

An abstract painting of a baby's face, composed of various colored brushstrokes and geometric shapes. The colors include shades of yellow, orange, red, white, and grey. The face is depicted in a stylized, non-representational manner, with the eyes and mouth suggested by the arrangement of the brushstrokes.

neonatal INTENSIVE CARE

Vol. 22 No. 7
November/December 2009

The Journal of Perinatology-Neonatology

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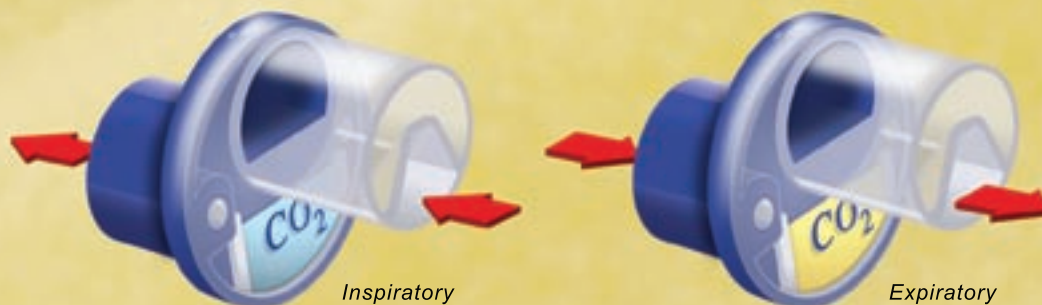


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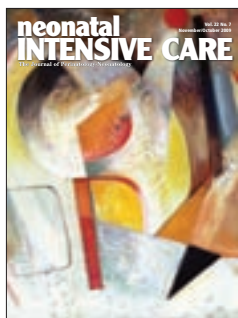
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Editorial

Perspective

A recent article posted on e-medicine by Brian Carter of Vanderbilt University reminds neonatal healthcare practitioners not to lose sight of their goals. Dr Carter raises the following questions: Who deserves access to neonatal specialty care? Who pays for it? Are the costs acceptable? Is the distribution of care equitable? Are some babies too small or sick for care? What outcomes are too burdensome? Who decides about who gets care? How are these decisions made? But Carter points out that many of these questions are often vaguely posed, if at all, and typically in reverse order. He says neonatal caregivers may also wonder, Why are we doing this? Did we make a difference? What were we trying to accomplish with our efforts? Failing to approach and try to answer these questions, he says, leads to moral uncertainty and distress. Another way to put the picture in perspective, he notes, is to posit the following questions before proceeding: what are the goals of neonatal intensive care? What place do guidelines have in ethical practice, and how should they be developed? What's good for the infant, and who says so? Neonatal caregivers, he says, can't simply say their job is to "save all babies," or "reduce infant mortality." The physical constraints of the NICU need to be considered, he says, and the ends to which care is provided should be kept in mind: Goals need to include more than the simple application of critical care technology, such as ventilators, monitors, medications, invasive devices, and a multiplicity of laboratory measurements, to sick and premature newborn patients. They should include stabilization of the newborn and, ultimately, facilitation of the transition to normal, extrauterine, neonatal physiology. This transition takes longer for some infants and may require significant intervention and support. The reversal of acute disease processes, such as infection and respiratory distress, is one recognized end to aim for. Care should be provided, he says, with a reasonable expectation of steady improvement, and shouldn't cause needless pain. When apportioning care, the "capacity for the newborn to enjoy and participate in the human experience over a life prolonged beyond infancy" must be considered. Carter also reminds us that "parents are considered to be the spokespersons [for infants], and thus their input must be considered, and that decisions should be shared and communicated among all parties." Finally, he says, data about outcomes can't rely solely on national, generalized information, because it may not apply to the local situation. Carter notes, "Perhaps the final consideration in answering these questions is that each day, healthcare professionals must work within the realities of the cases before them. Each patient has a unique set of problems that prompt action, moral reflection, and reevaluation. Each healthcare dilemma reminds caregivers of their limitations, including uncertainty, the human predicament, lack of knowledge, and decision-making abilities. All of these are tempered by the moral constraints under which they act. Healthcare professionals must, at times, accept the reality that tragic cases have tragic outcomes... [The practitioner is] asked to not only inquire, 'What good are we doing here?' but also to move toward defining goals for the individual patient."

Les Plesko, Editor

From E-medicine, Ethical Issues in Neonatal Care, Brian S. Carter, MD, FAAP, Professor of Pediatrics (Neonatology), Vanderbilt University School of Medicine; Co-director, Pediatric Advance Comfort Team, Monroe Carell Jr Children's Hospital at Vanderbilt. <http://emedicine.medscape.com>. From WebMD. All material on the website is protected by copyright, Copyright© 1994-2009 by Medscape.

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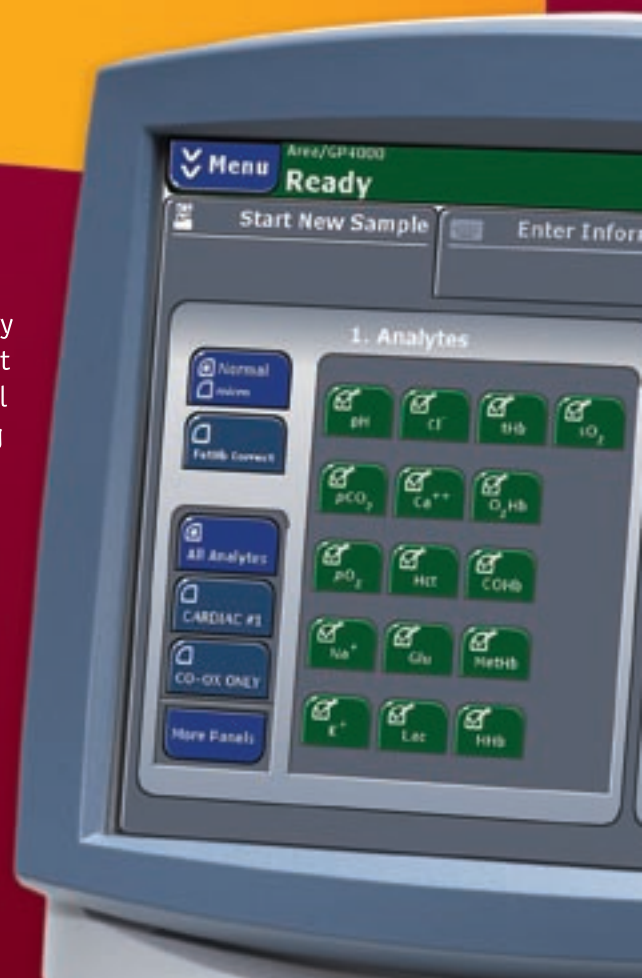
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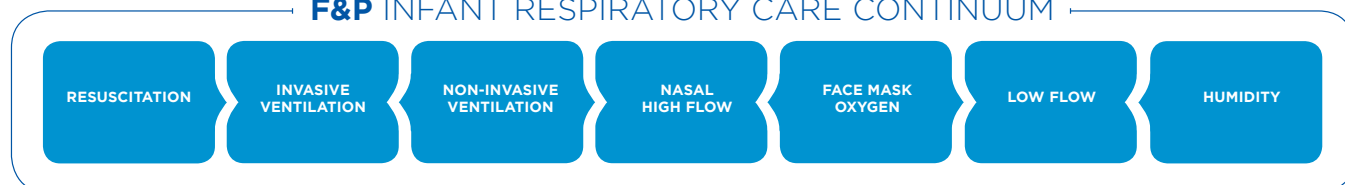
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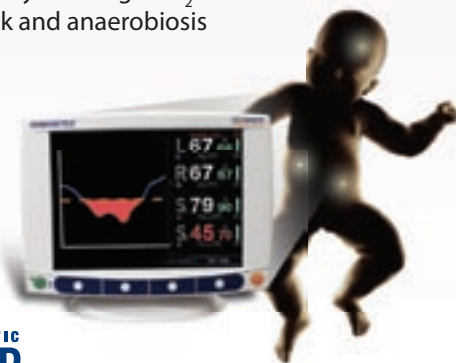
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WIC vs Breastfeeding

Benamanahalli K. Rajegowda, MD
Muhammad Aslam, MD

The Women, Infant and Children program (WIC) was started in the late 1960s during President Lyndon Johnson’s term and was fully implemented in 1972. The National Nutritional Survey in the 1960s and 1970s revealed that many low-income pregnant women and their children suffered from poor nutrition resulting in adverse health outcomes. This program has a long history of educating pregnant mothers about prenatal nutrition and providing supplemental nutrition to pregnant mothers, their infants, and children until age 5. The creation and implementation of the WIC program was a blessing for these families. The program provided age-appropriate food during a time when many families were offering their infants cow’s milk, which is nutritionally inadequate and can result in malnutrition and death. The benefits of breastfeeding were not fully discovered at that time. By providing formula, the government was allowing infants to develop healthier than if they were eating cow’s milk and solid foods. The program is administered by the federal agencies of United States Department of Agriculture at a national and state level. It provides nutritional guidelines and supplemental food offerings to mother-infant dyads based on pattern of infant feeding. There are three distinct patterns of infant feeding: 1. Mother is exclusively formula feeding; 2. Mother provides some breastfeeding and some formula feeding; and 3. Mother is exclusively breastfeeding.

The program continued to serve the nutritional needs of the mothers and infants with several modifications over the years. In the year 2004, the program subsequently included a breastfeeding initiative for the mothers. Exclusive breastfeeding is the norm for all mammals including humans, with the exception of a few contraindications. Exclusive breastfeeding for the first six months of life has health benefits for the mother and infant. The ecological advantage and the simplicity are of even of greater significance. Savings from cost of formula milk is

Dr Rajegowda, is Chief, Division of Neonatology, Lincoln Medical and Mental Health Center and Professor of Pediatrics at Weill Medical College of Cornell University. Dr Aslam is Neonatologist, Children’s Hospital Boston and Instructor in Pediatrics at Harvard Medical School. The authors sincerely thank breastfeeding coordinator and facilitator Ms Ilana Tubman and Ms Debra Waldkos, who are instrumental in improving exclusive breastfeeding among the authors’ urban, low socioeconomic population patients.

estimated to be about \$1,000 per year per infant. The Economic Research Service estimates that a minimum of \$3.6 billion dollars would be saved if breastfeeding rates increased to the Healthy People 2010 goals. The Healthy People 2010 goal is to have 60% of women to initiate breastfeeding in the immediate postpartum period, 50% to continue at 6 months and 25% at 12 months. The percentages are based on any breastfeeding and not exclusive breastfeeding per se. The most recent survey from 2005 is as follows:

Duration of breastfeeding	National (%)	NY State (%)	NY City (%)
1 month	60	50	40
3 months	32	25	23
6 months	12	8	10

From the above table it is clear that the rate falls short of Healthy People objectives in all three categories: national, NY State and NY City. In addition, half of the states have achieved breastfeeding initiation at birth, but only ten states meet program objectives for exclusive breastfeeding at 3 months and only 8 states (Alaska, California, Hawaii, Idaho, Oregon, Utah, Vermont and Washington) meet these objectives at 6 months.

The reasons for low rates of breastfeeding are multiple, including patient, family, and social issues, fear of peer pressure, loss of self esteem, loss of work, physical difficulties, and lack of support in the hospital along with short stay of the infant and the mother. Lastly, but most importantly, freely available commercial cow milk formula including the free formula provided by the WIC program to low-income mothers, may encourage women to choose formula or to choose formula along with providing breast milk.

All the WIC programs have trained nutritionists, who teach nutritional counseling to all low-income families at WIC visits. Even though they learn about the benefits of exclusive breastfeeding, most of the mothers prefer formula since WIC provides free formula on the basis of clientele preferences. It is the easy availability of the formula at the WIC program that is partially responsible for many women of low-income families not to breastfeed, exclusively or partially, to their infants even

with the counseling provided by the WIC and also outside the WIC in various community programs. Although the WIC program was started in the 1960s, the breastfeeding rate among the WIC clientele has largely remained the same. Recently, the WIC program has come up with some changes in the nutritional guidelines to mothers who are exclusively breastfeeding. They provide additional nutritional support to the mothers to help them continue breastfeeding until 6 months. After 6 months, the infant will receive iron fortified cereals, vegetables, fruits and meats but no formula. The food package is larger than the breastfeeding-bottle feeding package or the formula only package, which may attract some women to choose exclusive breastfeeding, since some women may have previously perceived the formula package as worth more.

In our view, in order to reach the Healthy People 2010 objectives, the WIC program should go even further to educate all women to exclusively breastfeed. WIC should provide nutritional support to the pregnant mothers and their infants up to 6 months without providing formula unless their healthcare providers determine contraindications to breastfeeding from medical, physical or technical reasons. WIC is a supplemental nutritional program; they should practice educating women on the importance of breastfeeding with major nutritional supplementation to women of low socioeconomic families. By improving the mother's nutrition and health, she can breastfeed her offspring without providing cow's milk formulas. We feel WIC may be one of the major deterrents to breastfeeding in the USA among low-income families. Times have changed from the 1960's and 1970's and we know so much more about breastfeeding in the 21st century, but the WIC program has not changed much. Around the world, communities are preaching to increase breastfeeding and exclusive breastfeeding including efforts in all of our Health and Hospital Corporations in NYC facilities. How can we preach breastfeeding on one end, while on the other end provide free formula to the low-income communities who quite possibly need the health benefits of breastfeeding even more. Many of the mothers who want to breastfeed do not want to miss the

opportunity in receiving formula from the WIC program. They think they are providing their infants with the "best of both worlds," but in reality their infants are missing out on many health benefits of exclusive breastfeeding.

This may be a radical statement, but we have worked all our lives with low socioeconomic families. Our staff has increasingly tried to help mothers to breastfeed. What we have heard from our staff is that WIC provides free commercial formula to the infants and the mothers would not miss the opportunity to receive it. This is one of the reasons they have made up their minds not to breastfeed exclusively. Also, while some of the mothers do exclusively breastfeed, they tell the WIC nutritionist that they are providing breast milk and formula so that they can have the formula in case of an illness or for later use in the infant's life.

The WHO/UNICEF Baby Friendly Hospital Initiative requires hospitals that desire a "Baby-Friendly" designation to not provide free formula, but instead pay for the formula just like for any of their other medical supplies. Paying for formula helps to realize the cost-benefit comparison of breastfeeding versus formula feeding. Ultimately, hospitals will see reduced payments to pay for their formula as they encourage and support mothers to breastfeed. The WIC program should similarly stop offering free formula to mothers and instead encourage all women to breastfeed. WIC should only provide mothers with nutritious foods so they can be healthy enough to breastfeed, and provide food for infants after 6 months of age. The same recommendation is voiced by the American Academy of Pediatrics in its statement, "Breastfeeding and the Use of Human Milk." WIC was developed during a time when infants were receiving nutritionally inadequate human milk substitutes and providing the infant formula milk seemed like the right answer at that time. However, now that we know the extensive short and long-term benefits of breastfeeding, WIC needs to re-think its mission and stop providing free formula. If WIC indeed changes its practices, we believe we can achieve the Healthy People 2010 objectives and save healthcare dollars.



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□ November-December 2009

WAO ASTHMA NEWS

World Allergy Organization featured the paper: Exploring the association between severe respiratory syncytial virus (RSV) infection and asthma (A). Does RSV cause A, or do those infants who later develop A have a genotype that both predisposes them to A and makes them more susceptible to severe RSV infection? That question is explored in this population-based study of hospitalization data from all Danish twins born alive between 1994 and 2000 (8280 twin pairs). The diagnosis of RSV infection was based on hospital diagnosis and/or RSV identification by ELISA. Presence of A was assessed by hospital discharge diagnosis and parental questionnaire. Among the children with RSV infections, 50% were hospitalized before the age of 6 mo and 75% before 12 mo. 95% had been hospitalized before 24 months. Twins hospitalized for RSV were more likely to have A. The data were subjected to statistical analysis and direction of causation (DOC) modeling. Monozygotic twins showed a higher correlation for A than dizygotic twins, suggesting a genetic component in disease susceptibility; but for RSV there was no such correlation, meaning that environmental factors play a larger role. When data were fitted to a DOC model, it was found that the best fit occurred for RSV infection resulting from the underlying susceptibility to A rather than vice-versa. Editor's comment: These data support the concept that RSV is associated with but does not cause A, implying unknown genetic factors are involved. Thomsen SF et al, *Am J Resp Crit Care Med* 2009; 179:1091-1097. From the World Allergy Organization Journal July 2009, Volume 2, Issue 7 ISSN: 1939-4551. Contact worldallergy.org.

OBSCENITY

When Zambia's healthcare workers went on strike, a newspaper circulated a photo of a naked woman giving birth outside a hospital where she'd been unable to get medical attention. The baby came out feet first, and soon died. The newspaper's editor sent the photos to the country's vice president, asking him to end the strike. Copies were circulated to the health minister and other leaders. The police arrested the editor, charging her with distributing obscene materials to corrupt public morals. As we went to press, she faced five years in prison. The president of the country called the pictures pornography. The photographer said the point of the photos had been missed. The strike ended after the government threatened to replace the healthcare workers. The photo was taken by the woman's husband. Reported by Barry Bearak in *The New York Times*, July 14.

DON'T DARE BREATHE

Prenatal exposure to a category of persistent environmental pollutant PCBs is associated with the strongest detrimental effects on fetal neurodevelopment, according to researchers at UC Davis. The study was conducted in Slovakia, where researchers recruited mother-and-baby pairs at delivery from a district known to have high PCB contamination from a plant operated from 1959 to 1984. The plant dumped chemical waste into a local river and on nearby land. Mother-and-baby pairs from a nearby town that did not have such a plant and had lower levels of PCB contamination were also enrolled. The researchers measured non-dioxin-like PCBs, dioxin-like PCBs and anti-estrogenic PCBs. They also measured babies' mental development and motor skills at 16 months and interviewed mothers to obtain information on other factors that might affect brain development, including the mothers' education levels, health status, and cigarette and alcohol use. Because of an overlap in the PCB levels between the two areas, the study focused on measuring the chemical loads in mother and child. The researchers found that only the two dioxin-like PCBs, #118 and #156, were associated with deficits in neurodevelopment. The non-dioxin-like PCBs as a group did not seem to have an impact on mental functioning. The researchers noted that Americans have been exposed to levels of PCBs comparable to those measured in Slovakia.

CUT OFF POINTS

The CDC recommendation for male circumcision as a way to curb the spread of HIV has engendered some debate. According to a US News & World Report blog, circumcision is not just a medical procedure but a religious and cultural one and in terms of the science, it's not clear how much circumcision will protect American men from being infected with HIV, where the virus is largely transmitted through homosexual contact. The blog added that there was also the potential for spreading misinformation. The writer noted that the CDC should evaluate the latest research carefully before deciding to take a cultural practice and turning it into a public health mission. According to an article in the *Jackson Clarion Ledger*, opponents of the recommendation argue that routine circumcisions would not impact STD transmissions in the United States, considering that 80% of all adult men are already circumcised. In addition, the article says, everyone doesn't view the procedure as medically necessary and opt not to do it.

FORMULAIC

The National Institute of Standards and Technology (NIST) has issued new certified reference materials for determining the concentrations of vitamins, minerals and other nutrients in infant and adult nutritional formula and similar products. The new Standard Reference Material (SRM 1849) for Infant/Adult Nutritional Formula was said to represent a significant improvement over current reference materials. The authors of the new guide noted that formula is one of the most regulated food items in the United States. At the time the original materials were published, the NIST did not have in-house methods to certify values for fatty acids, vitamins D and K, and many water-soluble vitamins, but now they do. Among other reasons for releasing new guidelines was that the material no longer presented the same analytical challenge as commercially available formulas. The new SRM contains certified values for 43 nutrients, including vitamins, minerals and elements, and 43 reference values for amino acids and nucleotides. NIST SRMs are intended to be used as controls in analytical chemical testing,

and are not intended to prescribe what a consumer product should contain.

LEAVE 'EM AT HOME

While car safety seats protect children from injury and death, the upright position infants are forced to assume can compress the chest wall and reduce airway size, resulting in lower levels of oxygen. So says a study that compared oxygen levels in 200 newborns while in a hospital crib, car bed and car seat. The mean oxygen saturation level was significantly lower in the car seat (95.7%) and the car bed (96.3%) compared to the crib (97.9%). Previous studies have found similar effects on premature infants; this study confirms the respiration of full-term infants is also affected by car seats and car beds. The study authors suggest these safety devices should be used only for protection during travel, and not as replacement for cribs.

DIABETES

Two new articles in the September/October issue of the *Journal of Obstetric, Gynecologic and Neonatal Nursing (JOGNN)*, published by the Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN), include timely study results and a literature review prior to American Diabetes Month in November. The first article is a report showing that new mothers with gestational diabetes are more likely to breastfeed than mothers with Type 1 or Type 2 diabetes. The study also suggests further research is necessary to develop breastfeeding support policies for women with diabetes. The second article is a literature review noting that nurses should explore better strategies to promote accurate risk perception, healthy diet, weight control and adequate physical activity in women with gestational diabetes. "Breastfeeding in mothers with diabetes," studied 94 women with diabetes for two years to determine factors that might influence breastfeeding rates. Results showed women with gestational diabetes intended to and breastfed more than women with Type 1 and Type 2 diabetes in the two weeks following childbirth. The authors found that after two weeks, a higher body mass index (BMI) and socioeconomic status were the more significant predictors of breastfeeding in diabetic women. They concluded that while women with gestational diabetes are more likely to breastfeed than women with pre-existing diabetes, further investigation is needed to determine whether this is because of their higher level of complications or simply perceived complications. As little information exists on factors that influence breastfeeding behaviors in diabetic women, identifying indicators can help nurses to develop better-targeted policies and interventions to support breastfeeding. The second article, "Beliefs and behaviors of women with gestational diabetes," shared results of an eight-article review. The authors' assessment determined that understanding common risk perceptions, health beliefs and lifestyle behaviors of women with gestational diabetes can help women's health researchers and clinicians develop appropriate intervention strategies to increase risk awareness, promote self-efficacy for healthy lifestyle behaviors and decrease rates of cardiometabolic disease in these women.

DON'T BELIEVE YOUR EARS

Mums-to-be are being advised not to use home Doppler devices to listen to their baby's heartbeat at home over fears that they may lead to delays in seeking help for reduced fetal movements. Researchers have pointed to a case of a woman who presented to a labor ward 32 weeks into her first pregnancy with reduced fetal movements. She'd noted a reduction in her baby's

movements two days prior, but had used her Doppler device, heard a heartbeat, and assured herself that everything was fine. The baby was delivered by cesarean section and had to remain in a special care unit for eight weeks. The researchers pointed out that a hand-held Doppler device assesses the presence of fetal heart pulsations only at the moment of use, and it is used by midwives and obstetricians to check for viability or for intermittent monitoring during labor. In untrained hands it is more likely that blood flow through the placenta or the mother's main blood vessels will be heard. The scientists found that a fetal Doppler device could be bought as cheap as about \$25 on ebay, and while it isn't meant to provide antenatal care, the manufacturer claimed, "you will be able to locate and hear the heartbeat with excellent clarity."

SHAKY START

Women with epilepsy who have seizures during pregnancy are more likely to give birth to preterm and LBW babies than women without epilepsy, according to researchers at Tai Pei Medical University in Taiwan. About 0.2 to 0.7% of pregnant women have epilepsy. Researchers analyzed records from 1,016 women with epilepsy who gave birth between 2001 and 2003. Of these, 503 had seizures during pregnancy and 513 did not. A control group of 8,128 women were selected for comparison. Women who had seizures during pregnancy had 1.36-times greater risk of having a baby weighing less than 2,500 grams, a 1.63-fold increased risk of giving birth before 37 weeks and a 1.37-fold increased risk of having a baby who was small for gestational age. The risk for a small baby was 1.34 times greater for women who had seizures compared to those who had epilepsy but no seizures. The researchers speculated that trauma caused by a seizures could rupture fetal membranes, increasing risk of infection and early delivery or that tension and injury may result from contractions in the uterus that occur during seizures.

NOT AGAIN

A Vermont woman is seeking legal recognition of her six-month-old twin fetuses that died in a car accident, potentially reopening the debate over abortion rights in the state. Some abortion-rights advocates have expressed concerns that revising state law to give legal recognition to fetuses could conflict with the Supreme Court ruling in *Roe v Wade*. The Vermont Supreme Court previously ruled that prosecutors cannot charge anyone for the death of a fetus in a motor vehicle accident. The court cited a common law tradition from the 17th century that ruled that a fetus must be born alive for it to be eligible for legal protection. Although 36 states have some form of fetal homicide law, Vermont does not, and the state Supreme Court said it will be up to the Vermont Legislature to revise the law. Fetal homicide laws nationwide have changed in recent years and have been invoked during debates over abortion rights. Reported by Medical News Today, from the AP/Barre-Montpelier Times Argus. Copyright 2009 The Advisory Board Company.

GOING UP

The average age of women giving birth for the first time is increasing worldwide but remains lower in the US than in other developed countries because of the nation's high teen birth rate, according to a National Center for Health Statistics report. The average age at first birth for women in the US was 25, compared with 29 in other developed countries. Of the 14 countries cited, US women had the lowest age at first birth in both years studied, 21.4 in 1970 and 25 in 2006. The UN noted that the teen birth rate in the US was more than eight times higher than in Japan,

seven times higher than in Denmark and Sweden, and more than three times higher than in Canada. In 1970, one in a hundred births was among women ages 35 and older, compared with one in 12 in 2006. The age of first birth is a significant indicator of future trends, such as birth defects, birthweight and the number of children women have, which affects population trends. The average age at first birth increased for all racial and ethnic groups between 1990 and 2006. The oldest average age at first birth was 28.5 years for Asian or Pacific Islander women, while the youngest was 21.9 years for Alaska Native women. The average age at first birth was 26 years for white women, 22.7 years for black women and 23.1 years for Hispanic women. Age at first birth increased in all 50 states, and the largest gain was in DC, Massachusetts and New Hampshire; the smallest in New Mexico, Mississippi and Oklahoma. The main reason for the increase is said to be the availability of the birth control pill. Reprinted from nationalpartnership.org, copyright 2009 The Advisory Board Company, from Medical News Today.

NO HARM

The New York Times reports: children who were exposed to anesthesia when their mothers underwent C-sections were no more likely to develop learning disabilities than those whose mothers delivered vaginally. Researchers at the Mayo Clinic reviewed records of 5,320 children until they were five years old. The group included 497 children who had been delivered via C-section, including 193 whose mothers received general anesthesia and 304 whose mothers were administered regional anesthesia. Overall, 921 children were diagnosed with learning disabilities by age 19. 20.8% percent of those delivered vaginally, with or without regional anesthesia, had developed a learning disorder, compared with 19.4% of those whose mothers were put under general anesthesia for a C-section delivery. Children whose mothers had C-sections and received regional, rather than general, anesthesia appeared to be at the lowest risk, with only 15.2% percent developing learning disabilities. The surprise finding led researchers to guess that regional anesthesia was more effective than general anesthesia in blocking stress hormones that are normally produced by a mother during labor and delivery. Such hormones are normally transferred to the baby, where they may have adverse effects on the brain. From The New York Times, July 30, reported by Roni Caryn Rabin.

MAKE ROOM

Neonatal units for preemies need redesigning for parents, according to Britain's National Childbirth Trust. A survey of UK neonatal units by the University of Warwick found one in 10 units didn't have a parent sitting room close to clinical areas where the babies were being cared for. A quarter of units had no single rooms for babies in which families could care for their newborn while preparing for discharge home. Few had playrooms or areas for siblings. Half of the units had a parents' support group and only a third had a one-to-one parent support scheme. Few facilities had policies for ways to involve families in care, or offered skin-to-skin bonding opportunities. Reported by the BBC.

BLOOD WORK

Researchers at Michigan State University are studying Michigan's archive of newborn blood spots to work on getting info about the cause of cerebral palsy. The focus will be on hormones, infection and blood clotting. The scientists will be using results of the state's newborn genetic screening program, extracting biological information. Researchers will also interview mothers about

pregnancy exposures and analyze health data recorded at birth.

SUICIDAL TENDENCIES

Mothers who experience a poor mother-infant relationship are more likely to think about killing themselves, according to a study at Boston University. Postpartum depression, with a risk of suicide, occurs in nearly 20% of new moms. Researchers studied a group of first-time moms who suffered from depression, isolation and difficulties in parenting. The mothers answered pre-treatment questionnaires and self-reported symptoms, and were also observed and videotaped while they played with their infants. A psychological test assessed if the moms felt their babies would be better off without them, or if the mom wanted to die. Seventeen of the 32 participants (53%), who comprised the highly suicidal group, experienced severe struggles with depression and had sleeping and eating problems. Researchers found that mothers with suicidal ideas had poorer self esteem than women who had few suicidal thoughts. The infants of the more suicide-prone mothers exhibited less positive behavior in the form of fewer smiles and more fussing. Infants of highly suicidal mothers were somewhat more passive and less engaged in the interactions. Most of the suicidal moms also had jobs that they gave up once they had their baby.

NO RISK

The risk of infant death following planned home birth attended by a registered midwife doesn't differ from risks of birth in a hospital, according to a Canadian study. The study looked at 2,889 home births attended by regulated midwives in British Columbia and 4,752 planned hospital births attended by the same cohort of midwives, compared with 5,331 physician-attended births in hospital. Women who planned a home birth had a significantly lower risk of obstetric interventions and adverse outcomes, including augmentation of labor, electronic fetal monitoring, epidural analgesia, assisted vaginal delivery, cesarean section, hemorrhage, and infection. According to the researchers at the University of BC, women planning birth at home experienced reduced risk for all obstetric interventions measured, and similar or reduced risk for adverse maternal outcomes. Newborns born after planned home births were at similar or reduced risk of death, although the likelihood of admission to hospital was higher.

EGG SCREENING

A new egg screening technique has resulted in a birth to a woman with 13 failed IVF treatments. Array Comparative Genomic Hybridization was used to screen eggs or embryos in an IVF cycle, evaluate all the chromosomes and select the most chromosomally normal embryos. Researchers at Care Fertility Clinic in Nottingham, England, found a way of speeding the analysis of the genetic material, getting it in 24 hours, which means that the mother can have IVF in the same cycle of treatment. In this case, eight eggs were tested, two found normal, and these resulted in the birth. The researchers cautioned that other promising techniques have proven to be duds, and that conclusions shouldn't be jumped to before more testing. Reported by the BBC.

EGG-CITING

Researchers have developed a technique for transferring hereditary materials from one female egg into another from which the transferred hereditary material has been removed. The eggs produced babies free of the mom's mitochondria, but had the mitochondria of the donated cells. Defective mitochondria

are linked to diabetes, cancer, infertility, Alzheimer's, Parkinson's and Huntington's diseases. The research holds the potential of allowing a couple to have a child who is biologically its own, but free of conditions associated with defects. Researchers created fertilized eggs and achieved three successful pregnancies in rhesus monkeys, which have resulted in four healthy newborns. Recent advances in the transfer of hereditary material and in microscopy facilitated the achievement. The technique didn't seem to pose any risk of chromosomal damage. Reported by Medical News Today.

NON FAT FETUS

Women who have weight-loss surgery before pregnancy may reduce the chances of having a kid who also turns out to be fat, according to a report in the Los Angeles Times. Researchers at the State University of New York studied 49 women who had undergone weight loss surgery and their 111 children. The study showed that the children born after their mother's surgery had reduced birth weight and waist circumference and were three times less likely to become severely obese compared with siblings born before the surgery. The kids also had improved cardiovascular markers, such as reduced insulin resistance and lower cholesterol and inflammation. While some women are worried that weight loss before pregnancy can result in fetal malnutrition, this hasn't been demonstrated, the researchers said. Reported by Shari Roan in the Los Angeles Times.

SOUNDINGS

Roni Caryn Rabin reported in the NY Times that a small placenta can endanger a fetus by limiting the delivery of food and oxygen. Researchers at Yale have developed an easy method of measuring the volume of the placenta during pregnancy. The technique uses ultrasound, and involves a formula for finding the placenta's volume using measurements that can be obtained during an ultrasound typically done halfway through a pregnancy. It uses the placenta's maximal width, maximal height and thickness at maximal height. The formula can be programmed into an ultrasound machine. From the New York Times, August 3.

SLOWER SIDS

Cases of SIDS have been falling in England, down 7%, according to the latest surveys. There were 264 such deaths in 2007 across England and Wales. The rate was highest among babies born outside marriage. The majority of deaths were among babies of a normal birthweight - 2,500 g and occurred between 28 days and one year. The rate among unmarried women was eight times that of babies born within marriage, 1.42 per 1,000 live births. The death rate among parents in the routine and manual occupations was twice that among those classified as managerial or professional. Rates were highest in mothers under 20. Reported by the BBC.

GHOST IN THE MEDIA MACHINE

Doctors have been attaching their names and lending their reputations to scientific papers that were drafted by ghostwriters working for drug companies, according to an expose in the New York Times. Senator Charles Grassley, an Iowa Republican, recently known for his spurious claims about so-called "death panels," is so concerned that he's putting pressure on the NIH, which underwrites much of the US's research, to crack down on the practice. But the NIH, while proclaiming its commitment to objectivity, said universities and research institutions should be the enforcers of policies regulating ghostwritten pieces. Recent revelations suggest that the practice is widespread.

Dozens of medical education companies across the country draft scientific papers at the behest of medical companies, and placing such papers in medical journals has become a standard marketing practice. Allegations of industry-sponsored ghostwriting date back to articles about fen-phen, the diet drug taken off the market in 1997. Evidence about the practice was recently revealed in a case dealing with menopause drugs, and its manufacturer's dealings with a medical writing company hired to prepare about 60 favorable articles. The articles were published in medical journals between 1998 and 2005, even after researchers found evidence about the drug contrary to info published by the company-paid researchers. While some journals have instigated more rigorous rules about author disclosure, others have been slow to react, according to Senator Grassley's office. A spokesperson for a university used by Grassley as evidence said that authors were responsible for the integrity of their work. But some bioethicists countered that institutions can't just blow off the subject. In interviews with The Times, some writers explicitly named as contributors to companies providing ghostwritten pieces made various excuses, admitting that, perhaps, mistakes were made in not naming corporate sources, but claimed that more rigorous requirements for disclosure were now in place. However, some writers also noted that they have to rely on research companies for getting vital background information and doing source searches. Information for the above is from the New York Times, August 19, "Senator Moves to Block Medical Ghostwriting," by Natasha Singer. For the record, Neonatal Intensive Care accepts articles from all sources, as long as the author and all affiliations are clearly named.

HEART ON YOUR SLEEVE

Doctors in New Delhi have stuck a heart back inside a baby who was born with the organ protruding from his chest. Ectopia cordis occurs in only five to eight of a million births. The baby was admitted with dehydration and a severe infection which he probably suffered because of an arduous train journey to reach the hospital, and doctors were surprised it had survived. The heart was covered with a synthetic membrane, and infected blood replaced in the baby's body. His blood was cooled to 18 degrees for an hour for the operation, in which the doctors "built a new home" for his heart. The doctors wrapped the heart in Gore-Tex, then in a layer of the child's skin, to substitute for his missing pericardium, then stuck the heart back in.

SPIT IT OUT

A saliva test could help spot which expectant women are likely to go into premature labor, according to researchers at the Maternal and Foetal Research Unit at King's College London. The researchers, noticing that progesterone played a part in preemie births, decided to monitor progesterone levels in saliva as a cheap and easy marker. They studied 92 women deemed to be at increased risk of having a preterm birth, and found the women who delivered spontaneously before 34 weeks had much lower salivary levels of progesterone than those giving birth at term, after 37 weeks. This measurable difference in progesterone was apparent at all gestational ages from 24 weeks onwards. The researchers noted that saliva is easy to collect, there's no need for a needle or a blood sample and said it would be wonderful if in the future a pregnant woman had merely to produce a little spit to find out if she was at risk of giving premature birth. Reported by the BBC.

FROM NICU TO PTSD

A new study from Stanford University School of Medicine followed 18 parents who had babies in the NICU. After four months, three had diagnoses of PTSD and seven were considered at high risk for the disorder. In another study, researchers from Duke University interviewed parents six months after their baby's due date and scored them on three post-traumatic stress symptoms: avoidance, hyperarousal, and flashbacks or nightmares. Of the 30 parents, 29 had two or three of the symptoms, and 16 had all three. According to a researcher, the NICU is very much like a war zone, with the alarms, the noises, and death and sickness. As such, parents of NICU infants experience multiple traumas, beginning with the early delivery, followed by witnessing traumatic medical procedures and life-threatening events, and also seeing other infants going through similar experiences. Parents of babies in NICUs are also often given serial bad news. As a result, the parents are likely to remain fearful and tend to become overly sensitive to any perceived abnormality in their child's subsequent condition. The study at Stanford found that fathers tended to hold it together in the NICU but fell apart afterwards. At four months after a child's release, 33% of the fathers and 9% of the mothers had PTSD symptoms. Such stress may take the form of nightmares or flashbacks. While their kid is still in the NICU, parents may feel panic every time a beeper goes off, or they may avoid the trauma by not visiting the unit or by emotionally distancing themselves from their child. Over time, they may develop depression, anxiety, insomnia, numbness, anger and aggression. Studies have shown that the risk of PTSD wasn't related to the condition of the child or length of stay in the NICU, but to the parents' style of coping. And it's often after the child is released from the unit that problems develop. Researchers noted that several months may pass until parents are ready to process their NICU experiences, at a point when no one else really wants to hear about it anymore. Experts say parents who are at risk for post-traumatic stress should be identified ahead of time and given help to prepare them for dealing with the initial trauma, but most hospitals are busy caring for infants, not parental emotional crises. Some hospitals pair parents of preemies in NICUs with NICU veterans who have gone through the experience, and this has helped. Researchers have also pointed out that PTSD can have an effect on the child itself, with parents who find it difficult to hold or look at their child, or who panic every time a kid, for instance, sneezes. Reported by The New York Times, August 25, 2009, "For Parents on NICU, Trauma May Last," by Laurie Tarkan.

PILOT PROGRAM

The drug 17P, a synthetic hormone which hasn't yet been approved by the FDA, is being promoted by Washington State Medicaid contractor Molina as a way to reduce preemie births and yet make a profit while serving Medicaid patients. Many insurers don't cover 17P because it's experimental. Washington State spends about 7% less in reimbursements for Molina members than it does on Medicaid members who have fee-for-service coverage. Premature babies account for one of Molina's largest expenses, with delivery costs for a fetus born at 26 to 28 weeks gestation averaging \$250,000 by the time the baby leaves the intensive-care ward. Some medical experts have said they're uneasy about Molina's advocacy of 17P, because there may be unrealized safety concerns with synthetic hormones. The New England Journal of Medicine published a paper on 17P studies sponsored by the NIH. In a randomized, double-blind study, women who received weekly injections of 17P were one-

third less likely to give birth before 37 weeks than those given a placebo. Molina started its 17P pilot program in Washington and has expanded its use to all 10 states in which it operates. Doctors can legally prescribe it. Reported by the Seattle Times.

SAYING THE RIGHT THING

An article in the August/September issue of *Nursing for Women's Health*, the clinical practice journal published by the Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN), offers situations and suggested responses nurses can use to help ease a difficult moment for families. "Will Our Baby Be Alive Again? Supporting Parents of Young Children When a Baby Dies," by Rana Limbo, RN, PhD, PMHCNS-BC, and Kathie Kobler, MS, APN, PCNS-BC, covers a variety of situations, including potential responses for early miscarriages and ectopic pregnancy, unborn babies diagnosed with life-limiting conditions and stillborn babies. The article covers a number of scenarios that nurses might see when a baby dies and appropriate ways to talk to and help families. In addition to responses, the article describes common questions children might ask or feelings they might show when a baby dies, as well as rituals, keepsakes and additional resources families can use to cope and move forward together. The article concludes by noting surviving children's need for parents who are emotionally available to them after the tragic loss of a baby and the important role that proper nursing support plays in the process.



HEY DOLL

Pregnant women are being given the chance to hold life-sized models of their fetuses, thanks to an invention that converts data from ultrasound and MRI scans. Jorge Lopes, a Brazilian designer, uses 3-D printing technology to create the plaster models, which went on display at an exhibition at the Royal College of Art in London, and the invention has already attracted the attention of medical experts. Mothers can see and feel their fetus at full scale and size.

TWO FOR ONE

An Indonesian mother has given birth to conjoined twins who share the same body and all their vital parts, except their heart and their heads. The boys were delivered in the Riau province via cesarean section. They can't be separated. The boy(s) have two heads, a pair of lungs, two arms and two hearts. They weighed 7 pounds.

MANY PAIRS

Reuters (via the internet) reports on an Indian village which has about 230 sets of twins, and no one knows why—perhaps, they say, it's the water. The village of Kodinji, unoriginally nicknamed "the twin village" has four times more twins than normal. At the time of the Reuter's article, five women in the village were pregnant with twins. A researcher noted that the residents weren't exposed to harmful drugs or chemicals. He said, "it's a virgin village," though that's doubtful, under the circumstances.

The oldest twins in the village are 65. Scientists haven't a clue about the reason for all the twins. The locals say it's the water that collects in the fields during the monsoons.

EXPANDING

BioMed Central, the world's largest open access publisher, announced that Bev Ackerman joined the company as Commercial Director. Ackerman comes to BioMed Central from medical publisher Taylor & Francis. BioMed Central reported that it is experiencing rapid growth in manuscript submissions, has many new products in development and sees many opportunities for partnerships and relationships with academic institutions, libraries and societies.

PRODUCT FEATURE: MONITORING

An interview with John Hoyt, senior project manager for Philips Healthcare.

What sets Philips Patient Monitoring products apart from other similar offerings?

For more than 25 years, Philips has been delivering solutions that acquire, analyze, and present patient data in ways that are meaningful for clinicians in the most challenging, data-rich clinical areas. Breaking down information for clinicians in a data intensive field helps them make informed decisions about patient care. We provide everything from compact, wireless transport monitors to our most powerful, modular monitors for the neonatology intensive care unit, high-acuity critical care, and obstetrical care.

How does SureSigns VS2 enhance the Philips Patient Monitoring portfolio?

As a world leader in patient monitoring, Philips is able to provide advanced solutions in a wide range of hospital settings including critical care, perinatal, ambulatory and emergency care, anesthesia, cardiac care, and the general ward. SureSigns VS2, along with the SureSigns VS3, enhances the overall product portfolio by providing a spot check solution that can be used in the space Philips Patient Monitoring has traditionally not occupied: the Med/Surg setting. In addition, the technology is usable out of the box, and is being well received on the general floor and in the Emergency Department (ED). The VS2 promotes Philips' effort to provide solutions that operate together with diverse systems, integrating into the universe of patient data.

How does the VS2 meet a market need and directly impact patient care?

The VS2 technology supports adults, children and neonates. The VS2 as well as the more advanced version VS3, are two spot check monitoring systems on the market that directly export data in HL7 format. This feature means that minimal software needs to be developed in order to integrate patient data taken at the bedside with the VS2 into the electronic health record (EHR). Philips' VS2 and VS3 do not require an intermediary piece of equipment to change data into HL7 format for an EHR. All that is required is some type of integration engine software and host, which most hospitals already have in place.

Applying this to a real-world setting, nurses can take a patient's vitals at the bedside using the VS2, including basic vital signs such as NBP, SpO₂, temperature and heart rate. This data is then automatically exported and, after flowing through an integration

engine, is then integrated into the patient's record. Without this technology, the nurse would take the patient's vitals, record them manually and then go into the EHR to input the data. By offering advanced technological solutions, we are able to save time and reduce transcription errors while increasing the amount of time nurses can spend having meaningful interactions with patients rather than documenting their chart and filling out paperwork.

The VS2 system was also designed to hold 100 complete patient records, which provides nurses the flexibility to visit many patients during rounds before validating the data in the EHR. In addition, the VS2 offers seven fields for patient ID information, depending on how the user records this in his EHR system.

What types of customers are purchasing the VS2?

The VS2 is currently available in South Africa, the Middle East, Australia, Western Europe, the United States and Canada. Customers currently include Med/Surg and general floor nurse managers as well as IT professionals at hospitals including leading research university, Oregon Health & Science University (OHSU), which also uses EPICCare EHR. IT departments, while not having daily interaction with the monitor, are able to recognize the value in the HL7 formatting, the automatic export via LAN or Serial, and that it can be integrated successfully with existing EHR systems. It was designed to do this with minimal IT support. The VS2 includes patient specific settings, inflation pressures and alarm settings which are designed specifically for neonates. A full suite of consumable supplies specifically designed for neonates are also available.

Discuss the educational services you offer to users of the VS2.

The VS2 is designed to be used out of the box. It is packaged with a DVD that provides a comprehensive overview for those who will be using the monitoring device. In addition, we provide a data export guide to be used by the IT department at the facility to help them set up the device to export data information to the hospital's EHR system. Due to the simplicity and ease of use, we are able to avoid taking nurses and hospital staff away from their jobs in order to attend complex training sessions with clinical trainers. Finally a quick reference card is also included which stays with the device after it is installed. This card is an easy way for nurses and technicians to quickly answer the most common questions that might arise during use.

What do you see on the horizon for this segment?

As EHRs become more widely adopted in hospitals across the US, Philips expects to help drive customer implementation of the VS2 by providing simple solutions to common hospital needs. The VS2 will reinvent the direction Philips is taking spot check devices by increasing the use of these devices into more areas of the hospital, improving clinician workflow and the way they integrate with hospital IT systems as well as positively impacting care by increasing time spent with patients rather than time spent documenting their care. This user-friendly approach puts customers first and makes integration of patient data with an EHR a more viable option for hospitals.

Bunnell AARC Preview

Information provided by Bunnell, Inc.

What new products will you be presenting at AARC?

Bunnell Incorporated will be promoting an upgrade to their Life Pulse High-Frequency ventilator that reduces its sound level output by 60%, from 58 dBA to 41 dBA. That makes the Life Pulse the quietest high-frequency ventilator available in the US. The Life Pulse is now 4 dBA below the American Academy of Pediatrics' recommendation for sound level in the NICU.

Discuss educational materials you'll be promoting at the convention.

Bunnell has developed a three booklet pocket reference series on the Life Pulse High-Frequency ventilator. The booklets cover "What" high-frequency ventilation is compared to conventional ventilation, "Why" high-frequency jet ventilation is effective and unique compared to other high-frequency ventilators, and "How" to use the Life Pulse to manage patients successfully. Also, a new training DVD is now available from Bunnell that includes a full in-service video, an alarms and troubleshooting video, and a patient management video. The DVD also contains a competency exam and a certificate of completion.

What speakers will your company be working with or featuring?

Bunnell is hoping to participate in the Respiratory Care Solutions Showcase at the 2009 International Congress in San Antonio, Texas. If our proposal is accepted, the presentation will focus on "The Life Pulse HFV: How it works & Why it's Effective."

Why should AARC participants visit your display?

AARC participants concerned about noise in the NICU will want to visit the Bunnell exhibit to hear how quiet high-frequency ventilation can be with new sound reduction technology. At 4 dBA below the American Academy of Pediatrics' recommendation the Life Pulse HFV is just a whisper. Participants will also want to pick up our new educational pocket references and training DVD. Whether they are new to the field of respiratory care or seasoned veterans, these materials will provide new insights into high-frequency ventilation.

PRODUCTS

PROBING

Respiratory Technology Corporation (dba Restech) announced that The Oregon Clinic, in Portland, has adopted the Restech Dx-pH Measurement System to detect acid reflux in the airway. The Restech DX-System is utilized by The Oregon Clinic, Gastrointestinal & Minimally Invasive Surgery Division's (GMIS) Foregut Program for the diagnosis and treatment of all diseases of the upper digestive system. Restech's Dx-System provides valuable information about patients' pharyngeal acid exposure and its role in various comorbidities, helping physicians diagnose the cause of each patient's symptoms more accurately, and treat the patient more effectively. The miniaturized pH sensor at the tip of the Dx-pH Probe measures pH in a non-liquid environment, such as the pharynx. By monitoring the pH levels in the pharynx, the Dx-System enables physicians to confirm or deny the presence of laryngopharyngeal reflux, and evaluate it as a possible contributor to their patients' symptoms. The Dx-pH

Probe's miniaturized, patented sensor is housed in the tear-drop shaped tip at the distal end of a thin trans-nasal catheter. An LED blinks during placement, allowing the medical personnel to confirm the proper placement in the oropharynx. The small size and minimally invasive position of the Restech Dx-pH Probe allows patients to carry on normal, everyday activities including eating, talking and sleeping with more comfort than conventional esophageal pH probes. The measurements taken by the pH sensor are sent wirelessly to a recording device which the patient carries throughout the study period. Upon completion of the study (usually 24 hours), the patient returns to the physician's office where the data is downloaded and presented graphically for analysis using Restech's custom Dx-pH DataView software. Contact restech-corp.com.

VITALITY

The new Philips SureSigns VS2 offers clinicians a more affordable spot check monitor for use with neonates, as well as pediatric and adult patients. The VS2's intuitive user interface can help reduce the amount of time necessary for clinician training, increasing the time they can spend on patient care. The VS2 is available in markets around the world, including South Africa, the Middle East, Australia, Western Europe and the United States. The VS2 is able to store up to 100 patient records at any given time, allowing clinicians to view stored records for all patients or a selected patient with a push of a button. In addition, the new optional wireless capability permits the user to easily transport the system from patient to patient to obtain needed data and securely transmit to a patient's electronic medical record. Like all other Philips SureSigns products, the VS2 is easy to install, learn, use, and support, with intuitive navigation and color displays that are bright and easy to read. The compact VS2 system offers essential measurements such as non-invasive blood pressure, SpO₂, temperature and heart rate for efficient basic vital signs measurement. Contact philips.com.

A Method for Standardizing the Fat Content of Human Milk for Use in the Neonatal Intensive Care Unit

Charles Czank, Karen Simmer, Peter E. Hartmann

Abstract

Background: Accurately targeting the nutritional needs of the early preterm infant is challenging when human milk is used due to the natural variation in energy composition. The purpose of this study was to develop and evaluate a simple method for reducing the variation in fat and energy content of human milk prior to fortification such that the infant receives a diet of known composition.

Methods: Milk was centrifuged at low speed to concentrate the fat into a cream layer and a predetermined volume of skim milk is removed to meet a specific fat concentration. The fat layer is then resuspended to produce reconstituted milk of a specified standard fat content.

Results: Using this method it was possible to reduce the coefficient of variation in fat content of six different samples of donor human milk from 19.3% to 2.6%. As fat globule size may be associated with fat absorption, the effect that centrifugation and resuspension had on human milk fat globule distribution was assessed by laser diffraction particle sizing. No difference in the particle distribution of the treated and untreated human milk was observed.

Conclusion: This method is accurate and simple, allowing for integration alongside current milk bank and NICU practices for use with both donor human milk and mother's own milk.

Background

The benefits of using mother's own milk and donor human milk

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for premature and sick infants in the neonatal intensive care unit (NICU) are well known.^{1,2} In particular, the use of human milk in the NICU is associated with decreasing the likelihood of infection and in turn reducing the length of stay in hospital and associated costs.^{3,4} Unfortunately, human milk is not adequate to meet the nutritional needs of the early premature infant⁵ and it is common practice to fortify the human milk prior to enteral feeding.⁶ Fortification provides essential vitamins and minerals at necessary levels not ordinarily found in human milk, and is especially required to meet the protein and energy needs vital for adequate growth. Current recommendations of reasonable nutrient intakes state that protein:energy ratios of between 2.5–3.4 g protein/100 kcal of energy are required for extremely low birth weight (ELBW) infants and 2.6–3.8 g protein/100 kcal for very low birth weight (VLBW) infants.⁷ However, given that the energy content of human milk varies widely,⁸ the desired protein:energy ratio may not be met, because the

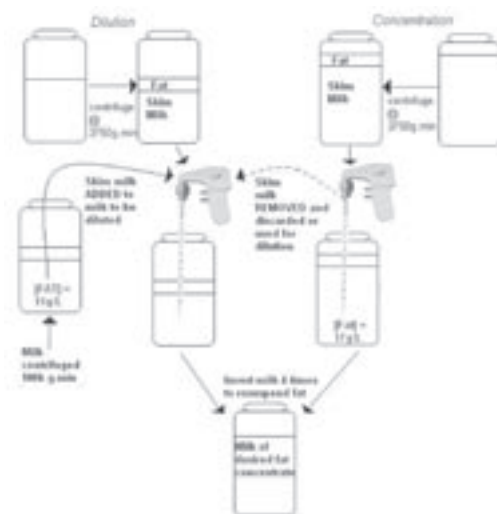


Figure 1. Schematic representation of method used to standardize energy content of breast milk for use in the NICU. Milk was firstly centrifuged at 3750 g.min at 4°C to concentrate the fat layer. A predetermined volume of skim milk was then removed if the fat concentration needed to be increased or added if the fat concentration needed to be decreased. The fat layer was then resuspended by four inversions of the vessel to produce reconstituted milk of specified fat concentration.

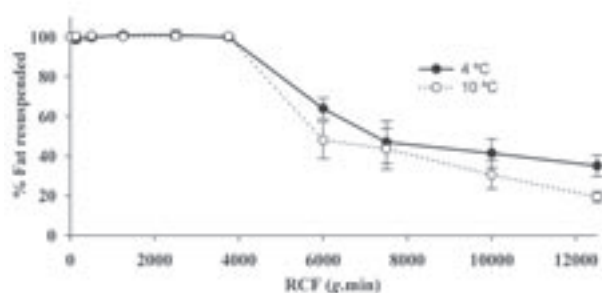


Figure 2. Relationship between percentage of fat resuspended by inversion of the container four times and relative centrifugal force (RCF). The maximum and therefore optimum RCF that allows for 100% fat resuspension is 3750 g.min. All data points are mean \pm SD (N = 6).

pre-fortification energy level of the human milk has not been standardized.

The total energy content of breast milk can be considered as the sum of the individual energy contributing components. Nutritionally, fat, lactose and protein are the most abundant energy sources contributing 9, 4 and 4 kcal/g (37.7, 16.7, 16.7 kJ/g) respectively.⁹ Fat is the most variable component of human milk (40 ± 16 g/l, Coefficient of Variation (CV):40%)¹⁰ compared to lactose (63 ± 2 g/l,¹¹ (CV):3.1%) and protein (9.2 ± 1.8 g/l, CV:19%)¹² and varies between mothers, throughout the day and during a breast expression.⁸ Often assumed human milk energy and protein content are used, which in turn may result in either a nutritional deficit once fortified or, conversely, a nutritional excess. The consequences of either under- or over- nutrition during this critical period of developmental programming may predispose the infant to a range of chronic disease states later in life.¹³⁻¹⁹

As fat is the most variable nutritional component and contributes over half of the energy to breast milk,²⁰ adjustment of the fat content to a specified level is a prerequisite to providing fortified human milk of a known energy content to meet the protein:energy needs of the preterm infant. The method

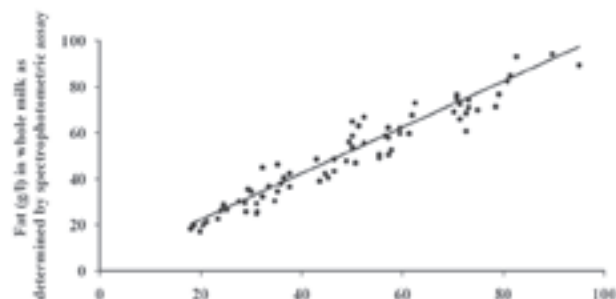


Figure 4. Correlation between fat content of milk as determined using the creamotocrit and spectrophotometric methods. ($R^2 = 0.93$, $n = 72$).

described here allows for standardizing the energy content of human milk prior to fortification, such that all infants will receive a standard level of energy from breast milk.

Methods

Samples were obtained from a store of breast milk donated to the Perron Rotary Expressed Milk Bank (PREM Bank), Subiaco, Western Australia. Mothers had given prior consent for their milk to be used in research. All samples were collected by the mother and immediately frozen prior to transportation to the milk bank and research laboratory.

The fat content of milk samples was determined by a spectrophotometric esterified fatty acid (EFA) method,^{8,21} as well as by using the creamotocrit method.²²

Samples of breast milk were thawed and 30 to 50 ml portions aliquoted into vessels. Skim milk and cream were separated by centrifugation at either 4°C or 10°C at a relative centrifugal

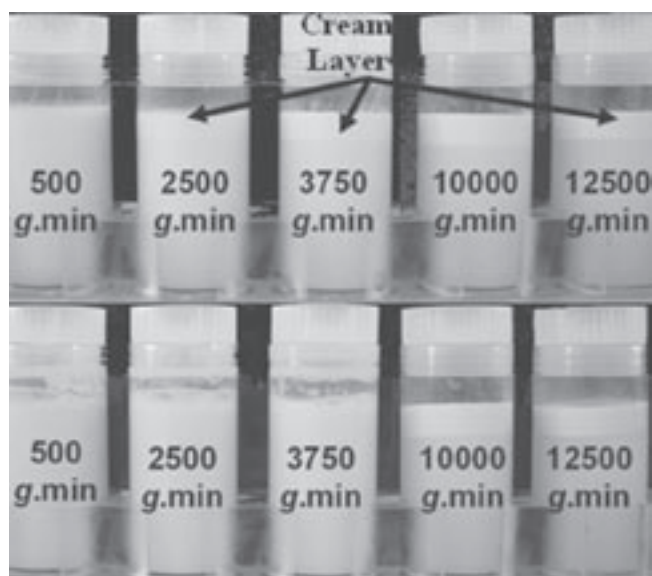


Figure 3. Examples of milk centrifuged at different relative centrifugal forces ranging from 125 – 12500 g.min before (top row) and after mixing (bottom row) illustrating resuspension of the cream layer (labelled).

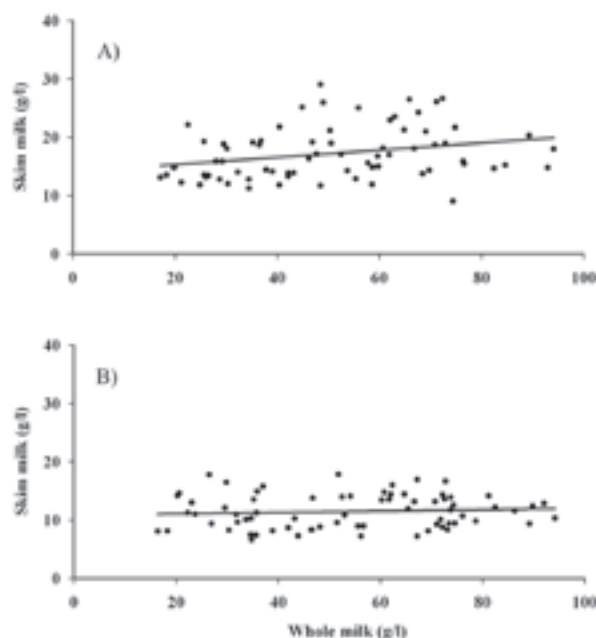


Figure 5. Relationship between fat concentration of whole milk and skim milk centrifuged at optimum resuspension RCF (A: 3750 g.min) and at “defatting” (B: 100,000 g.min). The skim milk fat content averaged 17.2 ± 4.5 g/l ($R^2 = 0.0772$, $n = 72$) and 11.5 ± 2.9 g/l ($R^2 = 0.0069$, $n = 72$) for samples centrifuged at 3750 g.min and 100,000 g.min, respectively.

Table 1: Initial fat content, volume of skim milk adjusted and final fat content of milk from six mothers to which the fat standardization applied

Human milk sample	Initial fat content (g/l)	Volume of skim milk adjusted (ml) ^a	Final fat content of reconstituted milk (g/l)	Percentage difference from target fat content
1	48.8	-0.4	49.8	0.53%
2	39.6	-9.0	52.2	2.9%
3	40.3	-8.4	50.4	1.12%
4	63.5	+13.3	49.1	0.18%
5	43.3	-5.6	50.5	1.28%
6	54.6	+5.0	49.5	0.77%
Mean	48.3		50.1	
SD	9.4		1.3	
%CV	19.3		2.6	

a: as determined using the equation described in text: Plus (+) refers to skim milk added and minus (-) refers to skim milk removed, b: target specified fat content was 49.3 g/L, CV%: Coefficient of variation, SD: standard deviation. All samples were 30 mL in volume.

force (RCF) and time needed to give a range between 125 to 12500 g.min (eg: 125 × g for 1 minute to 2500 × g for 5 minutes, respectively).

The volume of skim milk to be either removed or added was determined using the equation described below in the Results section. The container was then placed on a weighing scale and tared prior to adjustment and the required volume of skim milk adjusted carefully with a sterile pipette from below the fat layer (Figure 1). For those samples where skim milk was added to the milk, the skim was added above the cream layer prior to resuspension. The cream layer was then resuspended by inverting the container four times. All manipulations were performed at room temperature.

Freshly expressed breast milk from a term mother was aliquoted into sterile 5 ml containers and either frozen at -20°C or stored at 4°C overnight. Frozen milk was then thawed and both the thawed and milk stored at 4°C mixed and 1.0 ml samples of mixed milk taken prior to centrifugation. Milk was then centrifuged at the 3750 g.min at 4°C and the cream layer resuspended and another 1.0 ml sample taken from the reconstituted milk. Particle size was determined using a Mastersizer 2000 fitted with Hydro SM sample dispersion system (Malvern Instruments). Absorbance was adjusted to meet a target weighted residual of 1%, a dispersant refractive index of 1.33 was used and sample added to the dispersion unit until an obscuration target of 10–15% was achieved. Averaged data from ten repeated scans was analyzed with Dispersion Technology Software V4.02 (Malvern Instruments).

Results

Optimal relative centrifugal force for readily resuspending the cream layer: To allow the volume of skim milk to be adjusted to meet the specified total fat content, human milk was centrifuged to collect the cream in a layer at the top of the milk. It was necessary to determine the optimal RCF that allowed 100% fat resuspension, whilst still allowing the skim milk to be removed. This was achieved by centrifuging at RCF's ranging between 0 and 12500 g.min, sampling the skim milk, then resuspending the cream layer by four inversions of the centrifuged milk, followed by sampling of the reconstituted milk. By quantifying the fat content of the skim milk after centrifugation and of the reconstituted milk of six samples, it was determined that 3750 g.min was optimal for achieving 100% resuspension (Figure 2). When centrifuged at RCF's greater than 3750 g.min, either less than 100% fat resuspension was achieved or the fat layer did not resuspend (Figure 3). The effect of temperature on

the resuspension of the fat layer was assessed by centrifuging at either 4°C or 10°C. However, no effect on the level of fat resuspension was observed (Figure 2).

Fat content of skim milk after centrifugation: The fat content of the whole milk from six donors was determined by spectrophotometric assay and by creamotocrit with a mean ± SD of 49.2 ± 19.7 g/l (n = 72) and 53.92 ± 20.9 g/l (n = 72) respectively. A strong correlation ($R^2 = 0.93$) existed between the values determined by the two different methods (Figure 4). The fat content of the skim milk after centrifugation at 3750 g.min was 17.2 ± 4.5 g/l (n = 72). In comparison, the mean fat content of "defatted skim milk", produced by centrifuging for 100,000 g.min, was 11.5 ± 2.9 g/l (n = 72). The fat content of the skim milk did not correlate with whole milk fat content and remained relatively constant between samples (Figure 5).

Development of an equation for skim milk volume adjustment to standardize breast milk fat content

The relationship between total fat content in the whole milk, fat content in the skim milk after centrifugation at 3750 g min and final fat content after volume adjustment was used to develop an equation for skim milk volume adjustment to meet a specified fat content. The variables for this equation are defined below.

V_1 = Initial volume of milk (ml)
 V_2 = Volume of skim milk to be adjusted (ml)
 V_3 = Final volume of milk after adjustment (ml)
 C_1 = Initial fat content (g/l)
 C_2 = Content of fat in skim milk to be added or removed (g/l)
 C_3 = Desired fat content (g/l)
 Total grams of fat (F_T) is defined as a function of volume and content ie: $F_T = V_1 C_1 / 1000$
 Similarly, the total grams of fat in the skim milk (F_S) is defined as:
 $F_S = V_2 C_2 / 1000$
 The total grams of fat in the final adjusted volume (F_F) is defined as:
 $F_F = V_3 C_3 / 1000$
 As the final volume of milk and fat content was unknown, F_F was expressed as a function of F_T and F_S as the difference between the total grams of fat in the initial volume and the total grams of fat in the skim milk that is added or removed:
 $F_F = V_3 C_3 / 1000 = V_1 C_1 / 1000 - V_2 C_2 / 1000$
 F_F can be expressed as a function of the difference of in the initial and skim volumes and the final fat content.
 ie: $F_F = V_3 C_3 / 1000 = (V_1 - V_2) C_3 / 1000$
 $(V_1 - V_2) C_3 / 1000 = V_1 C_1 / 1000 - V_2 C_2 / 1000$
 Rearranged to give the skim milk volume to be adjusted (V_2) gives:
 $V_2 = V_1 C_3 - V_1 C_1 / (C_3 - C_2)$

Proof of concept

Samples of milk from six mothers were used to validate this method and demonstrate that the natural variation between samples could be greatly reduced. The aim was to standardize the fat content of the samples to 49.3 g/l with no greater than 5% variation between samples. This value was equivalent to an energy content of 75 kcal/100 ml assuming protein content of 10 g/l and lactose of 67 g/l. The initial fat content of the individual mothers' milk are illustrated in Table 1 and ranged from 39.6 – 63.5 g/l (mean = 48.3 g/l, CV = 19.3%). The individual fat contents of the six different milk samples, the target fat content and the assumed skim milk fat content of 17 g/l were inputted into the equation described above to determine the amount of skim milk to be removed from or added to each sample (Table 1). After centrifugation at 3750 g.min for 4°C, the skim milk volume was adjusted and the fat layer resuspended for each sample. The cream layer was noticeably easier to pipette through if the samples were kept on ice when being manipulated. Conversely, the cream layer was much easier to resuspend once the samples had returned to room temperature. The fat content of the reconstituted milk fat ranged from 49.1 – 52.2 g/l (mean = 50.1 g/l, CV = 2.6%).

Breast milk fat globule distribution in reconstituted breast milk after centrifugation and fat resuspension

Mean fat globule size \pm SD was $3.25 \pm 0.41 \mu\text{m}$ ($n = 27$). The fat globule distribution had a minor peak at $2 \mu\text{m}$ corresponding to a large number of small fat globules, a major peak at approximately $4 \mu\text{m}$, representing the majority of fat globules of average size and shouldering off down to a minor peak at around $12 \mu\text{m}$, representing a small number of very large globules. Frozen milk had a similar globule distribution to that of fresh milk except for slightly greater number of fat globules around $12 \mu\text{m}$. Fat globule distribution was not affected in the reconstituted milk and very closely resembled the particle distribution of the untreated whole milk for both the fresh and frozen samples (Figure 6).

Discussion and Conclusion

The basis of this method was to use low speed centrifugation to concentrate the fat globules into a cream layer, followed by the adjustment of the underlying skim milk and then resuspension of the cream layer. In order to accurately adjust the fat content of whole milk to a specified fat amount, an equation was developed for calculating the amount of skim milk to be either removed or added. Given the relatively low RCF used for this procedure it is likely that some fat would remain in the skim and it was therefore necessary to account for the amount of fat remaining in the skim when performing this calculation.

The samples chosen for the proof of concept studies had relatively low variation of 19.3% between samples, which was reduced to 2.6% by employing the method described. For these studies, an assumed value skim milk fat content of 17 g/l was used, which was derived from the average of 72 skim milk samples centrifuged at optimal RCF. Measurement of the fat content of the skim milk would decrease the variation between samples, but was not considered to be clinically important for either the milk bank or NICU. Nonetheless, assuming a skim milk fat content did result in a large decrease in the variability of fat between samples and contributed to less than 2.2% error in the final fat content of the reconstituted milk.

The effect that centrifugation and resuspension of the milk had

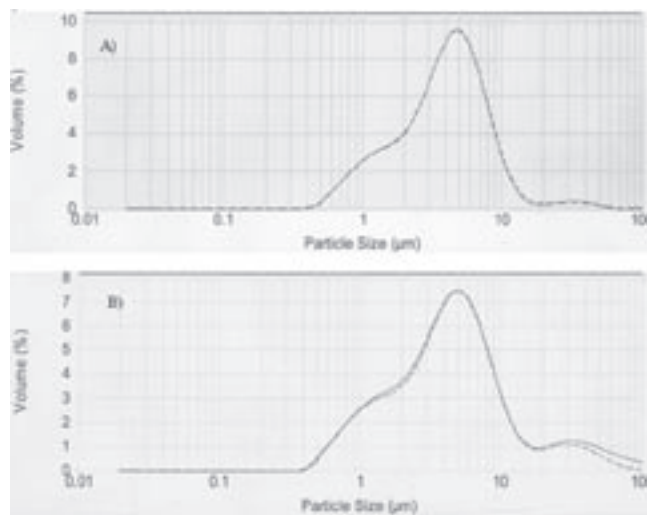


Figure 6. Particle distribution of untreated (solid line) and reconstituted (dashed line) fresh (A) and frozen (B) human milk.

on the fat globule size distribution was also investigated. Low temperatures are recommended for preventing microbial growth in human milk,²³ however it is not known how low temperatures affect the solidity of the cream layer and the ease of which the fat globules can be resuspended. Centrifuging at temperatures between 4°C and 10°C did not appear to affect the resuspension process. Subsequently, later centrifugation procedures were performed at 4°C to minimize any microbial growth. Fat globule size also may be important to infant gastric emptying and ability to absorb fat from the gut.²⁴

Centrifugation results in concentration of the fat globules into a dense cream layer at the top of the vessel, leading to the possibility of coalescence occurring and in turn altering the milk fat globule distribution. To test this hypothesis, samples of fresh and frozen milk, before and after manipulation were analyzed using laser diffraction particle sizing, a technology that has been successfully used for studying the particle distribution of bovine milk.²⁵ Results were similar to that of previous findings for human milk^{26,27} which employed more classical techniques such as coulter counters. Centrifugation and resuspension of milk did not alter the fat globule distribution, suggesting that coalescence does not occur under these conditions. The effect of centrifugation on milk proteins would be insignificant because much higher centrifugal forces are required for casein sedimentation²⁸ and the separation of small molecules (eg. lactose, oligosaccharides, peptides, hormones) from complex biological solutions cannot be achieved using centrifugation alone.

The method presented here has the potential for incorporation with current human milk banking protocols. While this study used a spectrophotometric assay for quantifying fat content of human milk, it was also demonstrated that the results from the simpler and quicker creamotocrit method correlated well with those derived from the more advanced spectrophotometric method. It is unlikely that most milk banks or NICUs would have access to a spectrophotometer, and the creamotocrit is an accurate and cost-efficient alternative for determining fat content of human milk. Using a creamotocrit it would be possible to determine milk fat content in the NICU or milk bank,

standardize the fat content of the milk prior to pasteurization, followed by appropriate fortification.

The validation of this method involved using assumed values of protein and lactose. Human milk composition is challenging to quantify outside the laboratory environment. Consequently, the concentrations of nutritional components in human milk are often assumed, contributing to inaccurate nutrition of the preterm infant. In recent years, human milk analysis equipment such as the MilkoScan (FOSS International) have become available that simultaneously determines protein, lactose and fat content in human milk. The equation presented here can be expanded to include these components in relation to total energy of the milk. Ideally all the variables including fat, protein, lactose and specified energy content can be inputted into the expanded equation and in combination with current fortification regimes, a standardized fortified human milk of known energy and protein content can be prepared that precisely meets the infant's nutritional recommendations. The method is also versatile, allowing for batch processing by employing a large capacity centrifuge or alternatively, for prescriptive use for standardizing the fat content of donor milk or mother's own milk to meet the needs of a particular infant. Finally, the simplicity of this method ensures that with minimal training, non-laboratory trained staff can utilize it to standardize the energy content of breast milk for use in the NICU.

References

- 1 Tully DB, Jones F, Tully MR: Donor milk: what's in it and what's not. *J Hum Lact* 2001, 17(2):152-155.
- 2 Wight NE: Donor human milk for preterm infants. *J Perinatol* 2001, 21(4):249-254.
- 3 Arnold LD: Cost savings through the use of donor milk: case histories. *J Hum Lact* 1998, 14(3):255-258.
- 4 Arnold LD: The cost-effectiveness of using banked donor milk in the neonatal intensive care unit: prevention of necrotizing enterocolitis. *J Hum Lact* 2002, 18(2):172-177.
- 5 Schanler RJ, Atkinson S: Human Milk. In *Nutrition of the Preterm Infant: Scientific Basis and Practical Guidelines* Edited by: Tsang RC, Uauy R, Koletzko B, Zlotkin SH. Cincinnati, Ohio: Digital Educational Publishing, Inc; 2005:333-357.
- 6 King C: Ensuring nutritional adequacy of human milk-fed preterm babies. In *Feeding and Nutrition in the Preterm Infant* Edited by: Jones E, King C. London: Elsevier Churchill Livingstone; 2005:31-53.
- 7 Tsang R, Uauy R, Koletzko B, Zlotkin S: *Nutrition of the Preterm Infant: Scientific Basis and Practical Guidelines*. Cincinnati, Ohio: Digital Educational Publishing; 2005.
- 8 Mitoulas LR, Kent JC, Cox DB, Owens RA, Sherriff JL, Hartmann PE: Variation in fat, lactose and protein in human milk over 24 h and throughout the first year of lactation. *Br J Nutr* 2002, 88(1):29-37.
- 9 Protein and Energy Requirements [<http://www.fao.org/docrep/003/aa040e/AA040E00.HTM>]
- 10 Jensen RG, Bitman J, Carlson SE, Couch SC, Hamosh M, Newburg DS: A. Human Milk Lipids. In *Handbook of Milk Composition* Edited by: Jensen RG. London: Academic Press Inc; 1995:495-537.
- 11 Newburg DS, Neubauer SH: Carbohydrates in Milks: Analysis, Quantities and Significance. In *Handbook of Milk Composition* Edited by: Jensen RG. London: Academic Press Inc; 1995:282-283.
- 12 Atkinson S, Lonnerdal B: Nitrogenous components of milk.
- 13 Buckley AJ, Jaquiere AL, Harding JE: Nutritional programming of adult disease. *Cell Tissue Res* 2005, 322(1):73-79.
- 14 Grino M: Prenatal nutritional programming of central obesity and the metabolic syndrome: role of adipose tissue glucocorticoid metabolism. *Am J Physiol Regul Integr Comp Physiol* 2005, 289(5):R1233-1235.
- 15 Koletzko B: Early nutrition and its later consequences: new opportunities. *Adv Exp Med Biol* 2005, 569:1-12.
- 16 Langley-Evans SC: *Fetal nutrition and adult disease: programming of chronic disease through fetal exposure to undernutrition*. Wallingford, UK: CABI Publishing; 2004.
- 17 Symonds ME, Stephenson T, Gardner DS, Budge H: Long-term effects of nutritional programming of the embryo and fetus: mechanisms and critical windows. *Reprod Fertil Dev* 2007, 19(1):53-63.
- 18 Wells JC, Chomtho S, Fewtrell MS: Programming of body composition by early growth and nutrition. *Proc Nutr Soc* 2007 66(3):423-434.
- 19 Schack-Nielsen L, Michaelsen KF: Breast feeding and future health. *Curr Opin Clin Nutr Met Care* 2006, 9(3):289-296.
- 20 Czank C, Mitoulas L, Hartmann PE: Human Milk Composition: Fat. In *Hale and Hartmann's Textbook of Human Lactation* Edited by: Hartmann PE, Hale T. Amarillo, TX: Hale Publishing; 2007:49-67.
- 21 Stern I, Shapiro B: A rapid and simple method for the determination of esterified fatty acids and for total fatty acids in blood. *J Clin Path* 1953, 6:158-160.
- 22 Lucas A, Gibbs JA, Lyster RL, Baum JD: Creamatocrit: simple clinical technique for estimating fat concentration and energy value of human milk. *Br Med J* 1978, 1(6119):1018-1020.
- 23 Arnold LDW, Tully MR: *Guidelines for the Establishment and Operation of a Donor Human Milk Bank*. HMBANA; 1994.
- 24 Thomaz ACP, Goncalves AL, Martinez FE: Effects of human milk homogenization on fat absorption in very low birth weight infants. *Nutr Res* 1999, 19(4):483-492.
- 25 McCrae C, LePoetre A: Characterisation of dairy emulsions by forward lobe laser light scattering—application to milk and cream. *Dairy J* 1996, 6:247-256.
- 26 Michalski MC, Briard V, Michel F, Tasson F, Poulain P: Size distribution of fat globules in human colostrum, breast milk, and infant formula. *J Dairy Sci* 2005, 88(6):1927-1940.
- 27 Ruegg M, Blanc B: The fat globule size distribution in human milk. *Biochim Biophys Acta* 1981, 666(1):7-14.
- 28 Lonnerdal B, Forsum E: Casein content of human milk. *Am J Clin Nutr* 1985, 41(1):113-120.

Downward Trend in Percutaneous Umbilical Blood Sampling at a Single Tertiary Care Center

Daniel Roshan, MD; Boris Petrikovsky, MD, PhD; Marianna Dubovska, MD; Michael J. Mobasser

Introduction

In the field of prenatal diagnosis, percutaneous umbilical blood sampling (PUBS) is one method that has been widely used in the past for its ability to obtain pertinent diagnostic information. Since its introduction in 1983 by Daffos and associates, PUBS was quickly adopted in many hospitals worldwide as a fast and accurate diagnostic procedure. However, within 10 years of its introduction, decline was already imminent. Technologic advancements in the early 1990s, including new devices (middle cerebral artery Doppler) and techniques (pre-implantation genetic diagnosis), have begun to replace the once popular PUBS. This study details the chronic downward trend of PUBS usage at a single tertiary care center and addresses the possible reasons for the decline.

Materials and methods

During the 8-year span between 1992 and 1999, 398 PUBS were performed at a tertiary care center. All PUBS procedures were performed using 20-gauge needles. Sampling was from the umbilical cord at its placental insertion under continuous ultrasound guidance using the free-hand technique. Approximately 2-3 mL of blood was drawn from the umbilical vein and sent to the lab for various tests. Gestational age at the time of the procedure ranged from 16-36 weeks.

Results

The 8-year study period was divided into two 4-year periods, 1992-1995 and 1996-1999. The 398 PUBS were split among four categories based on indications: 1. Fetal hematologic complications, 2. Fetal infections, 3. Rapid karyotyping, and 4. Fetal acid-base status. Each specific procedure had its own number and indication recorded for the given 4-year span, indicating a fraction of the total PUBS administered. Statistical analysis was performed using Fisher exact test and chi-square.

The fetal hematologic complications included diseases such as erythroblastosis fetalis, beta-thalassemia, hydrops fetalis, and Rh isoimmunization. Between 1992 and 1995 there were 117 PUBS related to fetal hematologic complications performed at the

tertiary care center. Between 1996 and 1999 that number became 89, a 24% drop ($p < 0.0001$).

The fetal infections included rubella, cytomegalovirus, varicella-zoster virus, and parasites (*Toxoplasma Gondii*). In the span of 4 years 1992-1995, 69 PUBS were performed. In the next 4 years 1996-1999, the number of PUBS had decreased to 3, which amounted to a 96% decline in the use of PUBS ($p < 0.0001$).

Rapid karyotyping has been used to diagnose chromosome abnormalities and genetic disorders, such as Down, Edwards, Turner, and Klinefelter syndromes, among others. In the first 4-year interval, there were 67 rapid karyotyping-related PUBS and in the second 4-year interval, that number dropped to 41. This change amounted to a 38% decrease.

Fetal acid-base status was used to diagnose hypoxia, other respiratory acidosis and alkalosis, as well as metabolic acidosis and alkalosis. The first 4 years of PUBS for fetal acid-base status yielded 11 procedures, while the following 4 years yielded only 1 PUBS test. This was a 91% drop in PUBS between the two 4-year intervals ($p < 0.04$). Overall, the number of PUBS fell from 264 between 1992 and 1995, to 134 between 1996 and 1999 (a decrease of 49%).

Discussion

There was a significant and dramatic drop of PUBS procedures in our tertiary care center. Several studies reported at other centers suggest the dramatic drop in PUBS is a widespread phenomenon and not just specific to our center.

There are a number of reasons that can be attributed to the decline in use of PUBS in maternal-fetal prenatal diagnosis. Firstly, there have been well-chronicled studies on the complications and difficulties associated with PUBS and the potential for fatal consequences for the fetus. Duchatel et al¹ reported their experience with 341 cases of PUBS. In 67 procedures there were 12 failures and 6 fetal deaths (8.96%), of which half were procedure related. In addition, 17 cases of fetal bradycardia were observed in this group.

Buscaglia et al² analyzed PUBS results over 9 year period. They claimed that the indications for PUBS had changed throughout

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these years because of rapid evolution of molecular biology. As a result, there were steady decreases in the use of PUBS between the time ranges of 1986-88 to 1991-92 and 1994; thus, prenatal diagnosis of hemoglobinopathies is not a major indication for second trimester PUBS and Rh alloimmunization as an indication is also dropping rapidly.

DNA probes have also taken the place of PUBS for many other indications. DNA probes allow prenatal diagnosis of fetal infections for which routine screening is undertaken. A dramatic decrease in prenatal diagnosis of congenital infections, toxoplasmosis, rubella and beta-thalassemia by PUBS can be observed by us as well as by others.

The most important factor in the diminishing use of PUBS could be the advent of the middle cerebral artery (MCA) Doppler. Numerous studies have shown the advantages that MCA Doppler has over PUBS.^{3,4}

Pereira et al⁵ compared noninvasive MCA Doppler and invasive test to diagnose fetal anemia.

Twenty-eight fetuses were followed up: 4 had severe anemia, 1 had moderate anemia, 3 had mild anemia and 20 were non anemic. Conventional management had a sensitivity and positive predictive value for moderate-to-severe anemia of 80% and 44%, with a false-positive rate of 56%. In the same patients, MCA Doppler may have better predictive accuracy for moderate-to-severe fetal anemia in fetuses with red blood cell alloimmunization.

Another technique which is changing the approach to prenatal diagnosis is pre-implantation genetic diagnosis (PGD). PGD is actually an alternative to prenatal diagnosis and refers to procedures that are performed on embryos prior to implantation. Many studies have shown clear advantages in using PGD, as it is superior in avoiding selective pregnancy termination and in that the child will be free of genetic diseases.^{6,7}

Conclusion

There was a significant decline in the number of PUBS performed in our center. If this decline is sustained on a nationwide basis, the level of fellow training and proficiency in this procedure is likely to decrease. We speculate the number of procedures to decrease further due to the utility of MCA Dopplers and pre-implantation genetic diagnosis that has developed over the past 5 years.

Recent advances in molecular and cytogenetic techniques have restricted the number of reasons for using PUBS. Therefore, regional maternal fetal medicine training centers should have enhanced cooperation to optimize teaching this procedure, have more fellows involved in each case, and create computer simulated models to enhance manual dexterity with the technique.

References

- 1 Duchatel F, Oury JF, Mennesson B, Muray JM. Complications of diagnostic ultrasound-guided percutaneous umbilical blood sampling: analysis of a series of 341 cases and review of the literature. *Eur J Obstet Gynecol Reprod Biol* 1993 53: 95-104.
- 2 Buscaglia M, Ghisoni L, Bellotti M, Ferrazzi E, Levi-Setti P, Marconi AM, Taglioretti A, Zamperini P, Pardi G.

- Percutaneous umbilical blood sampling: indication changes and procedure loss rate in a nine years' experience. *Fetal Diagn Ther* 1996. 11: 106-113.
- 3 Segata M, Mari G. Fetal anemia: new technologies. *Curr Opin Obstet Gynecol* 2004. 16:153-158.
- 4 Dukler D, Oepkes D, Seaward G, Windrim R, Ryan G. Noninvasive tests to predict fetal anemia: a study comparing Doppler and ultrasound parameters. *Am J Obstet Gynecol* 2003. 5:1310-1314.
- 5 Pereira L, Jenkins TM, Berghella V. Conventional management of maternal red cell alloimmunization compared with management by Doppler assessment of middle cerebral artery peak systolic velocity. *Am J Obstet Gynecol* 2003. 4: 1002-1 006.
- 6 Pellicer A, Rubio C, Vidal F, Minguez Y, Gimenez C, Egozcue J, Remohi J, Simon C. In vitro fertilization plus preimplantation genetic diagnosis in patients with recurrent miscarriage: an analysis of chromosome abnormalities in human preimplantation embryos. *Fert Ster* 1999. 7:1033-1039.
- 7 Wells D, Sherlock JK. Strategies for preimplantation genetic diagnosis of single gene disorders by DNA amplification. *Pren Diagn* 1999. 13:1389-140.

Regional Block vs General Anesthesia for Cesarean Section and Neonatal Outcomes: A Population-Based Study

Charles S. Algert, Jennifer R. Bowen, Warwick B. Giles, Greg E. Knoblanche, Samantha J. Lain, Christine L. Roberts

Abstract

Background: Anesthesia guidelines recommend regional anesthesia for most cesarean sections due to the risk of failed intubation and aspiration with general anesthesia. However, general anesthesia is considered to be safe for the fetus, based on limited evidence, and is still used for cesarean sections.

Methods: Cohorts of cesarean sections by indication (that is, planned repeat cesarean section, failure to progress, foetal distress) were selected from the period 1998 to 2004 (N = 50,806). Deliveries performed under general anesthesia were compared with those performed under spinal or epidural, for the outcomes of neonatal intubation and 5-minute Apgar (Apgar5) <7.

Results: The risk of adverse outcomes was increased for cesarean sections under general anesthesia for all three indications and across all levels of hospital. The relative risks were largest for low-risk planned repeat cesarean deliveries: resuscitation with intubation relative risk was 12.8 (95% confidence interval 7.6, 21.7), and Apgar5 <7 relative risk was 13.4 (95% confidence interval 9.2, 19.4). The largest absolute increase in risk was for unplanned cesareans due to foetal distress: there were five extra intubations per 100 deliveries and six extra Apgar5 <7 per 100 deliveries.

Conclusion: The infants most affected by general anesthesia were those already compromised in utero, as evidenced by foetal distress. The increased rate of adverse neonatal outcomes should be weighed up when general anesthesia is under consideration.

Background

Internationally, obstetric anesthesia guidelines recommend spinal and epidural over general anesthesia (GA) for most cesarean sections (CSs).^{1,2} The primary reason for recommending regional blocks is the risk of failed endotracheal intubation

and aspiration of gastric contents in pregnant women who undergo GA.³ While there is evidence that GA is associated with an increased need for neonatal resuscitation,⁴ evidence about specific delivery indications and about neonatal outcomes subsequent to resuscitation is limited. Previous studies have usually been single hospital-based and lacked power to confidently detect differences in a rare neonatal outcome such as a low 5-minute Apgar score (Apgar5), particularly among sub-groups such as emergency deliveries. Observational studies, generally unstratified by risk, are subject to confounding since emergencies such as an antepartum haemorrhage can be both an indication for GA and the cause of poor infant status at birth. A Cochrane Database of Systematic Reviews of anesthesia for CS included only two randomised studies with a total of 10 Apgar5 <7 events, and one trial with oxygen therapy as an outcome.⁵ That meta-analysis, and another which used cord blood acid-base status as the outcome,⁶ concluded that there was no evidence that regional anesthesia was superior to GA in regard to neonatal outcomes.

Although the use of GA for CS has declined while the use of regional techniques has increased,⁷ both planned and unplanned CS continue to be performed under GA. GA can be thought to be the quickest anesthesia method in an emergency since it avoids the possibility of a failed regional block. The purpose of this study was to determine the relative risks of neonatal resuscitation with intubation and of an Apgar5 <7 when CS was performed under GA compared with a regional block stratified by specific indications for CS and levels of risk to the fetus. A further purpose was to examine whether the risk of adverse events varied by level of hospital.

Methods

The study population included all liveborn infants delivered by CS in New South Wales (NSW), Australia from 1 January 1998 to 31 December 2004. Data were obtained from two de-identified linked population databases. The Midwives Data collection (MDC) is a legislated surveillance system of all births in NSW of ≥ 20 weeks gestation or ≥ 400 g birth weight. The Admitted Patient Data Collection has records of all hospital admissions, including ICD10 diagnostic codes related to the admission. Linked MDC and hospital birth admissions were available from 1998 to 2004. Non-linked data on anesthesia for CS was also available from the MDC for the years 2005 and 2006. The study was approved by the NSW Population and Health Services Research Ethics Committee and the University of Sydney Human Research Ethics Committee.

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The MDC collects information on maternal characteristics, pregnancy, labour, delivery and infant outcomes. It includes tick boxes for spinal, epidural and/or GA at delivery. In this study, regional block included any record where spinal and/or epidural anesthesia (including combined spinal/epidural) was recorded. The outcome and exposure measures in this study are reliably reported on the MDC.^{8,9} Compared with medical records, MDC reporting had excellent agreement beyond chance ($\kappa > 0.75$) for GA for CS, epidural and spinal anesthesia, neonatal resuscitation and Apgar5 score, and almost perfect agreement for CS. Only four CS deliveries in the study period did not have type of anesthesia recorded and only 84 (0.06%) were missing an Apgar5 score.

A CS was categorized as planned if performed prior to the onset of labor and as unplanned if performed after labor had begun. Deliveries where a regional block was recorded in addition to GA are referred to as conversions to GA and presumably represent failed regional blocks. Hospitals were grouped into three categories: large public, which are public hospitals providing high-risk obstetric care and 24-hour on-site anesthetic staff, other public, and private.

The primary infant outcomes were resuscitation requiring intubation of the neonate at the time of delivery and the 5-minute Apgar score (Apgar5), dichotomized as < 7 or ≥ 7 . An Apgar5 score of < 7 is associated with increased risk of infant mortality and neurological impairment.¹⁰ The rates of these outcomes for infants exposed to CS under GA were compared with CS under any regional block technique. The GA category in the analyses included those deliveries where both GA and regional block were used (converted regional blocks). To control for confounding by indication, comparisons were made for three pre-specified risk groups, defined by the indications for CS: low-risk pregnancies were planned repeat CS; moderate-risk pregnancies were for failure to progress and where fetal distress was absent; high-risk pregnancies were unplanned CS for fetal distress. All three risk groups were restricted to pregnancies with the following (low fetal risk prior to delivery) characteristics: maternal age 20 to 44 years, gestation 38 to 41 completed weeks, singleton pregnancy. Pregnancies with reported hypertension, oligohydramnios, polyhydramnios, antepartum hemorrhage, or care for a suspected fetal abnormality were excluded as these conditions could have been associated with both anesthesia choice and neonatal outcome. Births were further restricted to non-breech presenting live births > 10 th percentile of size for gestational age. Since the

10th percentile for females at 38 weeks in NSW is 2660 g, this was the minimum birth weight for inclusion in this analysis. Relative risks (RRs) and risk differences and their 95% confidence interval (CI) were calculated for each indication and/or risk group. The risk difference is the absolute difference in outcome rates between exposure groups and, in this study, measures the excess rate of adverse outcomes attributable to GA.

To examine the potential impact of variation in level of anesthetic care available, the risks of intubation and an Apgar5 < 7 were further stratified by hospital level for each risk group. The risk differences for each hospital category were calculated and presented as forest plots, and the heterogeneity of effect was assessed using the I-squared statistic (I^2).¹¹ The I^2 value estimates the percentage of variation across sub-groups (hospital levels, in this case), which is due to true heterogeneity of effect rather than chance.

Results

From 1998 to 2004, there were 592,125 deliveries. Annual deliveries declined by 0.9% from 85,072 in 1998 to 84,288 in 2004. The number of women delivered by CS rose steeply, up 41.5%, from 16,216 in 1998 to 22,904 in 2004. Over this period, the percentage of CS performed under GA declined (Table 1). The decrease in use of GA was greater for planned CS than for unplanned CS (25.0% versus 18.3%). Private hospitals had the lowest rate of GA use and other public hospitals had the highest rate. Data from the non-linked 2006 MDC showed a further decline in the use of GA: 1654 unplanned CS under GA (15.3%) and 1627 planned CS under GA (10.5%). The rate of failed regional blocks fell for both planned and unplanned CS, but the absolute numbers increased slightly due to the large overall increase in CS deliveries.

Of the 137,987 CS deliveries during the study period, 69,437 were pregnancies without apparent fetal risk factors prior to delivery. From these deliveries, three specific CS indication groups were selected, totalling 50,806 live births. The RR and risk differences for resuscitation requiring intubation and of an Apgar5 < 7 for the specific CS indication groups are shown in Table 2. For planned repeat CS deliveries performed under regional block, both intubation (0.09%) and an Apgar5 of < 7 (0.17%) were rare events. The RRs when GA was used for repeat CS were greatly increased, and in these otherwise low-risk deliveries, the excess risk attributable to GA was one intubation and two Apgar5 < 7 scores per 100 deliveries. The excess risk attributable to GA

Table 1: Caesarean section delivery frequencies for New South Wales 1998 and 2004

	1998 N (%)	2004 N (%)	Change in frequency relative to 1998 (%)
All planned CS	8800	12,930	+46.9
- intended GA	2193 (24.9)	1597 (12.4)	-27.2
- GA after regional block	153 (1.7)	162 (1.3)	+5.9
All unplanned CS	7416	9974	+34.5
- intended GA	1937 (26.3)	1468 (14.8)	-24.2
- GA after regional block	329 (4.5)	384 (3.9)	+16.7
CS in large public hospital	5913	8264	+39.8
- under GA	1397 (23.6)	1404 (17.0)	+0.5
CS in other public hospitals	6025	6954	+15.4
- under GA	2401 (39.9)	1564 (22.5)	-34.9
CS in private hospitals	4278	7686	+79.7
- under GA	814 (19.0)	643 (8.4)	-21.0

CS, caesarean section; GA, general anaesthesia.

Table 2: Effect of anaesthesia type, by caesarean section indication, on relative risk of neonatal outcomes.

Riskgroup/ Indication	Outcome	General anaesthesia events/N (rate %)	Regional block events/N (rate %)	Relative risk if general anaesthesia used (95% confidence interval)	Risk difference* (%) (95% confidence interval)
Low risk: planned repeat caesarean section	Resuscitation w/ intubation	46/4149 (1.11)	20/23,139 (0.09)	12.8 (7.6, 21.7)	1.0 (0.7, 1.3)
	Apgar5 <7	96/4146 (2.32)	40/23,134 (0.17)	13.4 (9.2, 19.4)	2.1 (1.7, 2.6)
Moderate risk: unplanned caesarean section for failure to progress	Resuscitation w/ intubation	71/2320 (3.06)	68/13,449 (0.51)	6.1 (4.3, 8.5)	2.6 (1.8, 3.3)
	Apgar5 <7	95/2319 (4.10)	70/13,446 (0.52)	7.9 (5.8, 10.7)	3.6 (2.8, 4.4)
High risk: unplanned caesarean section for foetal distress during labour	Resuscitation w/ intubation	139/2058 (6.75)	105/5759 (1.82)	3.7 (2.9, 4.8)	4.9 (3.8, 6.1)
	Apgar5 <7	158/2054 (7.69)	95/5757 (1.65)	4.7 (3.6, 6.0)	6.0 (4.8, 7.2)

*Rate in general anaesthesia sub-group minus the rate in the regional block sub-group, representing the excess number of adverse outcomes per 100 deliveries under general anaesthesia.

increased with the urgency of the indication for delivery, so that for foetal distress deliveries there were five extra intubations per 100 deliveries under GA and six extra Apgar5 <7 scores. Among the infants who did require intubation, those that had been delivered with GA had higher rates of an Apgar5 <7 compared with regional block: 42% versus 20% for planned repeat CS ($P = 0.06$), 51% versus 21% for failure to progress ($P < 0.01$), and 57% versus 34% for fetal distress as the indication ($P < 0.001$).

A separate group of 3,473 small-for-gestational-age infants delivered at 38 to 41 weeks by unplanned CS was also analyzed, 30.0% of whom were delivered under GA. These antenatally compromised fetuses had increased risks of both intubation (RR = 3.4, 95% CI 2.4, 4.8) and of Apgar5 <7 (RR = 4.3, 95% CI 3.1, 5.9), when the CS was performed under GA.

GA was more frequent in other public hospitals for all three of these risk groups. For the low-risk repeat CS deliveries, 22.5% were performed under GA in other public hospitals compared with 14.4% in large public hospitals and 9.0% in private hospitals. For the failure to progress risk group, the rate of GA was 25.4% in other public hospitals, 9.6% in large public hospitals and 9.4% in private hospitals. For unplanned CS for fetal distress, 39.0% of deliveries were by GA at other public hospitals, 24.0% of deliveries at large public hospitals, and 14.9% of deliveries in private hospitals.

Figure 1 shows the risk differences for resuscitation with intubation and for an Apgar5 <7 for each CS indication group, by hospital category. For all of the CS indications and across all of the hospital levels, the results favoured regional block over GA. The planned repeat CS group showed no variation by hospital level in difference in intubation rates (heterogeneity $I^2 = 0\%$), but there was strong heterogeneity for the Apgar5 score ($I^2 = 75\%$). This was influenced by private hospitals, which had both the lowest rate of Apgar5 <7 scores after GA (1.4%) and the highest rate after regional block (0.2%), resulting in the smallest risk difference (1.2 extra Apgar5 <7 scores per 100 deliveries under GA). For the failure to progress group, there was strong heterogeneity in the risk differences for intubation ($I^2 = 82\%$) and

the Apgar5 outcome ($I^2 = 52\%$). The heterogeneity was driven by the relatively high rate of intubation (5.4%) and Apgar5 <7 (5.4%) in large public hospitals after GA, whereas other public and private hospitals had intubation rates of <2.5% after GA. For the fetal distress indication group, there was strong heterogeneity in the risk differences for intubation ($I^2 = 72\%$) and weak heterogeneity for the Apgar5 outcome ($I^2 = 7\%$). This was mainly due to the relatively low rates of intubation (3.9%) and Apgar5 <7

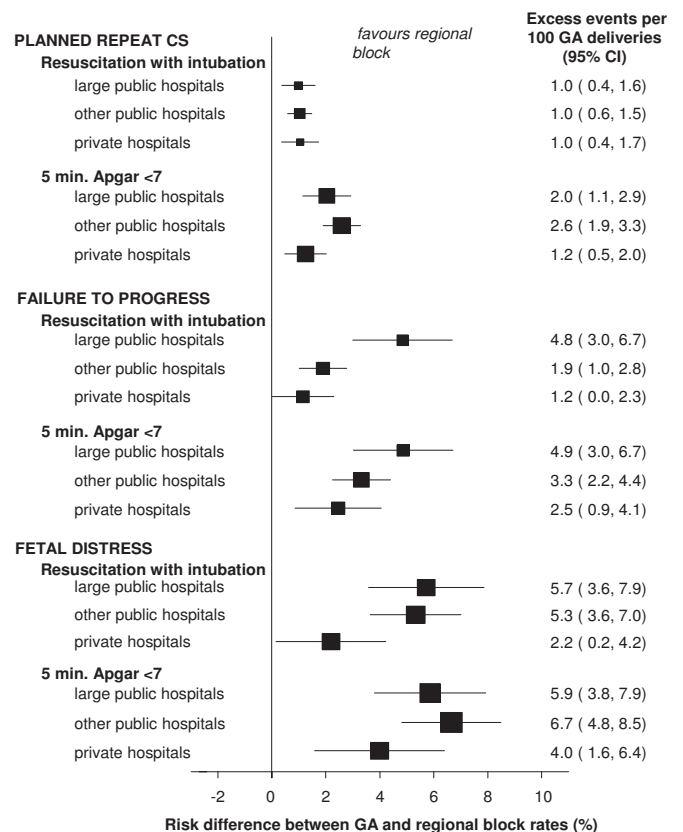


Figure 1. Risk differences for neonatal outcomes, for caesarean section under general anaesthesia compared with regional block, by caesarean section indication and hospital level.

(5.7%) in private hospitals after GA for this group.

Discussion

This is the largest study to compare the effect of anesthesia methods for CS on neonatal outcome, and controls for confounding by specification of both pregnancy risk and indication for CS. We have shown that there are significant risks to the neonate of both resuscitation requiring intubation and of a poor Apgar score at 5 minutes, for a range of delivery indications. The greatest RR of both adverse outcomes occurred in the low-risk planned repeat CS deliveries under GA, but the greatest excess in risk attributable to GA was for emergency deliveries for foetal distress where the infant would already have been compromised to some extent. Not only did GA increase the risk of intubation, but it also increased the probability that an intubated infant's Apgar5 score would be <7 compared with an infant intubated after a regional block.

Similarly to reports from other developed countries^{7,12,13} the use of GA for CS in NSW has decreased and the use of spinal anesthesia has become more widespread. However, GA was still used for 12.6% of CS deliveries in 2006 across all levels of hospitals in the state. This study provides strong evidence that the guidelines recommending regional block over GA for most CS are prudent and beneficial for neonates as well as for mothers.^{1,2} The RR of both intubation and a low 5-minute Apgar score were greatly decreased if a regional block was used for all three of the defined risk groups and across all three hospital levels. While this study is based on observational data, it did include a large number of deliveries drawn from an entire population. The CS indication groups make the comparisons meaningful and control for confounding. The result for the high-risk fetal distress group is arguably still subject to confounding by indication since the precise cause and degree of the fetal distress is not reported, although haemorrhage and maternal hypertensive disorders and preterm deliveries were excluded. The relative risk of an Apgar5 <7 strongly favoured regional block for this group (RR = 4.7 if GA was used), and it seems unlikely that selection bias could explain this away. The increase in rates of intubation as the urgency of the indication for CS increased was consistent with the increase in rates of Apgar5 <7.

Previous population-based studies of anesthesia for delivery in Tasmania did find significantly increased risks of intubation and Apgar1 <4 for both repeat and primary CS under GA,¹⁴ and an RR of intubation = 10.8 (95% CI 3.2, 36.0) when emergency CS was performed under GA.¹⁵ A recent US study, which included births from 14 university-based hospitals, showed an increased odds of both Apgar1 ≤ 3 and Apgar5 ≤ 3 but did not specify the indications for CS.³ Other observational studies have found an increased need for resuscitation when GA is used.⁴ However, these had limited statistical power for an Apgar5 outcome, and this continued to be a limitation in two more recent studies.^{16,17} Controlling or stratifying for the indication for CS is also usually absent. A study of 3,940 deliveries in a tertiary referral hospital did use three CS indication groups (that is, elective, urgent and emergency), which approximated the categories in this study. That study found that there was a significant increase in rates of intubation and low Apgar5 score for urgent and emergency CS, but was under-powered for the elective deliveries, and did not control for factors such as gestational age.¹⁸ Randomized trials of anesthesia in CS not only have had small numbers of deliveries,⁵ but may also have limited generalisability.¹⁹ For instance, the only randomised trial with more than five Apgar5 <7 events was

of pregnancies affected by severe preeclampsia.²⁰

A limitation to this study is that infant records were only available up to separation from the birth hospital, so longer term outcome data was not available. An Apgar5 <7 is usually associated with birth asphyxia,²¹ but it is unclear whether an Apgar5 <7 affected by GA has the same prognostic value. That the setback due to GA could be temporary is plausible to some extent for low-risk infants. The greatest burden may be on those infants already compromised in utero, as indicated by foetal distress, who in this study had significantly increased risks of both intubation and a low Apgar5 score if the delivery was performed under GA.

A strength of this study is the large, well validated, population-based data. Like all such databases, there could be some under-reporting of risk factors for CS. However, for maternal hypertension it has been shown that the more severe manifestations, which result in maternal morbidity, are more likely to be reported.²² If this holds true generally for pregnancy complications, risk factors are likely to have been well reported in cases of adverse neonatal outcomes. Variations in experience and skill level of anesthetists or obstetricians may have been partly responsible for differences in the risks associated with GA, as evidenced by the heterogeneity of outcomes by hospital category. However, all comparisons across all hospital levels favoured the use of regional block over GA.

Conclusion

Concerns about the effects of GA on the neonate have mostly focused on acid-base status, resuscitation and the Apgar score at 1 minute, with the presumption that the effect of GA on the infant is short lived.⁶ The increased rates of neonatal intubation after GA in this study represent harm in and of itself, and the persistence of low 5-minute Apgar scores suggests that deleterious effects may last longer than the immediate aftermath of delivery. The greatest absolute increase in the rate of intubation and of a 5-minute Apgar score <7 for deliveries performed under GA occurred in the most vulnerable infants: those that were delivered by emergency CS because of fetal distress. Clinicians considering the use of GA for a CS delivery should be aware of these possible consequences for the infant, for both planned and emergency CS.

References

- 1 American Society of Anesthesiologists Task Force on Obstetric Anesthesia: Practice guidelines for obstetric anesthesia: an updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia. *Anesthesiology* 2007, 106:843-863.
- 2 Cyna AM, Dodd J: Clinical update: obstetric anesthesia. *Lancet* 2007, 370:640-642.
- 3 Bloom SL, Spong CY, Weiner SJ, Landon MB, Rouse DJ, Varner MW, Moawad AH, Caritis SN, Harper M, Wapner RJ, Sorokin Y, Miodovnik M, O'Sullivan MJ, Sibai B, Langer O, Gabbe SG: Complications of anesthesia for cesarean delivery. *Obstet Gynecol* 2005, 106:281-287.
- 4 Gordon A, McKechnie EJ, Jeffery H: Pediatric presence at cesarean section: justified or not? *Am J Obst Gynecol* 2005, 193:599-605.
- 5 Afolabi BB, Lesi FEA, Merah NA: Regional versus general anesthesia for cesarean section. *Cochrane Database Syst Rev* 2006:CD004350.

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Metabolic Bone Disease in a Preterm Newborn: An Update On Nutritional Issues

Valentina Bozzetti, Paolo Tagliabue

Abstract

Osteopenia, a condition characterized by a reduction in bone mineral content, is a common disease of preterm babies between the tenth and sixteenth week of life. Prematurely born infants are deprived of the intrauterine supply of minerals affecting bone mineralization. The etiology is multifactorial: inadequate nutrients intake (calcium, phosphorus and vitamin D), a prolonged period of total parenteral nutrition, immobilization and the intake of some drugs. The diagnosis of metabolic bone disease is done by biochemical analysis: low serum levels of phosphorus and high levels of alkaline phosphatase are suggestive of metabolic bone disease. The disease can remain clinically silent or presents with symptoms and signs of rickets depending on the severity of bone demineralization.

An early nutritional intervention can reduce both the prevalence and the severity of osteopenia. This article reviews the pathophysiology of foetal and neonatal bone metabolism, focuses on the nutrient requirements of premature babies and on the ways to early detect and treat osteopenia.

Background

The continuous advances in intensive care of preterm newborns have led to a progressive decline of mortality in Institutions where facilities and expertise for respiratory resuscitation and respiratory distress syndrome are available. Infant mortality dropped among all races between 1980 and 2000. The survival rate depends on the gestational age of the newborn; actually the survival rates for very low birth weight (VLBW) are the following: for those weighing 501 – 750 g is 56% and for the ones above 750 is 88%.¹ However, the success in the survival achieved through an aggressive intensive care is not always paralleled by a subsequent fully healthy development of the newborn.

Among the common conditions of morbidity due to the prematurity (cerebral impairment, bronchopulmonary dysplasia, growth failure, retinopathy...) a growing interest is focusing now on the metabolic bone disease of the prematurity (MBD), also called osteopenia of prematurity. This condition is characterized

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by a reduction in bone mineral content (osteopenia), with or without rachitic changes, and is caused by several nutritional and biomechanical factors.

An inadequate supply of nutrients (vitamin D, calcium and phosphorus), a prolonged period of total parenteral nutrition, immobilisation and the intake of some drugs are the main factors involved in the pathogenesis of osteopenia.² The MBD usually occurs between tenth and sixteenth week of life, but it may remain silent until severe demineralization (a reduction of BMD of 20 – 40%) occurs.

The clinical picture is various, ranging from a totally silent condition to a clinical picture of overt rickets, with multiple fractures and other alterations, when the demineralization is severe. The purpose of this review is to focus on the recent advances in the understanding of the bone tissue metabolism and on the nutritional approach to prevent and to treat the MBD.

Magnitude of the Problem

The prevalence of MBD varies depending on gestational age, birthweight and kind of alimentation.

It occurs in up to 55% of babies born with weight under 1000 g³ and 23% of infants weighing < 1500 g at birth⁴ and it is especially frequent in babies under 28 weeks of gestation. The prevalence is 40% in premature infants who are breastfed, in contrast to 16% of those fed with a formula designed for preterm infants and supplemented with calcium and phosphorus.^{5,6} Preterm infants with a complicated medical course and delayed nutrition are also at high risk for MBD. Actually in western countries there is a trend of decrease of gestational age and birthweight, so the frequency of the MBD is expected to further increase.

Homeostasis of Calcium – Phosphorus: The homeostasis of calcium, phosphorus and magnesium is fundamental for structural matrix of the bone.

Calcium and phosphate represent the major inorganic constituents of bone. The highest amount of calcium (99%) and of phosphorus (80%) of the whole body is in the bone as microcrystalline apatite. Only 1% of the total body calcium is within the extracellular fluids and soft tissues. About the 50% of total serum calcium is in the ionised form and represents the biologically active part. A further 8–10% is bounded to organic and inorganic acid and the remaining percentage of calcium is protein-bound (80% to albumin, 20% to globulin). The formation

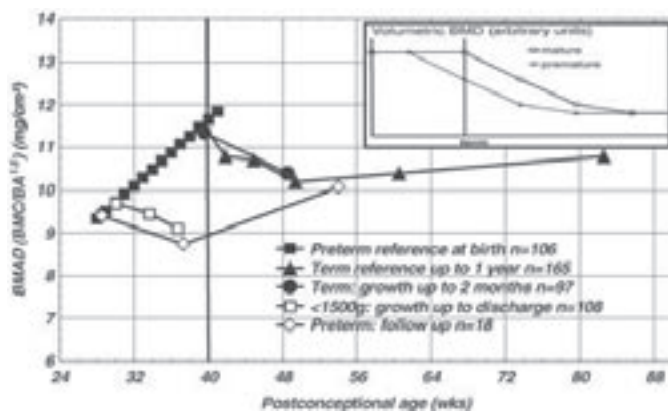


Figure 1. Physiological evolution of DEXA apparent bone mineral density during the last trimester of gestation (filled squares) and during the first year of life in healthy term infants (upper triangles) compared to that observed in preterm infants (open squares and lower triangles). (With permission from Ref [12]).

of the apatite takes place if calcium and phosphorus are simultaneously available in optimal proportions. Also magnesium is part of the bone matrix and the 60% of total body magnesium is in the bone.

Calcium and phosphorus homeostasis is a function of hormones, vitamin D and dietary intake, and depends on the intestinal absorption, skeletal accretion and reabsorption, and urinary excretion.⁷ Parathyroid hormone (PTH) is synthesised and secreted from the parathyroid glands in response to a reduction of serum level of ionised calcium. PTH regulates mineral metabolism and skeletal homeostasis through its action on target cells in bone and kidneys. It stimulates the reabsorption of calcium and excretion of phosphorus in the kidney and bone reabsorption of calcium. PTH also is able to activate the synthesis of calcitriol via stimulation of renal 25 (OH) D3-1-alpha-hydroxylase activities. In its active form, 1, 25(OH) 2 vitamin D, stimulates the renal reabsorption of calcium and phosphorus. The synthesis of calcitriol is inhibited by elevated serum levels of calcium and phosphorus.

The combined actions of PTH and calcitriol maintain the adequate concentration of calcium in the extracellular fluids. Kidneys contribute to maintain homeostasis of calcium; urinary calcium is one third derived from diet and the remaining from body stores, mostly bone. Diuretics, as furosemide, increase renal calcium excretion.

Prenatal bone physiology: The amounts of minerals required for a correct accretion of the skeleton are widely different depending on the age of the babies. The period of greater skeletal development is during the intrauterine life

and specifically during the last trimester. The bone volume increases significantly with gestational age and the high net bone formation activity is mainly due to modeling, with a rapidly increasing trabecular thickness (the trabecular thickening rate being approximately 240 times faster in the foetus than in the children). The mineralization process is determined by synthesis of the organic bone matrix by osteoblasts (osteoid) onto which calcium and phosphate salts are deposited. This process increases exponentially between 24 and 37 weeks of gestation, reaching the 80% of mineral accretion in the third trimester.⁸

During gestation the developing fetus receives supplies of energy, protein and mineral for adequate growth (1.2 cm/week) and bone development. At term the newborn skeleton has a high physical density (expressed as bone mass divided by bone volume). The fetal accretion of calcium and phosphate during the last three months of gestation is about 20 g and 10 g respectively, which represents accretion rates of 100–120 mg/kg/day for calcium and 50–65 mg/kg/day for phosphate.⁹

A very important role in skeletal accretion of the fetus is played by the placenta. In fact, the transfer of calcium from the mother to the fetus through the placenta occurs via an active transport done by the calcium pump in the basal membrane.¹⁰ There is a 1:4 maternal to foetal calcium gradient.¹¹ Moreover, the placenta is able to convert vitamin D to 1,25-dihydrocholecalciferol which is fundamental for transferring phosphate to the fetus.¹² The fetus is maintained hypercalcemic in a high calcitonin and estrogen environment which promotes the modeling/remodeling ratio in favour of modeling and thus increasing the endocortical bone.¹³ As a result, infants born prematurely will be deprived of the intrauterine supply of calcium and phosphorus affecting bone mineralization. It is well known that a chronic damage to the placenta may alter the phosphate transport; this explains why babies with intrauterine growth restriction may be osteopenic. Demineralization is also observed in infants born from mother with chorioamnionitis and placental infection.¹⁴

Maternal dietary intake of calcium is a factor implied in foetal bone accretion. A supplement of calcium (2 g from before 22 weeks of gestation) to women with a low dietary calcium intake resulted in higher bone mineral content (BMC) of the total body in infants born at term.¹⁵

Post-natal bone physiology: After birth the physical density of term newborns bones decreases by 30% in the first 6 months of life.¹³ This is mostly due to an enlargement of the marrow cavity size, which occurs faster than the increase in the cross-sectional area of the bone cortex.¹⁶ In term infants these postnatal changes are not accompanied by an increase in bone fragility and occur because bone is exposed to different conditions before and after birth.

Table 1: Minerals and vitamin D recommended intakes in growing preterm infants.

Requirements	ESPGAN [32] 1987	LSRO [31] 2002	Atkinson [33] 2005	Rigo [34] 2007
Calcium (mg/kg/day)	70–140	150–220	120–200	100–160
Phosphorus (mg/kg/day)	50–90	100–130	60–140	60–90
Vitamin D (I.U./day) (I.U./kg/day)	800–1600	90–225	200–1000 150–400	800–1000

First, there are important changes of hormonal environment: the reduction of maternal estrogens¹⁷ and a postnatal increase of PTH level mainly due to a reduction of the calcium supply by the placenta.¹⁸

As the serum calcium levels falls in the first day of life, PTH secretion is stimulated. During this transition the response of the parathyroid gland to falling levels of ionised calcium is blunted, as emphasized in a recent review article.¹⁹ This finally results in a physiological nadir in neonatal serum calcium levels within the first 48 hours of life. Of note, PTH level is still within the normal range for term babies or adult, but represents a decrease from fetal levels.

Many factors affect calcium absorption including the maternal vitamin D status, solubility and bioavailability of calcium salts, quality and quantity of calcium, amount and type of lipids and, obviously, gut function.

Calcium absorption from the intestine occurs both passively and through a vitamin-D dependent active transport mechanism. In a newly born preterm the low mineral content of human milk associated with a poorly efficient absorption of the developing gut determine a net reduction of calcium and phosphorus supply. Absorption of phosphorus takes place in the jejunum and depends on the dietary intake. The phosphorus supply regulates calcium absorption and retention: the higher is the phosphorus content of the diet, the higher is the calcium retention. However, an excessive amount of one decreases the absorption of the other.

Moreover, while in utero fetus experiments mechanical stimulation by kicking against the uterine wall, this kind of training is missing during the extrauterine life since preterm babies usually stay in the incubator.^{20,21} Inactivity due to immobilisation stimulates bone reabsorption by osteoclasts and urinary calcium excretion; furthermore the reduced muscle activity prevents the addition of new bone tissue.²² *Conditio sine qua non* for the physical activity to be beneficial is that an adequate mineral intake is guaranteed.²³

Figure 1 shows that during the third trimester of gestation, bone mineral apparent density (BMAD) increases at a faster rate in utero (term infants) than ex utero (preterm infants) according to gestational age. BMAD is an estimation of volumetric BMD (g/cm³) calculated as bone mineral content/bone area (BMC/BA). Figure 1 also shows that there is a sharp reduction in BMAD in neonatal age followed by a stabilization that lasts all the first year of life (black triangles). A similar event occurs in preterm babies: from birth to the term, mineral retention sharply diminishes comparing with the foetal life, while the skeletal growth remains high. This leads to a reduction of bone density (white squares). A catch-up mineralization occurs after discharge of VLBW so BMC spontaneously improves (white rhombs).

Among the other pathogenic factors, also problems related to inadequate supply of calcium to babies, which require parenteral nutrition and interference of several drugs, may contribute to determine preterm osteopenia with an increasing risk of bones fractures. The drugs mostly implied in pathogenesis of MBD include steroids, methylxanthines and diuretics. They stimulate osteoclasts activation, decrease calcium absorption, reduce osteoblasts proliferation and increase calcium renal excretion and hence increase the risk of poor bone mineralization.²⁴⁻²⁶

Neonatal mineral requirements: The requirements of calcium and phosphorus are based on demands for matching intrauterine bone mineral accretion rates. Supplying calcium and phosphorus in parenteral nutrition is a challenge because of limited solubility of these two minerals. Calcium and phosphorus's solubility in nutrition admixtures depends on temperature, type and concentration of aminoacid, glucose concentration, pH, type and concentration of calcium salts, and presence of lipid and so on.

In parenteral nutrition calcium is administered as inorganic salt and phosphorus may be administered as inorganic sodium and potassium phosphate or sodium-glucose phosphate or glycerolphosphate, which are quite soluble in water. The addition of cystein to lower pH of the parenteral admixtures improves the solubility of calcium and phosphorus. For all such reasons it is not possible to supply these minerals according to the physiologic requirements of the preterm to reach an adequate bone mineralization.

In the transition period, most of VLBW neonates receive full or partial parenteral nutrition with the goal to maintain normal levels of calcium and phosphorus. Hypocalcaemia, in fact, is a common event during the first days of life because of the sharp decrease of the calcium supply by the placenta and the delayed release of PTH due to the immature response of the parathyroid glands.

Parenteral administration of 50–75 mg of calcium/kg/day can prevent early neonatal hypocalcaemia in preterm infants. Through the parenteral administration of calcium and phosphorus (40–70 mg/kg/day and of 25–45 mg/kg/day respectively) it is possible to achieve 60 – 70% of intrauterine mineralization.²⁷ The best calcium to phosphorus ratio for bone mineralization is 1.7:1.²⁸⁻³⁰

In preterm babies receiving parenteral nutrition only limited amounts of vitamin D are required since calcium is given by vein and there is no need of calcitriol to facilitate the intestinal uptake. Moreover only the parent compound needs to be administered since the preterm infant is able to hydroxylate the inactive form to the active one since the 24th week of gestation. It is now generally accepted the daily recommended dose of vitamin D is 400 U.I./day.¹⁸

For the transitional period, when infants are weaned from parenteral nutrition to the enteral one, the aim usually is to maintain an adequate serum level of calcium and phosphorus. However the serum level of calcium is not a good marker of adequacy of calcium intake since the level is maintained stable at the expense of the bone. Therefore the clinicians should be aware that a normal serum level of both calcium and phosphorus are not guarantee for an adequate whole body accretion as in intrauterine life.

The enteral administration of calcium is fraught with many problems as regards the calcium bioavailability. Vomiting, large gastric aspirates, constipation and abdominal distension are quite common in preterm babies and the gut absorption capacity is impaired due to the immaturity of the gastrointestinal mucosa. Calcium absorption depends on vitamin D status, solubility of calcium salts, quality and quantity of lipid intake. Moreover, in preterm babies, vitamin D demands are influenced by body contents at birth which depends on the duration of gestation and maternal vitamin status. Current estimates of requirements for

calcium, phosphorus and vitamin D in growing premature infants vary among international sources of recommendations (Table 1).³¹⁻³⁴

The human milk content is inadequate for preterm requirements since the content of calcium and phosphorus in preterm human milk is 31 mg/100 kcal and 20 mg/100 kcal¹⁸ while the Life Science Research Office³¹ suggests, for premature formulas, a dose approximately 4–6 times higher (123 to 185 mg Ca/100 kcal and 80 to 110 mg P/100 kcal). Even when VLBW are fed at high feeding volumes (180–200 mL/Kg), assuming calcium and phosphorus absorption of 70% and 80% respectively, this would provide only one-third of the in utero level of absorbed calcium and phosphorus.⁶ Formula milk is richer in calcium and phosphorus than human one, but bioavailability is quite different. In formula fed infants, calcium absorption is usually less than with human milk, ranging from 35 to 60% of the intake. Hence the human milk intake has to be promoted, but a fortification with mineral and protein fortifier is necessary to achieve adequate nutrient intake.

With the current human milk fortifiers, containing highly soluble calcium glycerolphosphate, calcium retention reaches a level of 90 mg/kg/day (88% of the overall intake). However the new human milk fortifiers available in the market still do not allow intakes of calcium comparable with the values achieved during the last trimester of gestation (100–120 mg/kg/day) which are considered the target mineral accretion for preterm infants, nevertheless the use of multinutrient fortification of human milk for premature infants is currently recommended. A Cochrane systematic review and metaanalysis of human milk fortifiers, which however included studies on children who were not extremely preterm (the class at major risk) stated that the effects on bone mineralization were not conclusive.³⁵

Finally, it must be noted that high calcium supplementation of milk is not well tolerated; it is associated with high faecal calcium, prolonged gastrointestinal transit time and impaired fat absorption. All these effects are potential risk factors for developing necrotizing enterocolitis.

Clinical features and diagnosis: MBD remains silent until a severe demineralization occurs. The most evident clinical findings of osteopenia are deformity of the skull (diastasis of the suture, enlargement of the sagittal fontanelle and frontal bosses, craniotabe), thickening of the chondrocostal junctions and of the wrists, rib and long bones fractures. Softening and/or fractures of the ribs can cause pulmonary changes and respiratory distress, typically between 5 and 11 weeks of age.³⁶

Diagnosis of osteopenia is mainly done by serum analysis. Biochemically osteopenia is characterised by low serum levels of phosphorus and by an increase in serum levels of alkaline phosphatase that can reach values 5 times higher than the upper reference range used for adults.³⁷ It is useful dosing the isoenzymes of alkaline phosphatase since this enzyme is synthesised also by the liver and by the gut.

Backstrom and colleagues suggested that serum alkaline phosphatase levels higher than 900 U/l associated with a serum phosphate level lower than 1.8 mmol/l have a diagnostic sensitivity of 100% and specificity of 70%.³⁸ However the opinions in literature about the reliability of alkaline phosphatase to predict the status of bone mineralization are still conflicting.^{39,40}

Serum level of calcium is usually within the normal range due to effects of PTH on the bone. Low concentrations of calcium and phosphorus in the urine suggest an inadequate intake. This is mainly due by an increase of the tubular reabsorption of phosphate because of the low dietary intake and by an increase of PTH level that stimulates the reabsorption of calcium. Markers of nutritional status should be assessed baseline, and then weekly during the initial phase; once the newborn is stable, assessment must be done at the starting of total enteral nutrition and successively every 2–3 weeks. If MBD is diagnosed and nutritional supplementation is started, a periodic assessment of laboratory data is necessary to evaluate the response to treatment also when babies are discharged from hospital. The key clinical goal is to maintain normocalcemia and normophosphatemia and to avoid an excessive calciuria.

Once levels of ALP, calcium and phosphorus normalize, serum analysis can be performed monthly up to 6 months of age and then every 3 months.

X-rays examination may show fractures, thin bones and other alterations as reduction of thickness of the cortical, enlargement of the epiphysis, irregular border between growth cartilage and bony metaphysis.⁴¹ Dual energy X-ray absorbitometry (DEXA) is able to determine the bone mass content of neonates and can predict the risk of fractures^{39,42} since it is sensitive in detecting small changes in BMC and BMD. Its use is now validated in neonates both term and preterm ones. DEXA reflects most accurately the state of bone mineralization in preterm infants⁴³ but the examination involves radiations for the baby and the device is not portable. Quantitative ultrasound is simpler than DEXA and is non-invasive; it can be used bedside without moving the baby. Reference values are now available for infants. Quantitative ultrasound gives information about structure of the bone and about bone density.⁴⁴

Osteopenia has a good prognosis since the disease is self-resolving, provided that calcium, phosphates and vitamin D are appropriately administered to the babies.

The need for high calcium and phosphorus intakes in preterm infants after hospital discharge is still controversial. Few data are available about the optimal length, quantity and methods of providing supplemental minerals for preterm infants who are in stable growth. There are studies that show increased bone mineral mass in infants who receive formulas containing more minerals than the traditional ones up to 9 months.^{45,46} It has been shown, with studies assessing bone mineralization with quantitative ultrasound and DEXA, that preterm infants show a catch-up mineralization for the first year of life. There is no difference in late childhood of bone mineralization between term and ex-preterm infants⁴⁷ even though the biochemical evidence of metabolic bone disease during the neonatal period may have a long-term stunting effect which continues up to 12 years later. A recent study published on Journal of Perinatology⁴⁸ stated that children who were born prematurely with birth weights less than 1.5 kg tend to be significantly smaller for age and have lower lumbar spinal bone mineral content and density compared with children born at term gestation. The long duration of this complication provides further rationale for implementing any practice that can prevent this condition.⁴⁹

In the case of BMD of prematurity nutrition is both therapy and prevention. An adequate intake of minerals and of vitamin D,

with breast milk fortifier or formula with a content of minerals suitable for preterm infant's requirements, are necessary for a correct bone mineralization. A regular physical stimulation, when the preterm infant is clinically stable and is receiving adequate doses of calcium, phosphate and vitamin D, should also be included in the standard preventive approach.

Conclusion

An adequate nutritional intake of calcium, phosphorus and vitamin D and passive physical exercise may prevent abnormal bone-remodeling activity during first weeks of life and may optimize growth potential of preterm infants. It is important to recognize the biochemical signs of osteopenia in an early stage in order to be able to precociously implement the dietary intake and reduce the risk of bones fractures. The determination of alkaline phosphatase and of phosphoraemia seems to be useful in assessing the risk of metabolic bone disease and serum analysis need to be performed periodically in order to assess response to nutritional treatment. Through DEXA and quantitative ultrasound it is also possible to determine the state of bone mineralization and therefore to plan a nutritional intervention.

References

- Neonatal Research Network: Perinatal, mortality and morbidity information for infants born in the National Institute of child Health and Human Development (NICHD) Neonatal Research Network from 1997 to 2000. In From Avery's disease of the Newborn 8th edition. Elsevier Saunders; 2004:3-5.
- Demarini S: Calcium and phosphorus nutrition in preterm infants. *Acta Paediatr Suppl* 2005, 94(449):87-92.
- Mc Intosh N, DeCurtis M, Williams JR: Failure of mineral supplementation to reduce incidence of rickets in very low birth weight infants: conservative management and outcome. *J Pediatr* 1989, 9:326-9.
- Koo WWW, Sherman R, Succop P, Krug-Wispe S, Tsang RC, Steichen JJ, Crawford AH, Oestreich AE: Fractures and rickets in very low birth weight infants: conservative management and outcome. *J Pediatr Orthop* 1989, 9(3):326-30.
- Takada M, Shimada M, Hosono S: Trace elements and mineral requirements for very low birth weight infants in rickets of prematurity. *Early Hum Dev*. 1992, 29(1-3):333-338.
- Abrams AS: In utero physiology role in nutrient delivery and fetal development for calcium, phosphorus and Vitamin D. *Am J Clin Nutr* 2007, 85:604S-7S.
- Portale AA: Blood calcium, phosphorus and magnesium. In *Primer on the metabolic bone diseases and disorders of mineral metabolism* 4th edition. Edited by: Favus MJ. Philadelphia: Lippincott William and Wilkins; 1999:115-8.
- Greer FR, Tsang RG: Calcium, phosphorus and vitamin D requirements for the preterm infants. In *Vitamin and minerals requirements in preterm infants* Edited by: Tsang RC. NY: Marcel Deer; 1985:99-136.
- Sparks JW: Human intrauterine growth and nutrient accretion. *Semin Perinatol* 1984, 8:74-93.
- Kovacs CS, Kronenberg HM: Maternal-fetal calcium and bone metabolism during pregnancy, puerperium and lactation. *Endocr Rev* 1997, 18:832-72.
- Care AD: The placental transfer of calcium. *J Dev Physiol* 1991, 15:253-7.
- Weisman Y, Harell A, Edelstein S, David M, Spirer Z, Golander A: 1 alpha, 25-Dihydroxyvitamin D3 and 24,25-Dihydroxyvitamin D3 in vitro synthesis by human deciduas and placenta. *Nature* 1979, 281:317-9.
- Rigo J, Senterre J: Nutritional needs of premature infants: current issues. *J of Pediatrics* 2006, 149(5 Suppl):S80-88.
- Ryan S, Congdon PJ, James J, Truscott J, Horsman A: Mineral accretion in human fetus. *Arch Dis Child* 1988, 63:799-808.
- Koo WW, Walters JC, Esterlitz J, Levine RJ, Bush AJ, Sibai B: Maternal calcium supplementation and fetal bone mineralization. *Obstet Gynecol* 1999, 94(4):577-582.
- Rigo J, De Curtis M: Disorders of calcium, phosphorus and magnesium metabolism. In *Neonatal-Perinatal medicine: disease of the fetus and infant* 8th edition. Edited by: Martin RJ, Fanaroff AA, Walsh MC. Philadelphia: Elsevier; 2006:1492-1523.
- Toth P, Erdei G, Vasarhelyi B: Potential consequences of the sudden postnatal drop of estrogens level in preterm neonates. *Orv Hetil* 2003, 144:1719-24.
- American Academy of Pediatrics, Committee on Nutrition: Nutritional needs of LBW infants. *Paediatrics* 1985, 75:975-6.
- Hsu SC, Levine MA: Perinatal calcium metabolism: physiology and pathophysiology. *Seminars in Neonatology* 2004, 9:23-26.
- Miller ME: Hypothesis: fetal movement influences fetal and infant bone strength. *Med Hypotheses* 2005, 65:880-6.
- Miller ME: The bone disease of preterm birth: a biomechanical perspective. *Pediatr Res* 2003, 53(1):10-5.
- Rauch F, Schoneau E: Skeletal development in premature infants a review of bone physiology beyond nutritional aspects. *Arch Dis Child Fetal Neonatal Ed*. 2002, 86(2):F82-F85.
- Specker BL, Mulligan L, Ho M: Longitudinal study of calcium intake, physical activity and bone mineral content in infants 6-18 months of age. *J Bone Miner Res*. 1999, 14(4):569-576.
- Weiler HA, Wang Z, Atkinson SA: Dexamethasone treatment impairs calcium regulation and reduces bone mineralization in infant pigs. *Am J Clin Nutr* 1995, 61:805-11.
- Zanardo V, Dani C, Trevisanuto D: Methylxanthines increase renal calcium excretion in preterm infants. *Biol Neonate* 1995, 68:169-74.
- Venkataraman PS, Han BK, Tsang RC, Daugherty CC: Secondary hyperparathyroidism and bone disease in infants receiving long-term furosemide therapy. *Am J Dis Child* 1983, 137:1157-61.
- Riefen RM, Zlotkin S: Microminerals. In *Nutritional Needs of the Preterm Infant* Edited by: Tsang RC, Lucas A, Uauy R. Baltimore, Williams and Wilkins; 1993.
- Rigo J, De Curtis M, Nyamugabo K, Pieltain C, Gerard P, Santerre J: Premature bone. In *Nutrition and bone development. Nestlé nutritionworkshop Series Volume 41*. Edited by: Bonjour JP, Tsang RC. Philadelphia: Vevey/Lippincott-Raven; 1999:83-97.
- Koo WW, Tsang RC: Calcium, magnesium, phosphorus and vitamin D. In *Nutrition needs of preterm infant. Scientific basis and practical guidelines* Edited by: Tsang Rc, Lucas A, Uauy R, Zlotkin S. Baltimore: Williams & Wilkins; 1993:135-155.
- Rigo J, De Curtis M, Pieltain C, Picaud J, Salle BL, Santerre J: Bone mineral metabolism in micropremie. *Clin Perinatol* 2000, 27:147-70.
- Klein CJ: Nutrient requirements for preterm infants formulas. *J Nutr* 2002:1395S-577S.
- European Society of Paediatric Gastroenterology and Nutrition, Committee on Nutrition of the Preterm Infant: Nutrition and feeding of preterm infants. *Acta Paediatr Scand*

Suppl 1987, 336:6-7.

- 33 Atkinson S, Tsang RC: Calcium and phosphorus. In Nutrition of the preterm infant: scientific basis and practice 2nd edition. Edited by: Tsang RC, Uauy R, Koletzko B, Zlotkin SH. Cincinnati: Digital Educational Publishing; 2005:245-275.
- 34 Rigo J, Pieltain C, Salle B, Senterre J: Enteral calcium, phosphate and vitamin D requirements and bone mineralization in preterm infants. *Acta Paediatr* 2007;969-974.
- 35 Kuschel CA, Harding JE: Multicomponent fortified human milk for promoting growth in preterm infants. *Cochrane Database Syst Rev* 2004, 1:CD000343.
- 36 Glasgow JS, Thomas PS: Rachitic respiratory distress in small preterm infants. *Arch Dis Child* 1977, 52:268-273.
- 37 Bishop N: Bone disease in preterm infants. *Arch Dis Child* 1989, 62:1403-9.
- 38 Backstrom MC, Kouri T, Kuusela AL, Sievanen H, Kiovisto AM, Ikonen RS, Mäki M: Bone isoenzyme of serum alkaline phosphatase and serum inorganic phosphate in metabolic bone disease of prematurity. *Acta Paediatr* 2000, 89(7):867-73.
- 39 Ryan SW, Truscott J, Simpson M, James J: Phosphate, alkaline phosphatase and bone mineralization in preterm neonates. *Acta Paediatr* 1993, 82(6-7):518-21.
- 40 Faerk J, Peitersen B, Petersen S, Michaelsen KF: Bone mineralization in premature infants can be predicted from serum alkaline phosphatase or serum phosphate. *Arch Dis Child Fetal Neonatal* 2002, 87(2):F133-6.
- 41 Ardran GM: Bone destruction not demonstrable by radiography. *Br J Radiol* 1951, 24(278):107-9.
- 42 Rigo J, Nyamugabo K, Picaud JC: Reference values of body composition obtained by DEXA in preterm and term neonates. *J Pediatr Gastroenterol Nutr* 1998, 27:184-90.
- 43 Bruton JA, Bayleys HS, Atkinson SA: Validation and application of dual-energy X-ray absorptiometry to measure bone mass and body composition in small infants. *Am J Clin Nutr* 1993, 58:839-45.
- 44 Rubinacci A, Moro GE, Bohem G, De Terlizzi F, Moro GL, Cadossi R: Quantitative ultrasound for the assessment of osteopenia in preterm infants. *Eur J Endocrinol* 2003, 149:307-15.
- 45 Kurl S, Heinonen K, Lansimies E: Pre- and post-discharge feeding of very preterm infants: impact on growth and bone mineralization. *Clin Physiol Funct Imaging* 2003, 23:182-9.
- 46 Lapillonne A, Salle BL, Glorieux FH, Claris O: Bone mineralization and growth are enhanced in preterm infants fed an isocaloric, nutrient-enriched preterm formula through term. *Am J Clin Nutr* 2004, 80:1595-603.
- 47 Fewtrell MS, Prentice A, Jones SC, Bishop NJ, Stirling D, Buffenstein R, Lunt M, Cole TJ, Lucas A: Bone mineralization and turnover in preterm infants at 8-12 years of age: the effect of early diet. *J Bone Miner Res* 1999, 14(5):810-20.
- 48 Chang JM, Armstrong C, Moyer-Mileur L, Hoff C: Growth and bone mineralization in children born prematurely. *J Perinatol* 2008, 28(9):619-23.
- 49 Fewtrell MS, Cole TJ, Bishop NJ, Lucas A: Neonatal factors predicting childhood height in preterm infants: evidence for a persisting effect of early metabolic bone disease? *J Pediatr* 2000, 137(5):668-73.
- 6 Reynolds F, Seed PT: Anesthesia for Cesarean section and neonatal acid-base status: a meta-analysis. *Anesthesia* 2005, 60:636-653.
- 7 Bucklin BA, Hawkins JL, Anderson JR, Ullrich FA: Obstetric anesthesia workforce survey: twenty-year update. *Anesthesiology* 2005, 103:645-653.
- 8 NSW Department of Health: Validation Study: NSW Midwives Data Collection 1998. N S W Public Health Bull 2000 [<http://www.publish.csiro.au/nid/227/issue/5090.htm>].
- 9 Roberts CL, For JB, Lain SJ, Algert CS, Sparks CJ: Use and accuracy of reporting of general anesthesia for childbirth. *Anesth Intensive Care* 2008, 36:418-424.
- 10 Thorngren-Jerneck K, Herbst A: Low 5-minute Apgar score: a population-based register study of 1 million term births. *Obstetrics & Gynecology* 2001, 98:65-70.
- 11 Higgins JPT, Thompson SG, Deeks JJ, Altman DG: Measuring inconsistency in meta-analyses. *Br MedJ* 2003, 327:557-560.
- 12 The Information Centre: NHS Maternity Statistics 2005-06. [<http://www.ic.nhs.uk/statistics-and-data-collections/hospital-care/maternity/nhs-maternity-statistics-england-2006-2007>].
- 13 Bartussek E, Fatehi S, Motsch J, Grau T: Survey on practice of regional anesthesia in Germany, Austria, and Switzerland. Part 3: Methods in obstetric anesthesia. *Anesthesist* 2004, 53:993-1000.
- 14 Parsons SJ, Sonneveld S, Nolan T: Is a paediatrician needed at all Cesarean sections? *J Paediatr Child Health* 1998, 34:241-244.
- 15 Atherton N, Parsons SJ, Mansfield P: Attendance of paediatricians at elective Cesarean sections performed under regional anesthesia: is it warranted? *J Paediatr Child Health* 2006, 42:332-336.
- 16 Bowring J, Fraser N, Vause S, Heazell AEP: Is regional anesthesia better than general anesthesia for cesarean section? *J Obstet Gynaecol* 2006, 26:433-434.
- 17 Gori F, Pasqualucci A, Corradetti F, Milli M, Peduto VA: Maternal and neonatal outcome after cesarean section: the impact of anesthesia. *J Matern Fetal Neonatal Med* 2007, 20:53-57.
- 18 Ong BY, Cohen MM, Palahniuk RJ: Anesthesia for cesarean section- effects on neonates. *Anesth Analg* 1989, 68:270-275.
- 19 Black N: Why we need observational studies to evaluate the effectiveness of health care. *BMJ* 1996, 312:1215-1218.
- 20 Wallace DH, Leveno KJ, Cunningham FG, Giesecke AH, Shearer VE, Sidawi JE: Randomized comparison of general and regional anesthesia for cesarean delivery in pregnancies complicated by severe preeclampsia. *Obstetrics & Gynecology* 1995, 86:193-199.
- 21 Hogan L, Ingemarsson I, Thorngren-Jerneck K, Herbst A: How often is a low 5-min Apgar score in term newborns due to asphyxia? *Eur J Obstet Gynecol Reprod Biol* 2007, 130:169-175.
- 22 Roberts CL, Bell JC, Ford JB, Hadfield RM, Algert CS, Morris JM: The accuracy of reporting of the hypertensive disorders of pregnancy in population health data. *Hypertens Pregnancy* 2008, 27:285-29

Delivering Interventions to Reduce the Global Burden of Stillbirths

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Abstract

Background: Although a number of antenatal and intrapartum interventions have shown some evidence of impact on stillbirth incidence, much confusion surrounds ideal strategies for delivering these interventions within health systems, particularly in low-/middle-income countries where 98% of the world's stillbirths occur. Improving the uptake of quality antenatal and intrapartum care is critical for evidence-based interventions to generate an impact at the population level. This concluding paper of a series of papers reviewing the evidence for stillbirth interventions examines the evidence for community and health systems approaches to improve uptake and quality of antenatal and intrapartum care, and synthesises programme and policy recommendations for how best to deliver evidence-based interventions at community and facility levels, across the continuum of care, to reduce stillbirths.

Methods: We systematically searched PubMed and the Cochrane Library for abstracts pertaining to community-based and health-systems strategies to increase uptake and quality of antenatal and intrapartum care services. We also sought abstracts which reported impact on stillbirths or perinatal mortality. Searches used multiple combinations of broad and specific search terms and prioritised rigorous randomised controlled trials and meta-analyses where available. Wherever eligible randomised controlled trials were identified after a Cochrane review had been published, we conducted new meta-analyses based on the original Cochrane criteria.

Results: In low-resource settings, cost, distance and the time needed to access care are major barriers for effective uptake of antenatal and particularly intrapartum services. A number of innovative strategies to surmount cost, distance, and time barriers to accessing care were identified and evaluated; of these, community financial incentives, loan/insurance schemes, and maternity waiting homes seem promising, but few studies have reported or evaluated the impact of the wide-scale implementation of these strategies on stillbirth rates. Strategies to improve quality of care by upgrading the skills of community

cadres have shown demonstrable impact on perinatal mortality, particularly in conjunction with health systems strengthening and facilitation of referrals. Neonatal resuscitation training for physicians and other health workers shows potential to prevent many neonatal deaths currently misclassified as stillbirths. Perinatal audit systems, which aim to improve quality of care by identifying deficiencies in care, are a quality improvement measure that shows some evidence of benefit for changes in clinical practice that prevent stillbirths, and are strongly recommended wherever practical, whether as hospital case review or as confidential enquiry at district or national level.

Conclusion: Delivering interventions to reduce the global burden of stillbirths requires action at all levels of the health system. Packages of interventions should be tailored to local conditions, including local levels and causes of stillbirth, accessibility of care and health system resources and provider skill. Antenatal care can potentially serve as a platform to deliver interventions to improve maternal nutrition, promote behaviour change to reduce harmful exposures and risk of infections, screen for and treat risk factors, and encourage skilled attendance at birth. Following the example of high-income countries, improving intrapartum monitoring for fetal distress and access to Caesarean section in low-/middle-income countries appears to be key to reducing intrapartum stillbirth. In remote or low-resource settings, families and communities can be galvanised to demand and seek quality care through financial incentives and health promotion efforts of local cadres of health workers, though these interventions often require simultaneous health systems strengthening. Perinatal audit can aid in the development of better standards of care, improving quality in health systems. Effective strategies to prevent stillbirth are known; gaps remain in the data, the evidence and perhaps most significantly, the political will to implement these strategies at scale.

Introduction

In order to prevent stillbirths, high-impact interventions must be effectively delivered through health systems and reach high coverage. Despite calls for action to improve stillbirth outcomes, the strategies for delivering such interventions in health systems and in communities remain unclear. Consensus is needed on priority interventions, but also on strategies to deliver them.

Based on our analysis of the evidence for impact of 60 different peri-conceptual, antenatal, and intrapartum maternal interventions on prevention of stillbirths, we categorized

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interventions into one of four levels according to the strength and quality of the evidence, and, therefore, the level of confidence in recommending interventions for wide-scale delivery in programs. Five interventions of proven benefit in reducing stillbirths were identified: syphilis screening and treatment, use of insecticide-treated bednets in malaria-endemic areas during pregnancy, administration of heparin for certain maternal conditions including auto-immune and clotting disorders, and emergency obstetric care, including planned cesarean section for breech delivery in settings where access to referral-level care is good.

Strategies to deliver interventions with demonstrated or promising impact on stillbirths will need to employ a mix of service delivery modes, including family-community, outreach and clinical/facility-based platforms as used previously in the The Lancet Neonatal series and the World Bank Development report.

Family-community interventions can be taught or administered to mothers and/or other family members, and include the adoption of improved preventive practices and appropriate care-seeking for illness. Family and community care interventions include strategies for community mobilization and the empowerment of individuals and communities to demand quality health care services and find solutions to financial, logistical, and social barriers to care-seeking for maternal and neonatal illness. These services can be provided by various cadres of workers, and should be tailored to the community's social and cultural environment.

Outreach interventions may be provided through static health facilities or periodic community visits, and usually involve provision of a standardised intervention. These activities typically require less skill and training than clinical care services. Community-based, outreach interventions and interventions delivered at primary health clinics or peripheral facilities and district hospitals can be packaged as primary care interventions.

Facility-dependent clinical interventions may be delivered at secondary or tertiary care settings. Secondary care is hospital-based and specialist-dependent, involving surgical or other advanced interventions that primary care providers cannot perform. Few of the interventions we considered require tertiary care, the most complex level of intervention demanding highly specialised, technology-dependent solutions.

The specific mix of interventions recommended for delivery at various levels of care will depend upon the level of and distribution of capabilities and resources within the local health system as well as local prevalence of risk factors for stillbirth. Some interventions, such as Caesarean section and amniotic fluid volume assessment, require resources based at well-equipped facilities, whereas interventions such as multiple micronutrient supplementation can be delivered via relatively straightforward outreach services.

Results

In many settings, coverage of effective interventions that prevent stillbirth is low, in part because demand for these services is poor among the groups with the least resources, who stand to benefit most from accessing interventions. Financial, geographic, and cultural barriers to care-seeking, as well as perceptions of poor quality of services at health facilities, discourage the use of services. Community demand creation refers not only to efforts

to mobilize community awareness of health risks and promotion of best practices, but also to promote fiscal mechanisms to support uptake of these services. Demand creation is most effective alongside supply-side efforts to strengthen health systems and improve quality of service provision in facilities.

One of the major barriers to maternal and newborn health care is limited financial resources. A number of strategies have been developed to address demand-side barriers to accessing care, and thus incentivise care-seeking, especially in health emergencies. Strategies that have been employed in low-resource, rural settings include community emergency loan and insurance schemes. These schemes pool and manage capital to pay user/patient fees, transport and medication costs and follow-up care, as well as opportunity costs incurred during care-seeking such as missed wages, the combined costs of which can be catastrophic for families. Loans generally need to be repaid, whereas insurance schemes charge a fixed prepayment in exchange for the promise that a fraction or all of the cost of services will be reimbursed if utilised. These strategies spare families from the potentially catastrophic financial impact of obstetric complications, which have been documented to be as high as 34% of annual household income in Benin, and which are often higher at comprehensive essential obstetric care facilities that can provide emergency interventions such as c-section and blood transfusion compared to basic obstetric care facilities. The studies we evaluated described the implementation of community loan and insurance schemes for obstetric complications, but none reported the impact on stillbirths or perinatal mortality. Chiwuzie et al described a scheme to mobilize clans in Ekpoma, Nigeria to create emergency loan funds for obstetric complications, which occurred alongside upgrades to emergency obstetric services in local health facilities. Twelve of thirteen clans successfully launched loan funds and collected donations totaling US \$793, of which 80% was contributed by community members. In the first year, 456 loans were requested, 83% were granted, and 93% were repaid in full. Loans were used to pay for emergency transport, medications, blood transfusions and hospital fees [LOE: 2+].

Two other studies reported the implementation of community loan schemes in Sierra Leone and Nigeria. The project in Nigeria set up an emergency transport system that used private drivers charging a set fee for emergency transport and created a loan fund of US \$20,500, from which 18 loans were made in 9 months. In Sierra Leone, women from two chiefdoms that established community loan funds increased their utilization of obstetric services at the local government hospital. Several community-based insurance schemes relying on voluntary, flat-rate annual contributions for membership have reported increases in skilled attendance at delivery, with one study in the Democratic Republic of Congo reporting rates of skilled attendance 7 times higher among members of the insurance scheme compared to non-members. A much larger, nationwide social insurance scheme to provide for maternal and child health care in Bolivia increased ANC coverage and skilled attendance at birth by 50% in public facilities.

None of the studies evaluated loans or insurance for emergency obstetric care and pregnancy outcomes, and many schemes at community level were too small to measure meaningful changes in mortality rates, but the potential of these interventions to improve utilization of facility-based services and thus reduce perinatal mortality seems promising. Available evidence indicates

that with relatively little outside financial input, communities can successfully set up and administer loan funds for emergency obstetric transport and care, with relatively low default rates.

In addition to community loan schemes, a number of other strategies have been developed to minimize financial barriers to care-seeking, protect families from catastrophic costs of obstetric emergencies, and stimulate demand among poor or otherwise marginalized women. These strategies include conditional cash transfers and voucher schemes. Conditional cash transfers provide money to individuals or families, on the condition of their using specific health services such as antenatal care, skilled birth attendance at a facility, or postnatal services. Conditional cash transfers can reduce long-term indebtedness because they can be used to repay emergency loans from family, neighbors, banks, or community schemes. Voucher schemes are another relatively new strategy to generate demand; women given vouchers at the community level can redeem them for pre-specified services at participating health facilities. These are particularly useful in non-cash economies, and limit expenditures to transport and opportunity costs.

A national-level fiscal incentive program introduced in 2005 by the Indian government provides cash assistance to poor rural pregnant women at childbirth and postnatally for their first and second pregnancy, with additional funds for emergency transport and c-section. A similar program is in operation in Nepal, in which the government finances facility-based delivery in poor areas and provides conditional cash transfers to women who receive services at facilities as well as to their care providers. Several ongoing projects are evaluating the ability of voucher systems to increase access to obstetric care, as well as to preventive interventions. In India, the Government of Gujarat introduced voucher schemes to increase the access of poor women to antenatal, obstetric and neonatal health care. As part of a World Bank programme to improve pregnancy outcomes in western Uganda, 170,000 safe delivery vouchers were distributed to pregnant women covering services including c-section at a number of public and private service providers. In Tanzania, a nationwide voucher scheme was introduced to provide free or discounted insecticide-treated bed nets to pregnant women and mothers of young children to prevent malaria.

The critical role of formally trained professional health personnel—primarily physicians and nurses—in primary care and community settings is well recognized. Shortages of formally trained health workers in some countries has been underscored as a major barrier to implementation of key maternal and newborn interventions. Traditional Birth Attendants (TBAs) have a role in supporting women during labor but are generally not trained to deal with complications. TBA training can improve perinatal outcomes. The potential of TBA training to reduce perinatal mortality is promising, especially when TBA care is integrated with quality health services or health services strengthening activities.

In addition to TBAs and nursing cadres including nurse-midwives and nurse-aides, Community Health Workers (CHWs) are active in the health systems of many rural or underserved settings. With training, CHWs can function as community activists, opinion leaders, or health promoters, and can share their knowledge with community members, including pregnant women and their families. Because the availability, abilities, and prior training of CHWs vary significantly from setting to setting, relatively few

have been broadly integrated with public sector programmes and health systems to promote activities that could prevent stillbirth, although there is increasing focus on the use of CHWs to provide postnatal care for mothers and newborns. Despite considerable interest in the field, and increasing evidence for neonatal and maternal mortality reduction there is a paucity of data from studies on the effects of CHWs' activities on stillbirth outcomes.

In many low- and middle-income countries, particularly in rural areas, the most common cadre of health worker is the nurse-aide (also referred to as nursing aide, nursing assistant, auxiliary nurse/nurse-midwife, or nursing associate). Some initiatives have offered training to equip nurse-aides to deliver a broad spectrum of preventive and curative health care services. Because of potential cost savings and availability of nurse-aides, especially in rural settings, there is an interest in task shifting to nurse-aides or similar cadres in geographic areas with insufficient physicians and nurses to manage all deliveries.

Studies have reported very low perinatal mortality among births assisted by nurse-aides. Doctors and nurses at the hospital handled births of primigravidae and high-risk pregnancies, which had substantially higher perinatal mortality. While perinatal mortality rates are not comparable because of differences in risk profiles between the two groups, the study suggested that risk screening was effective and that nurse-aides' skills were sufficient to attend low-risk births in this setting.

In low-risk pregnancies, evidence suggests that antenatal and intrapartum care can be managed effectively by providers other than obstetricians. Midwives have long attended births, predating the field of obstetrics by many years. In modern practice, the term "midwife" refers to different groups of individuals with vastly different training levels, ranging from apprenticeship with no formal training. Midwives with significant formal midwifery training routinely provide antenatal care and health education, and have the requisite technical skills to provide safe birthing services for uncomplicated deliveries, and to recognize and refer patients to obstetricians or other specialists in cases of complications. Their approach is generally holistic, culturally sensitive, and centered on the preferences of the women in their care. Comparing trials of midwife- or general-practitioner managed care versus obstetrician-gynecologist led shared care, have found a non-significant reduction in perinatal mortality among births managed by midwives compared to those where physicians and midwives shared care for the parturient.

Continuous intrapartum support was associated with shorter labor, more spontaneous vaginal births and less need for intrapartum analgesia. Although the risk of stillbirth/neonatal death was non-significantly increased, the likelihood of c-section was lower. A Cochrane review found no difference in stillbirths or neonatal deaths when midwives provided antenatal social support to economically disadvantaged pregnant women at risk of low birth weight compared to controls who did not receive this support.

There is some evidence that midwifery training programs leading to improved midwifery skills can reduce intrapartum complications and perinatal outcomes, including reduction in stillbirth incidence. Improvements in practical obstetric skills of midwives followed training, and midwives appeared to manage low-risk births without increasing, and possibly reducing, rates of perinatal mortality. Technical skills in providing continuous

care during childbirth may be more influential on birth outcomes than provision of antenatal social support.

Neonatal resuscitation

Many intrapartum stillbirths as well as neonatal deaths are associated with acute intrapartum events such as cord accidents, hemorrhage, hypertension, or prolonged or obstructed labor. Some babies that appear to be stillborn at birth may be able to be resuscitated if immediate and appropriate resuscitation techniques are used; though these are technically neonatal deaths, they often are documented as stillbirths, especially in low resource settings lacking in diagnostic tools and technologies. Appropriate resuscitation skills are thus potentially important in reducing rates of early neonatal deaths which are often misclassified as stillbirth. It is thus important that all personnel involved in labor room care of the newborn should be fully trained in neonatal resuscitation.

A more controversial yet urgent issue concerns interventions to resuscitate asphyxiated newborns born at home in the absence of skilled attendance. Raina et al reported that TBAs in Haryana, India, were readily able to recognize birth asphyxia, but lacked modern resuscitative knowledge and skills. TBAs were found to use 6 different resuscitative techniques, but only 20% of the sample used more than 4 of these techniques, which were not assessed for their effectiveness. In rural India, it was reported that asphyxia-associated perinatal mortality was 70% lower among babies delivered by traditional birth attendants trained to perform resuscitation using a mucous extractor and bag-and-mask resuscitation device versus simplified resuscitative training. Overall perinatal mortality was 20% lower in the group of asphyxiated infants delivered by TBAs with advanced training compared with simplified training, but the sample size was small and the finding was not statistically significant.

There are only a few studies examining the impact on stillbirths/perinatal mortality of training health professionals or other individuals to perform neonatal resuscitation. One study reported a statistically significant decrease in perinatal mortality, while in the other study there was a decrease only in asphyxia-related deaths. There is some evidence of reduction in stillbirths and perinatal mortality after training health workers in resuscitation skills, but further evidence is needed from rigorous, ethically designed and controlled studies.

Other aspects

In low-/middle-income countries, the distance and time required to reach health facilities are often obstacles to care-seeking. Financial constraints may also impact a woman's ability to obtain transport to a hospital and these delays contribute to poor birth outcomes among those families with the least resources. Maternity waiting homes—lodgings for pregnant women close to or within hospitals—are a strategy to address these access barriers. The use of mothers' waiting homes is common in many Southern African countries but does not appear to have achieved high coverage elsewhere. Overall, this intervention is promising as a strategy to increase facility-based births, especially among the very poor and women with identified risk factors, and warrants further evaluation in large scale studies with more rigorous study designs.

In high- and moderate-income countries, most women deliver in hospital labor wards. When home births occur in high-resource settings, they are often deliberately planned by women who

have low-risk pregnancies and the financial means and access to have a facility-based birth. Home births are primarily attended by midwives with a philosophical orientation toward birth as a normal physiological process. The potential lack of medical interventions available in the home in case of life-threatening complications has rendered planned home births controversial in many high-resource countries. The constellation of factors leading women to choose planned home birth in low-and middle-income country settings differs from high-income country settings, and is largely a function of barriers to care including cost and distance; concerns about privacy, respect, and quality of care in facilities; as well as cultural preference for relatives or TBAs to assist with the birth. Maternal preferences as well as the safety of home-based birth may vary from setting to setting. Particularly in low-/middle-income countries, home-based births frequently occur in the presence of a family member or a TBA rather than a skilled birth attendant, which may limit or delay recognition of complications. Home births without skilled birth attendance or rapid access to emergency obstetric care in low-/middle-income countries are a well-known risk factor for adverse perinatal outcomes.

The Cochrane review comparing home-like versus conventional institutional settings for birth does not show any increased risk of perinatal mortality among planned home births with skilled care compared to hospital-based births, suggesting that for low-risk pregnancies, home birth with skilled care is a safe alternative to facility-based birth, and potentially leads to fewer unnecessary interventions. The available evidence is exclusively from high-income countries, however, and transferability of the findings to low-/middle-income country settings where home births without skilled attendants are common may not be appropriate, as caregivers have few opportunities to effectively triage high-risk women. Presence of a skilled birth attendant at home births could be a practical option to improve obstetric health care access, safety, and accessibility, particularly in areas without ready access to facilities, and for many women with uncomplicated deliveries, would potentially improve perinatal health outcomes. Studies that test the feasibility and impact on stillbirths/perinatal mortality of home-based births with skilled attendants are needed. Still, without a well-functioning health system including rapid emergency transport and access to operative delivery and blood transfusion, complications arising at home in the absence of a supportive environment would increase the risk of poor perinatal outcomes.

Discussion

Several innovative strategies have been examined to promote the utilization and quality of interventions to improve perinatal outcomes and prevent stillbirth; however, few have been tested at scale. These strategies include community-based schemes to generate demand and finance care where cost is a barrier, efforts to upgrade or evaluate the skills of health care providers, and innovative ways of re-organizing care to make obstetric care—particularly the subset of interventions that constitute emergency obstetric care—more accessible, affordable, and effective. Community demand-side interventions to improve accessibility and uptake of facility-based care appear to be effective in many settings, particularly where quality facility-based care is available but cost of services or transport impedes care-seeking. Although most studies of community-based loan/insurance schemes and financial incentives involve populations which are too small to assess statistically significant changes in birth outcomes, they offer promising models of improving

accessibility of care that may improve care-seeking while sparing families from catastrophic household expenditures. Similarly, maternity waiting homes have not yet shown a demonstrable impact on stillbirths due to limitations in size and design of the studies on this subject. The reported maternal and infant benefits of maternity waiting homes suggest that their availability for primiparas and high-risk pregnancies in areas with poor access to emergency obstetric care might prevent stillbirths. Sustainability of these schemes is challenging; public-private partnerships may offer one possible option for financing care.

Although evidence from rigorous studies is limited, a number of studies suggest that cadres of health workers other than physicians have an important role to play in the prevention of stillbirths. The impact of training TBAs in clean delivery and management of birth asphyxia is small but significant, suggesting that this important human resource should not be overlooked in community-based efforts to improve birth outcomes. In certain settings where doctors are unavailable, task-shifting to other cadres of health workers to perform c-section and neonatal resuscitation may be feasible, low-cost and effective.

Delivery approaches must be tailored to setting-specific needs and resource constraints. For example, in secondary or tertiary-care facilities in middle- or high-income countries, skills training in neonatal resuscitation for physicians in conjunction with perinatal audit may be sufficient to bring about significant improvements in quality of care for asphyxiated infants who would otherwise be misreported as stillbirths. In low-/middle-income-country settings where home births are common, facility-based care is perceived to be of poor quality, and financial barriers to accessing care are high, community-based demand creation strategies such as loan schemes and health promotion using community health workers could complement interventions to improve quality of care. Whether skilled birth attendants can effectively triage and refer high-risk births in rural areas of low-/middle-income countries, while safely attending low-risk births at home or in birthing centers, has not been adequately tested.

We propose some clear priorities for promoting the delivery of interventions in programs. Firstly, improving coverage of skilled birth attendance and emergency obstetric care is the top priority, as skilled attendance is consistently associated with reductions in intrapartum stillbirth and decreased maternal mortality. However, there are some areas of the world with such a dearth of skilled birth attendants that even aggressive and developed training programs cannot achieve a high proportion of births with skilled attendance in the short term. In these situations, there is positive but limited evidence from this review that training different cadres of community workers, including TBAs, to provide basic clean childbirth care and to refer complications has the potential to have a small positive impact on birth outcomes. TBAs have been successfully trained in some studies to work in tandem with other health workers and can build effective linkages with health systems for referrals.

Disappointingly, few interventions to detect problems late in pregnancy and during labor are supported by rigorous evidence. Observational and historical data from high-income countries suggests that the introduction of fetal monitoring in conjunction with the availability of c-section for fetal distress has led to significant declines in stillbirth rates, suggesting that monitoring technologies may be effective. Because cesarean section carries

higher risks of maternal morbidity and mortality, as well as adverse outcomes in subsequent pregnancies if access to care is poor, it is recommended that in low-resource settings, it be conducted only when clinically indicated.

The second priority is to address maternal infections, especially syphilis and malaria in endemic areas. Nearly 40% of the world's population lives in malaria-endemic areas, a known risk factor for stillbirth. Intermittent preventive treatment of malaria and use of insecticide-treated bed nets during pregnancy can protect women from maternal malaria during pregnancy and reduce stillbirth rates among women in their first or second pregnancy; these interventions can be provided using a combination of outreach and community-based strategies.

Thirdly, quality antenatal care offers an entry point to the health system and may increase the likelihood that women obtain timely emergency obstetric care. Although stillbirth is one of the most common adverse outcomes of pregnancy, stillbirth has been largely overlooked by policy makers and researchers. Many stillbirths could be prevented if pregnant women had access to quality peri-conceptional care, antenatal care, skilled attendance at birth, and emergency obstetric care for complications. While large evidence gaps remain, there is a compelling case that scaling up several interventions, particularly emergency obstetric care packages; screening and treatment for maternal infections especially syphilis, and malaria prevention and treatment could substantially reduce the burden of stillbirths in low-/middle-income countries. We also have parallel evidence from a range of delivery strategies addressing barriers to access to care, and task-shifting, including use of alternative cadres of non-physician health workers, which suggests that these interventions can be implemented and scaled up in situations where they are most needed. The largest remaining gap is for more widespread recognition and political commitment to reduce this massive loss of life of at least 3.2 million stillbirths, 1 million of which occur right at the time of birth.

Postnatal Quality of Life in Women After Normal Vaginal Delivery and Cesarean Section

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Abstract

Background: Cesarean sections might increase the incidence of surgical interventions and problems resulting from hospitalization and thus affect quality of life in women after delivery. This study aimed to compare quality of life in women after normal delivery and cesarean section.

Methods: This was a prospective study. A sample of women with normal delivery and cesarean section from 5 health care centers in Isfahan, Iran were entered into the study. Quality of life was measured using the SF-36 at two points in time (time 1: 6 to 8 weeks after delivery; time 2: 12 to 14 weeks after delivery). Data were analyzed to compare quality of life in the two study groups.

Results: In all, 100 women were interviewed (50 with normal delivery and 50 with cesarean section). Postnatal quality of life in both groups was improved from time1 to time 2. However, comparing the mean scores between the normal and cesarean delivery groups the results showed that in general the normal vaginal delivery group had a better quality of life for almost all subscales in both assessment times. The differences were significant for vitality (mean score 62.9 vs. 54.4 $P = 0.03$) and mental health (mean score 75.1 vs. 66.7, $P = 0.03$) at first assessment and for physical functioning (mean score 88.4 vs. 81.5, $P = 0.03$) at second evaluation. However, comparing the findings within each group the analysis showed that the normal vaginal delivery group improved more on physical health related quality of life while the cesarean section group improved more on mental health related quality of life.

Conclusion: Although the study did not show a clear-cut benefit in favor of either method of delivery, the findings suggest that normal vaginal delivery might lead to a better quality of life especially resulting in superior physical health. Indeed, in the absence of medical indications, normal vaginal delivery might be better to be considered as the first priority in term pregnancy.

Background

The extent of postnatal morbidity in vaginal delivery and cesarean sections has increasingly been recognized in recent years. The focus on obvious morbidity such as anemia, infections and hemorrhage has been widened to include other areas such as sexual functioning, backache, painful perineum and constipation. Screening for postnatal depression is also well established. However, the debate on the best practice (vaginal delivery versus cesarean section) to minimize postnatal morbidity still is a matter of controversy both from professionals' perspectives and from women's perceptions of the childbirth experience. Discussion about such issues goes beyond the scope of this paper but concerns about the increase in cesarean section rates remain unresolved, yet this increase is not associated with improvement in postpartum mortality or morbidity. A wide variation exists among countries worldwide, ranging from 0.4 to 40% of all deliveries performed. A study from Brazil, with a high rate of cesarean sections, found that doctors frequently persuaded their patients to accept a scheduled cesarean section for conditions that either did not exist or did not justify this procedure. The study suggested that the problem identified in Brazil may extend well beyond Brazil and should be of concern to those with responsibility for ethical behavior in providing obstetric cesarean sections in Iran.

In Iran elective cesarean sections have been increasing at alarming rate, and about 60% of women prefer to have cesarean to avoid labor pain or to determine the exact time of childbirth. A study from Tehran in 1999 reported that the rate for cesarean section was between 14.6 to 39.2 in 6 teaching hospitals and 78.5 in 2 private hospitals. Similarly, a study comparing teaching and private maternity hospitals in 2001 showed that the rates for elective cesarean section were 47% and 84%, respectively. Of these, 14% in teaching hospitals and 86% in private hospitals were performed due to maternal request. Also, a recent study on cesarean section rates in teaching hospitals in Tehran found

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Table 1: The characteristics of women in two groups

	Normal delivery (n = 50)	Caesarean section (n = 50)
	No. (%)	No. (%)
Age groups		
20–24	32 (64)	31 (61)
25–29	16 (32)	17 (34)
30–34	1 (2)	2 (4)
35 ≥	1 (2)	0 (0)
Mean (SD)	24.8 (3.68)	24.7 (3.17)
Educational status*		
Illiterate	2 (4)	0 (0)
Primary	11 (22)	13 (26)
Secondary	30 (60)	28 (56)
Higher	7 (14)	9 (18)
Employment		
Housewife	44 (88)	42 (84)
Employed	6 (12)	8 (16)
Number of children		
One	26 (52)	31 (62)
Two	24 (48)	19 (38)

Table 2: Comparing quality of life in women with normal delivery and caesarean section at 6 to 8 weeks postpartum

	Normal delivery (n = 50)	Caesarean section (n = 50)		
	Mean (SD)	Mean (SD)	95% CI for the difference	P
Physical functioning	79.5 (23.0)	77.2 (18.7)	10.6 to -6.0	0.58
Role physical	42.5 (37.2)	33.0 (33.6)	23.5 to -4.5	0.18
Bodily pain	62.8 (20.1)	62.1 (20.4)	8.7 to -7.2	0.85
General health	73.1 (19.0)	77.8 (15.0)	2.1 to -11.4	0.17
Vitality	62.9 (17.6)	54.4 (22.0)	0.56 to 16.4	0.03
Mental Health	75.1 (16.8)	66.7 (21.7)	0.67 to 16.1	0.03
Role emotional	50.6 (45.3)	38.0 (37.5)	29.1 to -3.8	0.13
Social functioning	68.2 (19.6)	63.2 (23.2)	13.5 to -3.5	0.24

Table 3: Comparing quality of life in women with normal delivery and caesarean section at 12 to 14 weeks postpartum

	Normal delivery (n = 50)	Caesarean section (n = 50)		
	Mean (SD)	Mean (SD)	95% CI for the difference	P
Physical functioning	88.4 (14.0)	81.5 (18.5)	0.36 to 13.4	0.03
Role physical	59.5 (39.4)	50.0 (38.4)	24.9 to -5.9	0.22
Bodily pain	71.9 (17.2)	70.7 (19.0)	8.3 to -6.0	0.75
General health	75.7 (18.4)	73.8 (18.2)	9.2 to -5.3	0.60
Vitality	61.1 (20.1)	64.3 (22.1)	5.1 to -11.5	0.45
Mental Health	74.7 (17.7)	72.3 (20.1)	9.9 to -5.1	0.52
Role emotional	62.0 (41.5)	60.6 (40.7)	17.6 to -15.0	0.87
Social functioning	70.5 (19.3)	71.5 (22.0)	7.2 to -9.2	0.81

that the elective cesarean section rate has doubled during a five-year period (6.2 in 1999 to 11.8 in 2003). Overall, the cesarean section increased from 35.4% of deliveries in 1999 to 42.3% in 2003.

Studies on either postnatal quality of life in general or studies that compare quality of life in new mothers after different types of delivery are limited. An investigation using psychometric evaluation of health-related quality of life measures in women after different types of delivery showed that women with vaginal delivery had a better health-related quality of life compared to those with elective or emergency cesarean sections. In particular, comparing health-related quality of life between three modes of delivery (vaginal, elective, and emergency cesarean) it was found that patients after vaginal delivery had higher mean physical health-related quality of life scores than after cesarean section, while mean mental health-related quality of life was similar among the three groups. In contrast, some investigators showed that in addition to variables such as the occurrence of pregnancy complications, life stress and less social support, cesarean delivery is a predictor of poorer mental health in postpartum women. However, there is currently no instrument available for measuring the mothers' health-related quality of life in relation to the mode of delivery, although recently the Mother-Generated Index (MGI) was developed to identify the areas of lives that are of most concern to mothers' quality of life, and the Maternal Postpartum Quality of Life (MAPP-QOL) questionnaire is intend to measure quality of life during the early postpartum period. The aim of this study was to examine whether postnatal health-related quality of life differed among women after different types of delivery. It was thought that this might help to provide information for evidence-based practice and assist women for informed decision-making. We used a generic health-related quality of life instrument to measure quality of life after normal delivery and cesarean section in a group of Iranian women.

Methods

This was a prospective study of quality of life of women living in Isfahan (a famous and historical city in the central part of Iran), and admitted for delivery in Isfahan health centers, affiliated to Isfahan University of Medical Sciences. In all a consecutive sample of 130 women

Table 4: The mean score differences within each group (time 2 scores minus time 1 scores)*

	Normal delivery (n = 50)	Cesarean section (n = 50)	
	Mean Difference (SD)	Mean Difference (SD)	P
Physical functioning	8.9 (24.2)	4.3 (24.2)	0.34
Role physical	17.0 (40.8)	17.0 (40.8)	1.0
Bodily pain	9.0 (22.9)	8.6 (21.5)	0.92
General health	2.5 (17.4)	-4.0 (16.0)	0.05
Vitality	-1.8 (22.1)	9.9 (16.3)	0.003
Mental Health	-0.4 (15.1)	5.6 (16.5)	0.06
Role emotional	11.3 (46.9)	22.6 (50.5)	0.24
Social functioning	2.3 (22.9)	8.3 (25.0)	0.21

* Positive values indicate improvements and negative values indicate deteriorations. Higher positive values indicate more improvements and higher negative values indicate more deterioration.

were approached during their antenatal care and agreed to take part in the study after childbirth. Applying inclusion and exclusion criteria, 100 women (50 with normal delivery and 50 with cesarean section) entered into the study and no one was excluded after entering. The recruitment was not based on the power calculation, and it was done post-hoc. Inclusion criteria were: age 20 to 40 by the time of delivery, having one or two children, experience of just one type of delivery method, having a maximum of one abortion in the medical history and receiving prenatal care. Exclusion criteria were: having history of dystocia or instrumental delivery, still birth, having a diseased or handicapped child, giving birth to a child with a weight of less than 2,500 grams, history of general medical conditions, disabilities, depression, drug intake, major psychological problems, having stress-inducing experiences such as loss of a family member, divorce, or family problems. Also, those with medical conditions such as low back pain, chronic constipation, urination problems, and breast problems before pregnancy were excluded from the study. A trained female nurse collected quality of life data at six to eight weeks after delivery, and 12 to 14 weeks postpartum. Normal delivery was defined as non-instrumental vaginal delivery and the type of cesarean section included both emergency and elective cesareans.

Since at the time of this study the Iranian versions of postnatal quality of life measures such as the MGI or the Quality of life was measured using the Iranian version of Short Form Health Survey (SF-36). It is a well-known generic health related quality of life instrument and translated into a variety of languages. It measures eight health related concepts: physical functioning, role limitation due to physical problems, bodily pain, general health perceptions, vitality, social functioning, role limitation due to emotional problems, and perceived mental health. The scores on each subscale range from 0 to 100, with higher scores indicating a better condition. The validity of the Iranian version of the SF-36 is well documented. In addition, demographic data were collected using a short questionnaire during the antenatal period and included age, educational level, employment status, and number of children as a proxy of childbirth experiences.

Results

In all 100 women were interviewed. The characteristics of the women in the two groups were very similar. The women's scores on the SF-36 at 6 to 8 weeks after delivery are shown in Table 2. The analysis indicated that in all subscales the normal delivery group showed a better condition, except for the general health

subscale. These differences were statistically significant for vitality and the mental health.

Comparing scores at 12 to 14 weeks postpartum, the results showed that the cesarean group had slightly higher scores in vitality and social functioning whereas for other subscales the normal delivery group scored higher. The difference was statistically significant for physical functioning (Table 3).

To compare the findings within each group, the analysis showed that the normal vaginal delivery group showed more improvements on physical health-related quality of life, while the cesarean

section group showed more improvements on mental health related quality of life. These were just barely significant for the general health subscale in favor of the normal delivery group and highly significant for the vitality subscale in favor of the cesarean section group.

Discussion

There are many studies that assess different problems resulting from normal vaginal delivery and cesarean section, but a few studies have focused on women's health-related quality of life per se. Thus, the findings of this study, although limited, could contribute to the existing literature and a better understanding of maternal health care outcomes.

We showed that there were differences between health-related quality of life among women after normal vaginal delivery and cesarean section. At first assessment (6–8 weeks postpartum) women after vaginal delivery scored significantly higher on the mental health and the vitality subscales compared to new mothers after cesarean section. Although these differences disappeared in the second assessment (12–14 weeks postpartum), the findings indicate that in the short-term vaginal delivery might prevent postnatal depression. There is a wide range of prevalence of postnatal depression among women from different countries. A recent review of 143 studies from 40 countries demonstrated that reported prevalence of postnatal depression ranged from 0% to 60%. Postnatal depression is associated with problems in the mother-infant relationship, which in turn have an adverse effect on the course of child cognitive and emotional development. However, recent evidence does not support significant differences in postpartum depression between women who had normal vaginal delivery or cesarean section. In addition, as suggested, postpartum quality of life may be influenced by factors other than type of delivery, such as mother-related factors (for example amount of blood loss, duration of gestation, first delivery or not, presence of co-morbid conditions) and child-related factors (for example the condition of the baby, such as his or her health condition, gender, and weight).

It is argued that postpartum mothers experience certain physical health problems that may affect their quality of life, future health, and health of their children. Yet, the physical health of postpartum mothers is relatively neglected in both research and practice. In our study at second assessment (12–14 weeks

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Human Resources for Maternal Health: Multi-Purpose or Specialists?

Vincent Fauveau, Della R Sherratt, Luc de Bernis

Abstract

A crucial question in the aim to attain Millennium Development Goal 5 (MDG5) is whether it can be achieved faster with the scaling up of multi-purpose health workers operating in the community or with the scaling up of professional skilled birth attendants working in health facilities. Most advisers concerned with maternal mortality reduction concur to promote births in facilities with professional attendants as the ultimate strategy. The evidence, however, is scarce on what it takes to progress in this path, and on the interim solutions for situations where the majority of women still deliver at home. These questions are particularly relevant as we have reached the twentieth anniversary of the safe motherhood initiative without much progress made. In this paper we review the current situation of human resources for maternal health as well as the problems that they face. We propose seven key areas of work that must be addressed when planning for scaling up human resources for maternal health in light of MDG5, and finally we indicate some advances recently made in selected countries and the lessons learned from these experiences. Whilst the focus of this paper is on maternal health, it is acknowledged that the interventions to reduce maternal mortality will also contribute to significantly reducing newborn mortality.

Addressing each of the seven key areas of work—recommended by the first International Forum on Midwifery in the Community, Tunis, December 2006—is essential for the success of any MDG5 program.

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We hypothesize that a great deal of the stagnation of maternal health programs has been the result of confusion and careless choices in scaling up between a limited number of truly skilled birth attendants and large quantities of multipurpose workers with short training, fewer skills, limited authority and no career pathways. We conclude from the lessons learnt that no significant progress in maternal mortality reduction can be achieved without a strong political decision to empower midwives and others with midwifery skills, and a substantial strengthening of health systems with a focus on quality of care rather than on numbers, to give them the means to respond to the challenge.

Background: As the international public health community marks the twentieth anniversary of the Safe Motherhood Initiative, more than 530,000 women still die each year from complications of pregnancy and childbirth, over 90% of them in South Asia and sub-Saharan Africa. Additionally, 10 to 20 million women annually suffer severe health problems as a result of pregnancy and childbirth, such as obstetric fistula or chronic infection. Seventy percent of maternal deaths are due to five major complications, the majority of which occur during labour, delivery and the post partum period. Approximately 15% of women will experience a complication during pregnancy, childbirth or the immediate postpartum period—most of which cannot be predicted, but almost all of which can be managed. Most maternal death and disability could be averted if: all pregnancies were wanted, all births were attended by skilled health professionals and all complications were managed in quality referral facilities offering emergency obstetric care. While the focus of this paper is on the second of these conditions, it must not be forgotten that a large part of maternal deaths could be avoided if all women had access to family planning and reproductive health services. It must also be acknowledged that the interventions to reduce maternal death also significantly contribute to reducing newborn mortality.

Saving mothers' lives is widely recognized as an imperative for social and economic development, as well as a human rights imperative, although until recently there has been limited evidence mapping such links. It is the basic right of every woman and baby to have the best available care to enable them to survive pregnancy and childbirth in good health. Yet, while

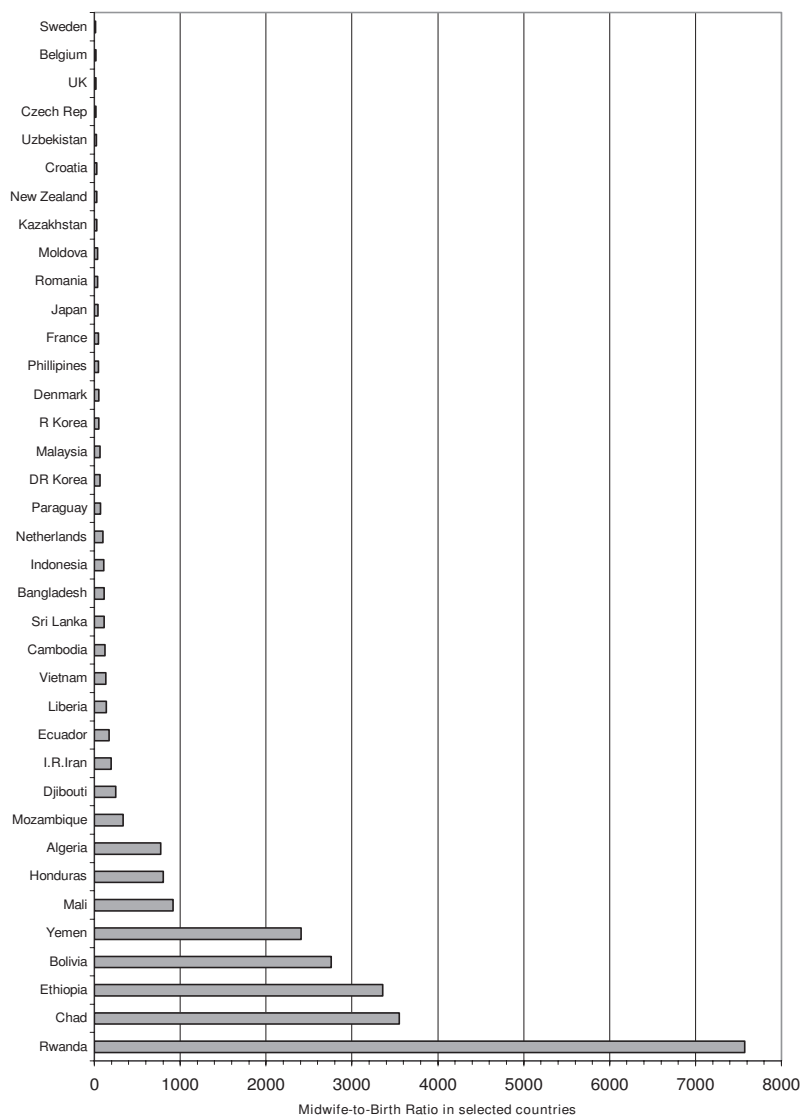


Figure 1. Expected births per midwife ratio in selected countries.

the techniques and strategies to address maternal health are well known and widely accepted, and the need for access to specialist emergency obstetric care services has a high level of evidence, the factor most neglected in the last decade was human resources required to implement these interventions. Although there is a general consensus that maternal mortality and morbidity cannot be reduced without midwives and others with midwifery skills, the numbers of these skilled providers have not significantly increased over the last two decades. Moreover, the actual numbers of skilled midwifery providers has started to decrease in some countries, as the result of migration, losses from HIV/AIDS and dissatisfaction with remuneration and working conditions. At the same time issues of quality of care remain crucial, particularly where health systems do not play their supportive role, as in many countries that have embarked in scaling up the number of community-based providers without giving sufficient attention to their skills. The World Bank estimates that maternal deaths would decrease by 73% if coverage of key interventions rose to 99%. Access to essential maternal health care services, however, is riddled with inequities. The lower a woman's economic status, the less likely she is to have skilled assistance at delivery and lifesaving emergency obstetric care. Geographical location, ethnicity and age are also related to disparities in access.

WHO initiated a decade of special attention to the health workforce with the World Health Report 2006, 'Working together for Health'. UNFPA, working jointly with the International Confederation of Midwives (ICM), plans to contribute to this global initiative on the health workforce by initiating in collaboration with their partners a global campaign to promote and rapidly scale-up the coverage of midwifery care. Midwives and others with midwifery skills are the representation of UNFPA's mandate within the health workforce, not only for their role in providing skilled delivery care, but also for their ability to deliver the essential sexual and reproductive health package in relation to maternal health. In addition, efforts to strengthen midwifery are also in line with UNFPA's mandate to promote gender equality, as midwives are key female members of the health workforce. However, for many reasons, some having to do with the fact that most midwives are women, there has been gross underinvestment, and sometimes no investment at all, in building or maintaining a cadre of professional midwives. In addition, midwives very often have low status within their community and receive little recognition. The vast majority of midwives thus suffer from the same gender-related inequalities as other women. The result has been insufficient investment in midwifery training, deployment and supervision, coupled with inadequate regulation and policies to support and protect

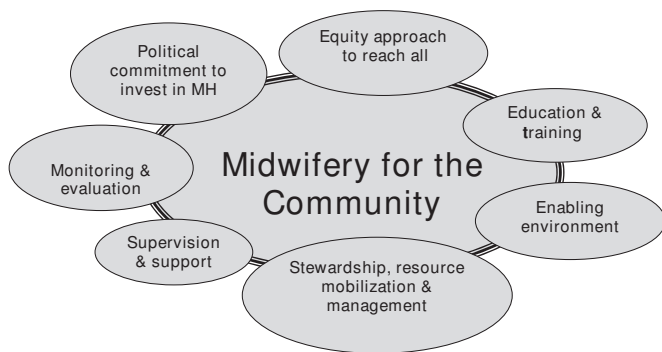


Figure 2. Framework for addressing issues of scaling-up midwifery for the community level.

midwives in their practice. Yet, without expert midwives to teach midwifery skills and supervise others, ensuring quality of care will not be possible and efforts to reduce maternal and newborn deaths will fail. A number of countries or states—particularly Sri Lanka, Malaysia, Tunisia, Thailand, Kerala, Tamil Nadu—have, however, successfully undertaken specific measures to make midwifery a respectful and attractive profession. Policy, advocacy and revision of regulatory systems were instrumental in order to professionalize midwifery and remove discriminatory legislation.

The Millennium Development Goal 5 highlights the crucial role of midwives and others with midwifery skills on the path to improved maternal health by including as its second indicator the proportion of births attended by skilled health providers. Although the percentages are not specified, it is assumed that the target for 2015, “universal access to a skilled birth attendant”, translates into between 90% and 100% coverage. Currently it is estimated that no more than 40% of births in low-income countries are assisted by properly skilled attendants—highlighting the large effort needed to reach the target of 90% coverage by 2015. According to WHO, an additional 334 000 midwives are required to fill this gap, not counting the number of doctors and other nurse providers. It can be argued that at least twice as many are required to achieve universal access to a full package of sexual and reproductive health care.

In the past few years, the international public health community has made two significant advances. One by incorporating in to the new global health partnerships the health care professional organizations such as the International Confederation of Midwives (ICM) and the International Federation of Gynecology and Obstetrics (FIGO). The other by highlighting the key role of human resources for health (HRH) in the failure of health systems and the need to address HRH in priority in health system strengthening initiatives (GAVI-HSS, GFATM, Global Business Plan, Global Campaign for Health MDGs, International Health Partnership, etc).

This paper aims at contributing to generating a massive effort to increase not only the coverage of all births by skilled attendants, but also the quality of this attendance by promoting the role of midwives and others with midwifery skills in improving maternal, reproductive and newborn health. The question, however, is whether countries should give priority to producing a relatively high number of multipurpose community-based providers to cover all villages or to produce a lower number of specialized, facility-based, professional and skilled maternal health providers.

Situation and challenges: Ensuring equitable access to a continuum of skilled care before, during and after childbirth, is recognized as a universal human right, and is critical for saving the lives of mothers and for their newborns. However, skilled care requires skilled providers—a scarce commodity in most low-income countries. Much of the efforts in the lead up to the 20 year marking of the Safe Motherhood Initiative (SMI), have focused on the barriers to skilled care are at birth, among which the lack of qualified human resources appears the most challenging.

The lack of skilled providers linked to a facility offering quality emergency obstetric and neonatal care (EmONC), is neither a new phenomena, nor is it only a problem of low-income countries. The need to invest in training of the midwifery workforce and ensuring that midwifery providers have appropriate life-saving skills have been topics of debate for many decades. Yet, as estimates for the proportion of births attended by a skilled provider shows, the majority of women in developing countries still give birth without such assistance and the data reveals huge disparities and inequity, with women in low income families having little options or opportunities to access such healthcare. However, the lack of access to health services occurs for a variety of reasons and not just because of lack of healthcare providers.

A skilled birth attendant (SBA) has been defined by the WHO in collaboration with the ICM and FIGO and has been endorsed by UNFPA, the World Bank and the International Council of Nurses in 2004. The definition builds on and seeks to add clarity to the initial definition in the 1999 Joint statement on Maternal Mortality and the one developed by the Interagency Group for Safe Motherhood in 2000, and sets better the minimal requirement for a skilled birth attendant. The 2004 definition states that a skilled birth attendant is: “an accredited health professional—such as a midwife, doctor or nurse—who has been educated and trained to proficiency in the skills needed to manage normal (uncomplicated) pregnancies, childbirth and the immediate postnatal period, and in the identification, management and referral of complications in women and newborns.”

As the above definition clearly shows SBAs are not a single cadre or professional group. SBAs are providers with specific midwifery competencies; they perform these competencies as professional midwives or, if trained in these competencies as general practitioners with midwifery competencies, or as nurses. Furthermore, not only must they have received proper training to carry out their tasks, but they must have developed the competencies to a level of proficiency. The total list of competencies for each type of skilled attendant will vary between the different professional groups, according to the scope of practice for each group. The list may even vary for cadres with same professional title in different countries, depending on the legislation and regulations and training curricula for each cadre. The common denominator, however, is the basic skills required to assist a woman during pregnancy, childbirth and after birth, including essential care to newborns—known internationally as midwifery skills and defined as core competencies. In addition, experts agree that the education of nurses and midwives must include development of problem-solving competencies, because the arrival of a woman at a referral facility is often the end of a long and complex decision-making process, influenced by the interpersonal relationships between the woman, her family members and the health providers.

Moreover it is known that to be effective, healthcare providers must work in a supportive enabling environment—which must include basic equipment and drugs as well as good communication and transportation systems—to ensure timely referrals when needed and have effective and supportive supervision. Yet, too often, the enabling and supportive environment is also lacking.

The core competencies required of any skilled birth attendant outlined in the 2004 WHO ICM FIGO statement were intended to apply to any health worker providing midwifery care at any level of the healthcare system, including the primary care level. Included within the core competencies are the basic EmOC skills to which essential neonatal care has been added, as well as essential maternal and neonatal healthcare for preventive and promotional care and care of women and newborn with no complications. The list of additional competencies was added in the 2004 statement to apply to those skilled birth attendants working in peripheral and or isolated settings, where referral to a district hospital is difficult. Whereas the ‘advanced skills’ are the surgical competencies required for comprehensive care (EmONC).

Contention however remains as to which maternal health providers should have these core competencies. Is it all maternal health care providers? And, who should have just the core and who should have advanced or additional competencies? Moreover, the discussion on which maternal health workers can be trained or up-skilled, to ensure they have the required competencies to a level of proficiency, is causing concern in many countries.

Even if there was a consensus on the above questions, there remains the issue of the maintenance of these competencies. And the issue of whether the legal and regulatory framework properly protects the rights of the healthcare provider to perform the life-saving interventions for maternal and newborn survival. Often they are seen as the prerogative only of physicians. Therefore, becoming competent, or scaling up the competencies of the maternity workforce, is only part of the overall issue to be addressed. To develop and implement a plan for the adequate production of their maternity workforce, the countries need to know how many of which type are needed, where they should be deployed, and how to retain them at their post, especially those working in rural areas.

Why have the critical midwifery competencies been so neglected?

One of the major reasons explaining why so many countries still have inadequate numbers of skilled midwifery providers is because those grappling with human resources have not paid attention to the need for ‘proficiency’ in the various competencies required to assist women and newborns. For too long it has been accepted that as long as the health worker received some (often too little) training in midwifery, this was sufficient. Too often there has been a lack of understanding and appreciation of the difference between competence—the ability to carry out a task to the required standard—and competencies, the discreet knowledge, skills, attitudes and experience required for individuals to perform their jobs correctly and proficiently.

Additional reasons for the current shortfall in midwifery skills in many low-income countries include the lack of understanding and appreciation of what the professional midwife can offer,

as well as an historical prioritisation on medical training of physicians over other healthcare providers. As argued in the World Health Report 2005, many countries facing current shortages of midwifery providers have been at the mercy of misguided, albeit well intentioned, advice from external donors recommending policy changes to create a multipurpose worker or seeing midwifery care as a voluntary occupation that can be performed by a traditional healer or traditional birth attendant.

Investing in a specialist midwifery provider is challenging in many countries because midwifery, as a predominantly female profession, does what is predominantly considered women’s work. The double burden of being a woman, herself subject to gender inequalities, as well as being a female worker, puts tremendous pressure on midwives who do a very emotional and stressful job that can lead to high levels of occupational ‘burn-out.’ Having responsibilities for their own home and child care, etc, and working with women in what some perceive as a female area—pregnancy and birth—is made even more difficult in those situations where women’s status is low and where assisting childbirth is seen as low status or culturally unclean. On a positive note however, where midwives are respected they can, by working in the community, in close proximity to families, have the potential for offering career aspirations to girls and young woman and in so doing, may contribute to efforts to address gender inequity.

The failure of governments to provide competent, skilled midwifery health workers has been seen by some as a blatant case of gender inequality or lack of gender sensitive health policy. Failure of governments to provide basic healthcare for the most vulnerable of its citizens at the most vulnerable time of life can be viewed in the light of the Committee on Economic, Social and Cultural Rights’ General Comment 14 as a failure of governance.

Why invest in midwives and others with midwifery skills? Investing in a specialist cadre of midwifery provider-professional midwives or others with midwifery skills—has been shown to make a difference in reducing maternal mortality in many countries. Indeed, historical evidence tells us that the countries that have succeeded in reducing their maternal mortality and morbidity have done so by ensuring skilled care at all births. In particular, they have achieved this by ensuring that all home births were undertaken by ‘trained and supervised midwives or, as in the case in Sweden and the UK, by making sure midwives not only referred all complicated cases—having first rendered first aid and offered first line management—but also reported all births and maternal deaths to the local public health physician or district health authority. Reviewing case studies from countries that have in recent years succeeded in reducing their maternal mortality ratio, Koblinsky suggested that, “assistance at birth by a skilled birth attendant in the home or any health facility, supported by a functioning referral system, can reduce the MMR down to around 50 or below.” The recent Lancet series on maternal survival also point to the value of midwives working as a team in health centres. Indeed, home delivery is not a good use of the time of scarce professionals, who should be concentrated in health centres.

For skilled attendants to effectively contribute to achieving the MDGs however, they must be accessible, offer affordable women-centred care, and must be seen as a member of the health system and to be credible. For this they must be technically competent. Being seen by the community as a

specialist in midwifery care contributes to credibility. The outstanding evolutionary feature of maternity-related health services in Sri Lanka and Malaysia is the pivotal role of trained and government employed midwives. They have been relatively inexpensive to both countries, yet they have been the cornerstones for the expansion of an extensive health system to rural communities. They have provided accessible maternity services in hospitals and communities, gained sustained respect from the communities they serve, and are described with affection and admiration by managers and policymakers in each country.' As found in a study on access to emergency obstetric care and human resources in Tanzania, there is a positive correlation between having a professional qualification and clients' willingness to use health services.

Professional midwives or others who meet the international definition of a midwife (regardless of their title) and practice according to ICM's evidence-based essential midwifery competencies do have all the essential basic midwifery competencies required for the provision of high quality skilled midwifery care, and more. Where they work in partnership with women and are acceptable by women and their communities, professional midwives (or those functioning with legal protection as a professional midwife) offer countries potential for meeting the broader reproductive health needs of communities, as well as contributing to universal primary health care for all. As history has shown, midwives can be most useful in helping to ensure that health services reach those in greatest need, the poor and hard to reach communities.

Quality or quantity? While there is a need to build the capacity of the maternity workforce in terms of quantity in order to reach out to all communities, it is even more important to consider quality. The debate on whether to prioritise quality or just have more numbers is at the heart of current discussions on skilled attendants, and strategic decisions are likely to have a strong impact on maternal mortality. Whilst everyone agrees it is not effective to look at human resources for health for a specific health issue in isolation, we argue that MNH services do have several unique characteristics that require specific attention when making decisions about the size, shape and production of the midwifery workforce. Specifically the need exists for high levels of technical competence in a number of very specific areas, both curative and promotive in nature. Maternal mortality reduction shows the greatest sensitivity to the presence of skilled maternal health providers. Appropriate curricula that ensure sufficient time for hands-on practical training to become competent to the level of proficiency in all the requisite areas, as complications can arise quickly and without warning. What is required is repeated reflexive and intelligent practice. Clinical instruction and mentorship are also paramount. Trainers must themselves be proficient in these competencies, although unfortunately in many low-income countries they are not.

Also required is gender sensitivity: Although this can apply to all health service access, lack of a female provider is perceived as one the major barriers to why women do not use maternal health care. Excellent inter-personal communication and cultural competencies are required, because of the high cultural sensitivity of pregnancy and birth. Nowhere else are interpersonal skills, linguistic skills and cultural appreciation more crucial to help the families with decision making in all aspects of reproductive health. Motivation for the job has been shown to be vital for providing quality care. Midwifery providers

must be available at all hours of the day and night—whenever birth takes place. Among the criteria that should be considered are demonstrating professionalism and positive attitude to patient, avoiding impersonal routine response, and resisting to corruption.

For all the above reasons it is essential that curricula and training programs prioritize midwifery skills—but sadly many current training programmes do not. Far too often, midwifery skills are seen as accessory, or add-on skills, and are afforded little time, typically at end of a programme, where there is little time for repeated hands-on practice.

In terms of numbers, the largest barrier to overcome is the need for sufficient teachers and trainers who are competent in education and in midwifery theory and in clinical practice. Deciding on numbers depends on a complex set of criteria: number of training institutions and teachers, caseload, overall education standards, reservoir of suitable entrants, but also recruitment policies, fiscal space and budget. Historically, a population base ratio has been used to estimate the number of midwives needed in a given country. The most widely used ratio of one midwife to 5000 population developed by WHO in 1993, assumes that one community midwife would be able to care for 200 pregnant women a year, including assisting at their births and giving postnatal follow up care. The ratio however does not take account of the skill-mix needed to care for obstetric emergencies, nor the different geographical circumstances, differences in fertility rate nor other personal or professional work demands on the midwife. UNFPA has recently called for using a new "births by midwife" indicator i.e. the number of births expected to be attended in all security by a qualified midwife (see Figure 1).

To achieve the right balance between numbers and quality, adequate funds and a cost-effectiveness analysis are necessary, in turn dependant upon having policies and strategies in place. To avoid repetition of past mistakes and the selection of misguided strategies, technical competence is critical to guide the decision.

Towards solutions: key areas—Time to scale up is limited. However, as countries like Indonesia have experienced, rapid scale up in numbers without ensuring full competencies of midwifery providers can be costly in terms of in-service training needs. It is also possible to improve access to skilled care by better utilization of existing staff, and training mid-level providers in tasks that are usually undertaken by physicians. Each country will need to take a considered approach, allowing fast scale-up while at the same time maintaining, or improving, quality. While there is a need to address the deficiencies in specific obstetric skills, especially surgical skills and specialist neonatal skills, it is the midwife who will ensure access to all. Graham et al estimate that on average there should be a minimum of five midwives for 1 obstetrician (or physician with obstetric skills). Midwives are also required to develop community capacity in order for communities to take their place in monitoring and evaluating maternity services and contributing to overall quality improvements.

Midwives and other midwifery providers perform best within a multi-professional team of health workers—including peers—but also support workers who can conduct some of the non-specialist midwifery tasks under their supervision. Physicians

with obstetric skills or mid-level providers with obstetric competencies (such as in selective surgical procedures) are best targeted at referral centers where surgery is possible. This partnership should be based on mutual respect and appreciation for each other's contribution, rather than on an outdated historical hierarchical model, which sees the midwife or other mid-level worker as subservient to the physician. In addition to training, capacity building and capacity-development require attention to structure, systems, roles, support, supervision, as well as logistics. Above all, any new initiative must have inbuilt from the beginning a robust monitoring and evaluation systems, not only to demonstrate when progress is being made, but also to monitor quality improvement and future decision making that is at the heart of any capacity-development initiative.

During the 1st International Forum on midwifery in the community held by UNFPA, ICM and WHO in 2006, a framework was proposed for rapid scale-up of midwifery providers, based on a capacity development model. The framework identifies seven interconnected areas of work

1. Policy, legal and regulatory frameworks; 2. Ensuring equity to reach all; 3. Recruitment and education (pre- and in-service), accreditation; 4. Empowerment, supervision and support; 5. Enabling environment, systems, community aspects; 6. Tracking progress, monitoring and evaluation, numbers and quality; 7. Stewardship, resource mobilization

All the above areas of work are interrelated, but political and legislative action must be in the forefront. The protection to which mothers and children are entitled under the right to health framework cannot be regarded as charity. It is an obligation of governments, irrespective of adverse conditions such as severe shortage of economic resources. While governments cannot be held responsible for the actual care or omissions of care given by individual practitioners, they are responsible for ensuring that adequate mechanisms are in place for regulation, delegation of authority and training of the providers and that appropriate policies are implemented. Legal and regulatory frameworks are also needed to protect midwifery and medical providers.

Action: create a coalition of interested stakeholders, including professional associations, to promote and influence policy changes. Such partnerships should be built on mutual respect and include community participation, for example civil society groups, from the start.

In all countries poverty is strongly associated with less access and use of healthcare, including skilled midwifery care at birth. Evidence shows that even in relatively low-income groups, women with higher levels of autonomy find it easier to access maternal health services. Furthermore, evidence shows that introduction of formal user fees and demands for payment under the table have a negative influence on utilization of maternal health care services, particularly during childbirth. The required action is to make equity a national cause, in collaboration with and involving from the beginning the wider stakeholder group, such as the other ministries, and civil society, NGOs, faith-based and private healthcare providers, media and parliamentarians.

Recruiting from and providing education within the local area can help ensure that service provision is culturally appropriate. Both pre-service and in-service education and training programmes should be based on a competency model, with

those who teach midwifery in clinical or classroom settings being themselves competent in midwifery and having undertaken adequate preparation for their role. More work is needed to ensure that pre-service midwifery programmes have a better client-centered basis. Improving quality of care depends on the new graduates' ability to practice their newly acquired skills in the real situation. There is a need to develop or strengthen accreditation systems, including ensuring periodic updating and professional continuing education programmes linked to re-registration or re-licensing. The necessary action is to promote national evidence-based standards for education programmes and institutions, ensuring that they are as important as evidence-based clinical standards and protocols. Incentive schemes may be needed in some situations, to encourage and support recruitment from local communities and/or recruitment from linguistically and culturally diverse communities.

The problems associated with getting staff to change their performance based on evidence are widely recognized. Because the majority of women will not encounter a problem during pregnancy, childbirth or after birth, few providers may have hands-on practice of managing complications. Indeed, many midwives working at the community level may never have experienced in their initial training some of the problems and complication that they may meet during their professional career. Providing midwives with supportive supervision which helps build their capacity is essential, more so for those working in isolated practice or small teams in the community. For supervision to build capacity it must go further than assessing records and reviewing case registers. It needs to be supportive, undertaken by clinically competent midwives, allow free and open discussion of clinical practices, and give an opportunity for providers to acknowledge their weaknesses. Supervision should empower midwives, should not focus on just filling in a checklist, and should be performed by provincial or national health offices. Supervision should be organized as a separate function from the management of the midwifery service, although linked to it and indeed in some areas supervisors may have responsibility for both. Supervisors need to be competent in midwifery and receive in-service and updating training in supervising midwifery practice.

Too often an enabling environment is missing—often due to failures in health system management. For example, frequently the essential drugs for EmONC are not included in the national drugs list. It is now well known that health care practitioners cannot carry out all their tasks and function effectively if they have concern for their own safety or that of their family, or if they are anxious about their own health or the health of their family. Caring for woman and newborns in an environment lacking essential drugs and equipment to save lives if a complication occurs is particularly stressful and de-motivating. Support from the local community and community leaders, and the active participation of men, are also vital to creating an enabling environment, despite the barriers to male participation. Actions to take are: total quality care improvements, quality circles, as well as needs assessments, clinical audits, community surveys, confidential enquiries into maternal deaths, investigations of near-miss cases: all can be used as means of improving quality of care. A continuous supply of essential drugs down to the community level must be assured.

Until recently, little attention has been paid to the need for permanent monitoring and periodic evaluation of large

midwifery programmes. Very few current programmes have built-in evaluation, and there is consequent uncertainty about their health outcomes, and thus their effectiveness. Most safe motherhood programmes rely on fairly standard process indicators such as the UN indicators that are most often used for measuring the availability and use of obstetric services, but do not take into account quality, which is the product of technical capacity and culturally appropriate response. In addition, lack of a universal benchmark to define a skilled birth attendant has not only caused confusion and lack of validity around this indicator, but has led to great variations and thus an inability to make comparative judgments on programmes. There are currently few reliable and tested tools to measure the midwifery competencies of healthcare providers, or to compare the performance and utilization of non-specialized midwifery providers against specialist provider. Regular monitoring should be established based on routine data collection with an emphasis on quality. Monitoring and evaluation should involve midwives and midwifery providers at the community level, so that midwives and the community members can use the findings. This is particularly important for evaluating training initiatives, where—for pragmatic reasons—descriptive, non-experimental designs calling for before-and-after studies are the only option for assessing effectiveness.

While it is acknowledged that most countries need to take incremental steps towards implementing comprehensive health policies to respond to the needs of all citizens, very few have a well designed systematic plan to achieve this. Forty African countries are currently engaged in developing and implementing their national road map for maternal and newborn care. Ensuring equitable midwifery care requires intensified actions and substantial investments, calling for increased funds, and better costing and budgeting. In many countries parliamentarians and senior policy makers are not fully aware of the issues around access to midwifery care at the community level and often fail to understand the complexities involved. Furthermore, studies show that decentralization efforts too often focus on financial and structural reforms and do not take sufficient account of the human resource dimension. Governments must provide sufficient expenditure and proportionate investment of public resources in the maternal health sector, and focus expenditure on rectifying existing imbalances in the provision of health facilities, health workers and health services. This includes ensuring that the privatization of the health sector does not create a threat to the availability, accessibility, non-discrimination, acceptability and quality of maternal and newborn health services. Policy makers must also recognize that, even where safe motherhood programmes are built on increasing access to institutional birth, women and newborns need access to community-based midwifery care ante and post-natally, as women are more likely to seek skilled care for birth if they have access to such care ante-natally.

The issue of requiring a dedicated skilled provider for maternal and newborn health is gaining momentum in many parts of the world—despite pressures for a generic multipurpose healthcare provider. A survey conducted by WHO in the Africa region showed that among the 31 African countries who responded to the survey (out of 46), only 14 had a HRH policy and plan, an HRH situation analysis and an HRH operational plan. For example, WHO-AFRO is about to publish a set of Midwifery Competencies for Africa, recommended by the Regional Committee in 2005 and developed through a series of

consultations with countries. It is hoped that countries will use these competencies as benchmarking for agreeing who meets the definition of a skilled attendant. There are also positive signs to show that the various country Road Maps for maternal and newborn health are offering important opportunities to integrate human resources issues in the national health plans and national sexual and reproductive health policies. Similarly in other regions there is a renewed interest in developing and supporting the specialist cadre of midwifery provider.

There are more examples of countries investing in increasing the numbers of multi-purpose maternal health providers, but some countries are also taking steps to strengthen and skill up their current midwifery providers, and/or creating a specialist cadre in an attempt to upgrade quality of obstetric care. For example, action has begun to re-establish midwifery in the south of Sudan, an area of huge deprivation following years of civil unrest which has left that part of the country with almost no health system. One of the first priorities undertaken with the assistance of the international donors following the signing of the Peace Accord has been to develop and initiate a program to train midwives for the community. Elsewhere in Africa, new programmes for direct entry into midwifery training have just started, such as in Zambia.

In Bolivia, with UNFPA support, plans have been agreed and work commenced to introduce a pre-service midwifery program, at provincial university level, so that the midwives from this program will be educated to a level equivalent of other healthcare providers such as nurses. The reason behind the decision to start such a programme is that, despite excellent results of the national insurance scheme, many women are still reluctant to be attended to by a professional provider until a problem arises, often too late. This is because in the rural areas, where the majority of families still live, people feel that healthcare providers at the facility do not respect the cultural requirements surrounding pregnancy and childbirth. This new program for professional midwives will have a large component on social and cultural issues, as well as on technical midwifery care. The work is being undertaken with technical support from Chile, which is one of the countries with the longest history of professional midwives in Latin America. Haiti is also in the process of re-opening the national school of nursing and midwifery, after many years of deterioration of their health system due to internal conflict.

In many parts of Asia the same positive signs can also be observed. In 2006, Pakistan took the decision to mount a large initiative to train more than 58,000 community midwives. The first intake of students commenced in the summer of 2007. The competencies for this program and the training of the midwife teachers were done in collaboration with and support from the ICM. The program for introducing this new cadre has not taken a traditional vertical approach, but has started with strengthening the regulatory and accreditation system, through fortifying the Pakistan Nursing Council, establishing a new Midwifery Association (affiliated with the ICM), and working with the State Examinations Boards. The MOH supported by partners has also strengthened the training infrastructure, including upgrading and refurbishing training schools, as well as updating the staff working in the facilities where students will also undertake part of their training and where it is hoped they will refer clients after their graduation when needed. Afghanistan has recently re-opened their schools of midwives, after having started with launching a competency-based pre-service training curriculum.

This successful programme allowed 1300 young midwives to graduate and make a dramatic impact on women's access to maternity care.

With the exceptions cited above, very few countries have embarked on a scheme for introducing a new cadre of professional midwife. Most countries in all regions have mainly focused on scaling up and skilling-up those who are already functioning as midwives, or supporting and retaining the midwifery providers working in isolated places. Mauritania for example is expanding an obstetric risk insurance mechanism aimed at sharing costs related to obstetric complications among all pregnant women on a voluntary basis. The budget includes a number of incentives (30%) and duty allowances (13%) to compensate facilities and staff for increased workload and is aimed at suppression of informal payments by clients. A mechanism of special incentives to ensure better retention of health professionals in remote areas has also been established, while noting that this initiative is not without its challenges, given the increasing competition from an uncontrolled and rapidly developing private sector.

Senegal on the other hand is focusing on strengthening management systems and capacity, especially at the district level. Professional staff are now receiving incentives and midwives, who are seen as the most cost-effective health professionals, are involved in maternal death reviews and focus groups to assist them in improving quality of care.

Rwanda is also undertaking a management approach to ensuring that skilled midwifery providers are available and accessible, free of charge and offering quality care. A recent survey has shown improvements in health center performance and higher productivity of health staff through output-based performance contracts.

Mozambique, Malawi, Senegal, Tanzania and a few other African countries have for some years successfully trained mid-level cadres (health officers and midwives), as well as general practitioners to provide comprehensive emergency obstetric care including surgery. Their initial skills were deficient in terms of maternal and newborn health, and therefore as generalists they were unable to meet the needs of mothers and newborns. These trained health professionals are highly cost-effective as their training (and other related costs) is less costly in regard to the comparable performance of obstetric specialists. Furthermore, there is evidence showing their high level of retention.

In Malawi, as in many African countries, professional midwives mainly conduct institutional births, yet the majority of births still take place at home. Also, like many neighbouring countries, Malawi suffers from a huge deficit of all human resources for health, including physicians, with a ratio of 1.6/100 000 (health workers/population). Addressing HRH challenges is very difficult, but action is being taken to expand training institutions to accommodate more students; increase enrolment of nurse/midwives and other healthcare providers; and to skill up competencies to gain community midwifery clinical experience. Moreover, a community-oriented curriculum has been developed to train District Health Officers, as a specific response to the huge numbers lost through migration. The programme includes a minimum of community health (25%), plus surgical and medical specialties, including midwifery skills. A post-graduate program has now also been added.

Zimbabwe, where maternal mortality increased between 1994 and 1999 from 283/100,000 to 695/100,000, is facing major challenges in relation to midwifery services, including high attrition rate (brain drain), inadequate midwife tutors, midwifery not seen as a lucrative post graduation career, and no recognition for the profession of midwifery. The curriculum has been revised, student midwives now have practical attachments (hands on experience), a new diploma in midwifery has been started, in-service training and on-the-job support (mentorship by a skilled midwife) are now standardized. Efforts to increase the capacities of training of teachers have resulted in development of a Masters with a major in Maternal and Child Health. WHO has also recently announced support for working in collaboration with the Royal College of Midwives (UK) to encourage some of the diaspora community who are in the UK working as midwife teachers to return for short stays to offer their services in Malawi.

In some countries the low rate of skilled attendance is not because there are insufficient providers, but because of insufficient posts in the public sector to employ all available healthcare providers, even if they are known to have the necessary skills. In Kenya, an initiative began in 2004 to explore if it were possible to empower retired midwives and to support them to return to work as semi-private practitioners, still linked to and supervised by the local facility, under authority of the District Management Team. This pilot project has proved to be highly effective in increasing the numbers of skilled midwifery providers working in the country—particularly at the community level, where almost half the births still take place. As in some other countries in the region, the age of retirement from public service is low in Kenya, currently 55 years of age. Many professional women, who have delayed their own pregnancies and childrearing until after they have completed their studies and have had little time to work, find this age too early. Many are still supporting children through higher education and out of necessity are required to keep earning an income. Although a formal evaluation of the initiative is not yet available, all stakeholders are enthusiastic with the preliminary results, and the MoH has now asked all donors to support this initiative. A decision has been made in the new national RH strategy to roll-out the programme across the country. One of the keys of the success of this initiative according to UNFPA and MoH has been the involvement of the community in selecting which retired midwives to support. Those that have been selected are valued in their respective communities and are being well used by the local families. Preliminary results show that referrals for complications have increased significantly particularly referrals from midwives who have been able to identify problems or potential problems early.

Conclusion

We hope to have conveyed the message that for the sake of mothers and newborns both scaling up coverage and skilling up quality of care are necessary. In the event of scarce resources, however, we support the option of giving priority to quality of care over coverage, offering an adequate number of skilled professionals strongly supported by a well performing system, rather than the option of a high number of multi-purpose workers based in villages without adequate capacity, authority and support. We do not believe, and the experience of Bangladesh and Indonesia seem to confirm, that a high number of community-based, multi-purpose workers can be properly supported and funded to achieve the desired objective. Also,

our message is that even though specialist skilled professionals are preferable, they cannot, and should not, work alone. We introduce a fundamental contrast between 'community-midwives', who we consider unable to fulfill the core life-saving functions and 'midwives in the community', who are midwives first, with all the skills attached to the definition. Overloading skilled professionals, particularly with tasks that can be done by others, is not cost-effective and can lead to burn out and poor quality. While 'multi-purpose community workers' can deliver other complementary services such as family planning and other primary health care services, it is not cost effective to produce multi-purpose workers with some midwifery skills. Properly trained specialist skilled attendants such as professional midwives may take 3 to 4 years to train, they can have additional skills and deliver a broad range of primary healthcare, provided doing so does not interfere with the provision and maintenance of the competencies required to be a skilled birth attendant. Developing the needed workforce to ensure that women and newborns have access to a competent midwifery provider requires a comprehensive plan, tailored to the specific situation in each country. We believe that the framework developed by the participants at the 1st International Forum on Scaling up Midwifery for the Community can help countries to develop such a plan, while keeping a focus on quality.

While countries should keep in mind from the beginning the long-term strategy consisting of most births taking place in health centres (even small facilities operated by teams of midwives) attended by skilled professionals operating in multidisciplinary teams, and backed up by accessible functioning referral hospitals, their health planners also need to be pragmatic and to consider possible 'interim strategies'. An example of one such strategy is professional midwives leading multi-purpose teams and supervising home births attended by other health workers. However, there must be time limits set for these interim strategies otherwise they might become permanent strategies, as was the case in too many settings over the past 20 years.

Our final message is that monitoring and evaluation must be built into all plans from the very beginning, including for interim strategies, in an effort to produce evidence on how best to develop a competent midwifery workforce in low-resource settings. There must be a greater focus on continuous monitoring and periodic evaluations. Furthermore, monitoring and evaluation must focus on qualitative as well as quantitative data and look at the performance of providers—measuring how they are performing and identifying the system barriers that prevent quality performance.

Postnatal Quality...continued from page 46

postpartum) women after normal vaginal delivery showed significantly higher physical functioning. This is consistent with recent findings by other investigators, where in a study of 141 new mothers it has been shown that the average period to reach full physical recovery was 3 weeks for vaginal delivery, 6 weeks for elective cesarean section, and more than 6 weeks for emergency cesarean section.

In three areas women after cesarean section scored higher on the SF-36. These were general health at first assessment and vitality and social functioning at second evaluation. We do not know why this occurred, but it is possible that mothers after cesarean section received more hospital care and thus showed a slightly better condition on these two subscales. A review of the literature indicated that a small numbers of women would request a cesarean section and this request is influenced by a range of personal or societal reasons including perceived inequality and inadequacy of care after vaginal delivery. Perhaps this means that new mothers after cesarean section receive more adequate care compared with care after vaginal delivery. However, since in our study mothers in the cesarean section group consisted of both emergency and elective cesarean section, one might argue that the findings were influenced by the fact that women with elective or emergency cesarean may experience rather different quality of life during postnatal period. This might explain the observed within group differences (Table 4).

Cesarean section is not simply a mode of childbirth, it is also an operation, and like any form of surgery, particularly emergency surgery, can cause health problems. Cesarean delivery increases the incidence of surgical intervention and problems resulting from hospitalization. It also puts financial pressures on families and society. A study comparing early postpartum sleep and fatigue for mothers after cesarean section and vaginal delivery found that mothers with vaginal delivery had less hospitalization and more total sleep time. In this study we also found that mothers in the normal delivery group reported a better health-related quality of life and slightly scored higher on the SF-36 questionnaire.

This was a small-sized study and thus the results should not be generalized. It is problematic to reach to a general conclusion from such a small study. It seems that there is still a need to carry out more robust and larger studies to find out which types of delivery could improve quality of life in new mothers. Future studies also should consider variables that are related to social and cultural research environment where the potential studies would be carried out. In addition we recommend the future studies include both general and specific measures in assessing postnatal quality of life among women.

Conclusion

Although our study did not show a clear benefit in favor of either methods of delivery, our findings suggest that normal vaginal delivery might lead to a better quality of life, resulting in superior physical health. Indeed in the absence of medical indications, normal vaginal delivery might be better considered as the first priority in term pregnancy.

Prioritizing Neonatal Medicines Research: UK Medicines for Children Research Network Scoping Survey

Mark A. Turner, Sara Lewis, Daniel B. Hawcutt, D. Field

Abstract

Background: The dosing regimen and indications for many medicines in current use in neonatology are not well defined. There is a need to prioritize research in this area, but currently there is little information about which drugs are used in UK neonatal units and the research needs in this area as perceived by UK neonatologists.

Methods: The Neonatal Clinical Studies Group (CSG) of the Medicines for Children Research Network (MCRN) undertook a 2 week prospective scoping survey study to establish which medicines are used in UK neonatal units; how many babies are receiving them; and what clinicians (and other health professionals) believe are important issues for future research.

Results: 49 out of 116 units responded to at least one element of the survey (42%). 37 units reported the number of neonates who received medicines over a 2 week period. A total of 3,924 medicine-patient pairs were reported with 119 different medicines. 70% of medicine-patient pairs involved medicines that were missing either a license or dose for either term or preterm neonates. 4.3% of medicine-patient pairs involved medicines that were missing both license and dose for any neonate. The most common therapeutic gap in need of additional research identified by UK neonatologists was chronic lung disease (21 responding units), followed by patent ductus arteriosus and vitamin supplements (11 responding units for both)

Conclusions: The research agenda for neonatal medicines can be informed by knowledge of current medicine use and the collective views of the neonatal community.

Background

At present there are several drivers for research about medicines for neonates. The dosing regimen and indications for many

medications in current use are not well defined. Up to 90% of babies receiving medication on a neonatal unit receive unlicensed or off label drugs. The recent European Union Regulation on Medicines for Paediatric Use requires studies in neonates to be included in licensing applications for medicines that could be used in the newborn. This will increase the number of trials in the newborn. There is a relatively small number of infants, particularly at gestational ages < 29 weeks. This leads to a need to prioritise research in this area, so that high quality research is carried out to answer important clinical questions from finite funding opportunities. The process of prioritization involves an assessment of disease burden and available medicines, as exemplified by the work done by the European Medicines Agency (EMA) for off-patent medicines. This should be coupled with assessments of the pattern of medicines use and the licensing status of medicines. Surveys of medication use in neonatal medicine have been performed before but not recently in UK.

The Neonatal Clinical Studies Group (CSG) of the Medicines for Children Research Network (MCRN) has a remit to develop the UK portfolio of neonatal medicines research. Part of this portfolio will relate to existing medicines. The CSG decided to start its portfolio development work with an examination of medicines use in UK neonatal units. The MCRN set up an Extended Neonatal Network (ENN) to support the development and delivery of the portfolio. The aims of this 2 week prospective scoping survey study were to examine whether the Extended Neonatal Network of the MCRN could be used: i) to establish which medicines are used in UK neonatal units, and their relative frequency of use; ii) to determine what clinicians (and other health professionals) believe are important issues for future research.

Methods

A scoping survey was devised by the authors and revised by members of the Neonatal and Pharmacy CSGs of the MCRN. The survey was circulated by e-mail to 116 neonatal units that are members of the MCRN Extended Neonatal Network (ENN) and similar groups in the devolved nations. Two reminders were sent by e-mail. The two week data collection period occurred at the convenience of each Unit (December 2007 – April 2008). The units were characterised by the level of care that they provide and their location within the UK. Medicines were grouped by clinical indications. Each unit counted the number of neonates who received each medicine giving a number of medicine-patient pairs.

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Results

Drugs Prescribed on Neonatal Units: Of the 116 units contacted, 45 units indicated which medicines they prescribed over a 2 week period with 37 reporting how many babies received each medicine during a 2 week period. The level of care provided by each unit and its location within the UK are given in Table 1 for responders and non-responders. The characteristics did not differ between responders and non-responders (chi-squared test, not significant). In total 3924 medicine-patient pairs were reported by the units, using 119 different medicines. The drugs prescribed to the greatest number of neonates were gentamicin (n = 417), benzylpenicillin (n = 350), vitamin K (n = 332), caffeine (n = 249) and dalivit (n = 242). 28% of medicine-patient pairs over the 2 weeks survey period had complete information available, i.e. licenses for use in term and preterm neonates with doses for both groups. On the other hand 4.3% of medicine patient pairs lacked both licences and doses in both term and preterm neonates. This latter group included medicines such as chlorhexidine (n = 95) and dexamethasone (n = 11). Excluding medicines whose license status was unclear (including heparin, hydrocortisone, phenytoin), a total of 70% of medicine-patient pairs had incomplete data for at least one criterion.

Therapeutic Gaps Identified: 37 units suggested one or more therapeutic gaps, providing 162 suggestions in total. The most common therapeutic gap was chronic lung disease (raised by 21 responding units), followed by patent ductus arteriosus and vitamin supplements (n = 11 for both). Full results for all aspects of the survey are available from the Extended Neonatal Network on request [sara.lewis@npeu.ox.ac.uk].

Discussion

The results of this survey are comparable with recent results from the USA. For example the most frequently prescribed medications on neonatal units in the USA were ampicillin and gentamicin. 28% of the medicine patient pairs involved medicines that were reported to have licenses and doses for both term and preterm neonates. This represents a high number of prescriptions for a relatively small number of medicines (mainly benzyl penicillin and gentamicin). The fact that 70% of medicine-patient pairs reported during the scoping exercise involved medicines that were lacking at least one piece of information suggests that there is a substantial research agenda in this area.

The methodology used here is simple, was acceptable to a range of neonatal units and provides a novel approach to estimating the impact of licensing status. The ENN provides a useful way to access UK neonatologists. One approach to assessing the impact of licensing status is to count the number of licences for neonatal medicines. For example among the new molecular entities licensed for use in a pediatric population in the US between 1998 and 2002 only 2% were licensed for use in the newborn period. Our methodology extends this approach by estimating the extent of medicines use in neonates that falls under a marketing authorization and the extent to which medicines use is not covered by a marketing authorization. A repeat survey in several years time would indicate how changes in the regulatory framework, such as the EU regulation, have impacted on patients.

Clinicians are aware of gaps in the therapies they can offer. This will help inform the future direction of neonatal pharmacological research. One exemplar is The Newborn Drug Development Initiative, which was organized in the USA by the FDA and

NIH Institute for Child Health and Human Development. This collaboration developed a process for deciding which drugs were most in need of study in this population (taking account of the nature of disease, outcome, drug characteristics, feasibility, methodology and ethics). Based on this work, criteria have been established for the investigation of a drug in the US neonatal population. The information we have gathered could be used in a similar dialogue between different stakeholders (eg parents, professionals, funders and regulators).

The limitations of this work include the incomplete response rate. This arose due to the lack of time among busy professionals to complete an unfunded survey. We acknowledge that the units who did respond may potentially represent a biased subset of units. However, we believe that the response rate was sufficient to yield a representative range of medicines used in this patient group. Our estimate of the extent of medicines use that lacks information relevant to prescribers is likely to reflect the true number of medicines requiring more information. We are also aware that the BNFC is not the only source of information about licensing status and dosing available. However, the study was designed and carried out through the UK's MCRN and the BNFC is well recognized, widely available, and is the national formulary of UK MCRN units. Comparisons with other sources would have detracted from our aim of contributing to UK prioritization. The denominator in this study is the number of medicine-patient pairs on a neonatal unit over a 2 week period. The 2 week period varied between units. The number of units, an increased response rate due to the flexibility of the design and the random nature of admissions to neonatal units are likely to have outweighed the potential for bias introduced by the lack of a standardised time point for the start of data collection. Future work could include an estimate of the number of neonates. However, that would introduce the need to standardize for variation between units in admission criteria and for variation in the gestational age profile.

We have presented a summary of the data. The results also indicate which units use which medicines and the likely numbers of neonates in each unit who use each medicine. This information will facilitate research by allowing the rapid identification of units who might be interested in a particular research project. We anticipate that similar studies will be conducted by national bodies across Europe. These studies will facilitate international cooperation in areas of common need as well as national prioritization.

Conclusions

To date, the agenda about research into medicines for neonates has been informed by the interests of individual investigators and funded on the basis of the quality of individual trials. Our results raise the possibility that the research agenda can also be informed by the extent of medication use and the collective views of the neonatal community. We speculate that this will facilitate rational priority setting by directing the community towards neglected areas (such as vitamin supplements) and be relevant to decisions about funding and collaboration at national and international levels.

A Trial of the ASV Mode Using the Hamilton G5 Ventilator in NICU

Heloisa Georgiev, RRT-NPS

Our NICU at Florida Hospital for Children in Orlando, trialed the Hamilton G5 ventilators back in May 2009. Infants who weighed between 760 grams and 6.8 kilos were placed on different modes such as APV/CMV, APV/SIMV and ASV. Out of all the patients who were placed on the ventilator, the one that definitely stood out the most was baby “A” who had been in our NICU for six months and weighed 6.8 kilos.

At that time baby “A” was being ventilated via the Babylog 8,000+ Draeger infant ventilator on Assist/Control mode with peak inspiratory pressures as high as 42 cmH₂O.

Taking into consideration that the patient weighed over 3 kilos, and his increased work of breathing on the assist/control mode, the decision was made to place him on the ASV mode (adaptive pressure ventilation) via the Hamilton G5. The staff had utilized the mode in the pediatric unit and felt very comfortable managing the patient.

Prior to making the switch, the patient’s minute volumes on the assist/control mode were carefully noted and recorded. The goal was to set a target percent minute volume that was similar to what the patient was generating before. Initial settings were: 100% target minute volume, PEEP +7 and 21% FiO₂.



Due to an initial increase in respiratory rate and patient generated (actual) minute volume, the percent minute volume was increased from 100% to 130% in an attempt to mimic his actual minute volume and provide the support demanded.

His respiratory rate decreased considerably fast after this change and he appeared to be a lot more comfortable. Peak inspiratory pressures continued to be in the high 30s cmH₂O range and tidal volume mid 30s to mid 40s mls.

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A capillary blood gas obtained an hour after placing him on the ASV mode. Results were: pH 7.56, PCO₂ 35, PO₂ 67, HCO₃ 31 and base excess +8. At that point the percent VE was weaned back to 100%, which translated in a target VE of 1.7 ml (very close to the previous amount on Babylog 8000+ Draeger ventilator).

Baby “A” dictated how he wanted to be ventilated, switching back and forth between breathing spontaneously with the aid of pressure support or receiving full controlled breaths from the ventilator. His respiratory rate remained stable in the mid 30s–40s whenever breathing spontaneously. There was a remarkable decrease in his work of breathing.



Another capillary blood gas was drawn 3 hours after being on the ASV mode at 100% VE which revealed pH 7.44, PCO₂ 44, PO₂ 48, HCO₃ 30 and base excess +5, the best capillary blood gas result the patient had had in days.

PIPs had decreased significantly to mid 20s without compromising the delivery of volume.

Baby “A” continued on the ASV mode for over 36 hours. Every capillary blood gas obtained during that time was within normal limits. He appeared very comfortable on the ASV mode. When the trial time was over, it was a difficult task to take him off the ASV mode and place him back on his previous ventilator/ settings.

The NICU staff was very pleased with the result they witnessed. Ventilating large infants in our NICU can be challenging at times. In utilizing the ASV mode, the infant was able to dictate how he wanted to be ventilated and it made weaning completely up to the patient. Pressure support was automatically adjusted as the patient’s lung compliance and resistance improved.



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