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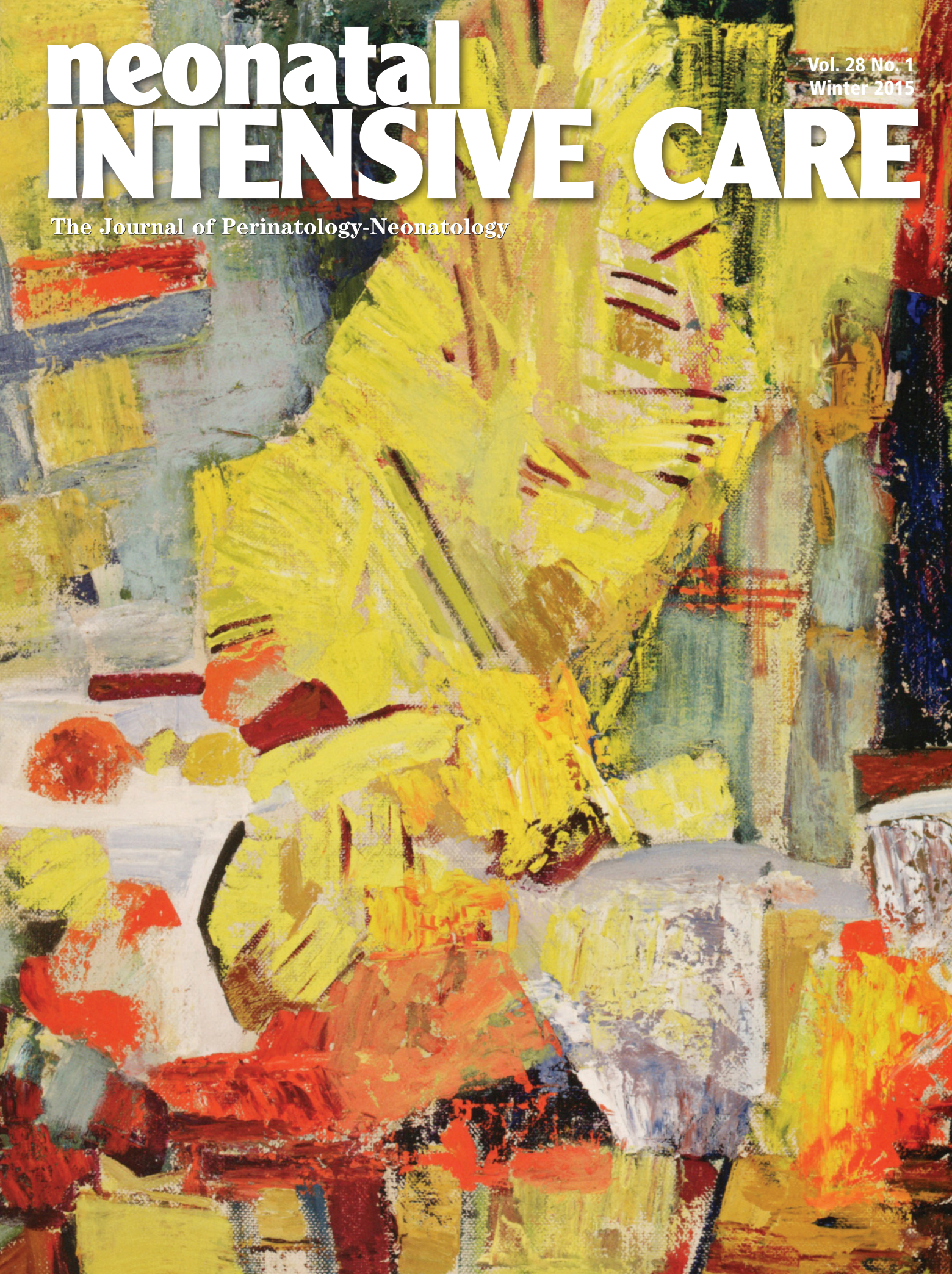
neonatal INTENSIVE CARE

The Journal of Perinatology-Neonatology



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1. American Academy of Pediatrics. Breastfeeding and the Use of Human Milk. Section on Breastfeeding. [originally published online February 27, 2012]. Pediatrics. DOI: 10.1542/peds.2011-3552

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1. Centers for Disease Control and Prevention. (2003) Guidelines for Environmental Infection Control in Health-Care Facilities. Recommendations of CDC and Healthcare Infection Control Practices Advisory Committee (HICPAC). MMWR, 52(RR10):1-42.

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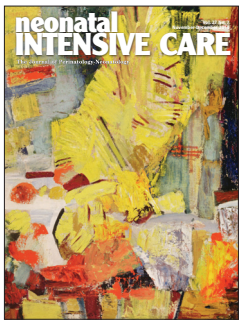

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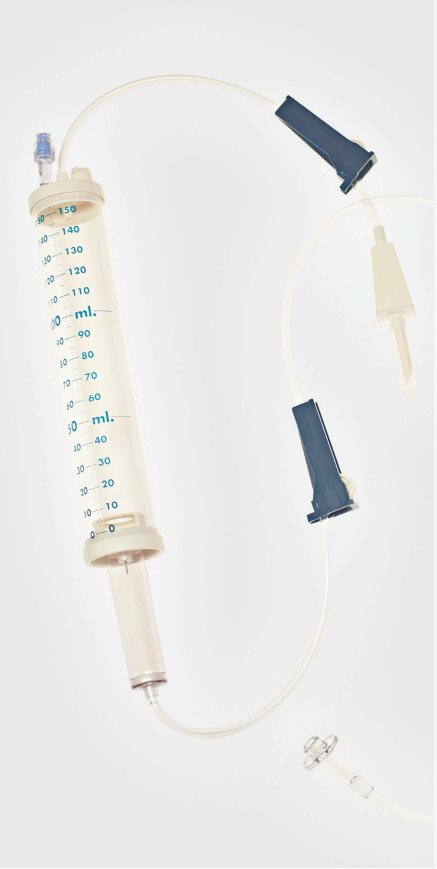

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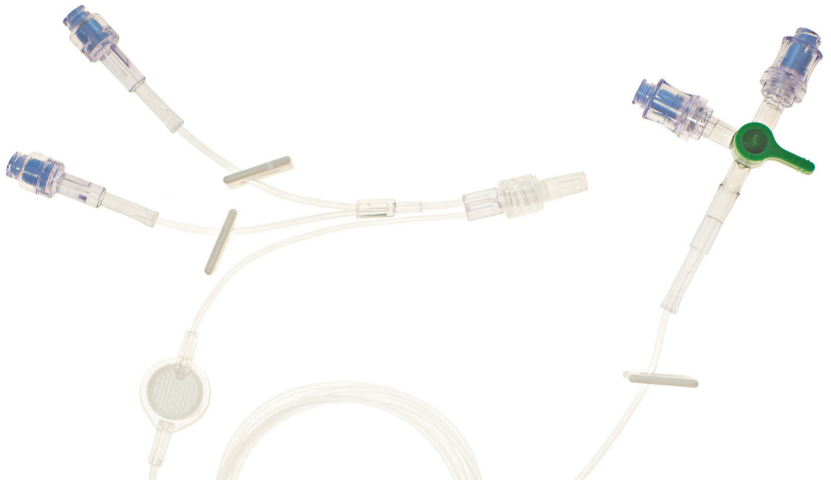

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Got Donor Milk?

Kayce Ryberg, BS

One in ten infants born in the United States is admitted to the neonatal intensive care unit (NICU). For these vulnerable infants suffering from prematurity, congenital and surgical anomalies, and low birth weight, human milk is the preferred source of nutrition. However, if a mother's supply is insufficient or if she chooses not to provide milk for her infant, donor human milk (DHM) should be a provider's next order.

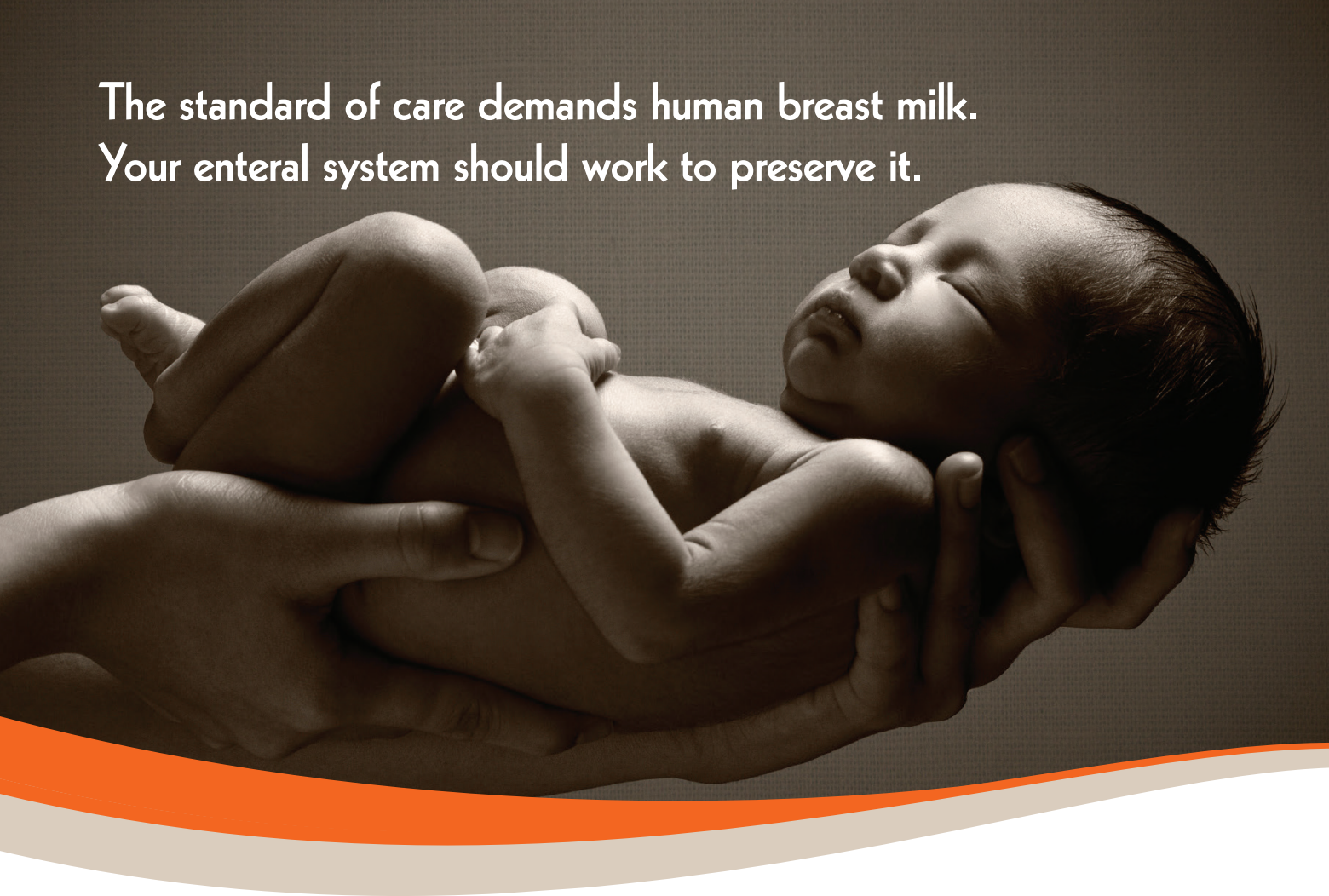
The American Academy of Pediatrics (AAP), World Health Organization (WHO) and the United States Surgeon General recommend exclusive breastfeeding for the first 6 months of life and then continuation of breastfeeding as other enteral nutrition options are introduced for 1 year or longer. These revered organizations make these recommendations based on the exceptional benefits human milk has over formula. Immediate health benefits include decreased respiratory tract infections, otitis media, and serious cold, throat, and gastrointestinal infections. Long-term benefits include protection from obesity, type I and type II diabetes, celiac disease, inflammatory bowel disease, asthma, atopic dermatitis, eczema, leukemia, and sudden infant death syndrome. Not only do premature infants experience these same benefits as well, but during their hospitalization in the NICU, an exclusive human milk diet also contributes to lower rates of sepsis, necrotizing enterocolitis (NEC), urinary tract infections, gastroesophageal reflux disease, diarrhea, and nosocomial infections, improved clinical feeding intolerance, improved visual acuity and neurocognitive outcomes, shorter hospital stay, and fewer hospital readmissions for illness in the three years after hospital discharge. With all the recent literature demonstrating these life-saving benefits, if a mother's own milk is unavailable, why isn't DHM readily ordered by NICU providers as the source for enteral feeding?

Several concerns regarding the use of DHM include associated costs, bacterial contamination, and insufficiency in meeting the higher nutritional requirements of vulnerable infants. When compared to the cost of mother's own milk or to formula, DHM is indeed more expensive. However, when comparing the cost of DHM, which helps protect against NEC, to the cost of an infant developing NEC, possibly requiring surgery, and extending their NICU stay an average of eleven days (42 if needing surgery), the potential savings for the hospital are significant. In regards to possible bacterial contamination, DHM is treated by Holder pasteurization to eliminate viral and bacterial pathogens. It is also cultured for bacterial growth afterwards and discarded if any bacteria are identified. Finally, when questioning whether DHM meets the nutritional needs of vulnerable infants, initial concern was warranted. Since DHM is commonly donated by women who have delivered infants at term, it generally has a lower energy and protein content than milk produced by mothers of preterm infants or than that of preterm formula. Randomized clinical trials comparing formula and DHM have shown that feeding with formula does increase short-term growth rates, but as previously mentioned, it is associated with a higher risk of feeding intolerance, sepsis, and NEC. So, which is better: ensuring growth or risking possible complications?

Thanks to fortification, a provider shouldn't have to worry about answering this question. Initial fortification made from bovine milk resulted in improved weight, length, and head circumference. Nevertheless, since these fortifiers were derived from a non-human source, subsequent research demonstrated that they posed the same risk of feeding intolerance, sepsis, and NEC as formula. Fortunately, this data led to the need and development of a liquid human milk protein-based fortifier (Prolact+ H^2MF), which is made from fortifying concentrated pasteurized DHM with nutrients, specifically protein and micronutrients. Furthermore, recent research has revealed that infants receiving an exclusive human milk-based diet, with early and rapid advancement of fortification using a donor milk derived fortifier, are associated with weight gain exceeding targeted standards and length and head circumference growth meeting targeted standards. This development of a liquid human milk fortifier has created the option for providing an all-human milk diet to vulnerable infants. The use of DHM should be routine in NICUs in order to reduce neonatal morbidity rates, and as healthcare professionals striving to provide the best evidence-based care possible, effort should be made to enhance the availability and affordability of DHM.

Kayce Ryberg is an NP Student at the University of Pennsylvania.

The standard of care demands human breast milk. Your enteral system should work to preserve it.



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1. Neu J, Polin R. Gastroenterology and Nutrition: Neonatology Questions and Controversies. Philadelphia, PA: Elsevier Saunders; 2012. 2. Jensen RG. Handbook of Milk Composition. San Diego, CA: Academic Press; 1995. 3. How NICU Syringe Choice Can Reduce Fat Loss in Human Breast Milk. NeoMed. 2014.

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News

☐ Winter 2015

'Superbugs' an Overseas Threat

An epidemic that could have global implications has hit India and among its many victims are tens of thousands of newborns dying because once-miraculous cures no longer work. These infants are born with bacterial infections that are resistant to most known antibiotics, and more than 58,000 died last year as a result, a recent study found. While that is still a fraction of the nearly 800,000 newborns who die annually in India, Indian pediatricians say that the rising toll of resistant infections could soon swamp efforts to improve India's abysmal infant death rate. Nearly a third of the world's newborn deaths occur in India. Researchers have already found "superbugs" carrying a genetic code first identified in India — NDM1 (or New Delhi metallo-beta lactamase 1). Health officials have warned for decades that overuse of antibiotics — miracle drugs that changed the course of human health in the 20th century — would eventually lead bacteria to evolve in a way that made the drugs useless. In September, the Obama administration announced measures to tackle this problem, which officials termed a threat to national security. Some developing countries have bacterial rates of resistance to antibiotics that are far higher than those in developed nations, with India the global focal point. Bacteria spread easily in India, experts say, because half of Indians defecate outdoors, and much of the sewage generated by those who do use toilets is untreated. The Indian government has begun a campaign to clean the country and build toilets, with Prime Minister Narendra Modi publicly sweeping a Delhi neighborhood. Some health experts and officials here say that these killer bugs are largely confined to hospitals, where heavy use of antibiotics leads to localized colonies. But India's top neonatologists suspect the large number of resistant infections in newborns in their first days of life demonstrates that these dangerous bacteria are thriving in communities and even pregnant women's bodies. In a continuing study in Delhi at several government-run hospitals that has so far included more than 12,000 high-risk newborns, about 70 percent of the babies' infections were found to be immune to multiple powerful antibiotics, confirming the results of earlier and smaller studies. – Article includes information from the New York Times. Copyright, New York Times

Practice Makes Perfect

Drager, a leading provider of medical and safety technology, announced that it had received the 2014 Frost & Sullivan Best Practices Award for its vision to invest in technological innovations in ventilation therapy and its ability to maintain superior customer relationships. The award recognizes excellence across several categories for outstanding achievement and superior performance in areas such as leadership, technological innovation, customer service and strategic product development. Drager received the award in the Growth Excellence Leadership category for mechanical ventilation equipment, and candidates were evaluated on specific market criteria, including total customer experience and product-service value.

Private NICU Better

Research from the Brown Center for the Study of Children at Risk at Women and Infants Hospital of Rhode Island has found that a neonatal intensive care unit with single-family rooms produces better results than one with a shared, open-bay arrangement. Researchers tracked outcomes in an open-bay NICU for 18 months before the unit was moved to a new single-family room facility. Then they tracked successive admissions to the new facility and compared them with the open-bay NICU results. There were no differences between the 151 infants in either type of intensive care unit in terms of gestational age at

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birth, race or maternal educational status or ethnicity. But the study found significant differences in medical outcomes. Infants in the single-family rooms weighed more at discharge and gained weight more rapidly. They needed fewer medical procedures, had increased attention, less stress, less lethargy and less pain.

Intervention Superiority Unclear

The era of fetal intervention has arrived in congenital heart care, but does performing prenatal catheter-based intervention on fetuses with aortic stenosis provide advantages? One expert says it's too soon to declare its superiority over current conventional strategies for management of hypoplastic left heart syndrome. Jack Rychik, MD, director of the Fetal Heart Program at The Children's Hospital of Philadelphia (CHOP) wrote an editorial commentary on this topic in response to a report on outcomes following fetal aortic valvuloplasty in the August 19 issue of Circulation, the journal of the American Heart Association. Congenital heart defects are the most common birth defects, affecting approximately 1 in 120 babies born. Among such congenital heart defects, one of the most challenging to treat is hypoplastic left heart syndrome (HLHS), in which the left side of the heart is severely underdeveloped. The left side has the job of pumping oxygenated blood into the aorta, the large artery that carries blood to the body. In a child with HLHS the mitral valve, which separates the two left chambers of the heart, is too small or completely closed, the left ventricle absent is very small, and the aortic valve, which separates the left ventricle and the aorta, is too small or completely closed. The current management of babies with HLHS is a three-staged set of complex surgeries, culminating in the Fontan procedure. At completion of the surgeries, the child is left with only half of a heart. It offers the chance at survival, a modern-day miracle compared to the situation just two decades ago, when HLHS was almost universally fatal. Nonetheless, mortality from HLHS remains high among all treatable forms of CHD. Only two of three babies born with HLHS survive to the completion of the third stage of surgery. An important factor contributing to the gains in survival rates in HLHS compared to 20 years ago is the capability of detecting the heart defect using prenatal ultrasound and the evolution of programs such as the Fetal Heart Program at CHOP, which brings together a multidisciplinary team to counsel and provide care for the mother carrying a baby with HLHS. CHOP houses the Garbose Family Special Delivery Unit, the first facility dedicated to healthy mothers delivering babies with known birth defects. An emerging new strategy for a subset of patients with HLHS is fetal aortic valvuloplasty. In this procedure the aortic valve is opened before birth in order to allow for increased blood flow and potential growth of the left ventricle. The procedure is appropriate for only a select group of fetuses that fulfill specific anatomical and physiological criteria that might predict a successful recruitment of the left side of the heart. Rychik' s journal commentary analyzes research findings in the same issue of Circulation by a group from Boston Children's Hospital, led by Dr Lindsay Freud reporting on outcomes of the first 100 patients to undergo fetal aortic valvuloplasty at that center. Of those, 88 survived to birth and 38 achieved a bi-ventricular circulation. The 11 percent fetal mortality rate is notable, says Rychik, because in utero demise for HLHS is extremely rare and is not anticipated in the absence of a fetal intervention. Furthermore, Rychik adds, after the fetal intervention "mortality is pushed out of the neonatal period into childhood." Continuing complications, including impaired left-ventricle performance and pulmonary hypertension, may cause the risk of mortality to persist into childhood and early adolescence. He adds, "In comparison, after staged reconstructive surgery, mortality is quite low after completion of the Fontan operation." More time and experience, and much additional research, are needed to evaluate the benefits and risks of fetal aortic valvuloplasty in comparison to the current conventional postnatal strategy, adds Rychik.

Baby Pictures That Aren't Just Cute

Careful and continuous monitoring is critical in a neonatal intensive care unit (NICU), where premature babies (defined as born after less than 37 weeks of gestation) cling to life, often surrounded by the deafening sound of machines and nests of tubes and wires. According to the World Health Organization, over one in 10 births worldwide are premature—an estimated 15 million babies each year, of which more than 1 million will die because of complications from their prematurity. Preemies require special care until their organs have fully developed. Palm-sized infants are placed in temperature-controlled incubators, feeding tubes are inserted through their noses and electrodes and sensors are attached to babies' sensitive skin to track their breathing, heart rate and oxygen levels. The monitoring devices are not only invasive and uncomfortable—they can place fragile babies at an even higher risk of infection. However, with advancements in wireless monitoring technology rapidly evolving, less invasive methods have the potential to provide better care. At Manipal University Hospital in Bangalore, India, Xerox researchers are reinventing heart and respiration monitoring with imaging technology, allowing for cost-efficient, more manageable detection without hardware attached. High-definition webcams record changes in infants' skin and track their heart rate through a videoplethysmographic (VPG) signal—a series of pulses extracted from the video that reflect the change in vascular blood volume with each cardiac beat. The camera then feeds the information into a computer, which takes into account movement and other factors to determine the baby's vital signs. Remarkably, with appropriate optics the camera can scan a child from a distance of more than three feet, making it unobtrusive as well as safe.

Test Pregnant Women

New research suggests that transfusing leukoreduced blood products from cytomegalovirus (CMV)-negative donors prevents the virus from being transmitted to very low birth weight (VLBW) infants. Some infants in the study, however, contracted the virus from their mother's breast milk, a minority of whom developed symptomatic disease or died from the infection, says a researcher report in JAMA Pediatrics. Based on the findings, researchers recommended that pregnant women who may give birth to a VLBW infant be tested for CMV before delivery, and told about the potential risks of breastfeeding their infants if they do test positive for the virus. And longer-term studies are needed to understand whether asymptomatic CMV infection has long-term effects on these infants. To better understand the risk of CMV transmission associated with CMV-seronegative and leukoreduced blood products, as well as breast milk, the researchers at Emory University enrolled 539 VLBW infants who had not received a blood transfusion, and their mothers (n=462), within the infants' first five days of life. CMV seroprevalence was 76.2% among the women in the study. By 12 weeks after birth, 6.9% of the infants developed CMV infection. Of these 29 infants, five developed symptomatic disease or died. There were more than 2,000 transfusions given to 310 of the infants, and none of the transfusions was associated with CMV infection. However, breast milk tested positive for CMV in 27 of the 28 infants who developed postnatal infections.

Touched by an Angel

Preterm babies benefit from a type of soothing, rhythmic touch known as the M Technique, according to a pilot randomized controlled trial. The researchers at St. Louis Children's Hospital observed positive effects on weight as well as on physiologic and behavioral measures in babies who received the technique during a 5-week period relative to a matched control group. The M Technique is composed of structured, stroking movements, done in a set sequence at a set pressure and speed. It has been shown to be useful in many patient populations, including critically ill patients and hospice patients. The M stands for manual—a structured, manual method of touch—which distinguishes it from massage.

Staff Don't Not Getting Any Closure

What does it mean for expectant mothers and hospitals when there are large-scale closures of maternity units? Researchers at The Children's Hospital of Philadelphia provide an inside view from hospital staff members in Philadelphia, where 13 out of 19 obstetric units closed in a 15-year period. The researchers found that sharp surges in patient volume in the remaining units strained the healthcare system, eroded workforce morale, and fragmented care for mothers and babies until hospitals adjusted to added demands. In a previous study, published in 2012, the team reported that infant mortality rates in Philadelphia rose by nearly 50 percent over a three-year period after a series of hospitals began closing obstetric units in 1997. Those mortality rates subsequently leveled off by 2007. In contrast, the current study did not analyze patient outcomes, but instead summarized responses and conclusions from key hospital staff members asked about their experiences from 1997 to 2012. Over that timespan, 13 out of 19 hospital maternity units shut down within the city of Philadelphia. The researchers conducted semistructured interviews with 23 informants at 11 hospitals whose maternity units remained open. Six hospitals were in Philadelphia and five were in the surrounding suburbs; none were identified in the paper. The research says that dramatic surges in delivery volume were the greatest challenge. Maternity units averaged 58 percent in increased volume, resulting in frequent overcrowding, understaffing and lower staff morale. Moreover, the overall patient mix shifted toward poorer patients who were more likely to receive late or no prenatal care. From 1995 to 2009, the surviving obstetric units had on average a three-fold increase in patients with public insurance or no insurance.

KUB Moves Forward

Kubtec, a developer of low dose digital radiography (DR) systems, announced FDA approval of the KUB 250, the first truly portable low-dose digital X-ray system dedicated to the neonatal intensive care unit (NICU). Compact and lightweight, the KUB 250 is the world's highest-resolution low-dose imaging system available for neonates. When imaging high-risk infants in the NICU, it is critical to track subtle changes in pathology while maintaining the focus on low dose. Present day digital X-ray systems maintain pixel resolution in the 150-170 micron range, thereby sacrificing high-resolution images in order to keep the radiation dose low. The poor image quality may require facilities to take additional X-rays of the neonate to confirm pathology or PICC line placement, which in turn defeats the purpose of imaging with reduced radiation exposure. The KUB 250 introduces the world to the first digital X-ray system to image with 96 micron resolution, providing pediatric radiologists

with the highest quality images possible at the lowest dose every time. The KUB 250 eliminates the need to take additional X-rays, minimizing radiation dose to the infant by as much as 40% for each acquired image. Featuring the smallest footprint in its class, the highly mobile KUB 250 fits easily beside incubators in the NICU. The system features an articulating arm for decubitus views and a lightweight DR detector that slides directly into the incubator slot, eliminating the need to move the neonate and reducing stress. Additionally, as a dedicated system for the NICU, the KUB 250 decreases risk of cross-contamination from other areas of the hospital.

'Key' Promotion

Following six years of distinguished service as a local respiratory sales executive, Michael Dougherty, BS, RRT-NPS has been promoted to the position of Key Application Field Manager for Neonatal & Respiratory Care with Dräger's marketing team. Dougherty will oversee and execute the marketing and product management of Dräger's neonatal product portfolio including; jaundice management, warming therapy, and transport devices. He joins an elite team that is focused to provide innovative and cost-effective solutions for the hospital/medical segment of Dräger.

NICU Staff Added

Additional doctors and paramedical staff have been posted and adequate facilities have been created in all 64 neonatal care centres in the government hospitals and government medical college hospitals in the Salem region of India to prevent the death of newborn babies due to preterm birth complications, according to C.N. Mahesvaran, Mission Director, National Health Mission. Mr. Mahesvaran told journalists that an adequate number of ventilators and other equipment were given to these centres. The joint directors and deputy directors of health services and the doctors and other staff attached to these units were put on alert. He said the NICU at the Mohan Kumaramangalam Hospital already had five ventilators. After the deaths of the newborn babies, 13 more ventilators were rushed to the unit. At present, 75 newborn babies were treated at the NICU, of which 15 were in a critical condition. Replying to a question on the complaints of shortage of doctors and paramedical staff at the government hospitals, Mr. Mahesvaran said recruitment of doctors was a continuing process. The government proposed to recruit 2,200 doctors and 700 nurses shortly. With this, every hospital would get 15 more nurses.

RSV Guidelines Developed

New evidence-based guidelines for the prevention of Respiratory Syncytial Virus (RSV) for high-risk infants in the U.S. have been published by the National Perinatal Association. The guidelines are an important resource for healthcare providers and parents of at-risk infants in the midst of the annual RSV season, which occurs every fall through spring. The "National Perinatal Association 2015 Respiratory Syncytial Virus (RSV) Prevention Guidelines," were developed in collaboration with a number of leading experts in this field, including Ram Yogev, a former member of the American Academy of Pediatrics, Committee on Infectious Disease. The guidelines are based on the most recent research available in accordance with the FDA indication for palivizumab, a monoclonal antibody that has been shown to significantly decrease the severity of RSV in premature, at-risk infants. RSV is a virus that causes mild, cold-like symptoms in adults, children and most full-term infants. In premature and "at-risk" infants, RSV can cause severe disease and remains a very serious health concern. The RSV prevention guidelines issued by the National Perinatal Association documents that prevention of RSV is the best approach for at-risk groups. Hospitalization is decreased by 55% for infants treated with palivizumab who were born prematurely at less than 36 weeks gestation who have chronic lung disease or bronchopulmonary dysplasia, and is decreased by 80%, for those born between 32-35 weeks' gestation. For this vulnerable population, prevention is the best medicine. The full set of NPA guidelines can be accessed at: www.nationalperinatal.org/rsv.

Benefits of Busy Units

New research suggests that in the UK, specialist neonatal units that treat a large volume of infants were found to have much greater survival rates than less busy units. Specifically, the research found that the chances of survival were 30% higher for babies born prematurely after 27-32 weeks of pregnancy, and 50% higher for babies born after less than 27 weeks of pregnancy. Neonatal units were classified as being high-volume if they gave at least 3,480 days of care each year to babies born prematurely after less than 32 weeks of pregnancy. Previous studies have been carried out that have found that low-volume neonatal units are associated with increased mortality rates. The majority of these studies have been carried out in the US rather than the UK, where the variability in neonatal unit volume is particularly wide. In the UK in 2003, perinatal centers were reorganized into managed clinical networks (MCNs), providing some of the benefits of a centralized service while allowing smaller, low-volume perinatal centers to remain open to offer services locally. Emphasis is placed on transferring women with a high risk of delivery at less than 27 weeks gestation to units with a higher

care level or high-volume if required. Since the formation of the MCNs, the number of prematurely born infants in higher care level units has increased significantly, as has the transfer rate between units, although the effect that this change has had on clinical outcomes has remained unclear.

SCID Screening Test Approved

The Food and Drug Administration has granted marketing of the EnLite Neonatal TREC Kit, the first FDA-cleared test to screen for severe combined immunodeficiency (SCID) in newborns. The EnLite Neonatal TREC Kit requires a few drops of blood from the newborn's heel. After it has dried on filter paper, the Kit can detect whether the T-cell receptor excision circles (TREC DNA) are low or missing from the newborn's blood sample. TREC DNA is a specific type of DNA that is normally absent or present in low amounts in newborns with SCID compared to healthy infants. Further testing is necessary to confirm a SCID diagnosis. The FDA reviewed a clinical study of about 6,400 blood spot specimens from routine newborn screening, of which 17 had confirmed SCID. The EnLite Neonatal TREC Kit correctly determined all 17 SCID samples. It was also found that the kit could detect very low TREC DNA values associated with SCID. Every state is recommended by the U.S. Department of Health and Human Services to screen newborns for SCID as well as other genetic, endocrine, and metabolic disorders.

Medical Care Goes 3-D

In February of 2012, a medical team at the University of Michigan's C. S. Mott Children's Hospital, in Ann Arbor, carried out an unusual operation on a three-month-old boy. The baby had been born with a rare condition called tracheobronchomalacia: the tissue of one portion of his airway was so weak that it persistently collapsed. This made breathing very difficult, and it regularly blocked vital blood vessels nearby, including the aorta, triggering cardiac and pulmonary arrest. The infant was placed on a ventilator, while the medical team set about figuring out what to do. The area of weak tissue would somehow need to be repaired or replaced—a major and dangerous operation in so small a patient. The team consulted with the baby's doctors at Akron Children's Hospital, in Ohio, and they soon agreed that they had just the right tool for this delicate, lifesaving task: a 3-D printer. The University of Michigan researchers began by taking a CT scan of the baby's chest, which they converted into a highly detailed, three-dimensional virtual map of his altered airways. From this model, they designed and printed a splint—a small tube, made of the same biocompatible material that goes into sutures—that would fit snugly over the weakened section of airway and hold it open. It was strong but flexible, and would expand as the boy grew—the researchers likened it to "the hose of a vacuum cleaner." The splint would last for three years or so, long enough for the boy's cells to grow over it, and then would dissolve harmlessly. Three weeks after the splint was implanted, the baby was disconnected from the ventilator and sent home. In May of 2013, in The New England Journal of Medicine, the researchers reported that the boy was thriving and that "no unforeseen problems related to the splint have arisen."

Psych Support Helps

New research out of New Zealand suggests significant benefits with psychiatric support for mothers in the Neonatal Intensive Care Unit. Data were collected retrospectively about 204 mothers referred to a Level 3 NICU Psychiatric Consult Liaison Team over 2 years. This included medical, demographic and treatment information about both mother and infant. The results found that most mothers (69%) were referred within a week of birth, and 100 (49%) of the referred mothers received a psychiatric diagnosis. Psychiatric follow-up was recommended for 13% on leaving the NICU and additional follow-up referrals were made for another 16%. Mothers with more than one initial reason for referral, a past psychiatric history, receiving therapeutic services, receiving a psychiatric diagnosis and receiving pharmacotherapy were all significantly more likely to have follow-up recommended on discharge. Researchers concluded that approximately one-sixth of mothers in the NICU were referred, a large proportion received a psychiatric diagnosis, and over a quarter required follow-up after discharge, indicating the importance of the service.

Screen All Newborns?

While sudden cardiac death is undeniably devastating to a patient's family, friends and often to whole communities, cardiology experts disagree on whether to screen all US children for underlying heart problems that put them at risk for a sudden cardiac arrest (SCA). A person suffering a SCA requires immediate interventions to survive. A diverse group of uncommon congenital heart defects and genetic conditions may put a child in danger of SCA, and at least two-thirds of these defects and conditions can be identified by an electrocardiogram (ECG), the test that analyzes the heart's electrical function. Much of the current debate centers on the practicalities and cost of universal ECG screening. Victoria L. Vetter, MD, MPH, a pediatric cardiologist and medical director of Youth Heart Watch in the Cardiac Center of The Children's Hospital of Philadelphia, strongly advocates using ECGs to screen all newborns, children and teenagers in primary care facilities or in clinic or community settings. "Many of the conditions responsible for sudden cardiac arrest and death are subtle and not evident as they are genetically based and are silent until a sudden arrest occurs," said Vetter. "To prevent SCD, a predisposing disease condition must be identified and early intervention provided." These medical interventions for high-risk individuals include medications, lifestyle modifications, and use of implantable defibrillators in a small minority of those affected. Vetter says that people can be trained to administer and interpret the screening ECG and that the cost per test is nominal. Furthermore, she says, gaps in evidence about the utility of ECGs for screening should be addressed by further research, rather than dismissing its potential value.

Use of Plastics Studied

US researchers have warned that premature babies are being exposed to high levels of a potentially dangerous chemical in plastics. A Johns Hopkins Bloomberg School of Public Health study suggested babies may be exposed to high levels of a phthalate called DEHP in medical equipment. Some US healthcare providers have banned the use of DEHP, and other products were available, the researchers said. The UK is currently re-evaluating its position on phthalate use in devices. Evidence on the safety of phthalates in humans has been inconclusive, but European regulators have classified DEHP as possibly carcinogenic to humans. Newborn babies in intensive care were in a high-risk population for exposure to DEHP, regulators said, because they were dependent on multiple medical devices. From July 2015, France will become the first country to ban the use of DEHP-containing tubes in neonatal, pediatric, and maternity units. A preliminary EU report on the safety of DEHP in medical devices published in September concluded that the potential replacement for DEHP in medical

devices needs to be balanced with the benefits they bring in treatment, but that wherever possible low-release material should be used. In the UK, the Medicines and Healthcare products Regulatory Agency is re-evaluating its position on the safety of medical devices containing DEHP and is reviewing the EU report.

SPOTLIGHT ON OXIMETRY

Covidien

Describe the oximetry products your company offers.
Covidien offers Nellcor monitors, sensors and alarm management systems, designed to enhance clinician efficiency and effectiveness.

Recently, Covidien became the first company to receive FDA clearance for a motion-tolerant bedside pulse oximeter portfolio that is also compliant with ISO 80601-2-61 (International Organization for Standardization) standards for pulse oximetry.

The Nellcor Bedside Respiratory Patient Monitoring System incorporates the latest Nellcor digital signal processing technology for accurate, reliable readings even during low perfusion and other forms of signal interference, providing clinicians with access to the most critical information regarding their patients' respiratory status. With continuous SpO2 and pulse rate monitoring capabilities, plus trending data and SatSeconds alarm management, the technology offers clinicians the ability to detect respiratory complications earlier and intervene sooner.

SatSeconds alarm management technology, built into the Nellcor N-600x Bedside Pulse Oximetry Monitor offers a safe, practical way to reduce clinically insignificant alarms. The SatSeconds alarm management function analyzes desaturation events by multiplying the duration (seconds) by the number of percentage points the patient exceeds the alarm limit. Clinicians can set SatSeconds alarm management technology limit to 10, 25, 50 or 100. Once the limit is set, only events that equal or surpass the set limit cause the alarm to sound.

The LoSat expanded accuracy feature of Nellcor SpO2 adhesive sensors with OxiMax technology assures clinicians of the industry's widest accuracy range (60% to 100% SpO2) when used with the Nellcor N-600x bedside pulse oximetry monitor. 1 This allows improved patient assessment at challenging lower saturation levels. The low saturation feature in Nellcor adhesive sensors offers clinicians the ability to monitor patients accurately and non-invasively in lower SpO2 ranges.

Covidien also offers the Nellcor N-65 Portable Pulse Oximetry Monitor, an economical, easy-to-use handheld device, as well as the Nellcor N-85 Portable Pulse Oximetry Monitor with Microstream technology, a convenient, handheld device that accurately provides both SpO2 and etCO2 values.

Tell us about your company's R&D pertinent to oximetry.
Covidien is proud of the funds it allocates to research and development activities that have made it a market leader in innovation of medical products, including pulse oximetry. Our commitment to innovation in pulse oximetry monitoring is evident with the expansion of our R&D center in Boulder, Colorado. Nellcor brand R&D efforts are well supported, and Covidien currently has numerous research and development projects in process.

The Covidien commitment to R&D efforts is evident in meeting technology recommendations for CCHD screenings with pulse oximetry, established by the United States Department of Health and Human Services: Screening should be performed with pulse oximeters that are motion tolerant, report functional oxygen saturation, have been validated in low perfusion conditions, have been cleared by the FDA for use in newborns and have an accuracy of ±2 digits.[1]

1. Kemper AR, Mahle WT, Martin GR et al. Strategies for implementing screening for critical congenital heart disease. Pediatrics. 2011;128(5):e1259-1267.

What type of training and user support programs do you offer?
Through the Professional Affairs and Clinical Education (PACE) Online Platform, (www.covidien.com/PACE), Covidien offers a variety of free, clinical and non-clinical education modules online, including courses intended to develop clinician understanding of pulse oximetry technology, CCHD screening, and initiatives in patient care. Covidien is committed to promoting CCHD awareness activities to ensure clinicians understand how to use pulse oximeters to generate reliable readings. In fact, Covidien offers specific education about recommendations for early screening and monitoring for congenital heart disease in infants. Additionally, Covidien offers complimentary in-servicing and on-site clinical support for customers.

Discuss the cost of your oximetry products.
Pricing is generally structured with multiple pricing tiers based on a customer's commitment/compliance levels within their Group Purchasing Organization or Integrated Delivery Network contract arrangements. Other good information: Monitoring a wide range of critical respiratory parameters, the Sensing Systems of Covidien help caregivers provide faster, more informed interventions for their patients.

The above information provided by Nicole Malcolmson, Senior Product Manager, Covidien.

In this feature, Neonatal Intensive Care interviews clinicians and healthcare providers about the actual application of specific products and therapies. Participating in the interview are Michael H. Goodstein, MD, FAAP, Attending Neonatologist, Clinical Associate Professor of Pediatrics (Penn State U.) Director, York County Cribs for Kids Program York Hospital Office of Newborn Medicine, and Judith A. Bannon, BSBA, Executive Director and Founder, Cribs for Kids.

Neonatal Intensive Care: What is the Cribs for Kids Program; when and why was it started?
Michael H. Goodstein/Judith A. Bannon: Cribs for Kids began in 1998 when 5 babies died in their sleep within a two-month period. These 5 babies, along with 90% of all of the babies who died suddenly and expectedly in the three preceding years in Allegheny County (Pittsburgh) Pennsylvania, had two things in common: they were all found in unsafe sleeping environments, i.e., in bed with parents or siblings or on couches and they were from low-income households.

NIC: What do you hope to accomplish by this program?
MG/JB: The mission of Cribs for Kids is to help reduce infant mortality, specifically infant sleep related deaths, through education of parents, families, and communities about infant sleep safety. Anybody who will interact with an infant should be aware of the recommendations of the American Academy of Pediatrics for safe sleep. These recommendations are evidence-based and form the basis for the Eunice Kennedy Shriver National Institute for Child Health and Human Development's "Safe to Sleep" campaign which is an extension of the "Back to Sleep" campaign which began in 1994. In addition to education, any family identified as not being able to provide a safe sleep environment for their baby is provided with a Pack 'N Play and additional safe sleep materials, so no baby should ever have to sleep in an unsafe environment that could increase the risk of a sleep-related death- whether due to suffocation, strangulation, or sudden infant death syndrome.

NIC: Is there a particular problem facing new parents today that Cribs for Kids addresses head on?
MG/JB: Cribs for Kids directly addresses the issue of infant sleep-related deaths through consistent messaging of safe sleep and promoting a culture of infant sleep safety. Expectant and new parents are barraged with information about infant care throughout the pregnancy and after the birth of the child. Unfortunately, sometimes parents receive conflicting information and not all of the information is accurate. It is critical that families receive accurate information so they can make the best choices for the safety and health of their child. We know that infant sleep safety information is critical—these sudden unexpected infant deaths or SUID's are the third leading cause of infant mortality (exceeded only by prematurity and congenital malformations) and the leading cause of post-neonatal infant mortality. Approximately 3500 infants in the US die from sleep-related deaths every year. This is equivalent to one death every 2 to 3 hours of every day of the year. This is a silent tragedy that we are giving voice to.

NIC: How do you work with hospital to make your information and resources available to new parents? Are there materials you provide to health professionals on safe sleep for baby that would enable them to share what Cribs for Kids does?
MG/JB: We started the Hospital-Based Infant Sleep Safety (ISS) Initiative in 2008. It was developed at WellSpan York Hospital in York, PA and research on the program shows a positive impact on provider and parental knowledge on safe sleep, as well as on parental behaviors. It is a comprehensive infant sleep safety initiative, targeting education of staff, families, and the general community. The program consists of three components: watching a DVD on infant sleep safety, nurse modeling of safe sleep and providing reinforcement of the education from the DVD, and the signing of acknowledgement statement that the family has received and understands the information. The initiative developed a culture of infant sleep safety at the hospital and all new families receive standardized education to maintain a safe sleep environment at home. The program has undergone improvements periodically through PDSA cycles. These findings have been replicated by others who have used a similar educational model. We know that this program has excellent potential for widespread replication because it is already happening. Once we started reporting our positive outcomes at research meetings, we began to receive requests for information on the program and assistance with reproduction. We created a series of documents explaining the necessary steps for both program development and achieving and maintaining culture change. (Available online at: http://www.cribsforkids.org/hospital-initiative-toolkit/) Expansion relies on diffusion of innovation theory that innovators or champions need to be identified at sites to help promote the program. These opinion leaders are responsible for recruiting agents of change to help adopt the program and solve roadblocks. The program itself is inexpensive in terms of supplies and even manpower. The educational DVD (Safe Sleep for Your Baby: Right from the Start) only costs $20 and it is available to PA birthing hospitals at no cost through a Department of Health grant. All the forms including a safe sleep policy, brochures and educational flip chart can be downloaded for free. The only transient expense involves the time to provide staff education, and the education can be used for required continuing education credits.

Input on questions was provided by the editing staff at Neonatal Intensive Care. If you would like to participate in this feature, as a company or healthcare provider, please contact Steve Goldstein at s.gold4@verizon.net.

The program continues to grow with the support of PA Department of Health and the National Cribs for Kids Program. But the safe sleep initiative has spread outside the borders of PA. Working through the Maine Children's Trust, over 1/3 of their birthing hospitals have received comprehensive education on ISS, following a pattern of success they have had with implementing the Period of Purple Crying program. We also have provided assistance at the state level to TN, WV (Our Babies, Safe and Sound), OH, AR, and NM.

We are now introducing The National Safe Sleep Hospital Initiative. Developed by Cribs for Kids in conjunction with Halo Innovations, this is a hospital certification program which recognizes hospitals that demonstrate a commitment to community leadership for best practices and education on infant sleep safety. The initiative has 3 levels of Safe Sleep Certification, with each step up the ladder requiring an expansion toward a more comprehensive safe sleep program, culminating in the designation of Certified Safe Sleep Champion.

There are many benefits to this program. It gives hospitals a road map to achieving a successful culture of infant sleep safety, but still allows them to individualize the program for their specific local needs. It allows the hospital to move in a step-wise fashion so that goals remain achievable and lead to safe sleep success. The program provides all the materials for staff and family education, so there are no large costs involved which could otherwise prevent participation. Easy, on-line access allows for documentation of program compliance at no cost to the institution. Once certified a hospital can display their Certification medallion in their birth center, NICU and marketing materials.

The new hospital program has early supporters and has been endorsed by Kids in Danger, National Center for the Review & Prevention of Child Deaths, ASIP (Association of SIDS and Infant Mortality Programs), Ohio Hospital Association, Ohio Chapter of the AAP, and the Children's Safety Network.

This program is well-aligned with the Maternal Child Health Bureau's vision of reducing infant mortality through the promotion of infant sleep safety as outlined in Dr. Lu's Collaborative Improvement and Innovation Network (COIN). Data continue to accumulate about the importance of both provider education to families about safe sleep and consistent modeling in the hospital environment. All the information behind the program (including a brief slide show) can also be accessed at: http://www.cribsforkids.org/hospitalcertification/.

In this feature, Neonatal Intensive Care interviews clinicians and healthcare providers about the actual application of specific products and therapies. Participating in the interview is Keira Sorrells, Director and Founding Member of Operations for the Preemie Parent Alliance.

Deb Discenza: What is the Preemie Parent Alliance and how did it start?
Keira Sorrells: The Preemie Parent Alliance is a network of organizations from across the country. Each organization was founded by and/or is run by a parent of a preemie and each organization provides some form of support for parents who currently have a baby in the NICU or have since been discharged. It was born out of a meeting of like-minded preemie parents in the fall of 2010. Each parent invited to the meeting had already made a significant impact on the lives of other parents and each had a desire to collaborate on ways we can all work together to provide the best possible support for families all over the world.

DD: What groups comprise of the Preemie Parent Alliance?
KS: We have 24 member organizations throughout the US. Our members are located in Washington, Texas, Mississippi, Ohio, Illinois, Tennessee, Pennsylvania, Connecticut, New York, Virginia, Washington DC, Massachusetts, Iowa, Maryland, and New Hampshire.

Our members are:
- Dallas Preemie Parents
- Eli's Hope
- Families Blossoming
- Fragile Beginnings Preemie Parent Alliance
- Graham's Foundation
- Hand to Hold
- Holding Tiny Hands
- It's a Preemie Thing
- Keep 'Em Cookin
- Little Giraffe Foundation
- National Perinatal Association
- NICU Helping Hands
- Nurtured by Design
- Papas of Preemies
- Preemie: Lessons in Love, Life & Motherhood
- Preemies Today
- PreemieWorld
- Skyler's Gift
- Teenie Preemie
- The Foundation for Prematurity
- The Saving Grace Project
- The Tiny Miracles Foundation
- Zoe Rose Memorial Foundation

Input on questions was provided by the Deb Discenza, Founding Member of Preemie Parent Alliance. If you would like to participate in this feature, as a company or healthcare provider, please contact Steve Goldstein at s.gold4@verizon.net.

DD: Why an alliance of preemie parent support groups?
KS: Data from the CDC tells us that there are 500,000 babies born preterm every year just in the United States alone. That means there are families who find themselves in challenging, overwhelming, and traumatic life circumstances that need help navigating life with a preemie. It is my personal belief that no single organization can serve all the needs of all these families and do it well. However, by working together we can get much closer. By sharing ideas, partnering on projects, and creating that centralized voice for the preemie parent we have the power to change lives and affect standards of care guidelines with the single purpose of ensuring that every parent of a preemie feels empowered and supported.

DD: What types of projects has PPA taken on to help the preemie parent community? The professional community?
KS: We have already done a lot to help both the parent and professional communities and have more coming:

1) We unveiled the NICU Parent's Bill of Rights which is a listing of items that we hope will help NICU professionals understand a parent's mindset while in the NICU, encourage the parents to be involved in the care of their babies, foster a relationship with the families built on trust and mutual respect, and ultimately empower these parents when the time comes that they must take their baby home. The Bill can be downloaded from our website at this link: http://bit.ly/PreemieRights
2) We were also very excited to be involved with the National Association of Neonatal Nurses (NANN) this past year as they developed their Discharge Planning Module. We provided a review panel of parents that went through each topic the module covered and offered suggestions on how to best reach and teach the parents.
3) We have also provided parents to review articles for NANN's Advances in Neonatal Care.
4) Several of our parent leaders are a part of the newly created Psychosocial Support workgroup with the National Perinatal Association.
5) Additionally, we have parent panels who have presented at the NANN conference in October 2013 and have two upcoming panel presentations at NEO Conference and the National Association of Perinatal Social Workers

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In this feature, Neonatal Intensive Care interviews clinicians and healthcare providers about the actual application of specific products and therapies. Participating in the interview is Steven C. LeCroy, MS, CRTT, EMT-P.

Neonatal Intensive Care: How often do neonates need some type of ventilation support?
Steve LeCroy: The numbers might surprise a few folks. According to the American Heart Association almost 10% of all neonates require some form of respiratory support at birth, and almost 4 out of every 1000 births will require mechanical ventilation. The bigger questions everyone should be asking is how often do clinicians get the opportunity to manually ventilate a patient in this age group? And when they do is it safe and effective? And I think the answer to the first part is not very often, unless of course they work in the NICU or labor and delivery. And the second answer I suspect that in many cases it may not be safe or effective. For most clinicians ventilating neonates and small infants would be considered a low probability, high risk and high liability event.

NIC: Why might clinicians have difficulty manually ventilating newborns and infants?
SLC: The first and most obvious reason is opportunity, they just don't do it enough. It's very difficult to get good hands on training, we all know mannequins are a good start but are nothing like the real thing. Even though manual ventilations are considered a BLS skill it's important to recognize that a BLS skill does not equate to an easy skill. There's also the psychological aspect of treating babies and infants. If the average clinician is presented with a 60 year difficulty breathing patient the stress level is most likely pretty low. If the same clinician is presented with a 6 day old patient with difficulty breathing the stress level can be overwhelming. It's like asking the average driver to drive a race car and telling them it's just a car.

NIC: What complications can be caused by improper manual ventilation techniques?
SLC: There is a wide range of problems associated with poor manual ventilation techniques. Injuries can range from the development of a pneumothorax or chronic lung disease from too high of an inspiratory pressure to hypoxia from under ventilation both of which can lead to bad outcomes. Improper ventilation rates and volumes can also lead to major acid/base balance problems. For example under ventilating can not only create an hypoxic state leading to neurological problems, but can create a hypercapnic situation, and as most RT's know a high CO2 can cause a drop in pH putting a patient into respiratory acidosis a situation in which neither organs nor medications work very well.

NIC: What are the recommended starting PIP and PEEP pressures for small infants and newborns?
SLC: First, we should probably define the terms PIP and PEEP. PIP or peak inspiratory pressure is the maximum pressure exerted on the airway at the end of inspiration. PEEP is Positive End Expiratory Pressure or the pressure that remains in the airways at the end of expiration. Both PIP and PEEP are measured in centimeters of water or cmH2O. Clinicians that routinely treat adults are less concerned about PIP, however I believe that's about to change. Adult manual ventilation techniques could be a discussion for another day. According to the Neonatal Resuscitation Program guidelines the recommended starting PIP should be 20 cmH2O pressure and the initial PEEP should be 5 cmH2O pressure. However, some newborns may require higher pressures to get chest rise, for example those born with surfactant issues.

NIC: What type of equipment is typically used for manual ventilation of infants and newborns?
SLC: There are 3 basic types of manual ventilation devices a Bag-valve-mask, hyperinflation bag, and a t-piece resuscitator. Each of these devices has its pros and cons and I would recommend that all clinicians consider those pros and cons before selecting a device.

NIC: What are your thoughts regarding using a bag-valve-mask on small infants or neonates?
SLC: This one is easy, many infant BVMs don't come with a manometer or a PEEP valve, even though most manufacturers have them as options. Without a manometer or PEEP valve I can safely say that it's impossible to know the PIP and PEEP pressures being used. Even with a manometer and PEEP valve it's extremely unlikely that PIP and PEEP pressures are consistent. I would argue that a BVM without a manometer and PEEP valve is the most dangerous piece of resuscitation equipment in use today. If you currently use a BVM without a manometer or PEEP valve and you had to testify due to a bad outcome how would you answer if asked what pressures where use? Or did your ventilation technique meet the standard? I think the answer to both questions is pretty clear. The one positive aspect of a BVM is they don't need an oxygen source to work since they self-inflate. For those that use a BVM and believe they can feel lung compliance are probably mistaken.

Input on questions was provided by the editing staff at Neonatal Intensive Care. If you would like to participate in this feature, as a company or healthcare provider, please contact Steve Goldstein at s.gold4@verizon.net.

Studies have shown that feeling lung compliance while using a BVM is highly overrated.

NIC: What about a hyperinflation bags?
SLC: Hyperinflation bags or anesthesia type ventilation bags have been around for years. I think most respiratory clinicians would agree that using a hyperinflation bag is one of the most difficult skills to master. It's been my experience that it takes significant training and experience to properly ventilate a patient using such a device. I've heard clinicians say you need what they call an "experienced hand." From having experience with hyperinflation bags it does take a lot of feel to maintain the proper pressures. I've heard respiratory therapist comment that they prefer a hyperinflation bag because they get a better feel for lung compliance. This may be true for the more experienced users, I doubt that's the case for the average or infrequent user.

NIC: What is a t-piece resuscitator?
SLC: A t-piece resuscitator is a manual ventilation device that does not have a bag and has the ability to set and control PIP as well as PEEP. The device attaches directly to the patient interface and ventilation is accomplished by placing a finger over a hole on the exhalation side. Most t-piece resuscitators have an in-line manometer for continuous monitoring of the pressure and can also be used to provide CPAP.

NIC: Which one of the manual ventilation devices would you recommend?
SLC: Without a doubt the t-piece resuscitator. In my opinion it is the safest most effective manual ventilation device regardless of the skill level of the clinician. I'm sure there are RT's out there that will disagree they will argue that they want a device where they can feel lung compliance, a skill I believe to be poorly developed especially in inexperienced hands.

NIC: What makes a t-piece resuscitator a good option for manual ventilation?
SLC: The first and most obvious reason is ease of use. The proper technique for both the BVM and hyperinflation bag can be difficult to master, those that teach I'm sure can sympathize with that. The only negative to using a t-piece resuscitator is that you have to have a constant gas flow. However, I believe the problem I know about is the problem I can manage. No device is perfect, but when the risks and benefits of each device are compared the advantages of a t-piece outweighs the risk.

NIC: Any final thoughts when it comes to manually ventilating infants and newborns?
SLC: Each clinician should be asking themselves the same question. How comfortable am I with the equipment I'm using? Be critical! It's not about the clinician it's about the patient. Even if you have years of experience are you using the most effective safest equipment. There are only three ways to handle a situation you can ignore it, prepare for it which includes training and equipment, or you can take out more insurance. Either way the balls in your court.

Steven C. LeCroy, MS, CRTT, EMT-P, is a retired captain/ paramedic from St. Petersburg Fire & Rescue, an adjunct instructor at St. Petersburg College, a 35-year respiratory therapist and an expert witness in over 75 legal cases across the U.S. He is currently the Clinical Manager at Mercury Medical.

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conference. Each presentation is based on helping the NICU professional get inside the head of a parent to understand what a day in the life of a preemie parent is like and how our NICU experiences shape and mold us into the parents we will become. We provide teaching points and encourage the professionals to continue in their work of developing relationships with parents that offer the parents hope, no matter the outcome, as well as building a foundation of confidence for when the parents must take their medically fragile infants home.

DD: What should the neonatology community know about PPA in terms of its usefulness to them and to their families in their care?
KS: We are a group of inspired, dedicated parents who want to partner with the neonatology community to help ensure that we aren't just saving preterm babies but are encouraging the entire family unit to thrive.

Parenting a preterm infant is an experience unlike any other and only those who have walked a mile in our shoes can truly understand what that means. The experience cannot be taught in a textbook. We are here to make the jobs of neonatal professionals easier by supporting parents and NICU units to send their fragile babies home with parents who are empowered and will be strong advocates for their babies throughout the entirety of their lives.

Learn more about Preemie Parent Alliance here: www.PreemieParentAlliance.org

Learn more about the Preemie Parent Alliance members here: http://bit.ly/PPAGroups

In this feature, Neonatal Intensive Care interviews clinicians and healthcare providers about the actual application of specific products and therapies. Participating in the interview is Dr Sergio Golombek, MD MPH, FAAP, Professor of Pediatrics and Clinical Public Health.

Neonatal Intensive Care: In the past few years there's been an increasing emphasis on providing human milk to babies in the NICU, why is this the case?
Sergio Golombek: Human milk feeding is associated with substantial benefits to the health and development of infants, especially premature infants. The American Academy of Pediatrics recommends that all preterm infants receive human milk (including donor milk if mother's own milk is unavailable). (Pediatrics 2005;115:496-506)

NIC: We understand that your unit now uses 100% human milk for certain subsets of the babies. Who gets the 100% human milk diet and why?
SG: At our Regional Neonatal Center at the Maria Fareri Children's Hospital at Westchester Medical Center we, of course, recommend human milk to ALL babies that are admitted. After reviewing the literature, our group decided that we needed to provide the best possible nutrition to micro preemies, so when the mothers want to provide their milk, we support them as best as we can. While her own milk supply is increasing, we will supplement it with donor human milk. Our protocol includes, whenever possible, exclusive human milk (appropriately fortified) for babies less than 1500 grams birth weight.

NIC: How do you respond to questions raised in the medical literature and elsewhere about the comparative growth of babies on 100% human milk diet versus those who receive formula or other nonhuman products in their diet?
SG: The worldwide standard is that human breast milk is the preferred food for infants as endorsed by medical entities, including the American Academy of Pediatrics (AAP) [American Academy of Pediatrics. Breastfeeding and the Use of Human Milk. Section on Breastfeeding. [originally published online February 27, 2012]. Pediatrics. DOI: 10.1542/peds.2011-3552.], the World Health Organization (WHO), New York State Department of Health (NYS DOH), the US Surgeon Surgeon General. Studies have shown that an exclusive human milk based diet decreases the incidence of NEC and parenteral nutrition days (Sullivan S: An exclusively human milk-based diet is associated with a lower rate of NEC than a diet of human milk and bovine milk-based products. J Pediatr 2010 Apr;156:562-7). We know now that the caloric content of human milk is often < 20 cal/oz, with the fat content being the most variable component. The "secret" of improving growth in these babies then would be in fortifying the breast milk appropriately. An interesting study recently published by Dr Hair et al. in the Journal of Pediatrics compares the growth of babies 750-1250 grams birth weight providing human milk cream as a supplement to the diet, and concluded that these babies had improved weight and length velocity compared to the control group.

NIC: An article recently published indicated that mother's own breast milk is the leading cause of transmission of CMV to infants in the NICU. Do you have any concerns about transmitting either CMV or other infectious agents through the use of large volumes of donor milk products?
SG: I think that when you use a product that is made with all the appropriate standards, that should not be a concern. As you are aware, there were several recent reports about tainted and contaminated breast milk that was bought through the internet. Evidently, that is not the way to obtain "good quality" milk!

NIC: How do you encourage and support mother's to produce milk for their own babies in your NICU?
SG: At our Regional Neonatal Center at the Maria Fareri Children's Hospital at Westchester Medical Center we definitely encourage every mother to provide breast milk for their babies. We are fortunate to have a marvelous Lactation Consultant (Rhonda Valdes-Greene, RNC, MSN, IBCLC) who supports all of our mothers, including facilitating the rental of breast pumps for home use. We have several breast-pumping rooms throughout our NICU, so the mothers can pump whenever they need to. All of our NICU nurses continuously provide support and encouragement for the mothers to continue pumping, and supply the families with whatever they need to bring their babies the milk from home.

NIC: There have been sporadic reports of shortages of donor milk in some NICUs. Have you experienced such shortages and how do you get around them when they occur?
SG: Fortunately, we have not run into that problem!

NIC: Donor milk and donor milk-based products are rather expensive compared with cow-milk based infant formula. How has your unit dealt with this cost differential?
SG: At our Regional Neonatal Center at the Maria Fareri Children's Hospital at Westchester Medical Center, undoubtedly, cost is an issue. We have previously decided to do whatever is best for our babies, and many of the things that are used at a high acuity-high complexity (we have one of the highest case-mix

Input on questions was provided by the editing staff at Neonatal Intensive Care. If you would like to participate in this feature, as a company or healthcare provider, please contact Steve Goldstein at s.gold4@verizon.net.

index in New York State) are very costly (for example, inhaled nitric oxide, palivizumab for RSV prophylaxis, IV ibuprofen for PDA). The use of pasteurized donor milk is also included in this category, but human milk is very complex and provides the precise nutrients, immunities and gastrointestinal benefits these babies need to thrive, in the short and long term. (Chandehari et al., BMC Research Notes, 2012; S188). Few studies have shown that extremely premature infants fed with 100% human-milk based products had lower expected NICU length of stay and total expected costs of hospitalization (Ganupathy V – Barriers to successful lactation – BF Med 2012 Feb:29-37)

NIC: If the director of an NICU were to tell you that he has a low NEC rate (4 to 5%) and was wondering if they should try the 100% human milk diet, what would you advise?
SG: The advantages of human milk are not "only" decreasing NEC rate. There are several described short and long term effects, for example:

- Long term follow-up of 300 preterm infants at 7.5 to 8 years by Lucas et al. who received HM demonstrated a significantly higher IQ with an 8.3 point advantage after adjustments over infants who received no maternal HM (Lucas et al., Lancet 1992;339:261) (other studies that support this: Roze et al., BMJ Open 2012;2:e000834; Isaacs et al., Pediatr Res 2010;357-362; Vohr et al., Pediatrics 2006;118:e115 ; Hack et al., NEJM 2002;346:149)
- Decrease in sepsis/NEC/death by proportion of mother's milk days (Corpeleijn et al., Neonatology 2012;102:276-81)
- There is a dose-response relationship between the amount of HM feedings over the entire NICU stay and neurodevelopment outcomes at 18 months of age (NICHD Glutamine trial), and also with severity of ROP (Hylander – J Perinatol 2001;21:356 - Schanler et al., Pediatrics 2005:116:400 – Okamoto et al., Pediatr Intern 2007;49:894)
- Protect, develop and program many body systems through synergistic functions (eg., immunomodulatory, anti-inflammatory, gut-colonizing, epigenetic mechanisms)
- Increased lactase activity; decreased GI permeability; more rapid attainment of full feedings; better feeding tolerance

NIC: What other benefits have you seen from the use of a 100% human milk in your NICU?
SG: It's better for babies, for their mothers. It definitely improves the relationship that the mother (and family!) have with their baby in the NICU. Remember that the family is not a visitor in the NICU – so anything that we can do to improve their experience, and to help them through the difficult time of having a sick baby in the NICU, should be welcomed and encouraged!

NIC: You recently attended the Second International Human Milk Science and Innovation Conference. What were the most interesting clinical takeaways from the conference?
SG: To start with, the opportunity of visiting (again!) the Prolacta plant was amazing. It is an incredible place, and an eye-opener to everything that is involved in the production of pasteurized breast milk.

The conference allowed me to network with other neonatologists, dietitians and nurses that are covering many aspects of investigation related to breast milk, from basic sciences to the latest clinical research.

One of the best talks was by Alan Lucas, M.D., University College London, London, England: "A Challenging Evolutionary and Scientific Adventure in Breast Feeding Medicine", where he reviewed decades of practice of breastfeeding, lots of his own research and sprinkled it with his marvelous sense of humor!

The review of their own experience by Christoph Fusch, M.D., McMaster University, Hamilton, Ontario, Canada: "Individual Fortification & Implications; Optimal Growth" showed us that it is possible to look at the future when we will nourish babies "individually."

The talk by Jonathan M. Fanaroff, M.D., J.D., Case Western Reserve University School of Medicine, Cleveland, OH: "Informed Consent—Helping Families Make Decisions" clarify very important aspects of what we do routinely in our NICU while we are taking care of newborn babies, and William Rhine, M.D., Stanford University School of Medicine, Palo Alto, Calif.:"Overview of Clinical Research on Human Milk in Neonatal Intensive Care" talk encouraged all of us to continue doing research! (Even on his birthday!)

Neonatal Sepsis: A Review

Sandra Sundquist Beauman, MSN, RNC-NIC

Abstract

Sepsis has always been a concern in the care of infants. Pierre Budin (1), in his book, "The Art of Nursling" published in 1907 discussed the protection of the neonate, referred to as a 'weakling.' During an outbreak of a respiratory infection, "We obliged every wet nurse to wash her face and hands, and change her uniform each time she went to feed the weaklings."(1, p 56) Handwashing was a required and monitored activity in the NICU long before so much focus was spent on handwashing in other areas of healthcare. The initial scrub upon entrance into the NICU is only required in the operating area outside the NICU. Many other measures have taken place over the years, including the universal screening of mothers for Group B streptococcus and careful observation for chorioamnionitis. Causative organisms and rates of both early onset and late onset sepsis have changed but both still occur in both term and preterm infants. The risk factors, both neonatal and maternal for early and late onset sepsis, signs and symptoms of sepsis including some new methods to recognize the earliest signs of sepsis and recommendations for and interpretation of the septic workup will be discussed. In addition, a discussion of infection prevention, including some available bundles for prevention of central line associated blood stream infection and ventilator associated pneumonia are included.

Rates of sepsis are reported by various groups and in various countries with different results. Rates are generally higher in the preterm/low birth weight population with rates reported around 26/1000 live births for infants less than 1000 grams birth weight and 8/1000 live births for infants between 1001-1500 grams birth weight (2). Culture proven sepsis in all birth weights in the U.S. is reported at the rate of 0.77 to 1 per 1000 live births (2). Obviously the rate of sepsis is extremely high in the lower birth weight population according to these reports, and the rate of mortality is also higher in very low birth weight (VLBW) infants with sepsis than in term infants with sepsis. Camacho-Gonzales, Spearman, Stoll (3) report that the leading cause of morbidity and mortality amongst preterm infants remains infection, usually sepsis. Much of the work done over the past 10 years focusing on preventing preterm births found that in many cases, the reason for the preterm birth was related to the presence of infection in the mother, commonly chorioamnionitis (4). Tita and Andrews (5) report that clinical chorioamnionitis is present in 40-70% of pregnancies resulting in preterm delivery as compared to 1-13% of term deliveries. In many cases, particularly for the extremely preterm infant, this results in infection and sepsis.

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Definitions

Sepsis is defined as the presence of infection in the blood stream. Another term used often is culture-proven sepsis. In many cases, infants exhibit systemic signs of infection in the absence of a positive culture. This may be related to the low bacterial colony count often seen in neonates. For this reason, it is recommended that blood cultures be obtained with a minimum of 1 ml of blood as any less than this decreases the chance of actually growing out and identifying the organism (6; 7). Early-onset sepsis (EOS) is usually defined as sepsis that is diagnosed within 3 days of birth in the term infant and 7 days in the preterm infant (8). In addition, the causative organism of EOS should be tracked back to a maternal/perinatal source in order to meet the definition. Late onset sepsis (LOS) is often defined as the onset of sepsis from the 3-day or 7-day mark, depending on gestational age until 30 days of age (9). While late-onset sepsis is often associated with a hospital-acquired or nosocomial infection, it may also be from an organism acquired from a maternal source. For instance, Group B streptococcus (GBS) may be a causative bacteria for EOS as well as LOS. In either case, it may be acquired from the mother. Bizzarro et al(9) also identified a subset of infants who had the symptoms of sepsis from 30 days of age to 152 days. They referred to this group as the "late, late onset" group. Hornik et al (10) identify LOS as sepsis manifesting from 4 days of age to 120 days of age.

Risk Factors

Many studies have shown a higher risk of sepsis in the newborn of mothers who receive inadequate prenatal care or are members of a lower socioeconomic group, which may, in fact, be co-contributing factors. Women of lower socioeconomic groups are less likely to have access to adequate prenatal care. In addition, premature or prolonged rupture of membranes greater than 18 hours, substance abuse, chorioamnionitis, colonization of the maternal genital tract, presence of a urinary tract infection, antenatal antibiotic administration, and multiple gestation have been identified as maternal risk factors as well as eating contaminated food resulting in Listeria infection (10; 11; 12). Chorioamnionitis is difficult to diagnose prenatally and may be under or over-diagnosed. Chorioamnionitis is defined by the presence of an unexplained fever (greater than 38C), and at least one other sign, including purulent amniotic fluid, uterine

tenderness, maternal and/or fetal tachycardia or leukocytosis which is reported in 70-90% of cases (13). Chorioamnionitis may also be asymptomatic in the mother with diagnosis made at delivery or upon pathologic evaluation of the placenta. This is referred to as histological chorioamnionitis. Neonatal risk factors for sepsis include low birth weight, low gestational age (< 37 wks), prolonged antibiotic use, and use of invasive tubes/lines such as central catheters, endotracheal tubes, IV catheters, feeding tubes, and urinary catheters (9; 12). The observed higher risk of infection in lower gestational ages may be related to prolonged hospitalization and use of additional invasive devices.

Causative organisms for EOS and LOS differ and have changed somewhat over the years. The incidence of early onset GBS has fallen dramatically following maternal universal screening for GBS colonization and prenatal antibiotic administration (12). Eschereciacoli (e.coli) is now a common organism seen in EOS and is the leading cause of sepsis related mortality (11). With the increased use of antenatal antibiotics, some studies have found an increase in ampicillin resistant e. coli, particularly in the low birth weight infant. However, the rate of non-GBS EOS has remained unchanged in other studies (14). Overall, GBS and e. coli account for 70% of EOS cases (11).

Causative organisms in LOS vary somewhat by individual neonatal units. However, the most common organisms are from coagulase-negative staphylococci (CoNS) (15). CoNS is often seen as a non-pathogenic bacteria as it is colonized on the skin and therefore may be mistaken for contamination in a positive blood culture. Therefore, specific criteria for determining the validity of a positive blood culture are helpful (refer to septic work up section in this article). Staphylococcus aureus, e coli, GBS as well as Klebsiella and Pseudomonas are also common bacteria in LOS (12).

Signs of sepsis in the neonate

Many septic infants have non-specific signs of illness, particularly in the early stages. These non-specific signs include decreased activity or muscle tone, poor feeding, apnea/bradycardia or other respiratory symptoms (11). Because of this very non-specific presentation of sepsis, many more infants receive a septic evaluation and potentially, antibiotic treatment than are actually septic. Infants may also have negative lab indications for sepsis in the early stages, again, making it difficult to identify which infants should receive antibiotics and for how long. With more and more information available to indicate the adverse effects of antibiotic exposure, efforts to decrease the infant's exposure to antibiotics are important.

One sign of impending sepsis is heart rate variability or lack of variability. This concept is very comparable to loss of heart rate variability in the fetus prior to delivery that indicates distress. Several researchers have studied this phenomenon. Markers that are seen early in the course of sepsis are reduced heart rate variability and transient decelerations. Griffin et al (16) found that infants with these "high risk" heart rate characteristics were 5 to 6 times more likely to have sepsis, urinary tract infection or death within the next 24 hours. However, it should be noted that this is not diagnostic. The purpose of recognizing these characteristics are to evaluate further for sepsis. The loss of variability or transient decelerations occur in relation to the cytokine release associated with the onset of sepsis (17). This is also observed with urinary tract infections, in the absence of sepsis, with necrotizing enterocolitis with or without positive blood cultures, respiratory deterioration leading to intubation and after procedures in which anesthetics or anticholinergic medications are given (17). One encouraging aspect of using heart rate characteristics as an alerting signal is that it may provide a sign long before the infant becomes symptomatic in other ways such as the onset of apnea/bradycardia, changes in white cell counts or onset of glucose instability, thermoregulatory changes and respiratory deterioration (18). The difficulty is that heart rate characteristics are often transient until late in the clinical picture so difficult to recognize with usual clinical monitoring capabilities. In addition, this may provide an early warning sign in the presence of LOS but has not been studied in infants at risk for EOS. Ultimately, a high index of suspicion for sepsis is absolutely imperative. Evaluation of risk factors along with clinical signs and laboratory evaluation are more helpful than any alone.

Table 1. General Infection Prevention Measures

- Handwashing
- Equipment cleaning between patients or use of individual use equipment
- Regular incubator changing and cleaning
- Wipe-down of bed space each shift with disinfectant
- Adequate cleansing prior to skin puncture

Infection Prevention

Infection has been recognized as a major contributor to poor outcome in all ages of patients. Extended length of stay and mortality are often the resulting outcomes in the adult population. In the neonatal population, poor neurologic development or outcome can be added to that list. The neurologic system of the neonate is still developing, even for those born at term. For that reason, the neurologic system is at particular risk for damage and resulting poor outcome in the presence of other shorter term complications associated with sepsis such as hypoxia, persistent pulmonary hypertension, acidosis, hypo or hyperglycemia and others.There are four specific types of healthcare associated infections that are of particular study and interest in the adult population. These are central line associated blood stream infection (CLABSI), catheter-associated urinary tract infection (CAUTI), ventilator associated pneumonia (VAP) and surgical site infection (SSI) (19). Specific bundles have been developed to combat infection risk in each of these areas, again in the adult population. Work in the neonatal population has centered on prevention of CLABSI, VAP and SSI with CLABSI receiving the most effort. Central catheters are used commonly in the neonate providing more opportunity to evaluate the effectiveness of various measures to decrease the risk of infection.

Regardless of the portal of entry and in the absence of any of the device/risk factors, certain measures are known to be effective against infection (Table 1). Handwashing is known to be the most effective measure to prevent infection. In addition, some have investigated the additional advantage of universal gloving for patient contact (20; 21) in both the neonatal and adult populations. Harris, Pineles, Berlton et al (21) compared usual care to gown and glove care with the primary outcome of transmission of Methacillin Resistant Staphylococcus Aureus or Vancomycin Resistant Enterococcus. They found no difference in transmission of these organisms with these additional measures. Yin et al (20) studied several units in a children's hospital, including the Neonatal Intensive Care Unit

Table 2. Measures to Decrease Central Line Associated Blood Stream Infection

Catheter insertion:
1. Meet general infection prevention measures (table 1)
2. Dedicated team for placement and maintenance
2. All supplies required available at bedside before insertion
3. Maximalsterile barrierprecautions
4. Face mask worn by those within 3 feet of sterile field
5. Perform skin antisepsis with povodone-iodine or CHG

Catheter maintenance:
1. Daily assessment of catheter need
2. Dressing integrity and site cleanliness assessed daily. Change PRN.
3. Dressing change following sterile technique, if indicated.
4. of a closed system for infusion, blood draws, and medication administration
5. "Scrub the hub" prior to any catheter entry (15 seconds and allow to dry)
6. IV tubing change using sterile or aseptic technique

Adapted from: Wirtschafter et al, 2010, Schulman et al, 2011; Fisher et al, 2014.

(NICU). They already practiced universal gloving during the respiratory syncytial virus season and noticed a lower rate of infection during this time. They extended the universal gloving requirement to 12 months per year versus the previous 9 months per year and found a statistically significant decrease in hospital associated infection and CLABSI in the NICU. Actual monitored glove use rates were not reported. Kaufman, Blackman, Conaway & Sinkin (22) more recently published a randomized clinical trial in which nonsterile gloves were used in one group of patients and usual handwashing practices in another. This group showed a significantly lower rate of infections in the group of infants whose caretakers used gloving in addition to handwashing practices vs handwashing only. Larson, Cimiotti, Haas et al (23) compared isolates from clean hands to isolates from infected patients over a three year period. They found these isolates were significantly different, indicating that the infection did not come from the healthcare worker's hands. Controversies about universal gloving in the NICU include concerns about less actual hand hygiene, lack of skin to skin contact with neonates who experience a significant amount of input from tactile stimulation and the concern that parents believe this is necessary to protect their infant even after discharge. When practiced, universal gloving is usually done with clean and not sterile gloves. There are concerns that the gloves are not without some amount of bacteria themselves, sitting in an open box where multiple people access the gloves, hopefully with clean hands but certainly not sterile hands.

Specific bundles have been developed to target specific portals of entry. In the neonatal population, the CLABSI prevention bundle has been well-developed. Several collaboratives exist or have existed to examine the effect of various measures, implemented in a specific, systematic method that repeatedly resulted in a drop in CLABSI rates (24, 25, 26). Table 2 shows common measures implemented to decrease CLABSI in the NICU.

Other bundles have been developed for VAP and SSI prevention although these have not been as widely adopted or systematically implemented. Part of the difficulty with measuring outcomes is that the definition of VAP is very challenging in the neonate since many intubated infants also have lung disease that may progress to chronic lung disease that is very difficult to differentiate from pneumonia on x-ray. Therefore the Centers for Disease Control (CDC) definition of VAP which includes specific changes on x-ray is difficult to match to the clinical picture (27). Many measures from adult VAP bundles have been implemented in the neonate and most would not be harmful and may help, although some do increase cost such as changing out ambu bags daily (28) and having two suction set ups. Perhaps one of the measures that has received the most attention in the neonate is oral care. The adult recommendation is to perform regular oral care with an antiseptic solution (26). The issues of oral contamination are different in adults who have teeth, some may have periodontal disease and food sources of bacteria. Neonates are just becoming colonized in the NICU and it is important that the colonization occur in a natural manner with non-pathogenic bacteria to prevent colonization with pathogenic bacteria. Therefore, many are investigating the use of colostrum for oral care in neonates, both as a measure to prevent VAP but also to aid in the development of colonization of the gastrointestinal tract in a more normal manner, particularly for infants who are nothing per os (NPO) for a period of time after birth. Gephart & Weller (29) summarize the studies that have been performed but point out that the intervention of colostrum swabbing of the mouth is not consistently applied, monitored or reported in the studies. Certainly, it is known that the gastrointestinal tract of the infant is eventually colonized with organisms native to the mother's breast milk. These organisms are abundant in colostrum as well as containing other protective components. While it is, as yet, unknown if the administration of oral colostrum will prevent VAP, sepsis or necrotizing enterocolitis, it does not present a risk to the infant and may be advantageous (29). Table 3 shows elements of a VAP bundle developed for neonates although there is not yet adequate evidence to support the effectiveness of these in the neonatal population (30).

Surgical site prevention has not received much attention in the neonatal population but the risk of either surgical site infection or sepsis following surgery is a concern. In NICUs with high surgical procedures, this is certainly an important population. These infants are often in the NICU for a longer period of time than their gestational age equivalents without surgical needs. One measure to address concerns of infection is the administration of pre and post-operative antibiotics. The adult guidelines advise a single dose of antibiotics within 1 hour of the incision (19). In addition, specific antibiotics are recommended for specific procedures. It is not known if this timing is as important in the neonate as in the adult or if a different time interval is more important. However, it is known that prolonged antibiotic use without specific indications can be detrimental. In addition, the specific antibiotic that is best for which surgeries, if different, is not known. Thermoregulation and glycemic control are important measures in the neonate, even in the absence of stresses such as surgery. Hypothermia and hyperglycemia have been linked with increased infection risk in adults (19). It is unknown if this risk is the same in neonates but hypothermia and hypo/hyperglycemia are known to be detrimental to the neonate. Therefore, attention to these details should be increased during and after surgical procedures. The risk of hypothermia and hypo/hyperglycemia are particularly high due to the stress response during and after surgery as well as the surgical environment. Inadequate pain management contributes further to these complications. Romanelli, Anchieta et al (32) document the increased risk of blood stream infections in the neonatal surgical population, highlighting the need to pay particular attention to this population as well. In their study, non-invasive ventilation was protective for sepsis.

Other areas of potential concern as sources of infection in the neonate include maintaining skin health and integrity and proper management of gastric tubes. Recommendations for neonatal skin care can be found in the Neonatal Skin Care Guidelines available from the Association of Women's Health and Neonatal Nursing (33). Mehall, Kite, Saltzman et al (34), Matlow, Kitai, Kirpalani et al (35) and Hurrell, Kucerova, Loughlin et al (36) demonstrated the colonization of bacteria in neonatal gastric tubes in three different studies. Mehall, Kite, Saltzman et al (34) found tubes were heavily contaminated after 7 days of dwell time. Furthermore, feeding intolerance occurred in 24 of 32 patients whose feeding tubes were contaminated and none whose tubes were not contaminated. It is unknown from this study whether contamination may have occurred prior to 7 days as tubes were only cultured at 7 days. Hurrell, Kucerova, Loughlin et al (36) compared colonization of feeding tubes through which breast milk, breast milk with fortifier and formula were fed. Colonization was seen as early as 48 hours with organisms such as Enterobacteriaceae, S Marcescens and Kelbsiella pneumonia. These organisms were also associated with outbreaks. Matlow, Kitai, Kirpalani (35) showed colonization of the hub of the enteral tube with pathogenic organisms. These organisms were found on both the outside and inside of the feeding tube hub highlighting the importance of careful technique in the management of connections and disconnections to avoid introduction of pathogenic organisms. While no bundles have been developed to decrease this infection risk, there are several measures that just make sense. These include taking care when placing, connecting and disconnecting the tubes, and critically evaluating the need for an indwelling tube or limiting dwell time if left indwelling.

Laboratory Indications of Sepsis

The septic work up consists of several basic laboratory evaluations. The complete blood count (CBC) is an important evaluative indication of infection but not diagnostic. Indications of infection in the CBC include a low white blood cell count, low platelet count and high immature neutrophil count. The immature to total (I:T) neutrophil ratio of greater than 0.3 is an indication of infection. However an abnormal CBC may be helpful but a normal CBC does not rule out infection. The c-reactive protein (CRP) is a commonly evaluated marker of acute inflammation. It is non-specific to infection as it can be increased for other reasons as well, including meconium aspiration, hypoxic or traumatic tissue injury and other sources of stress resulting in an inflammatory response (37). It is most useful in a neonatal septic work up when measured serially. Since it takes 24 to 48 hours to rise and may not rise as dramatically in preterm infants, it is not a very helpful marker in determining the presence of infection (12). There are several other chemical markers that are being investigated to aid in a more accurate and earlier diagnosis of sepsis in the neonate. Procalcitonin, cytokines, including interleukin 6, interleukin 8,tumor necrosis factor, neutrophil CD64 and metabolomics as well as other markers such as cell surface markers and inter alpha inhibitor proteins have been studied in order to quickly and positively identify infants with sepsis (12, 38). All of these markers are elevated in the presence of inflammation. Some, such as the CRP can be elevated even when the source of the inflammation is not infection and others, such as neutrophil CD64 appear to provide a more positively predictive value, that is to say, identify infants who are likely to be infected (38). Procalcitonin and interleukin-6 have been studied in the cord blood. This could potentially provide a very early sign of EOS.

Table 3. Ventilator Associated Pneumonia Prevention Bundle Elements

- Meet general infection prevention measures (Table 1)
- Performance of daily assessments of readiness to wean
- Use of noninvasive ventilation whenever possible
- Keep ventilator circuit as closed system, including when suctioning and draining condensation
- Prevent unplanned extubation/reintubation
- Change ventilator circuit only when visibly soiled or malfunctioning
- Avoid gastric over-distention
- Maintain separate suction canisters and tubing for endotracheal tube and oral suctioning
- Suction catheters as single-use (with the exception of closed ET suction catheters)
- Oral care with human milk or sterile water (if no human milk available) every 3-4 hours
- Elevate head of bed 15-30 degrees

Adapted from: Ceballos et al, 2013; Smulders et al, 2013.

Steinberger, Hofer and Resch (41) found the two markers together to be very sensitive and specific in predicting infants who had EOS. Procalcitonin was shown to have a very high negative predictability, in other words, it was very likely that infants were identified who were unlikely to be septic but the positive predictive value was reported at about the same level as CRP (39, 40) Procalcitonin, cytokines and other markers show promise in predicting sepsis and some studies have shown greater accuracy in prediction of LOS (41). Even so, further studies are needed to determine what combination of markers may be most predictable and at what time point.

The gold standard for a diagnosis of sepsis is a positive blood culture. However, this is often not achieved in cases of symptomatic neonatal sepsis. Infants may have lab values indicating sepsis such as a decreased white count, elevated I:T ratio and elevated CRP, along with other physical signs such as a deterioration in respiratory status and yet, the blood culture is negative. This may be related to the low bacterial colony count often found in neonates (7). In about 75% of neonates, the colony count in the presence of sepsis is higher than in adults. For this reason and the concern of blood loss, low volume (0.5 ml) blood cultures have been the traditional practice. As has been discovered more recently, there are a significant number of septic infants who have a low colony count bacteremia. In this population, the low volume blood culture results in a false negative blood culture which leads to difficulty in decision making about treatment with antibiotics. In addition, two blood cultures from two sites are recommended to provide additional information about possible contamination. Organisms that may be responsible for LOS may also be contaminants. Two blood cultures performed meticulously in which both grow out the same organism provides reassurance that the bacteria is indeed the source of the sepsis. In this manner, antibiotics can be adjusted specifically to target the source of the infection.

Blood cultures from infants with high bacterial colony counts will grow more rapidly. These infants are also often more symptomatic. Most blood cultures become positive within 48 hrs if they are indeed positive (11). A negative blood culture at 48 hours, along with absence of other markers of sepsis like specific markers of the CBC and serially elevated CRP levels may be reassuring in stopping antibiotics earlier in some infants. However, in severe cases, the blood culture may become positive within a few hours. So while a definitive determination

of the specific bacteria may not be available until 5 days, there are often markers that can be used to indicate the presence or absence of infection, the category of bacteria involved and along with other markers can be used to target specific antibiotics. This information is helpful in antibiotic stewardship efforts.

Cerebral spinal fluid (CSF) evaluations are recommended as part of the septic work up in certain circumstances. Infants who have risk factors for sepsis but appear healthy may not benefit from performance of a lumbar puncture (11). Meningitis occurs in about 23% of infants with a positive blood culture, a level higher than previously believed (43). In addition, Garges, Moody, Cotten et al (44) found that 38% of infants with a negative blood culture had meningitis. So, while the performance of routine lumbar punctures as part of the septic work-up remains controversial, it is also recognized as an important piece of evidence to aid in selection of antibiotic type and length of treatment. The CSF cultures may be negative within hours of starting antibiotics and values are difficult to interpret in the presence of maternal antibiotics given prenatally. Garges, Moody, Cotten et al (44) studied CSF results that may be indicative of infection in infants ≥34 weeks gestation and found that meningitis can occur in the presence of normal CSF glucose, protein and white cell count. The only indication of meningitis in their study was a positive CSF culture. This was a retrospective study and also performed in term and late preterm infants so has some limitations but offers valuable information as well. Others found that CSF values may be less predictable in VLBW infants (11).

Management of Infection

The most basic management of sepsis is the administration of antibiotics. However, the challenge of resistant organisms and other risks of antibiotic overuse must be balanced with treating infections early and adequately. Frequent and early antibiotic administration came about in the days of rapid onset GBS. Since the onset of GBS sepsis can be so rapid and devastating, infants were often given antibiotics for a longer time and with only risk factors or soft signs of infection. More recent studies have shown an increased risk of growth of resistant organisms, onset of candidiasis and increased risk of morbidity and mortality with overtreatment with antibiotics (45). Neonates must become colonized with normal flora bacteria which helps fight off pathogenic bacteria. If antibiotics are administered, the normal flora bacteria are decreased in diversity and number, potentially allowing pathogenic bacteria to proliferate, resulting in an increased risk of late onset infection. In the Neonatal Research Network, affiliated with the National Institute of Child Health and Human Development, it was found that infants with more than 10 days of exposure to antibiotics had a 3-fold increase in risk of necrotizing enterocolitis (NEC) and each additional day of antibiotics increased the risk of NEC by about 20% (46).

Therefore, careful attention to which antibiotics are most effective against the specific causative bacteria, limiting extended antibiotic dosing to cases of confirmed sepsis and limiting the length of antibiotic exposure, particularly when ruling out sepsis or infection are important steps in antibiotic stewardship. Specifically, the symptomatic infant with abnormal neutrophil dynamics in the white blood cell count and the presence of risk factors indicate the need for antibiotic coverage as well as infants with respiratory distress and other positive risk factors. However, once initial blood culture results are available, consideration of limiting antibiotic administration is also important. The latest recommendations of the American Academy of Pediatrics Committee of the Fetus and Newborn (45) recommend that antibiotics be discontinued within 48 hours in situations where the probability of sepsis is low. Other situations where antibiotic limitation should be considered are around surgical procedures or other invasive procedures where no infection is present but the risk may be increased.

Specific antibiotics should be chosen once positive blood culture results are available. Ampicillin and gentamicin are common broad spectrum antibiotics used for EOS. These are optimal choices as they are effective against e.coli and GBS, the most common bacteria in EOS (11). Third generation antibiotics, specifically a cephalosporin such as Cefotaxime may be an alternative to an aminoglycoside such as Gentamicin. However, there is both an increase in the risk of resistant organisms and invasive candidiasis (47). A cephalosporin may be preferred in the presence of confirmed or suspected meningitis due to its ability to penetrate the CSF. For LOS, vancomycin is often preferred since the primary class of organism is CoNS which is sensitive to vancomycin. In addition, an awareness of the specific antibiogram for the hospital as well as the NICU helps in narrowing antibiotic choices in LOS even before final blood culture results are available.

Decisions about length of antibiotic treatment are important in avoiding consequences of over-exposure to antibiotics as well. In the scenario of low probability infection or what is commonly referred to as "rule out" sepsis it is usually recommended that antibiotics be discontinued by 48 hours when a preliminary blood culture result and serial CBC and CRP evaluations are available. In situations where sepsis has been culture proven, it is recommended that the infant be treated for 10 days (48). In the presence of meningitis, treatment may continue for 14 or 21 days, depending on the organism involved (45).

Conclusion

Sepsis remains a concerning and all too common complication of prematurity, both in the beginning of life and later, during the NICU stay. Various measures to decrease the risk are known to be effective but not to eradicate the possibility of infection completely. Therefore, one must be alert to the earliest signs of sepsis. Certain diagnostic measures are helpful in identifying infants who are septic but the value of keen observation cannot be overstated. Finally, quick and definitive treatment for infants who are septic is important while also ensuring that risk is not increased by over-exposure to antibiotics.

References

1. Budin, P. The nursling: The feeding and hygiene of premature & full-term infants. 1907. The Caxton Publishing Company: London. Available at: http://babel.hathitrust.org/cgi/pt?q1=infection;id=uc1.b5242429;view=1up;seq=152;start=1;sz=10;page=search;num=54#view=1up;seq=154
2. Weston, Pondo, Lewis, et al. The burden of invasive early-onset neonatal sepsis in the united States. 2005-2008. Pediatric Infectious Disease journal. 2011;30:937-941.
3. Camacho-Gonzalez A, Spearman PW, Stoll BJ. Neonatal infectious diseases: evaluation of neonatal sepsis. PediatrClin North Am 2013; 60:367- 89.
4. Hyun Jeon J, Namgung R, Park MS, Park KI, Lee C. Positive maternal C-Reactive Protein predicts neonatal sepsis. Yonsei Med J. 2014;55(1):113-117.
5. Tita AT, Andrews WW. 2010. Diagnosis and management of clinicalchorioamnionitis. Clin.Perinatol.37:339–354.

6. Schelonka RL, Chai MK, Yoder BA, Hensley D, Brockett RM,Ascher DP. 1996. Volume of blood required to detect common neonatalpathogens. J. Pediatr. 129:275–278.
7. Connell TG, Rele M, Cowley D, Buttery JP, Curtis N. How reliable is a negative blood culture result? Volume of blood submitted for culture in routine practice in a children's hospital. Pediatrics. 2007;119:891–896.
8. Bedford Russell AR. Neonatal sepsis. Paediatrics and Child Health. 2010;21(6):265-269.
9. Bizzarro MJ, Dembry LM, Baltimore RS, Gallagher PG. Changing patterns in neonatal Escherichia coli sepsis and ampicillin resistance in the era of intrapartum antibiotic prophylaxis. Pediatrics. 2008;121:689–696.
10. Hornik CP, Fort P, Clark RH, Watt K, Benjamin DK, Jr, Smith PB,Manzoni P, Jacqz-Aigrain E, Kaguelidou F, Cohen-Wolkowiez M.2012. Early and late onset sepsis in very-low-birth-weight infants from alarge group of neonatal intensive care units.Early Hum. Dev. 88:S69–S74.
11. Simonsen KA, Anderson-Berry AL, Delair SF, Davies HD. Early-onset sepsis. ClinMicrobiol Rev. 2014;27(1):21-47.
12. Shah BA, Padbury JF. Neonatal sepsis: An old problem with new insights. Virulence. 2014;5(1):170-178.
13. Martinelli P, Sarno L, Maruotti GM, Paludetto R. Chorioamnionitis and prematurity: a critical review. The Journal of Maternal-Fetal and Neonatal Medicine, 2012; 25(S4): 29–31.
14. Shane AL, Stoll BJ. Neonatal sepsis: Progress towards improved outcomes. Journal of Infection. 2014;68:S24-S32.
15. Dong Y, Speer CP. Late-onset neonatal sepsis: Recent developments. Arch Dis Child Fetal Neonatal Ed. 2014;0:F1-F7.
16. Griffin, Lake, Bissonette, Harrell, O'Shea & Moorman. 2005. Heart rate characteristics: Novel physiomarkers that predict neonatal infection and death.Pediatrics. 116(5): 1070-1074.
17. Sullivan BA, Grice SM, Lake DE, Moorman JR, Fairchild KD. Infection and other clinical correlates of abnormal heart rate characteristics in preterm infants. The Journal of Pediatrics. 2014;164:775-780.
18. Fairchild & O'Shea. 2010. Heart rate characteristics: Physiomarkers for detection of late-onset neonatal sepsis, Clinics in Perinatology. 37(3):581-598
19. http://www.cdc.gov/hai/ Accessed 12/20/14
20. Yin J, Schweizer ML, Herwaldt LA, Pottinger JM, Perencevich EN. Benefits of universal gloving on hospital-acquired infections in acute care pediatric units. Pediatrics. 2013;131(5):e1515-20. Epub 2013 Apr 22.
21. Harris AD, Pineles L, Berlton B, Johnson JK, Shardell M, Loeb M et al. Universal glove and gown use and acquisition of antibiotic-resistant bacteria in the ICU: a randomized trial. Benefits of Universal Glove and Gown (BUGG) JAMA. 2013 Oct 16;310(15):1571-80.
22. Kaufman DA, Blackman A, Conaway MR, Sinkin RA. Nonsterile glove use in addition to hand hygiene to prevent late-onset infection in preterm infants randomized clinical trial. JAMA Pediatrics. 2014;168(10):909-916.
23. Larson, Cimiotti, Haas, Nesin, Allen. Gram-negative bacilli associated with catheter-associated and non-catheter-associated bloodstream infections and hand carriage by healthcare workers in neonatal intensive care units. Pediatric Critical Care Medicine. 2005. 6(4):457-61.
24. Fisher D, Cochran KM, Provost LP, Patterson J, Bristol T, Metzguer K, Smith B, Testoni D, McCaffrey MJ. Reducing central line-associated bloodstream infections in North Carolina NICUs. Pediatrics. 2013 Dec;132(6):e1664-71.
25. Schulman J, Stricof R, Stevens TP, Horgan M, Gase K, Holzman IR et al. Statewide NICU central-l ine-associated bloodstream infection rates decline after bundles and checklists. Pediatrics. 2011;127:436-444.
26. Wirtschafter DD, Pettit J, Kurtin P, Dalsey M, Chance K, Morrow HW, et al. A statewide quality improvement collaborative to reduce neonatal central line-associated blood stream infections. Journal of Perinatology. 2010;30:170–181.
27. Coffin SE, Klompas M, Classen D, Arias KM, Podgorny K, Anderson DJ, et al. Strategies to Prevent Ventilator?Associated Pneumonia in Acute Care Hospitals. Infection Control and Hospital Epidemiology, 29:S1, A Compendium of Strategies to Prevent Healthcare?Associated Infections in Acute Care Hospitals (October 2008), pp. S31-S40. Published by: The University of Chicago Press on behalf of The Society for Healthcare Epidemiology of America.
28. Van Der Zwet WC, Parlevliet GA, Savelkoul PH et al. (2000). Outbreak of bacillus cereus infections in a neonatal intensive care unit traced to balloons used in manual ventilation. J Clin Microbil 38; 4131-4136.
29. Gephart SM, Weller M. Colostrum as oral immune therapy to promote neonatal health. Advances in Neonatal Care. 2014;14(1):44-51.
30. Smulders CA, van Gestel JPJ, Bos AP. Are central line bundles and ventilator bundles effective in critically ill neonates and children? Intensive Care Med (2013) 39:1352–1358.
31. Ceballos K, Waterman K, Hulett T, Makic MBF. Nurse-Driven Quality Improvement Interventions to Reduce Hospital-Acquired Infection in the NICU. Advances in Neonatal Care. 2013;13(3):154-163.
32. Romanelli RMdC, Anchieta LM, Carvalho, EAdA, Silva LFdGe, Nunes RVP, Mourao PM et al. Risk factors for laboratory-confirmed bloodstream infections in neonates undergoing surgical procedures. The Brazilian Journal of Infectious Disease. 2014;18(4):400-405.
33. Association of Women's Health Obstetric and Neonatal Nursing. Neonatal Skin Care. (3rded). 2013. AWHONN:Washington D.C.
34. Mehall JR, Kite CA, Saltzman DA, Wallett T, Jackson RJ, Smith S. Prospective study of the incidence and complications of bacterial contamination of enteral feeding in neonates. J Pediatr Surg. 2002;37:1177-1182.
35. Matlow, A.G., Kitai, I., Kirpalani, H., Chapmen, N.H., Corey, M., Perlman, M., Pencharz, P., Jewell, S., Phillips-Gordon, C., Summerbell, R., Ford-Jones, E.L. (1999). A randomized trial of 72-versus 24-hour intravenous tubing set changes in newborns receiving lipid therapy. Infection Control and Hospital Epidemiology, 20(6): 487-493.
36. Hurrell E, Kucerova E, Loughlin M, Caubilla-Barron J, Hilton A, Armstrong R, et al. Neonatal infectious feeding tubes as loci for colonization by members of the Enterobacteriaceae. BMC Infectious Diseases 2009, 9:146-154.
37. Hofer N, Zacharias E, Müller W, Resch B. An update on the use of C-reactive protein in early onset neonatal sepsis: current insights and new tasks. Neonatology 2012; 102:25-36.
38. Elawady S, Botros SK, Sorour AE, Ghany EA, Elbatran G, Ali R. Neutrophil CD64 as a diagnostic marker of sepsis in neonates. J Investig Med. 2014 Mar;62(3):644-9.
39. Lencot S, Cabaret B, Sauvage G, Laurans C, Orsonneau JL, Caillon J et al. A new procalcitonin cord-based algorithm in early-onset neonatal infection: for a change of paradigm. Eur J ClinMicrobiol Infect Dis.2014 Jul;33(7):1229-38. Epub2014
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Quality and Safety Indicators for Human Milk and Donor Milk Use in the NICU

Elena Taggart Medo

The chronic shortage of donor milk has triggered widespread rationing to such a degree that many preterm babies are now being denied access because they don't fit into the narrow definition of babies who "qualify". Mounting evidence of short and long term improved outcomes has prompted more neonatal units to use donor milk when mother's milk supply is short or unavailable.[1] While they are unable to meet the growing demand, community milk banks are asking legislators to create new laws that could very well violate anti-trust rules. These new laws would attempt to prevent mothers from sharing their milk outside the tax exempt milk banking system while refusing to acknowledge the legitimate role of commercial milk banks. In an attempt to maintain a steady supply, hospitals are now forced to place numerous small orders at multiple milk banks across the country. Even so, they often receive only a fraction of what they ordered. In the desperate race to procure human milk, the question of quality and safety is not given sufficient scrutiny.

To further complicate things, hospital staff are challenged when trying to assess the quality and safety of donor milk because very little information is being provided by most milk banks. Many milk banks fail to provide a nutritional label, instead labeling their donor milk as "preemie milk" or "mature milk" although there is no legal definition for either label claim and many of the milk banks have different definitions for those same terms. Some milk banks test the raw milk before processing and others bypass microbiological testing before processing, choosing to test after thermal treatment and taking the risk of heat stable toxins remaining. Even after Holder pasteurization, 50% of pathogens remain according to a Brazilian study.[2] Most milk banks fail to test for adulteration and instead, rely on the honor system and self-exclusion by donors to safeguard recipient babies from potential drug or alcohol exposure.

In its purest form human milk is truly remarkable and potentially lifesaving, but it is not magic. It can become contaminated from various sources, 1) either from within the breast through maternal infectious disease or exposure to drugs or alcohol, 2) as it is being pumped through exposure to biofilms on pump kits or collection bottles, 3) if it is stored or held at unsafe temperatures and, 4) if it is not screened for bacterial contamination prior to processing.[2] At a minimum, human milk is a food and like all foods, the quality of the raw food is the best indicator of the quality of the processed food.

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When the source of breast milk moves farther away from a healthy mother nursing her own healthy baby, things begin to get more complicated. The increased use of breast milk, especially for immune compromised neonates, calls for a higher standard than the status quo.[3]

As hospital staff and risk managers review practices, it is important to ask appropriate questions relevant to the source of the donor milk.

Mother's Own Milk: Clearly the best option, mother's own milk, pumped and stored, still carries an element of risk. Knowing the risk allows hospitals to better manage the risk.

Questions to consider:

1. Is the mother non-infectious, drug and alcohol free? Should mother's milk be subject to quality or safety testing by the hospital and is the hospital liable for harm to the baby if the milk is not tested?
2. Have the mothers in your NICU been counseled on the risks of bringing milk from other women into the NICU to feed their babies? Has your hospital considered developing a qualification program to allow this practice, especially when mother is unable to provide fresh breast milk or when mother is deceased and the community wishes to help?
3. Mother's own milk falls short of the protein and minerals needed to sustain growth for very low birth-weight preterm infants. How is the baseline of protein in mother's milk measured in your unit? Protein levels range from .8 g/dL to 2.8 g/dL. Are you using an average value to calculate fortification? What form of fortification should be used with mother's milk? Is the fortifier commercially sterile? If not, what is the allowable bio-burden and what pathogens are tested?
4. How often should the pump collection kit be cleaned? By what method? Is there a protocol to reduce the risk of biofilm formation on pumps and collection kits similar to those on ventilator tubes? How often are the NICU pumps tested for contamination?
5. How is mother's milk handled in the NICU? Are there evidence based protocols to support your practice?

Donor Breast Milk: Raw milk provided by healthy, qualified donors and tested prior to processing to assure bacteriological safety, purity and nutritional quality provides the second best option for feeding preterm infants. Optimally, donor milk should always be combined with any amount of mother's milk available

since each mL of mother's own milk contains approximately 1.2 million immune cells.[4]

Questions to ask your donor milk vendor:

1. What is the process for donor screening? How recently has the blood been tested? How is the donor's blood screened and for what diseases? How often are the donors re-tested? Do the blood test results come directly from the lab?
2. What testing is conducted on the raw milk to determine whether it is fit for human consumption? Thermal processing cannot make up for high bacterial counts in raw milk or prevent the potential for heat stable toxins remaining after thermal treatment. What microbiological testing is done prior to processing and what are the milk bank's allowable limits for each pathogen? How is the milk bank testing for spores which are difficult to culture?
3. What method is used to thaw the milk? Controlled temperature? Room temperature? Ask for evidence of validation for this method to show how elevated colonies of bacteria, yeast or mold, are prevented especially if the starting bio-burden is unknown.
4. How large is the production lot? How many donors in each lot? If only 2-3 donors, levels of major nutrients may be low. A recent study illustrated that the variation in the amount and composition of human milk oligosaccharides in donor milk processed by a community milk bank was significantly lower than mother's own milk.[5]
5. What thermal process is used to heat treat the donor milk? What is the total time that the donor milk is subjected to elevated heat including the time it takes to come up to temperature, the hold time and the cool down time? What are the major nutrient values pre and post processing? How is protein quality assessed? Rather than relying on generic data, specific data should be provided by each individual milk bank, based on analysis of their commercially available donor milk.
6. Is the thermal processing method validated or approved by any State or Federal entity? What is the demonstrated log kill? Holder pasteurization does not eradicate the spores of b. cereus, a heat resistant pathogen that can also produce toxins. With this in mind, what is the milk bank's strategy to reduce the risk of b. cereus contamination?[6]
7. Is the processed donor milk commercially sterile? If not, how can you assess risk if there are spores or heat stable toxins remaining?
8. Has your hospital (including risk management) visited the milk bank to inspect their processes, protocols and laboratory results?
9. Is there a nutritional value indicator that can be used to establish the baseline of quality expected for donor milk (levels of total and true protein, fat, lactose and total calories.)
10. If claims of biologically active components are being made, does the milk bank possess data to support such claims?

The use of donor milk is growing rapidly, especially with high risk preterm infants. Small milk banks that previously served only a few full terms babies in the past are now supplying donor milk to intensive care units in many states. Given the lack of consistent quality and safety standards, hospitals must begin to demand transparency and the detailed information needed to qualify vendors of donor milk products, regardless of whether they are commercial processors or tax exempt community milk banks.

References

1 More hospital NICUs moving to 100% human milk, http://www.chron.com/disp/story.mpl/metropolitan/7697313.html

2 Microbiological quality of human milk from a Brazilian milk bank, Álvaro B Serafini, Maria Cláudia D P B André, Márcia A, et al, Departamento de Microbiologia, Imunologia, Parasitologia e Patologia do Instituto de Patologia. Tropical e Saúde Pública da Universidade Federal de Goiás. Goiânia, GO, Brazil, Rev Saúde Pública 2003; 37(6), www.fsp.usp.br/rsp Serafini AB et al, Revista de Saúde Pública, ISSN 0034-8910 versão impressa. Rev Saúde Pública 2003; 37(6)

3 http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/PediatricAdvisoryCommittee/UCM235629.pdf

4 http://lactationnarration.com/index.php/2012/02/how-many-cells-are-in-your-breast-milk/

5 Human Milk Oligosaccharides In Banked Donor Milk Compared To Mother's Milk In The NICU, Carolin Marx, Renee Bridge, Alison Wolf, Wade Rich, Jae H Kim and Lars Bode. University of California, San Diego, San Diego, CA. (The FASEB Journal. 2012;26:625.2) © 2012 FASEB, 625.2

6 Landers, S Updegrove, K. Bacteriological Screening of Donor Human Milk Before and After Holder Pasteurization, BREASTFEEDING MEDICINE, Volume 5, Number 3, 2010, [a] Mary Ann Liebert, Inc., DOI: 10.1089=bfm.2009.0032.

7 Donor Human Milk Bank Data Collection in North America, An Assessment of Current Status and Future Needs, ,Elizabeth A. Brownell, MA, PhD, Mary M. Lussier, RN, BSN, IBCLC, Victor C. Herson, MD, James I. Hagadorn, MD, MS, Kathleen A. Marinelli, MD, IBCLC, FABM, FAAP, J of Human Lactation, October 28, 2013.

Truly Genetic Sonogram: Computer Assisted Detection of Fetal Syndromes and Abnormalities — Perestroika in Prenatal Diagnosis

BM Petrikovsky, MD, PhD

Currently, comprehensive sonograms, also referred to as level-2 sonograms, are routinely performed between the 16th and 21st weeks of pregnancy. [1] This ultrasound examination is also called an anomaly scan. The first ultrasound examination during pregnancy is done between the 11th and 13th weeks of gestation in conjunction with maternal blood screening for chromosomal abnormalities. The detection rate of chromosomal abnormalities, in particular, trisomy 21, 13 and 18, approaches 90%, especially when combined with biochemical screening. Most experienced sonographers however can identify major chromosomal abnormalities based on a thorough ultrasound examination alone. [2] In the review of our ultrasound practice, outcomes over a five-year period, all 48 fetuses with trisomy 13 or 18 were correctly identified based on an ultrasound examination alone. In addition, 112 out of 134 fetuses with trisomy 21 were diagnosed through this process. Sonographic markers, which include enlarged nuchal fold, vetriculomegaly, choroid plexus cists, pyelectasis, echogenic bowel, shortened long bones, hypoplasia of the mid phalanx of the fifth finger, hiatus between the first and second toe, absent breast buds and enlarged iliac wing angles, are very helpful in identifying affected fetuses. [1,2]

This paper seeks to share our experience with a computer-assisted program, which was used to identify abnormal fetuses using an international computer database. This technique is similar to software that identifies a criminal by comparing a fingerprint found at a crime scene to many millions saved in a database. We used a similar system. The software works by overlapping various sonographic features of fetuses we are studying over analogous features from the database containing various genetic abnormalities and other fetal syndromes. The newly developed program includes three steps:

Step one: obtaining the necessary images.
Step two: overlapping the images of the fetus over the analogous features from the computer database.
Step three: identifying abnormal fetuses and making the appropriate diagnosis.

The main focus of the investigation concentrates on the fetal face, since extra-cranial abnormalities (including: dilated renal pelvises, echogenic foci in the heart, short bones etc.) are much easier to identify. Lately, the fetal face has become the focus of a growing number of studies. [3-5] Facial malformations are present in more than 250 fetal syndromes with serious clinical implications. [6] Several techniques can be employed in automated facial feature analysis. The traditional and most common approach is to extract surface data (typically, polygon mesh surface representation). This technology has become more tenable as the equipment to collect the images has become less expensive, faster, and more portable. Initially, the affected and control fetal faces were aligned so that corresponding features across different faces could be easily identified and compared. An initial set of features was computed using geometric feature commutation algorithms and simple statistical evaluation. Pattern recognition and machine learning algorithms were then applied to the initial feature set to generate the optimal diagnostic signs and classifiers that best discriminated the affected and control faces. The alignment defined the correspondence of facial features on different faces by mapping a face on the. The basic idea of the alignment algorithm is to gradually adjust the orientation and position of the face data set so as to minimize the total distance between the face dataset and the template face period. The morphed face served as an intermediate step in building a feature – preserving correspondence between points across different faces. This alignment process builds a correspondence function that mapped a vertex on the template face to a point on an aligned one. This allows us to define features (e.g. regions) on the template face, which could then be automatically mapped to all other face datasets. Planes and targets of facial synography are as follows.

Facial planes required for computer assisted genetic sonogram:

Section plane	Facial structures
Midsagittal	Forehead Nasal bones and soft tissues Upper lip Hard palate Tongue Inferior lip Chin
Parasagittal	Maxilla Upper lip Nasal base and nares Mandible Ears

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Transverse	Orbits Malar arches Maxilla Upper lip Hard palate Superior dental arcade Tongue Inferior lip Mandible
Coronal	Anterior mouth-nose view Orbits Hard palate Retropalatine region

In paying attention to various parts of the face, we concentrate, first, on the fetal tongue and ears. An excellent review of fetal tongue abnormalities was put together by K. Nicolaides at al [5] who wrote "antenatally, an enlarged tongue protruding though an open mouth can be demonstrated in the midsagital view of the face. In our study, a specific search for this feature was undertaken especially in those cases…suggestive of trisomy 21 and the Beckwith-Wiedemann syndrome; microglossia was diagnosed in 50% of the cases. It is possible that in these conditions there is a progressive enlargement of the tongue with advancing gestation to account for the higher incident of microglossia at birth."

Comments

Aneuploidy screening with serum analytes and nuchal translucency measurements has greatly increased the detection of chromosomal abnormalities. Non-invasive prenatal testing using cell-free DNA has the ability to detect trisomy 21 with 99% certainty and with a false positive rate of 0.15% or less. [8-11] Many doctors use non-invasive prenatal testing as a secondary screening for women at high risk. Current screening algorithms target trisomies 18 and 21. However, trisomy 21 accounts for only 50% of prenatal aneuploidies, whereas trisomy 13, 18 and 21 together comprise two thirds. [12, 14] In view of the above, we believe that the entire approach to prenatal diagnosis should be different and should consist of universal non-invasive screening in the first trimester using free-cell DNA followed by a genetic sonogram at 16/18 weeks using the computer database. Abnormal genetic sonographic results should be followed by an invasive prenatal test if the prospective parent seeks a diagnosis with 100% certainty.

References

1 Fetal Disorders; Diagnosis and Therapy. In Maternal-Fetal Medicine principles and Practice. Creasy R, Resnik R (ED). Saunders 6th ed. 2009, chapter 17.
2 Petrikovsky BM Fetal Disorders. Wiley-Liss reprint 2014.
3 Anderson C, Matias A, Merz E. Fetal face: The whole picture ultrasound in Med 2012, 33: 431-40
4 Norton ME, Jelliffe-Pawlowski LL, Currier R. Chromosome abnormalities detected by current prenatal screening and noninvasive prenatal testing Obstet Gynecol 2014; 124: 979-86
5 Nicolaides KH, Salvesen DR, Snijders RSM, Gosden GM. Fetal facial defects. Fetal Diagn Ther 1993; 8, 1-9.
6 Benacerra F B. R. Ultrasound of Fetal Syndromes. Churchill Livingstone NY, 2004, 2nd edition.
7 Fang S, McLaughlin J, Fang J, et al. Automated diagnosis of fetal alcohol syndrome using 3D facial image analysis. Orthod Craniofac RES OCR. 2008, 11 (3), 162-171
8 Bianchi DW, Platt LD, Goldberg JD, Abuhamad AZ, Sehnert AJ, Rava RP, et al. Genome-wide fetal aneuploidy detection by maternal plasma DNA sequencing. Obstet Gynecol 2012; 120: 957
9 Ashoor G, Syngelaki A, Wagner M, Birdir C, Nicolaides KH. Chromosome-selective sequencing of maternal plasma cell-free DNA for first-trimester detection of trisomy 21 and trisomy 18. Am J Obstet Gynecol 2012; 206: 322.el-5
10 Sparks AB, Struble CA, Wang ET, Song K, Oliphant A. Noninvasive prenatal detection and selective analysis of cell-free DNA obtained from maternal blood; evaluation for trisomy 21 and trisomy 18. Am J Obstet Gyecol 2012; 206:319. el-9.
11 Norton ME, Brar H, Weiss J, Karimi A, Laurent LC, Caughey AB. Non-invasive Chromosome Evaluation (NICE) Study: results of a multicenter prospective cohort study for detection of fetal trisomy 21 and trisomy 18. Am J Obstet Gyecol 2012;207:137.el-8.
12 Alamillo CM, Krantz D, Evans M, Fiddler M, Pergament E. Nearly a third of abnormalities found after first-trimester screening are different than expected: 10-year experience from single center. Prenatal Diagn 2013;33:251-6.
13 Wellesley D, Dolk H, Boyd PA, Greenlees R, Haeusler M, Nelen V. Rare chromosome abnormalities, prevalence and prenatal diagnosis rates from population-based congenital anomaly registers in Europe. Eur J Hum Genet 2012;20:521-6.
14 Petrikovsky BM, Hallahan TW, Macri JN, First Trimester Aneuploidy Screening. Female Patient 1999, 24;41-49.

Skin to Skin Contact in the O.R. Between Partners and Newborns: No-Cost and Low-Technology

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Abstract

Purpose: To examine [1] if partners who attend their partners' Cesarean sections in the operating room (O.R.) and experience skin-to-skin contact (SSC) with the newborns have increased relational rating on partner-child bonding, and [2] if the newborns display somatic stability compared to pre-intervention.

Data Sources: This mixed methods translational research inquiry used three data sources: infant axillary temperatures pre- and post-intervention; infant crying times in minutes/seconds pre-, intra-, and post-intervention; and partners' reflections on the intervention. All were measured in a sample of 30 partners and 30 newborns.

Conclusions: Temperature stabilization/normalization was statistically significant using a local temperature policy range, but not significant using a national range. Infant crying times were significantly reduced by the intervention, including an effect on crying time during the post-intervention observation period. These findings were the same for infants of both majority and minority race mothers. Finally, maternal partners expressed increased satisfaction with their SSC experience.

Implications for Practice: This no-cost early intervention for families increases partner satisfaction, establishes positive relational ratings between partners and newborns, and offers somatic benefits to the infants. Healthcare systems could implement this immediately as a low-technology and low-risk evidence-based improvement without increasing delivery room costs.

Introduction

Beginning in 2008, a global economic recession deepened the financial crisis in the U.S., leading to escalating joblessness, poverty, and homelessness. Scarcity of resources placed more parents and their newborns at risk (Kirmeyer & Hamilton, 2011; Mishel & Shierholz, 2013; U.S. Department of Commerce, 2011). Meanwhile, fiscal pressure increased in American healthcare delivery systems, where competition for treatment dollars was rigorous. The financial basis of stressors threatening parents and their infants was widely acknowledged. However, few means beyond the Patient Protection and Affordable Care Act of 2010 emerged to effectively combine the need for reducing health care costs with improvements in the support of families with newborns (Obamacare Facts, n.d.).

Nonetheless, the demographics of motherhood have undergone several positive changes in the past decade. There has been a reduction in teenage births. There have been increases in the number of mothers age 25 or older as well as those with some college education before their first delivery. These developments decrease economic risks (Livingston & Cohn, 2010).

Still, most families with newborn infants can be characterized as young, simply due to the biologic age limits of child-bearing, and not always adequately educated for the harsh realities of the current job market. Families with newborns also tend to live in rented apartments or other temporary housing and thus face a heightened risk of housing loss. These parents experience a peak need for income as their family is enlarging, while wages may stagnate or worsen owing to the recent trends of the U.S. economy (Mishel & Shierholz, 2013). This fiscal background led to a search for no-cost, low-technology methods to decrease risks for newborns born into families bearing the brunt of the recession.

Purpose

The purposes of this translational research study were to determine if [1] partners who attended their partners' Cesarean sections (CS) and experienced skin-to-skin contact (SSC) with the infants for a minimum of ten minutes, within two hours post-operatively, had improved relational rating on partner-child bonding, compared to the partners' reported feelings of relation pre-birth and pre-intervention and [2] if the infants would display somatic stability (stable axillary temperatures, decreased crying intra- or post- intervention), compared to the infants' axillary temperatures and minutes of crying observed pre-intervention.

A secondary consideration was to ascertain if the SSC experiences of minority races was similar to those of majority race families and their newborns. This sample of partners and newborns were in inner-city hospitals, with geographic locations where many, if not most, families experience higher socioeconomic risks. The principal investigator (PI) theorized SSC as a no-cost method for healthcare organizations to increase support of early relational attachment in families experiencing increased risks due to the economic recession's effect on an already struggling young family. Examples of these risks included poverty, joblessness, alcohol and drug addiction, immigration, lack of steady food supply, and homelessness.

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Erlandsson, Dsilna, Fagerberg, and Christensson completed a randomized controlled trial in 2007 that influenced this study. These researchers discovered decreased crying, increased states of drowsiness, and improved pre-feeding (breastfeeding) behavior following analysis of two-hour periods of SSC with fathers and their newborns post-CS (2007). Recognizing that mothers were not offered SSC during or after CS, paternal SSC was implemented as an alternative, so infants could benefit from the known positive effects of SSC. Important differences between that original research and this study were: (1) the randomly assigned 29 pairs were not identified by race; (2) all partners were described as "fathers". The Erlandsson et al. study was completed in a hospital where members of the royal family of Sweden deliver their infants. Could the positive effects of SSC with fathers and their infants studied in Sweden be translated to an inner-city hospital delivery experience in the U.S.?

SSC has positive effects for infants and parents, as signified by its global spread after early reports of its use with newborns. In 1978, in Bogota, Columbia, a shortage of incubators and staff for premature infants led Dr. Edgar Rey Sanabria to institute SSC with mothers (Rodgers, 2013) whose infants subsequently exhibited improved feeding and growth, and stable temperatures (Feldman, 2004). SSC quickly spread to first-world countries and further research on its effects commenced, with SSC defined as "holding the baby naked against the mother's or father's skin near the chest" (Marin Gabriel, et al., 2010, p. 1630). Use of SSC early after birth led to improved breastfeeding outcomes, cardio-respiratory stability, less infant crying, and no obvious short- or long-term negative effects, as reported in a Cochrane Collaborative meta-analysis of 34 studies with 2177 participants (Moore, Anderson, Bergman, & Dowswell, 2012).

Researchers on SSC outcomes have also suggested positive effects on pain control, breastfeeding, temperature stabilization, and crying in the newborn, as well as parental attachment. The Baby Friendly Initiative, launched in 1991 by the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF), cited a growing body of evidence supporting the benefits of SSC, including regulating infant heart rate, breathing, and temperature, and stimulating feeding behavior (Vincent, 2011). The World Health Organization handbook published in 2003 on SSC (also referred to as "Kangaroo care") overtly supported the use of SSC, especially in resource-poor environments. Susan Ludington-Hoe, Ph.D., created a database listing the researched effects supporting use of SSC, updated weekly (January, 2014).

SSC and pain control/crying in the newborn: SSC was a potent analgesic in 30 infants undergoing heel stick, randomly assigned to SSC rather than lying in a crib during the procedure (Gray, Watt, & Blass, 2000). A standardized pain profile and salivary and serum cortisol levels showed evidence of reduced bio-behavioral pain responses in preterm infants undergoing SSC during heel stick (Cong, Ludington-Hoe, & Walsh, 2011). Since all newborns have developing central nervous systems, no matter their gestational age, this response reduction could theoretically also occur in term newborns. Combining SSC with other pain-reduction interventions may also have an additive effect. Scoring infants for pain during heel stick with a sample of 136 healthy term newborns randomly assigned to four groups including SSC alone, SSC with breastfeeding, sucrose alone, and SSC with sucrose, resulted in both the SSC/sucrose and the SSC/breastfed groups demonstrating significantly lower pain scores (Marin Gabriel, et al., 2013). Newborns who received a Hepatitis B vaccine injection, when randomly assigned to SSC, cried less, reached a calmer state sooner, and trended toward more rapid heart rate decrease after the pain (Kostandy, Anderson, & Good, 2013).

SSC and temperature stabilization: SSC appears to be linked with temperature stability in newborns. Greater thermal stability was found in 137 randomly assigned term and near-term newborns undergoing SSC, with an average rise of 0.07C (Marin Gabriel, et al. 2010). Increased thermal risks are associated with CS, a common example being a lowered operating room environmental temperature adjusted for the comfort of the operating room team, coupled with rapid decreases in body temperature due to evaporative heat loss in the amniotic fluid-covered newborn. In 34 mother-baby pairs randomized to SSC or routine care, CS-delivered infants who experienced SSC within one hour of delivery were not at risk for hypothermia (Gouchon, et.al, 2010).

SSC and parental attachment: Fifteen fathers were interviewed to explore their experience being the baby's caretaker while the mother was undergoing CS; their answers suggested that fathers took on more child care duties as they got to know their infant better (Erlandsson, Christensson, & Fagerberg, 2008). Most countries have established culturally-rooted infant-care practices. The Russian practices of separation of mother and infant after birth and swaddling were examined for their effects on mother-infant interaction, using varying combinations of modes of infant clothing, SSC, and rooming in. A two-hour period post-birth without SSC was not compensated for by later rooming-in (Bystrova, et al., 2009). Father-infant SSC was advanced as an alternative to mother-infant SSC after analysis of parental touch of the infant, parent speech directed toward the infant, and infant crying (Velandia, Uvnas-Moberg, & Nissen, 2012). Parent-infant interaction improved, maternal stress decreased significantly, and infants learned to respond to parental style in preterm infants undergoing SSC (Tallandini & Scalembra, 2006).

A pregnant woman's employment status is significantly related to major depressive symptoms, with low education, low support, acute stressful events, lack of money for basic needs, marital strain, and country of birth also significantly related (Fall, Goulet, & Vezina, 2013). Infants of depressed mothers display impaired attachment, angry and negative affect, and their attention/arousal responses are altered (Canadian Pediatric Society, 2004). When at-risk populations show higher rates of depressive symptoms related to these stressors, mothers could possibly benefit from the early decrease in depressive indicators found in the self-reported depression scales of 30 mothers of full-term infants providing daily SSC to their infants for varying time lengths up to one month of age. The lower scale values continued until one month postpartum, without significant differences at two and three month measurements. Reductions in physiologic stress and depressive symptoms were noted in mothers, which likely also benefited their infants (Bigelow, Power, MacLellen-Peters, Alex, & McDonald, 2012).

Support of parents using SSC may be vital to its beneficial effects. Of 20 parents interviewed after SSC, many responded positively, except when nursing support was not well versed in the practice, or appeared insensitive to parent needs (Lemmen, Fristedt, & Lundqvist, 2013). The outcomes of multiple research

study results on SSC supported the need for nurse-enablement of successful SSC experiences for parents and infants (Campbell-Yeo, Fernandes, & Johnston, 2011). No associated costs have been identified with SSC, but implementation factors were identified as crucial to its success, including accurately assessing the infant's clinical stability, staff education needs on supporting SSC, institutional support for the practice, and familial factors, such as parent availability for SSC, parent education, and motivation (Chong Lee, Martin-Anderson, & Adams Dudley, 2012).

SSC and socioeconomic status: The effects of SSC in regard to socioeconomic status have been infrequently addressed. An analysis of community-based SSC in two districts of Bangladesh, India, with high infant mortality and poverty rates revealed that mothers were likely to practice SSC if taught to do so. However, they performed SSC in a "token manner unlikely to improve health or survival" (Ahmed, et al., p. 361). Implementation of SSC reveals problems such as staff fearing the time demands of SSC, increased education needs, and lack of supportive infrastructure to support change. The need for support from the organizational culture and healthcare administration and well-developed communication processes to sustain SSC becomes important in supporting families using SSC with their newborns (Haxton, Doering, Gingras, & Kelly, 2012).

Methods

Setting

This study was conducted at two U.S. hospitals. The first was a regional medical center, which received low birth-weight infants and had an identified high-risk prenatal population; the second was a community hospital that transferred high-risk pregnant women and low birth-weight infants after stabilization, as well as those infants below 32 weeks gestation. Two sites were used to increase data collection opportunities for the study. Both were located in inner city neighborhoods of Milwaukee, Wisconsin.

The two sites care for differing populations: the regional medical center had a large Black population with the highest rates of unemployment and poverty in the city; the community hospital's majority population was Hispanic, also with high rates of unemployment and poverty. In "Empty Cradles", a series of newspaper stories about infant mortality, Milwaukee Journal Sentinel reporters found that the "disparity between Milwaukee's black and white infant mortality rates was among the worst in the nation" (Stephenson & Herzog, 2012). A review of the population census at the research sites currently includes the largest percentage of Black mothers in the city at the regional medical center, compared to other Milwaukee hospitals. The obstetric census is 48% Hispanic in the community hospital, per hospital administration census review, with many of these mothers being recent immigrants.

Participants

Enrolled participants included 30 maternal partners and 30 infants, the latter being included via maternal consent for a minor. Maternal partners were solely identified by the mother, which included spouses, life partners, relatives, friends, and neighbors. All maternal partners were age 18 or over, due to state adult informed consent guidelines. The age range of partners was 20-51 years, averaging 32.5 years. Partners unable to read/write sufficient English to participate by giving their signature and answering the questionnaire were included via interpreter. Partners not included in the study were those who identified a dermal rash, respiratory illness, or other conditions such as contagious disease or intoxication, excluding them from entering the operating room [see Table 1].

Table 1: SSC in the O.R. Demographic Data

	Mothers n=30	Maternal partners n=30
Age	Range: 18-24 years (Mean 27.96, Median 27.5)	Range: 20-51 years (Mean 32.5, Median 30.5)
Alaska Native/ American Native	1	0
Black	5	5
Hispanic	18	19
White	6	6

Enrolled newborn infants were born via non-emergent Cesarean section to mothers age 18 or over, with the lower age range restriction due to state adult informed consent guidelines for a minor. Maternal age range was 18 to 42 years, with a mean of 27.96 years, SD = 5.72. All infants were over/=37 weeks completed gestation, without congenital anomalies or major complications, and without need for resuscitation (intervention needed to establish heart rate or respirations immediately after birth).

Three women were enrolled but later deemed ineligible: In one case, the infant was transferred to the Neonatal Intensive Care Unit before data collection could be completed; in a second case, the alternate partner refused after the first partner signed the consent but then left the hospital; in the third case, the partner decided against participation after the mother had consented.

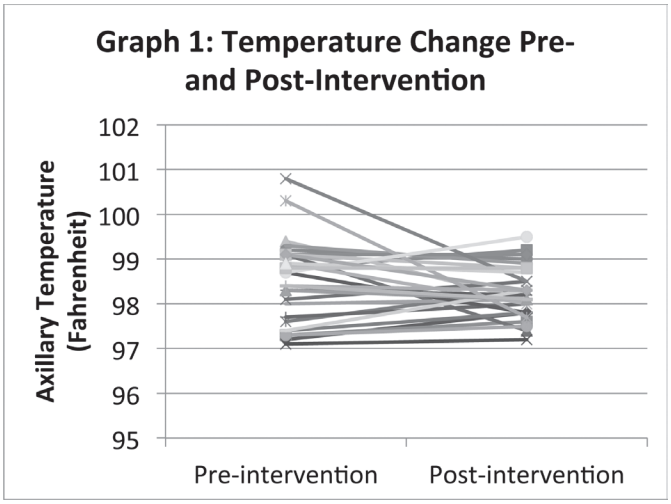
Measures

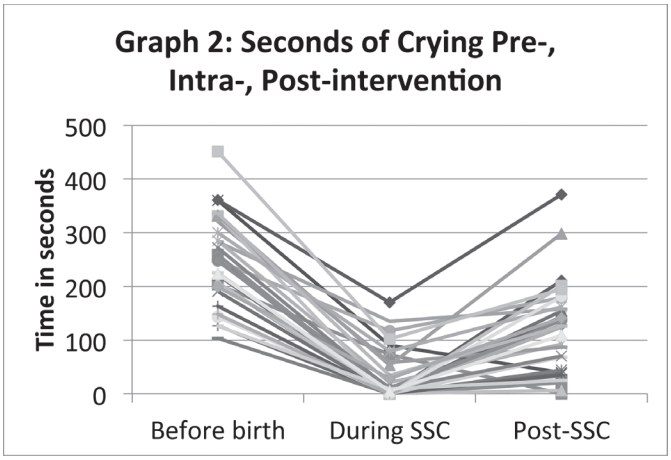
Both quantitative and qualitative variables were measured:

- Quantitative: (1) Axillary temperatures Fahrenheit (F) of the infants were measured before the intervention and in the observation period post-intervention. (2) The minutes/seconds of infant crying were measured pre/intra/post-intervention. (3) The race and age of both mother and maternal partner were recorded.
- Qualitative: A five query questionnaire asked partners first about their age and race, with the latter three questions qualitative in nature: partners were asked for their estimation of feelings of protectiveness toward the infant, both during pregnancy and then post-intervention experience, with "protectiveness" defined for the partner, and to identify if there was any change in their plans for involvement in the infant's future care.

Procedure

The Institutional Review Boards of the University of Michigan-Flint and the two hospital study sites, both in the Wheaton Franciscan Healthcare system, approved this study. Maternal partners gave informed consent for their participation after an oral explanation, and were enrolled within the two-hour pre-operative period. Mothers gave their consent for their unborn infants during the same time period. Copies of the consent form were given to mother and partner. Following consent acquisition, the PI informed the obstetrician, anesthesiologist, and the labor





and delivery RN (circulating nurse assigned to the mother's care) that the infant would undergo SSC with the partner via study protocol.

The partner was prepared to enter the O.R. after the circulating nurse/PI obtained operating room attire for the partner. Female partners were informed that they could retain their brassiere/camisole if desired, and then lift up the garment for SSC in the O.R. The circulating registered nurse (RN) or the PI accompanied the partner into the O.R., and seated the partner at the mother's side/head of the O.R. bed. The partner was seated on a chair, rather than a stool or backless seat, for the partner's safety. The PI briefly reiterated procedure to mother and partner.

Immediately following birth by Cesarean section, the infant was placed on a pre-warmed radiant warmer, dried, stabilized, and initial vital signs checked by the infant team. The PI recorded the first axillary temperature and length of infant crying in minutes/seconds. The pre-intervention observation time period varied, lasting from birth until the practitioner (MD/Neonatal Nurse Practitioner [NNP]) approved the infant's status to undergo the intervention. Tasks such as identification band placement, trimming of umbilical cord, bulb syringe use in infant's mouth/nares, and measurements were also sometimes performed. The infant was weighed pre-intervention. A hat was placed on the infant and a pre-warmed bath blanket brought to the radiant warmer.

After checking with the O.R. team to determine there was no impediment to going forward with SSC, the PI prepared the partner with verbal directions, via interpreter as needed: Open the jacket, hold the infant to chest with two hands, the infant would be positioned [upright between nipples], and informing mother and partner that the infant would be brought to them. The PI then stated: "I'm putting the baby skin to skin now". The infant was then transferred to the partner at the mother's side, with hat on, warmed blanket wrapped around the couplet, and with the partner's hands remaining on the infant, rather than outside of the blanket. To increase the surface area of actual skin contact during SSC, the infant was not diapered. SSC continued for 10 minutes/0 seconds; during the intervention, the PI recorded crying duration. Ten minutes was the time period allowing SSC prior to the mother being transferred to the recovery area and assuming SSC herself, and also allowing time for the partner to assess the experience afterwards. Tasks such as bulb suctioning, giving sucrose, body/head measurements, or foot printing proceeded if they did not expose infant unduly (skin exposure exceeding a hand or foot) or necessitate a change in position (loss of SSC between infant and partner).

After 10 minutes, the infant was returned to the radiant warmer and the second temperature check was performed. The PI would verbally alert the infant's nurse to signal that infant care tasks could resume. The post-intervention observation period was matched exactly to the minutes/seconds of the pre-intervention time period, and duration of crying was recorded.

Following the post-intervention time period, the PI administered the oral questionnaire to the partner and recorded responses. This was completed nearby, in an anteroom to the O.R. or in the mother's recovery room, to decrease the length of separation for mother and partner. Last, the PI checked with both mother and partner for any questions or concerns about the intervention.

Qualitative Analysis

Content analysis of the latter three questions of the five-question questionnaire analysis was completed using multiple readings of the compiled answers of the maternal partners reflecting on the lived experience of the partner, followed by identification of key words in the responses, and naming of overarching themes supported by the key words.

Statistical Analysis

The first two questions on the partner questionnaire were quantitative [age and race], and were analyzed using range, median, and mean computations, as well as a listing of the races reported by mother and partner. Quantitative analysis was completed using SPSS, version 20 (information available at www.ibm.com/SPSS_Statistics). Changes in pre- and post-intervention axillary infant temperatures were analyzed using 2x2 analysis; the McNemar test (information available at https://statistics.laerd.com/spss.../mcnemars-test-using-spss-statistics.php) was applied to detect if the infant's temperature changed from in-range to out-of-range, or out-of-range to in-range. The total times of crying per minutes pre-, intra-, and post-intervention ratios were compared via a paired samples test. Subgroup analyses were completed to assess the results for only those infants of maternal minority race. Sub-analysis of infants of maternal minority race and temperature changes was completed using the MeNemar test for in- and out-of-range temperature, and the paired t-test was used to evaluate infant mean temperature. Sub-analysis of infants of maternal minority race and crying times was completed via paired t-test.

Results

Analysis of Maternal Partner Questionnaire

Responses to the first question on the questionnaire showed partners were of both sexes with an age range of 20 to 51 years, averaging 32.5 years. Race was listed according to simple numbers (see Table 1).

Qualitative data were obtained via partner responses to the last three questions of the questionnaire and reviewed using content analysis of the narrative data. Following multiple readings of the recorded answers to the three questions posed to maternal partners and examining their lived experience reported in their own words, the over-arching theme emerging from the analysis was "increased satisfaction", supported by four foundational refrains: relational, protectiveness, emotional, and yearning.

Analysis of Infant Axillary Temperatures

Normal axillary newborn temperature is defined as 97.7 to 99.3 degrees F (36.5-37.4 degrees C). This range is used nationally and endorsed by the Committee on Fetus and Newborn of the American Academy of Pediatrics (2004). However, the policy of the hospital system of the two research sites had a different range: 97.8-99 degrees F. Since individual practitioners and hospitals may define normal axillary temperature ranges differently, temperatures were categorized using both ranges. This contrast in analyses highlights the possible effect on SSC practice when the range contracts or expands.

Using the local policy temperature range, abnormal temperatures occurred in 17 of 30 infants pre-intervention, 11 of whom had normal temperatures post-intervention. Of 13 infants with normal temperatures recorded pre-intervention, all but two continued to have a temperature in the normal range post-intervention. The McNemar test was significant at .022 ($p< 0.05$), although the paired samples t-test comparing change in mean was not significant at .120 ($p< 0.05$). Using the AAP temperature range (2004), abnormal temperatures occurred in 9 of 30 infants pre-intervention, six normalizing post-intervention. Of 21 infants with normal temperatures pre-intervention, all but one remained normal post-intervention. Using the McNemar test, the proportion of infants who had normal temperatures post-intervention was not statistically significant. Additionally, the paired samples t-test did not show a statistically significant difference in mean ($p<0.05$) [see Graph 1].

Analysis of Infant Crying Times

After collecting data on the minutes/seconds of infant crying time pre-, intra-, and post-intervention, these variables were used to create the mean ratio of crying time vs. total time. The mean ratio of crying times pre-intervention was .6966, intra-intervention .0552, and post-intervention .3353. Comparison of crying times pre- and post-intervention, pre-and intra-intervention, and intra- and post-intervention were all statistically significant at less than .001 ($p<0.001$). Infant crying times were significantly reduced by the intervention, including an effect on crying time during the post-intervention observation period [see Graph 2].

Sub-Analysis of Infant Axillary Temperatures for Infants of only Minority Race Mothers

Maternal races included 18 Hispanics, six Whites, five Blacks, and one Alaskan/American Indian [see Table 1]. Because this study was created, in part, to determine if previous results reported by Erlandsson, Dsilna, Fagerberg, and Christensson (2007) were generalizable to minority populations, a sub-group analysis of only minority race women and their infants' temperatures and crying times was completed; the number of subjects in the sub-group was 24.

The mean temperature pre- and post-intervention data of infants of maternal minority race were analyzed using a paired samples test, which was not significant at .079 ($p < 0.05$). Using the more stringent hospital temperature ranges, the McNemar test was not significant at 0.021 ($p<.05$). There was no statistically significant change in pre- and post-intervention axillary temperatures when examining only the infants of maternal minority race.

Sub-Analysis of Infant Crying Times for Infants of Only Minority Race Mothers

In a paired samples test, crying times for the infants of minority race mothers pre- and post-intervention, pre-and intra-intervention, and intra- and post-intervention were all statistically significant ($p <0 .001$). Infants of minority race mothers displayed crying times similar to those of infants of maternal majority race. Infant crying times were significantly reduced by the intervention, including an effect on crying time during the post-intervention observation period.

Discussion

The purpose of this study was to determine if partners who attended their partners' CS and experienced SSC with the infants would express improved relational rating on partner-child bonding, and if the infants would display somatic stability during SSC.

Maternal Partner Questionnaire

The five-question survey administered to the maternal partners was designed to identify both quantifiable data and lived-experience themes. A study of SSC dyadic interaction resulted in decreased maternal stress, better mother-infant interactive style, and better infant ability to respond to the parental interactive style (Tallandini & Scalembra, 2006). As the basis for the questionnaire, this description of maternal responses to SSC helped shape the questions on the partner's relational attachment to the newborn and about feelings of protectiveness.

- Question 1: "What is your age?" Eliciting the partner's age revealed a slightly older average of 32.5 years than the maternal average of 27.96 years, perhaps reflecting the varying types of partners enlisted by mothers, including older relatives and neighbors (See Table 1).
- Question 2: "How do you identify your race on documents like a driver's license?" A review of the partners' race showed a majority of 19 Hispanic, and two minorities of five Black and six White partners. This is nearly matched by the reported maternal races, and reflects the make-up of the inner-city neighborhoods surrounding the research sites (See Table 1).
- Question 3: "Feeling protective toward a baby can be described as wanting to make sure the baby is always safe, well-fed, and growing normally. While Mom was still pregnant, did you feel this way toward the baby?" Twenty-one respondents answered only "Yes". Comments made by the other nine respondents reflected on their interpretation of feeling protective, which also extended to the mother: "Yes, felt protective" (Partner # 9), "Yes, of course" (Partner # 7), "I felt more relaxed, better knowing that my baby was doing good" (Partner # 26). "Tried to keep her, make sure she's comfortable, there for her [also] for baby. I didn't, I

told her not to carry, nothing strenuous. Last week she fell. Worried about her last week" (Partner # 29).

- Question 4: "Now that you have held the baby during the Cesarean section, do you have more/less/the same protective feelings toward this baby?" No respondents answered "less"; 24 answered "more" or used "more" in comments, such as partners who answered: "I think more. More than I thought possible" (Partner # 27), and "Yes. Stay with him forever, makes me want to be even more involved" (Partner # 11). Five answered "same" or used "same" in their comments, with one partner using "same" and "more" in his comments (Partner # 25). Two respondents mentioned the infant's sex: "More. It's my first boy" (Partner # 20) and "More, now I have a daughter, have it somewhat better than me" (Partner # 23). Fifteen partners commented on the infant's presence and needs alone: "More now that the baby is out" (Partner # 32); "I feel more protective" (Partner # 30); "Si, yes. I felt the warmth and the feeling of always wanting to protect and care for the baby" (Partner # 21), and "The same. Pretty protective of my kids" (Partner # 10).
- Question 5: "Did holding the baby during the Cesarean section make any change in how much you want to be involved in the baby's care?" All 30 respondents offered comments, with 14 partners offering a clear "Yes", and 11 stating "No" with their statements. All responses were positive about the partner's involvement and in some cases, about the SSC experience: "Yeah, it was affirming, encouraging beyond the normal doubts about how you will be caring for the baby" (Partner # 1); "Yes, almost cried. Feels incredible" (Partner # 8); "Gonna be there for him; No change" (Partner # 9); "Si, yes. I felt the warmth and the feeling of always wanting to protect and care for the baby" (Partner # 21); "Yes. How can I say this? It affects how I feel about this baby, in a very good way" (Partner #15).

Partners' answers also reflected a satisfaction with the SSC experience: "I feel more relaxed. Better knowing my baby is doing good" (Partner # 26) was the statement of a partner who had not attended the mother's three previous CS. Another partner spoke of the effect of SSC on his infant: "Protective. I was really nervous but I feel like I have to take care all the time. I want to be a more better father, like I am now. When I was holding, I say "Thanks, God, for giving me this beautiful baby. I was holding strongly, I relaxed, then the baby relaxed too, and did better with the breathing and everything" (Partner # 28). In some cases, the partner was unrelated to the mother and infant, yet expressed attachment: "No, I was already all in. Not sure who the father is, so . . .but I'm there for her" (Partner #29). Feelings of attachment and a protective attitude were summarized by one partner as: "Yes, positive change. Since the one I know this is my baby. Now she's out of Mom's womb, the C-section went fine, now it's my turn as a parent and father" (Partner #32).

High-frequency word use included: affirming, encouraging, be involved, more involved, happy, good, warmth, protective. These terms suggest a positive response toward the infant and the SSC intervention. Key phrases included: "always want to be in her life", "there for her", "always going to be taking care of her", "be there for him", "very involved", "stay with him forever". The phrases indicate an overt, acknowledged state of attachment between partner and infant.

Four supporting themes emerged from analysis:

1. Relational: The intervention experience of SSC evoked feelings of a bond between partner and infant
2. Protectiveness: This feeling was directed toward the infant in present time. Several partners also alluded to the future in their remarks.
3. Emotional: The SSC encounter elicited positive emotions toward both the infant and the intervention
4. Yearning: Partners expressed the desire to be with the infant and to have planned involvement with the infant's care.

Analysis of the responses suggested an overarching theme of increased satisfaction. Partner responses point to this enhanced satisfaction being a focus in both their reactions to the infant and having the birth experience enhanced by the SSC intervention.

Infant Axillary Temperatures for the Whole Sample and Infant Axillary Temperatures for Infants of Only Minority Race Mothers

In this sample, SSC was not detrimental to term newborn temperature maintenance post-birth; as visualized in graphed results, there is minimal variance (see Graph 1). One objective was to detect somatic stabilization, characterized by infant temperature and out-of range temperatures. The local policy-based analysis showed normalization in 11 infants with abnormal pre-intervention temperatures, and stabilization in 11 infants out of 13 with normal temperatures pre-intervention. This statistically significant change was not repeated when the wider AAP range was analyzed. There may be a benefit based on the AAP's policy on newborn temperature range, which might be confirmed with a larger sample, since among the 30 infants, only nine started out of range. The results suggest that infants experiencing SSC with a partner after CS will likely normalize or stabilize their axillary temperatures.

Minority race infants were no different than majority race infants in temperature stabilization and normalization. Again, statistically significant change was seen when using the local policy range, but not with the AAP temperature policy range. With more minority women in a larger sample, it would be more likely to find a significant statistical change in temperature. It seems likely that infants of minority race mothers will benefit from the same temperature stabilization effect as infants of majority race mothers.

Infant Crying Times for the Whole Sample and Infant Crying Times for Infants of Only Minority Race Mothers

A second objective was to measure somatic stability in infants by measuring crying times, positing that the infant who cries more is experiencing more discomfort and destabilization, ranging from evocation of the startle reflex to pain. A statistically significant reduction in crying time was evident, most marked during SSC itself, but extending into the post-SSC period as well, as shown in Graph 2. The infant undergoing SSC with a maternal partner is more likely to exhibit less crying during and after SSC, with increased somatic stabilization.

Infants of minority race mothers displayed crying time results similar to those of majority race infants. Results for minority race infants were consistent with the whole group analysis, with crying time being significantly decreased intra- and post-intervention. Minority race inner-city newborns undergoing SSC during CS will likely benefit in the same ways as majority race newborns.

Limitations

Quantitative: A key limitation in this study is the number of subjects. A larger sample with concomitant increase in power would increase the probability of detecting statistically significant differences with the infants of minority race mothers and temperature changes measured against the AAP's recommended guideline.

Qualitative: The questionnaire was deliberately designed with the exclusion of open-ended questions to limit the amount of time the partner was separated from the mother and newborn for its completion, although partners were allowed to comment freely. The questionnaire was given to the partner within 10 minutes of the SSC intervention. Allowing more time between the intervention experience and questionnaire administration for reflection by the partner, and allowing a longer time period to complete the questions, would possibly encourage more in-depth answers and self-analysis.

Parental experience: In pre-operative conversations with the PI, several partners and mothers used the word "dread" as they spoke of the anticipated O.R. experience. Although all the mothers had experienced a previous CS and were familiar with hospital routines, some partners stated they had never been inside a hospital before, much less an O.R. Their decreased eye contact and lack of facial expressiveness reinforced the PI's impression of fear. Orientation to the unit and a review of what they might see/hear/smell, as well as time for questions about their expectations, would be useful to decrease anxiety and allow increased focus on the SSC event.

Nursing: Nursing resistance to changing routines in the O.R., which are highly task-oriented, should be addressed before implementing SSC during CS. In this study, the greatest frequency of questions from staff related to anticipated disruptions in their work. Anecdotal comments by nurses to the PI included expressions of frustration: "Well, I guess I just gotta wait now" and, "Now I don't have anything to do for 10 minutes", in response to the infant being placed in SSC. Some nursing staff refused the offer to resume non-disruptive tasks like foot printing of the infant: "No, I'll just wait, I don't want to bug the family", and "I'll do other stuff while I'm waiting". Comments characterized SSC as an interruption rather than part of the routine.

Parents reported sensitivity to staff attitudes and practices in their support of SSC, making SSC success partially dependent on staff encouragement (Lemmen, Fristedt, & Lundqvist, 2013). On the way to establishing SSC as a care modality for families, common obstacles found in the operating room include cultural, traditional, technological, and physical barriers that must be addressed (Mangan & Mosher, 2012). The O.R. is a highly technical environment with a hierarchical structure and routine-based work. Broaching these topics openly in a discussion of how to integrate SSC in such an ordered environment is crucial to successful integration into the O.R. routine.

Implications for Practice

Results suggest SSC with a maternal partner is a no-cost early intervention for families that increases satisfaction in partners, establishes positive relational ratings between partner and newborn, and offers somatic benefits to the infant. Healthcare systems could implement this immediately as a low-technology and low-risk solution, as a means of offering assistance to families experiencing the increased risks of global recession and increased costs associated with a newborn, without escalating delivery room costs. Further study is warranted on infant-to-mother SSC during CS, focused on at-risk families. A longitudinal study of continued partner interaction with the infant could also address questions of long-term effects after initial SSC.

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References

- Ahmed, S., Mitra, S.N., Chowdhury, A.M.R., Camacho, L.L., Winikoff, B., & Sloan, N.L. (2011). Community kangaroo mother care: Implementation and potential for neonatal survival and health in very low-income settings. Journal of Perinatology, 31, 361-367. doi: 10.1038/jp.2010.131.
- American Academy of Pediatrics. (2004). Committee on Fetus and Newborn. Policy statement: Hospital stay for healthy term newborns. doi: 10.1542/peds.2009-3119
- Bigelow, A., Power, M., MacLellan-Peters, J., Alex, M. & McDonald, C. (2012). Effects of mother/infant skin-to-skin contact on postpartum depressive symptoms and maternal physiological stress. Journal of Obstetric, Gynecologic, & Neonatal Nursing, 41, 369-382.doi: 10.1111/j.1552-6909.2012.01350.x.
- Bystrova, K., Ivanova, V., Edhborg, M., Matthiesen, A.-S., Ransjo-Arvidson, A.-B., Mukhamedrakhimov, R., Uvnas-Moberg, K., & Widstrom, A.-M. (2009). Early contact versus separation: Effects on mother-infant interaction one year later. Birth, 36, 97-109. doi: 10.1111/j.1523-536X.2009.00307.x
- Campbell-Yeo, M., Fernandes, A., & Johnston, C. (2011). Procedural pain management for neonates using nonpharmacological strategies: Part 2: Mother-driven interventions. Advances in Neonatal Care, 11, 312-318. doi: 10.1097/ANC.0b013e318229aa76
- Canadian Pediatric Society, Psychosocial Paediatrics Committee. (2004). Maternal depression and child development: Position Statement [PP 2004-03]. Paediatric Child Health, 9, 575-583. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2724169/pdf/pch09575.pdf
- Chong Lee, H., Martin-Anderson, S., & Adams Dudley, R. (2012). Clinician perspectives on barriers to and opportunities for skin-to-skin contact for premature infants in Neonatal Intensive Care units. Breastfeeding Medicine, 7, 79-84. doi: 10.1089/bfm.2011.0004
- Cong, X., Ludington-Hoe, S.M, & Walsh, S. (2011). Randomized crossover trial of kangaroo care to reduce biobehavioral pain responses in preterm infants: A pilot study. Biological Research for Nursing, 13, 204-216. doi: 10.1177/1099800410385839
- Department of Reproductive Health and Research. (2003). Kangaroo mother care: A practical guide. World Health Organization. Retrieved from http://whqlibdoc.who.int/publications/2003/9241590351.pdf
- Erlandsson, K. Christensson, K., & Fagerberg, I. (2008). Fathers' lived experiences of getting to know their baby while acting as primary caregivers immediately following birth. The Journal of Perinatal Education, 17, 28-36. doi: 10.1624%2F105812408X298363
- Erlandsson, K., Dsilna, A., Fagerberg, I., & Christensson, K. (2007). Skin-to-skin care with the father after cesarean birth and its effect on newborn crying and prefeeding behavior.

Birth, 34, 105-114. doi: 10.1111/j.1523-536X.2007.00162.x
- Fall, A., Goulet, L., & Vezina, M. (2013). Comparative study of major depressive symptoms among pregnant women by employment status. Springerplus, 2, 1-11. doi: 10.1186/2193-1801-2-201
- Feldman, R. (2004). Mother-infant skin-to-skin contact (Kangaroo care): Theoretical, clinical, and empirical aspects. Infants and Young Children, 17, 145-161.
- Gouchon, S., Gregori, D., Picotto, G., Patrucco, G., Nangeroni, M., & Di Giulio, P. (2010). Skin-to-skin contact after cesarean delivery. An experimental study. Nursing Research, 59, 78-84. doi: 10.1097/NNR.0b013e318ld1a8bc
- Gray, L., Watt, L., & Blass, E.M. (2000). Skin-to-skin contact is analgesic in healthy newborns. Pediatrics, 105, e14. Retrieved from http://pediatrics.aappublications.org/content/105/1/e14.full
- Haxton, D., Doering, J., Gingras, L., & Kelly, L. (2012). Implementing skin-to-skin contact at birth using the Iowa model. Nursing for Women's Health, 16, 220-229. doi: 10.1111/j.1751-486X.2012.01733.x.
- Kirmeyer, S.E. & Hamilton, B.E. (2011). NCHS Data Brief: Childbearing differences among three generations of U.S. women (No. 68). Retrieved from U.S. Department of Health and Human Services, Center for Disease Control and Prevention, National Center for Health Statistics website http://www.cdc.gov/nchs/data/databriefs/db68.htm
- Kostandy, R., Anderson, G.C., & Good, M. (2013). Skin-to-skin contact diminishes pain from Hepatitis B vaccine injection in healthy full-term neonates. Neonatal Network, 32, 274-280. doi: 10.1891/0730-0832.32.4.274
- Lemmen, D., Fristedt, P., & Lundqvist, A. (2013). Kangaroo care in a neonatal context: Parents' experiences of information and communication of nurse-parents. The Open Nursing Journal, 7, 41-48. doi: 10.2174/1874434601307010041
- Livingston, G., & Cohn, D. (2010). The new demography of American motherhood. Retrieved from http://www.pewsocialtrends.org/2010/05/06/the-new-demography-of-motherhood/
- Marin Gabriel, M.A., Martin, I., Lopez Escobar, A., Fernandez Villalba, E., Romero Blanco, I., & Touza Pol, P. (2010). Randomized controlled trial of early skin-to-skin contact: Effects on the mother and the newborn. Acta Paediatrica, 99, 1630-1634. doi: 10.1111/j.1651-2227.2009.01597.x
- Marin Gabriel, M.A., del Ray Hurtado de Mendoza, B., Jimenez Figueroa, L., Medina, V., Iglesias Fernandez, B., Vazquez Rodriguez,, M., Escudero Huedo, V., & Medina Malagon, L. (2013). Analgesia with breastfeeding in addition to skin-to-skin contact during heel prick. Archives of Disease in Children Fetal Neonatal Edition, 98, F499-F503. doi: 10.1136/archdischild-2012-302921
- Mangan, S., & Mosher, S. (2012), Challenges to skin-to-skin kangaroo care: Cesarean delivery and critically ill NICU patients. Neonatal Network, 31, 259-261. doi.org/10.1891/0730-0832.31.4.259
- Mishel, L., & Shierholz, H. (2013). A decade of flat wages: The key barrier to shared prosperity and a rising middle class (# 365). Economic Policy Institute, Briefing Paper. Retrieved from http://www.epi.org/publication/a-decade-of-flat-wages-the-key-barrier-to-shared-prosperity-and-a-rising-middle-class/
- Moore, E.R., Anderson, G.C., Bergman, N., & Dowswell, T. (2012). Early skin-to-skin contact for mothers and their healthy newborn infants (Review). Cochrane Database of Systematic Reviews, 5, 1-1231. doi: 10.1002/14651858.CD003519.pub3
- Obamacare facts: Dispelling the myths. (n.d.). Benefits of ObamaCare: Advantage of ObamaCare. Retrieved from http://obamacarefacts.com/federal-poverty-level.php
- Rodgers, C. (2013). Why kangaroo mother care should be standard for all newborns. Journal of Midwifery & Women's Health, 58, 249-252. doi: 1111/jmwh.12010
- Stephenson, C., & Herzog, K. (2012, April 12). Empty cradles/Confronting our mortality crisis: Disparity in infant mortality rates in Milwaukee widens. Milwaukee Journal Sentinel. Retrieved from http://www.jsonline.com/news/milwaukee/milwaukee-infant-mortality-rate-drops-overall-but-disparity-worsens-sp54t7f-148680905.html
- Tallandini, M.A., & Scalembra, C. (2006). Kangaroo mother care and mother-premature infant dyadic interaction. Infant Mental Health Journal, 27, 251-275. doi: 10.1002/imhj.20091
- U.S. Department of Commerce, Economics and Statistics Administration, United States Census Bureau. (2011). Child poverty in the United States 2009 and 2010: Selected race groups and Hispanic origin. Retrieved from http://www.census.gov/content/dam/Census/library/publications/2011/acs/acsbr10-05.pdf
- Velandia, M., Uvnas-Moberg, K., & Nissen, E. (2012). Sex differences in newborn interaction with mother or father during skin-to-skin contact after Caesarean section. Acta Pediatrica, 101, 360-367. doi: 10.1111/j.1651-2227.2011.02523.x
- Vincent, S. (2011). Baby friendly news: Skin-to-skin contact. Part one: Just an hour of your time. The Practising Midwife, 14, 40-41.

Pilot Study to Compare Two Nasal Airway Interfaces in Neonates on Non-invasive Neurally Adjusted Ventilatory Assist

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Abstract

Background: The use of non-invasive ventilation in neonates is increasing. Previous studies have focused on type and timing of non-invasive ventilation and not on the type of interface used. Multiple nasal interfaces are available for use with CPAP and non-invasive ventilation but none of these interfaces have been studied with NIV NAVA.

Objectives: To compare the functionality and short term physiologic outcomes of two nasal airway interfaces used with NIV-NAVA: Medin nasal prongs (FDA approved) and RAM nasal cannula (off-label use).

Methods: This as a prospective, single factorial, crossover study. Ten neonates on NIV NAVA were examined on each nasal airway interface. Short term physiologic outcomes of each nasal airway interface was measured via vital signs and ventilator parameters for a period of 20 minutes on each nasal airway interface. Statistical analysis was performed using ANOVA. ($p < 0.05$).

Results: Neonates were as clinically stable with the RAM as with the Medin but the Medin required lower peak inspiratory pressure despite higher leaks. There were no differences in other ventilatory variables and vital signs.

Conclusion: RAM nasal cannula may be an acceptable alternative to the Medin nasal prongs.

Introduction

Noninvasive ventilation (NIV) is a ventilatory mode that has been shown to increase dynamic lung compliance and tidal volume and improve arterial blood gas when compared to CPAP.[1] This type of ventilation is limited by poor synchrony from lack of a reliable flow trigger from large air leaks. Asynchronous ventilation can result in diaphragmatic dysfunction, higher ventilator weaning failure, increased use of analgesics and sedation, and other co-morbidities associated with increased intensive care unit time.[2-4] Synchronized non-invasive ventilation (NIV) is now available using Neurally Adjusted Ventilatory Assist (NIV-NAVA) that utilizes a neural trigger to provide positive pressure ventilation in proportion to the electrical activity of the diaphragm (Edi), a reflection of the respiratory neural drive.[5] Edi is measured via transesophageal electrodes positioned at the level of the crural diaphragm.[6] When ventilated with NIV-NAVA, the ventilator is able to adjust flow to compensate for variable air leaks around the nasal airway interface and through the mouth for leaks as high as 92%.[7]

Neonates presents a special challenge with nasal airway interfaces due to their small size and small tidal volumes.[2] Multiple neonatal nasal airway interfaces are available for non-invasive ventilation, but many are cumbersome and put the neonate at risk for nasal septal erosion and pressure sores around the face.[2]

Figure 1 shows the two nasal airway interfaces: Medin (Medin Medical Innovations, Munich, Germany), FDA approved for CPAP, bi-level CPAP and synchronous non-invasive positive pressure ventilation; and RAM (Neotech, Valencia, CA.), approved only for oxygen delivery in neonates. However, because of its less complaint design, compared to a standard nasal cannula, RAM may allow for higher flow and pressure delivery for NIV.[8] Although studies have shown that the RAM cannula delivers CPAP effectively,[8] there are no studies that show the short term physiologic outcomes of the RAM cannula on NIV-NAVA.

This study was done to compare the effects of these two nasal airway interfaces during ventilation with NIV-NAVA to evaluate if a difference exists with regard to short term physiologic outcomes.

Materials and Methods

This was a prospective, crossover study of ten neonates comparing Medin and RAM during ventilation with NIV-NAVA to evaluate short-term physiologic effects. The study population was a convenience sample of neonates who were stable on NIV-NAVA ventilation. The study was approved by the IRB and informed consent was obtained.

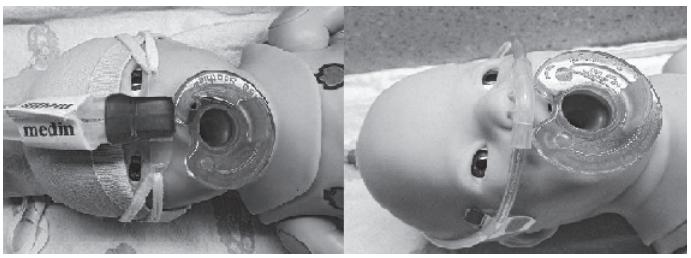

Figure 1: Medin nasal prongs and RAM nasal cannula. (Pacifier used for the mannequin only and not during the study).

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Each neonate was studied for 20 minutes each on RAM, Medin and then on RAM again. Chinstraps were used on all neonates during the study but pacifiers (as shown in Figure 1) were not. Measurement of vital signs and ventilator parameters were collected for a period of 20 minutes during each study period. There was a 10-minute stabilization period after changing interfaces. Proper positioning of the Edi catheter was confirmed by on-line analysis on SERVO-I software. Other than F_IO_2, (adjusted to keep the oxygen saturation (S_p0_2) in the range of 88-96%) all ventilator parameters were kept constant.

The independent variable was the type of ventilatory nasal airway interface. Dependent variables were: heart rate (HR), respiratory rare (RR), S_p0_2, blood pressure (BP), Edi P, Edi M, peak inspiratory pressure (PIP), and F_IO_2. Data output, stored in one-minute increments, were downloaded to a flash drive, and imported into Microsoft Excel for analysis. Data were averaged over the 20-minute period for all variables.

Statistics - SAS (SAS Institute Inc., Cary, NC) using ANOVA. A $p < 0.05$ was considered significant.

Results

Ten neonates were enrolled in the study. 60% were males, 90% were delivered via cesarean section, 40% received steroids prenatally, and 90% received surfactant postnatally. Mean birth weight was 1623±1019 grams, and mean gestational age was 29.5±4.1 weeks. Mean study weight was 1618±928 grams, and mean study age was 10±14 days. Diagnoses included Respiratory Distress Syndrome (6 neonates), pneumonia (2 neonates), pulmonary hypertension and pulmonary insufficiency of prematurity (1 neonate each). The NAVA level ranged from 1-3 cm H_2O/mcV and remained constant throughout the study period. PEEP was 5 cm H_2O. The peak inspiratory pressure alarm was 40 cm H_2O, apnea time 10 seconds and Edi trigger 0.5 mcV.

Figures 2 show the vital signs and ventilatory parameters. Differences were significant for PIP being lower for neonates on the Medin compared to the RAM and more leakage at the nasal airway interface on Medin than when on RAM. There were no differences in other variables. No neonate went into back-up ventilation during the study.

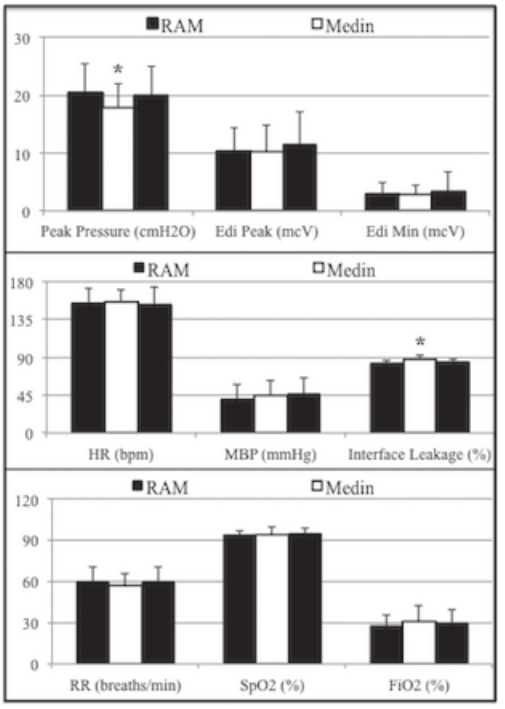

Figure 2: Comparison vital signs and ventilatory parameters for RAM and Medin (n=10). Peak pressure was lower and leakage at the interface was higher with Medin. Bars – mean ± SD, * $p < 0.05$.

Discussion

Studies in neonates, including a Cochrane review, compared nasal interfaces in the delivery of CPAP[9,10] but no studies have been done evaluating these interfaces with NIV or specifically with NIV NAVA. The use of NIV in neonates is increasing but previous studies have focused on the type and timing of NIV, not on the type of interface.[11]

NIV NAVA utilizes a neural trigger and biofeedback to regulate the inspiratory pressure delivered[12] so any increase in actual pressure delivered to the lungs is a result of an increase in respiratory drive (Edi). Although PIP was higher on RAM, there was no increase in Edi suggesting that this increase in PIP was not due to a patient response but possibly in the way PIP is determined between the two interfaces. When ventilating with NIV-NAVA the actual PIP delivered to the lungs is dependent on the leak at the nasal airway interface, through the mouth and into the stomach.[7] There is no accurate way to measure transpulmonary pressure with NIV-NAVA so we chose to measure PIP at the ventilator rather than at the nares due to the different interface mechanism. Medin has an inspiratory and expiratory arm with pressure drop off at the nasal interface. The expiratory side therefore sees a lower pressure than the inspiratory side. RAM has two long inspiratory limbs leading to the nasal interface and the y-connector is proximal to these inspiratory limbs. Therefore there is less drop-off of pressure between the inspiratory and expiratory arms at the y-connector of the circuit where it is connected to the RAM, distant from the nares. The algorithm in the ventilator will then raise the inspiratory pressure to increase the pressure difference between inspiratory and expiratory limbs. This most likely accounts for the observed 20% increase in PIP on RAM. Although we did not measure transpulmonary pressure directly, we assume the delivered pressures were comparable because clinical stability, assessed by vital signs, S_p0_2, and F_IO_2, on both nasal airway interfaces was similar. The clinical implication managing neonates on NIV NAVA is the awareness that the higher PIP noted at the ventilator on RAM is interface, not patient related.

PEEP was kept consistent throughout all the studies. Edi M supports regulation of end-expiratory lung volume and has been shown to change with modifications in PEEP.[13] There was no difference in Edi M suggesting that both nasal airway interfaces were equally successful in maintaining PEEP.

Leaks make comparing different CPAP nasal airway interfaces and devices challenging.[14] The Servo-i determines leakage at the interface by comparing inspiratory to expiratory volumes. Seeing that the double inspiratory arm interface design with RAM does not allow for patient generated expiratory flow, any measurements made by the ventilator are spurious and the leakage difference noted is therefore meaningless. Additionally, the neural trigger used for NIV NAVA works independent of leaks and the ventilator adjusts the flow on a breath by breath basis to compensate for variable air leaks.[7] Patient controlled changes in Edi secondary to variable PIP delivery to the lungs and not the leakage measurement of the ventilator drives this compensation[7].

Seeing there was no difference in Edi noted it is reasonable to assume that the leakage was actually similar between the interfaces.

This study was limited by only comparing the Medin and RAM interfaces. The study had few patients with similar diagnoses limiting the ability to determine if the nasal airway interfaces would function differently in various disease states. Neonates were not randomized and were on RAM for hours prior to the first 20-minute study period. The third 20-minute study period of retesting the RAM was comparable to the first study period so it was felt that the 20-minute time period was sufficient to generate reliable data.

Conclusion

Neonates on NIV NAVA were as clinically stable with the RAM (used off-label for NIV) as with the Medin (FDA approved for NIV). Users may anticipate needing higher PIP with RAM that is due to the device design and not patient related. It may be reasonable to do larger trials to further evaluate RAM as an acceptable interface for neonates on NIV.

References

1 Bhandari V, on behalf of the NICHD Neonatal Network. Synchronized nasal intermittent positive pressure ventilation and neonatal outcomes: a retrospective study. Pediatrics. 2009;124:517-26.
2 Deakins K. Non-invasive respiratory support in the neonatal intensive care unit. Clinical Foundations. 2011;8:2-5.
3 Kallet R, Diaz J. The physiologic effects of noninvasive ventilation. Resp Care. 2009;54:102-14.
4 Bhandari V. Synchronized ventilation in neonates: A brief review. Neonatology Today. 2011;6:1-6.
5 Sinderby C, Beck J. Neurally Adjusted Ventilatory Assist (NAVA): An Update and Summary of Experiences. Neth J Crit Care. 2007;11:243-52.
6 Sinderby C. Neurally adjusted ventilatory assist (NAVA). Minerva Anestesiol. 2002;68:378-80.
7 Beck J, Reilly M, Grasselli G, Mirabella L, Slutsky AS, Dunn MS, et al. Patient-ventilator interaction during neurally adjusted ventilatory assist in low birth weight infants. Pediatr Res. 2009;65:663-8.
8 Ramanathan R, Crotwell D, DiBlasi RM. A novel means for delivering nasal intermittent positive pressure ventilation (NIPPV) in infants: The nasal cannula. Resp Care. 2012;Open Forum Abstracts.
9 De Paoli A, Davis P, Faber B, Morley C. Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates. Cochrane database of systemic reviews. 2008;23.
10 Bushell T, McHugh C, Meyer M. A comparison of two nasal continuous positive airway pressure interfaces--a randomized crossover study. J Neonatal Perinatal Med. 2013;6:53-9.
11 DiBlasi RM. Neonatal noninvasive ventilation techniques: do we really need to intubate? Resp Care. 2011;56:1273-97.
12 Sinderby C, Beck J. Proportional assist ventilation and neurally adjusted ventilatory assist - better approaches to patient ventilator synchrony? Clin Chest Med. 2008;29:329-42.
13 Emeriaud G, Beck J, Tucci M, Lacroix J, Sinderby C. Diaphragm electrical activity during expiration in mechanically ventilated infants. Pediatr Res. 2006;59:705-10.
14 Schmalisch G, Fischer H, Roehr CC, Proquitté H. Comparison of different techniques to measure air leaks during CPAP treatment in neonates. Med Eng Phys. 2009;31:124-30.

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Feb 11.
40. Park IH, Lee SH, Yu ST, Oh YK. Serum procalcitonin as a diagnostic marker of neonatalsepsis.Korean J Pediatr. 2014;57(10):451-6.
41. Steinberger E, Hofer N, Resch B. Cord blood procalcitonin and Interleukin-6 are highly sensitive and specific in the prediction of early-onset sepsis in preterm infants. Scand J Clin Lab Invest. 2014;74(5):432-6.
42. Vouloumanou EK, Plessa E, Karageorgopoulos DE, Mantadakis E, Falagas ME. Serum procalcitonin as a diagnostic marker for neonatal sepsis: A systematic review and meta-analysis. Intensive Care Medicine. 2011;37(5):747-62.
43. Isaacs D, Barfield CP, Grimwood K, McPhee AJ, Minutillo C, Tudehope DI. Systemic bacterial and fungal infections in infants in Australian neonatal units. Australian Study Group for Neonatal Infections.Med. J. Aust. 1995; 162:198–201.
44. Garges HP, Moody MA, Cotten CM, Smith PB, Tiffany KF, Lenfestey R, Li JS, Fowler VG, Benjamin DK. Neonatal meningitis: what is the correlation among cerebrospinal fluid cultures, blood cultures, and cerebrospinal fluid parameters? Pediatrics. 2006;117:1094–1100.
45. Polin RA, Committee on Fetus and Newborn. Management of neonates with suspected or proven early-onset bacterial sepsis. Pediatrics. 2012;129:1006–1015.
46. Alexander DF. Why should there be an NICHD? Pediatrics2011 Feb;127(2):325-33. Epub2011 Jan 3.
47. Manzoni P, Farina D, Leonessa M, et al. Risk factors for progression to invasive fungal infection in preterm neonates with fungal colonization. Pediatrics. 2006;118(6):2359– 2364.
48. Nizet V, Klein JO. Bacterial sepsis and men- ingitis. In: Remington JS, Klein JO, Wilson Christopher B, Nizet V, eds. Infectious Dis- eases of the Fetus and Newborn Infant. 7th ed. Philadelphia, PA: Saunders; 2010:222–275.

Efficacy of Hydrochlorothiazide and Low Renal Solute Feed in Neonatal Central Diabetes Insipidus with Transition to Oral Desmopressin in Early Infancy

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Abstract

Background: The treatment of central diabetes insipidus (DI) with desmopressin in the neonatal period is challenging because of the significant risk of hyponatremia with this agent. The fixed anti- diuresis action of desmopressin and the obligate high fluid intake with milk feeds lead to considerable risk of water intoxication and hyponatremia. To reduce this risk, thiazide diuretics, part of the treatment of nephrogenic DI, were used in conjunction with low renal solute feed and were effective in a single case series of neonatal central DI. Aim: We evaluated the efficacy of early treatment of neonatal central DI with hydrochlorothiazide with low solute feed and investigated the clinical indicators for transition to desmopressin during infancy.

Methods: A retrospective chart review was conducted at Princess Margaret Hospital, Perth of neonates diagnosed with central DI and treated with hydrochlorothiazide, between 2007 and 2013. Four newborns were identified. Mean sNa and mean change in sNa with desmopressin and hydrochlorothiazide treatment were recorded along with episodes of hyponatremia and hypernatremia. Length and weight trajectories during the first 12 months were assessed.

Results: The mean change in sNa per day with hydrochlorothiazide and low renal solute feed was 2.5-3 mmol/L; on desmopressin treatment, the mean change in sNa was 6.8-7.9 mmol/L. There was one episode of symptomatic hyponatremia with intranasal desmopressin with no episodes of hyponatremia or hypernatremia during treatment with hydrochlorothiazide or following transition to oral desmopressin. Transition to oral desmopressin between 3 to 12 months of age was associated with good control of DI. Following introduction of solids, sNa remained stable but weight gain was slow. This improved following transition to desmopressin in one infant.

Conclusions: Hydrochlorothiazide with low renal solute feed is a safe and effective treatment option in neonatal central DI. However, transition to desmopressin should be considered early in infancy following initiation of solids to facilitate growth.

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Introduction

Central Diabetes Insipidus (DI) in newborns and infants is due to the deficiency of arginine vasopressin (AVP) from the posterior pituitary and is associated with septo-optic dysplasia and other midline malformations [1]. DI should be considered in polyuric neonates with elevated serum sodium and osmolality and an inappropriately low urine osmolality (<300 mosm/kg). Polyuria is characterized by a urine volume in excess of 2 l/m2/24 h or approximately 150 ml/kg/24 h at birth [2]. Desmopressin acetate (1-deamino-8-D arginine vasopressin) is the long acting synthetic analogue of vasopressin, without its vasoconstrictive effect, and is the current therapeutic agent of choice in the management of patients with central DI [1]. It binds to the V2 vasopressin receptor on the distal tubules and collecting ducts of the kidney to increase water reabsorption.

Desmopressin is available in oral, nasal and parental preparations and there is a high degree of dose variability between the different forms. In general, the oral dose is about ten times greater than the intranasal dose while the SC dose is 10 times more potent than the intranasal dose [3]. There is also marked inter-individual differences in sensitivity to the drug. These factors make establishing the correct dose and frequency of administration difficult. The fixed anti-diuresis action of desmopressin and the high fluid intake necessary to meet caloric requirements of newborns with milk feeds [4] increase the risk of hyponatremia and make the management of newborns with central DI challenging and difficult.

Thiazide diuretics are used in nephrogenic DI and have been used effectively in a case series of 3 newborns with central DI when desmopressin treatment caused varying sNa levels [5]. The principal action of thiazide diuretics is at the distal convoluted tubule and inhibits the Na-Cl cotransport, inducing natriuresis. Prolonged administration leads to reduction of extracellular fluid volume with water and sodium reabsorption at the proximal tubules. This leads to reduced water and sodium delivery to the distal tubules with resultant reduction in urine output [6]. This theory only partly accounts for the reduction in urine volume. Animal models have shown that the thiazide diuretic, hydrochlorothiazide, also acts at the inner medullary collecting ducts and enhances water reabsorption by increasing osmotic and diffusional water permeability. This direct action plays an important role in reducing urine volume [7]. The antidiuretic

Table 1 Renal solute load (RSL) in feeds

Feed	RSL (mOsm/L)
Breast milk	93
Standard formula	135-260
Cow's milk	308
Nan®HA	95

Nan®HA: commercially available formula.

effect of hydrochlorothiazide was more pronounced with low sodium diet with diminishing of the effect with high sodium intake [8]. The sum of dietary nitrogen, sodium, potassium, chloride and phosphorus determines the solute load to the kidneys, and, therefore, the urine osmolality [9]. Urine output increases proportionately to the renal solute load (RSL) in feeds in the presence of normal renal function and hence low renal solute feed is used concurrently with thiazides to reduce urine volume. Breast milk has the lowest renal solute load and in non-breast fed babies, commercially available formula with low renal solute load is used. (Table 1) [10].

The successful use of thiazide diuretics with low renal solute load was first documented in a case series of three infants with central DI [5]. However, transition from hydrochlorothiazide to desmopressin is warranted with increasing solid intake. Rivkees et al. has suggested transition at 12 to 24 months of age when infants are on at least 80% of solids for their calorie intake [4]. In the following case series of four newborns with central DI, we aim to review the efficacy of hydrochlorothiazide and low renal solute feed in the treatment of central DI by presenting the clinical response of these infants and their transition to oral desmopressin.

Methods

The Princess Margaret Hospital Newborn Service is the sole provider of tertiary neonatal intensive care for Western Australia. There are approximately 690 admissions per year. Review of discharge diagnoses over 2007-2013 identified 4 newborns with central DI treated with hydrochlorothiazide. A retrospective chart review of these patients was conducted to characterize their clinical features and management. Diabetes insipidus was diagnosed by the presence of hypernatremia (sNa > 150 mmol/L), high serum osmolality (>300 mOsm/L) and low urine osmolality (<300 mOsm/L). The co-existence of other pituitary hormone deficiencies was also reviewed.

During the treatment period in which the newborns were either on desmopressin or hydrochlorothiazide, mean sNa (SD) and mean change in sNa (SD) per day were reviewed; the latter was calculated against time, using sodium measurements taken > 8 hours apart. Episodes of hyponatremia (sNa <130 mmol/L) and hypernatremia (sNa >150mosm/L) were documented. The age of the infant and reason for transition from hydrochlorothiazide to oral desmopressin was also recorded. Growth parameters during the first 12 months were assessed. Informed consent according to Institutional HREC procedures was obtained from parents for this case series.

Results

There were 4 newborns treated for central DI with thiazide diuretics. DI was secondary to septo-optic dysplasia in 3 newborns and to holoprosencephaly in one newborn. The newborns were born at term with diabetes insipidus manifested in the first week of life. In the three newborns with septo-optic dysplasia, there were coexistent hormone deficiencies including growth hormone, thyroxine and cortisol. DI was isolated in the case (S4) with holoprosencephaly.

Intranasal desmopressin was the first drug instituted in 2 newborns . Wide fluctuations in sNa levels on desmopressin initiated a change to hydrochlorothiazide with low renal solute load feed and led to stabilisation of sNa levels. The subsequent 2 newborns with central DI were commenced on hydrochlorothiazide as the first line drug. The dose of hydrochlorothiazide was 2 to 3 mg/kg/day in two divided doses. The diuretic was used in conjunction with expressed breast milk or commercially available Nan® H.A. The response to hydrochlorothiazide, with sNa levels in normal range, was seen within the first 24 hours.

The mean sNa and mean change in sNa (SD) on treatment with desmopressin and hydrochlorothiazide are demonstrated in Table 2. sNa levels are more stable with hydrochlorothiazide . This is demonstrated in the sNa profile in a newborn with DI (S1) in Figure 1. Transition to oral desmopressin was initiated at 12 months of age in two infants when on significant solid intake except for S2 wherein desmopressin was commenced at 3 months of age in the background of difficult to control DI with gastroenteritis. The initial desmopressin doses ranged from 10 to 50 mcg (Table 3). There was one episode of symptomatic hyponatremia with intranasal desmopressin in the neonatal period. Importantly, there were no episodes of hyponatremia or hypernatremia during the neonatal period

Table 2 Mean sNa and mean change in sNa (mmol/L) per day on treatment with oral desmopressin and hydrochlorothiazide (HCT)

S	Mean sNa (SD)			Mean change in sNa (SD)		
	Desmopressin (IN)	Desmopressin (IN)+ HCT	HCT+ Low RSL	Desmopressin (IN)	Desmopressin (IN)+ HCT	HCT+ Low RSL
1	139	144.2	141.0	6.8	5.3	3
	+/−10.5	+/−5.4	+/−4.7	+/−5.6	+/−4	+/−2.7
2	142.7		143.5	7.9	-	2.7
	+/−8.5		+/−2.5	+/−6		+/−1.6
3			142.4		-	2.5
			+/−3.0			+/−2.4
4			142.2		-	2.55
			+/−2.9			+/−2.9

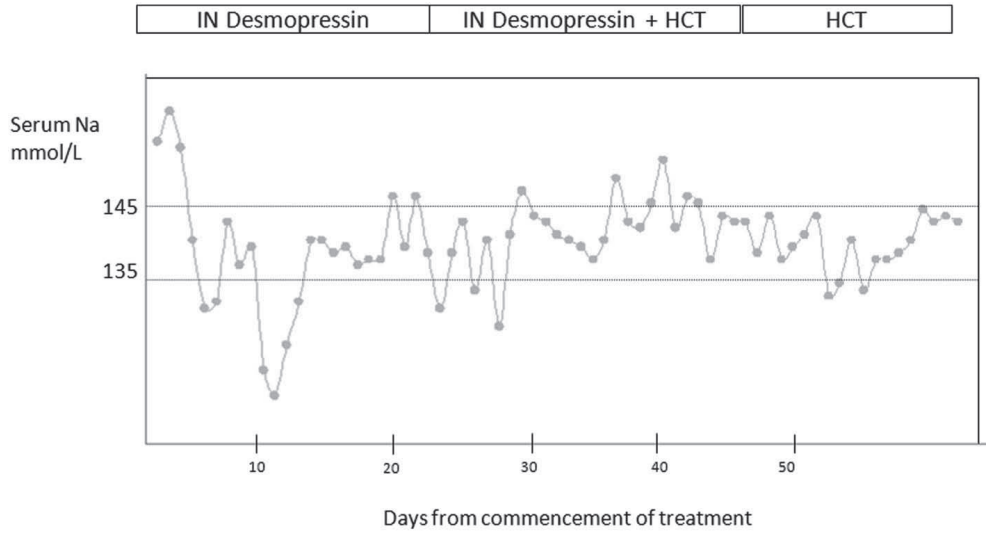

Figure 1. Serum Na profile in newborn with DI (S1) on intranasal desmopressin and Hydrochlorothiazide (HCT).

associated with hydrochlorothiazide and after transition to oral desmopressin. Other pituitary hormone deficiencies were carefully monitored and supplemented in the 3 cases with septo-optic dysplasia.

Discussion

Desmopressin is an effective treatment for central DI; however the risk of hyponatremia is a significant adverse effect and reported for all formulations [11]. This case series demonstrates that hydrochlorothiazide combined with low solute feed resulted in less variability in sNa compared to desmopressin therapy in newborns with central DI and is a safer option in the neonatal period.

Thiazide diuretics are used in the management of nephrogenic DI [12] and their use has extended to central DI [5,13] though still not common practice. Chlorothiazide was used as the diuretic in a dose of 5 mg/kg every 12 hours and increased urinary osmolality in an infant with DI from 50 mOsm/L to 100-150 mOsm/L [5]. This modest increment in urine osmolality is a relatively large increase considering the limited neonatal renal concentrating capacity. Chlorothiazide is not licensed for use in Australia and hence we used hydrochlorothiazide at a dose of 3 mg/kg/day as used in nephrogenic DI. The drug was administered as a suspension (1 ml = 10 mg) formulated in the hospital pharmacy. Although thiazide diuretics are generally well tolerated in newborns, the clinician should be aware of the potential risk of hypokalemia which may occur during episodes of gastroenteritis. We confirm the observations of Rivkees et al. [3,4] in the case series presented here that the combined use of hydrochlorothiazide and low renal solute formula feed is effective in managing central DI whilst the patient is maintained on a liquid diet. Hydrochlorothiazide was easy to administer and did not cause any episode of hyponatremia or hypernatremia.

By 12 months, most infants have nutritious choices from the wide variety of foods eaten by the rest of the family [14] and the renal solute load will vary depending on the protein intake. If a low renal solute diet is maintained, the sNa may be stable with hydrochlorothiazide therapy as in S1 who remained on low renal solute formula until one year of age with supplemental solids. However, she failed to gain weight although her length was not compromised. Her growth improved significantly following institution of oral desmopressin as demonstrated in Figure 2. In S4, the sNa level was high at 12 months of age as she was on standard formula with no reduction in volume of feeds with minimal solid intake. We infer from both these cases that the efficacy of hydrochlorothiazide is reduced with

Table 3 Transition from hydrochlorothiazide to oral desmopressin

S	Etiology	Age of transition	Reason for transition	Dose of desmopressin (oral)	F/U: growth
1	SOD	12 months	Failure to thrive	50 mcg BD 10.5 mcg/kg/	Improved growth
2	SOD	3 months	Acute gastroenteritis with low K; difficulty in maintaining Na	25 mcg BD 4.5 mcg/kg/day	-NA*-
3	SOD	6 months	Failure to thrive	10 mcg BD 3.3 mcg/kg/day	No improvement in growth; concerns regarding compliance
4	HPE	12 months	Failure to thrive Hypernatremia	50 mcg BD 10 mcg/kg/day	No improvement in growth but growth impaired due to underlying condition

*NA: not available.
SOD: Septo-optic dysplasia.
HPE: Holoprosencephaly.

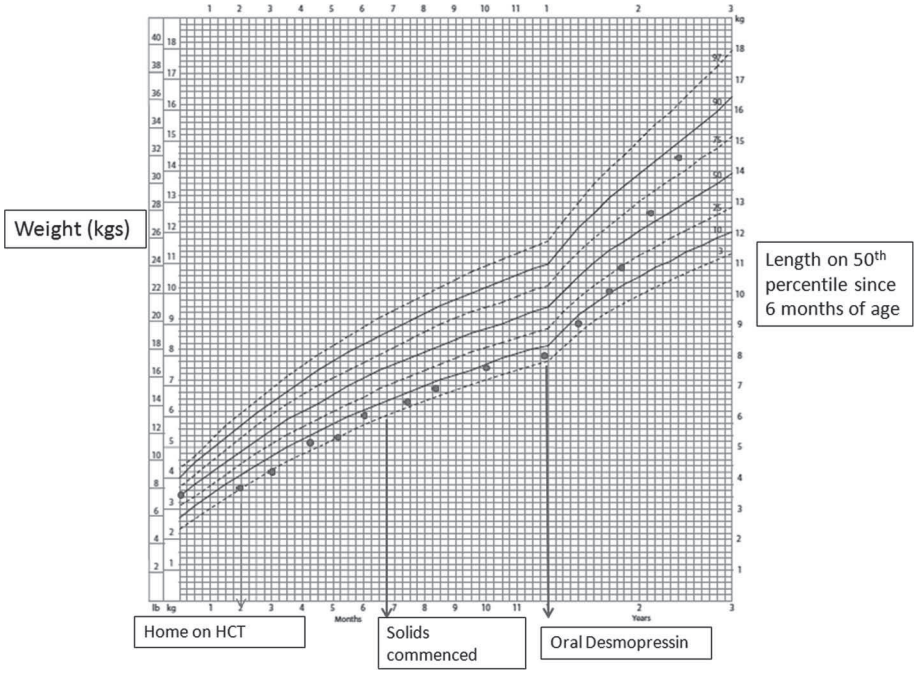

Figure 2. CDC growth chart of S1 demonstrates catch up growth after transition from hydrochlorothiazide (HCT) to oral desmopressin.

increased renal solute load. It should be noted that growth in S4 remained poor following institution of desmopressin due to her underlying medical condition (holoprosencephaly) [15]. Based on our findings from these cases, hypernatremia is a late clinical indicator but transition should be considered at an early stage of infancy before the infants are on significant solid intake. Weight loss of 0.8 to 1.5 kg was demonstrated in 4 patients (7-17 years) with vasopressin resistant DI when commenced on hydrochlorothiazide with regain of weight on cessation of the drug [8] which the authors believe is secondary to the natriuresis induced by diuretic. Chronic diuretic therapy also causes losses of potassium, magnesium and zinc and can inhibit protein synthesis and growth [16].

Intranasal and SC desmopressin have been used in central DI in infants and recently, there is increasing use of oral desmopressin. Blanco et al. compared the sNa profile of 6 infants with SC and 4 infants with intranasal desmopressin in infants aged less than 12 months of age and found that SC desmopressin was effective and better at maintaining sNa in range than intranasal desmopressin though symptomatic hyponatremia was not observed in either group [17]. However, symptomatic hyponatremia with central pontine myelinolysis has been described in a malnourished 3 year old with holoprosencephaly on intranasal desmopressin [18]. Use of oral desmopressin during the newborn period was earlier limited to case reports as in Table 4 [19-22]. An oral preparation was first used in view of difficulty with administering intranasal solutions in a patient with cleft lip/palate [20]. These first case reports were followed by a case series of infants with central DI [23]. Oral desmopressin was commenced at diagnosis (7-300 days) in 11 infants with central DI with a median initial dose of 2mcg/kg/day (0.26-18.5). Oral desmopressin was found to be superior to the intranasal form with less sNa fluctuations and has been increasingly used as treatment in majority of infants and toddlers [24]. The dose of desmopressin in infancy was lower at 1.1 (0.9-1.4) mcg/kg/day while the median oral dose in older children was higher at 9.5 (4.2-17.0) mcg/kg/day. Our experience with the use of oral desmopressin outside the neonatal period has been similar with doses ranging from 3.3 to 10.5mcg/kg/day associated with good efficacy and relatively stable sNa levels. In our centre, oral desmopressin (Minirin 200mcg) is dissolved in 20 ml of water and the required dose is administered with a syringe. This increasing safety and efficacy data of oral desmopressin supports the early transition to oral desmopressin.

Conclusion

In conclusion, we report our experience of 4 neonates with central DI treated with hydrochlorothiazide and low solute feeds, which supports this as a safe and effective alternative to desmopressin for treatment of central DI during the neonatal period. Our results, however, suggest that hydrochlorothiazide

Table 4 Use of oral desmopressin in infants <3 months of age

Case	Author	Etiology	Initial Rx	Age of oral desmopressin	Oral dose	Oral dose preparation
1	Stick [19]	Midline defect	IN	D33	5 mcg OD increased to BD dose	Intranasal solution
2	Atasay [20]	Intracranial haemorrhage	IN	D73	(5 mcg/day) 2.5 µg/kg/day, twice daily	Minirin® tablet, 89 µg,
3	Ozaydin [21]	ECP syndrome**	Oral	< 1 month	2.5 mcg/kg/day, twice daily	Minirin® tablet, 89 µg,
4	Kollamparambil [22]	Transient	IV	2 months	4 mcg/day in divided doses	-NA*-

*NA: not available.
**ECP syndrome: ectrodactyly and cleft lip/palate.

therapy should be limited to the neonatal and first few months of age. Transition to desmopressin should occur early during infancy, at the time of initiation of solid nutrition, in order to facilitate growth.

References

1 Oiso Y, Robertson GL, Norgaard JP, Juul KV: Clinical review: treatment of neurohypophyseal diabetes insipidus. J Clin Endocrinol Metab 2013, 98(10):3958-3967.
2 Di Iorgi N, Napoli F, Allegri AE, Olivieri I, Bertelli E, Gallizia A, Rossi A, Maghnie M: Diabetes insipidus—diagnosis and management. Horm Res Paediatr 2012, 77(2):69-84.
3 Rivkees SA: The Management of Central Diabetes Insipidus in Infancy: Endocrinology Touch Briefings. ; 2008:66-68.
4 Rivkees SA, Dunbar N, Wilson TA: The management of central diabetes insipidus in infancy: desmopressin, low renal solute load formula, thiazide diuretics. J Pediatr Endocrinol Metab 2007, 20(4):459-469.
5 Pogacar PR, Mahnke S, Rivkees SA: Management of central diabetes insipidus in infancy with low renal solute load formula and chlorothiazide. Curr Opin Pediatr 2000, 12(4):405-411.
6 Crawford JD, Kennedy GC: Chlorothiazide in diabtes insipidus. Nature 1959, 4665:891-892.
7 Cesar KR, Magaldi AJ: Thiazide induces water absorption in the inner medullary collecting duct of normal and Brattleboro rats. Am J Physiol 1999, 277:F756-F760.
8 Earley LE, Orloff J: The mechanism of antidiuresis associated with the administration of hydrochlorthiazide to patients with vasopressin resistant diabetes insipidus. J Clin Invest 1962, 41(11):1988-1997.
9 Ziegler EE, Fomon SJ: Potential renal solute load of infant formulas. J Nutr 1989, 119(12 Suppl):1785-1788.
10 Fomon S: Potential renal solute load: considerations relating to complementary feedings of breast fed infants. Paediatrics 2000, 106:1284.
11 Rizzo V, Albanese A, Stanhope R: Morbidity and mortality associated with vasopressin replacement therapy in children. J Pediatr Endocrinol Metab 2001, 14:861-867.
12 Crawford JD, Kennedy GC, Hill LE: Clinical results of diabetes insipidus with drugs of the chlorothiazide series. N Engl J Med 1960, 262:737-742.
13 Chaudhary H, Bhakhri BK, Datta V: Central diabetes insipidus in newborns: unique challenges in management. Pediatr Endocrinol Rev 2011, 9(1):476-478.
14 National Health Medical Research council: Infant Feeding Guidelines. Canberra: National Health and Medical Research council; 2012.
15 Dubourg C, Bendavid C, Pasquier L, Henry C, Odent S, David V: Holoprosencephaly. Orphanet J Rare Dis 2007, 2:8.
16 Dorup I: Magnesium and potassium deficiency: its diagnosis, occurrence and treatment in diuretic therapy and its consequences for growth, protein synthesis and growth factors. Acta Physiol Scand Suppl 1994, 618:1-55.
17 Blanco EJ, Lane AH, Aijaz N, Blumberg D, Wilson TA: Use of subcutaneous DDAVP in infants with central diabetes insipidus. J Pediatr Endocrinol Metab 2006, 19(7):919-925.
18 Rivas-Crespo MF, Minones-Suarez L, SS GG.: Rare neonatal diabetes insipidus and associated late risks: case report. BMC Pediatr 2012, 12:56.
19 Stick SM, Betts PR: Oral desmopressin in neonatal diabetes insipidus. Arch Dis Child 1987, 62(11):1177-1178.
20 Atasay B, Berberoglu M, Gunlemez A, Evliyaoglu O, Adiyaman P, Unal S, Arsan S, Ocal G: Management of central diabetes insipidus with oral desmopressin in a premature neonate. J Pediatr Endocrinol Metab 2004, 17(2):227-230.
21 Ozaydin E, Aycan Z, Yusufoglu AM, Cetinkaya E, Ergen S, Unal S, Köse G: Management of central diabetes insipidus with oral desmopressin in a patient with ectrodactyly and cleft lip/palate (ECP) syndrome. Turk J Pediatr 2009, 51:89-93.
22 Kollamparambil TG, Mohan PV, Gunasuntharam K, Jani BR, Penman DG: Prenatal presentation of transient central diabetes insipidus. Eur J Pediatr 2011, 170(5):653-656.
23 Karthikeyan A, Abid N, Sundaram PC, Shaw NJ, Barrett TG, Hogler W, Kirk JM: Clinical characteristics and management of cranial diabetes insipidus in infants. J Pediatr Endocrinol Metab 2013, 8:1-6.
24 Ooi HL, Maguire AM, Ambler GR: Desmopressin administration in children with central diabetes insipidus: a retrospective review. J Pediatr Endocrinol Metab 2013, 11:1-6.

Inadvertent Intravenous Administration of Maternal Breast Milk in a Six-Week-Old Infant: a Case Report and Review of the Literature

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Abstract

Background: Accidental intravenous administration of an enteral feeding can be fatal or cause complications such as sepsis, acute respiratory and circulatory failure, acute renal failure, hepatic insufficiency, coagulation disorders and severe permanent neurological sequelae. These "wrong route" errors are possible due to compatible connections between enteral feeding systems and intravascular infusion catheters.

Case presentation: We report a six-week-old male infant who received a 5 ml intravenous infusion of breast milk. Within five minutes of administration the child developed tachycardia and tachypnea, accompanied by a sudden decrease in oxygen saturation on pulse oximetry to 69%. The infant received supplemental oxygen via nasal cannula and was transferred to the pediatric intensive care unit. Broad-spectrum antibiotics were administered for 48 hours. Vital signs returned to normal within a few hours. Neurological follow-up through 3 years did not reveal any neurodevelopmental abnormalities.

Conclusion: Development of specific enteral feeding connections, which are incompatible with intravascular catheter connections, is needed urgently to prevent a misconnection with potential morbidity or mortality of children.

Background

Accidental intravenous administration of enteral feeding can cause severe complications including sepsis, multi-organ failure and death [1-6]. Tubing and catheter misconnections are an important and underreported problem in healthcare [7]. In addition to peripheral and central intravenous catheters and various feeding tubes, peritoneal dialysis catheters, epidural catheters and tracheostomy cuff inflation tubes also have had misconnections [7-10]. In many cases the outcome was fatal [3,5,7,11]. We report a six-week-old male infant who received 5 ml of breast milk intravenously and recovered completely. We discuss the medical management of this patient, and administrative measures and practices we propose to prevent future incidents.

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Case presentation

Postnatal assessment of a male newborn, delivered at 40 weeks gestation (birth weight 4.065 kg, height 52 cm), revealed malformation of the ribs and vertebral column with duplications of thoracic vertebrae, hypoplasia of the right lung, and partial liver herniation through a small diaphragmatic defect into the right hemithorax. On the 48th day postpartum, a simply herniotomy was performed for a right inguinal hernia. On the first postoperative day feeding was started via a nasogastric tube. To promote mother-infant interaction, the mother was instructed in enteral feeding procedures via the nasogastric tube. However, the mother administered 5 ml expressed breast milk intravenously with a syringe. The infant experienced an immediate decrease of oxygen saturation with pulse oximetry of 69%, developed sinus tachycardia of 195/min and tachypnoea with a respiratory rate of 84/min. Blood pressure remained normal, and oxygen saturation normalized following supplementation with nasal cannula oxygen using flow rates of 3-4 L/min. Due to the imminent risk of microembolism and nonspecific activation of coagulation, the infant was transferred to the intensive care unit. Chest X-ray did not reveal infiltrates, pleural effusions or a pneumothorax. Both an electrocardiogram and echocardiography did not show acute right ventricular overload. Ampicillin was given intravenously for a total of 48 hours. Laboratory values one, six and 12 hours after the incident neither revealed evidence for an infection, renal or hepatic dysfunction, a metabolic or coagulation disorder nor myocardial damage. Cerebral ultrasound was normal two hours after the event. Microbial cultures of expressed breast milk were negative. There was no microbiotic evidence of cytomegalovirus in expressed breast milk. The respiratory rate normalized within 1.5 hours, and the heart rate within 2 hours. Four hours after the incident, supplemental oxygen was discontinued. The infant's blood pressure and temperature were stable throughout the incident. The child was transferred to the pediatric surgical ward 24 hours after the incident and discharged on the third postoperative day without the nasogastric tube. Follow-up examinations through 3 years of age showed normal neurological development.

Discussion

There are few reports of medical injury due to catheter misconnections in scientific journals; however, they are only the tip of the iceberg worldwide [5,7]. Through 2006, more than 300 cases of misconnection errors have been reported to the United States Pharmacopeial Convention [5]. These events are often

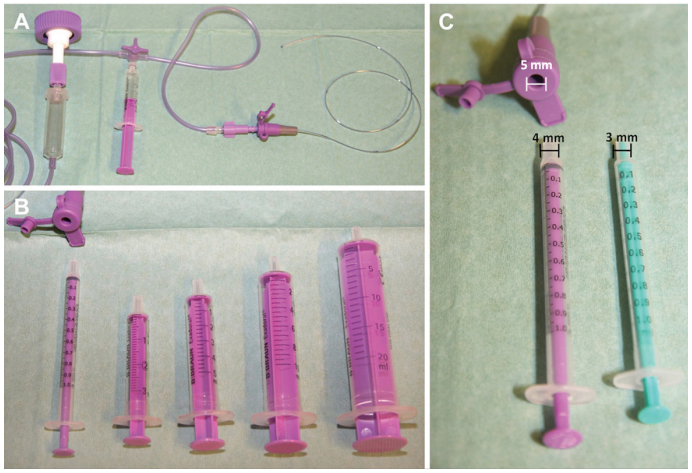

Figure 1. Specific tubing and equipment for enteral nutrition. (A) Gastric tubing with specific adapter for connecting enteral feeding tubings with built-in three-way stopcock, to which only specific food syringes can be connected. (B) and (C) Specific entry of a gastric tubing, which has a larger opening of 5 mm in diameter for connection of specific food syringes of different sizes (1 ml, 3 ml, 5 ml, 10 ml and 20 ml). Food syringes (color purple) have a larger cone with a diameter of 4 mm in comparison to an intravenous syringe (color green) cone (diameter 3 mm) for intravenous infusion systems. The intravenous syringe cone (green syringe) is too small and does not fit into the entry of gastric tubing (color purple). An additional safety feature is the consistent color coding (purple) for all parts used for the application of food.

fatal and occur in a wide variety of settings [5,7]. Affecting adults [1-3,6,12-17], infants and children [4,5,18-20]. An important lesson from these reports is that experience does not prevent wrong route errors.

Intravenous infusion of enteral feeding may lead to respiratory [15,18-20], renal [3] or hepatic insufficiency [3,18], diffuse myocardial damage [12], metabolic acidosis [18], coagulation disorder [12], increased production of stool [19,21], anaphylactic reactions [12,21], sepsis [1,2,4,6,13,14,18] and death [3,11,22]. Multi-organ failure may not be linked directly to high output septic shock [3,18]. Seizures and permanent neurological impairment have been described in a preterm infant [18]. Some of the clinical features may be explained by microembolism of fat globules and water insoluble particles, as well as an immune response to foreign antigens [3,12]. Cytomegalovirus infection in infancy caused by intravenously infused contaminated breast milk, bypassing the gastrointestinal barrier, has not been reported, however it is prudent to consider this risk. The composition of the enteral feeding, the volume, and the rate of administration are likely to be related to the severity of symptoms. The rarity of reported cases, however, prevents definite conclusions.

Management of most cases has been supportive and included oxygen supplementation and mechanical ventilation [3,5,13,18], diuretic therapy [12,23], peritoneal dialysis [3], steroid administration [12,15,19], and circulatory support with fluid resuscitation and catecholamines [1,3,12,13,15,18]. Broad-spectrum antibiotics were administered and then tailored to the results of blood and feeding cultures [1,3,12,13,15,23]. Heparin has been administered in some cases as prophylaxis to prevent thromboembolic events [12,15]. Plasmapheresis and exchange transfusion in an adult and a preterm infant have been reported to improve oxygenation and stabilize hemodynamics, respectively, in an attempt to remove foreign antigens and toxins [13,18]. Since the first report of obvious intravenous administration of an enteral feeding [12], numerous strategies have been proposed to further reduce wrong route errors [4,5,7,15,18,20]. In order to prevent such misconnections, tubings should always be traced to the point of origin connection before any infusion is initiated, including enteral feeds. Enteral feeding syringes and pumps should always be labeled. Education and instruction of all caregivers is necessary. One of the safest preventive measures which has been taken in our hospital after a causality analysis of the reported case, is the use of tubings that are specifically designed for enteral feeding (Figure 1). Government sponsored manufactures standards should identify this situation as solvable at the manufacturing stage and mandate individual non-interchangeable design for intravenous tubing and enteral feeding catheters.

Systematic or institutional practices and procedures should be designed to reduce medical errors, for example, the use of an electronic health record with instructions to avoid errors and the use of Six Sigma as a management system for process improvement [24]. A Hospital Safety Committee consisting of a multidisciplinary group should be established and given the mandate to ensure continuous quality improvement in patient safety [25]. More published reports of such medical errors are required to create guidelines for the optimal course of action to take in such cases.

Conclusion

Wrong route errors are associated with a high morbidity and mortality risk. Specifically designed non interconnecting tubing should be used to prevent consequences that can arise from misconnected enteral feeding tubing. Medical staff and associated caregivers should be instructed in the use of enteral feeding tubing to prevent route errors.

References

1 Stellato TA, Danziger LH, Nearman HS, Creger RJ: Inadvertent intravenous administration of enteral diet. J Parenter Enter Nutr 1984, 8:453–455.
2 Casewell MW, Philpott-Howard J: Septicemia from inadvertent intravenous administration of enteral feeds. J Hosp Infect 1983, 4:403–405.
3 Ulicny KS Jr, Korelitz JL: Multiorgan failure from the inadvertent intravenous administration of enteral feeding. J Parent Enter Nutr 1989, 13:635–660.
4 Vanitha V, Narasimham KL: Intravenous Breast Milk Administration—A Rare Accident. Indian Pediatr 2006, 43:827.
5 Ryan CA, Mohammad I, Murphy B: Normal neurologic and developmental outcome after an accidental intravenous infusion of expressed breast milk in a neonate. Pediatrics 2006, 117:236–238.
6 Stapleton GN, Symmonds KL, Immelman EJ: Septicaemia resulting from inadvertent intravenous administration of enteral nutrient solution: a case report. S Afr Med J 1988, 73:542–543.
7 Joint Commission on Accreditation of Healthcare Organizations, USA: Tubing misconnections–a persistent and potentially deadly occurrence. Sentinel Event Alert 2006, 36:1–3.
8 Patel PC, Sharif AM, Farnando PU: Accidental infusion of total parenteral nutrition solution through an epidural catheter. Anaesthesia 1984, 39:383–384.
9 Singh S, Loeb RG: Fatal connection: death caused by direct connection of oxygen tubing into a tracheal tube connector.

Anesth Analg 2004, 99:1164–1165.
10 Drake JM, Crawford MW: Near-miss injection of an anesthetic agent into a cerebrospinal fluid external ventricular drain: special report. Neurosurgery 2005, 56:E1161.
11 Takeshita H, Yasuda T, Nakajima T, Mori S, Mogi K, Ohkawara H, Nara M, Kishi K: A death resulting from inadvertent intravenous infusion of enteral feed. Int J Leg Med 2002, 116:36–38.
12 Wallace JR, Payne RW, Mack AJ: Inadvertent intravenous infusion of milk. Lancet 1972, 1:1264–1266.
13 Ong BC, Soo KC: Plasmapheresis in the treatment of inadvertent intravenous infusion of an enteral feeding solution. J Clin Apher 1997, 12:200–201.
14 Ramsay SJ, Gomersall CD, Joynt GM: The dangers of trying to make ends meet: accidental intravenous administration of enteral feed. Anaesth Intensive Care 2003, 31:324–327.
15 Sen I, Raju RS, Vyas FL: Inadvertent central venous infusion of enteral feed: a case report. Ann R Coll Surg Engl 2008, 90:1–2.
16 Burdon JT, Morton AM, Conway SP: Accidental intravenous administration of enteral feeds by a patient with cystic fibrosis. Clin Nutr 1995, 14:313–315.
17 Nicholson Roberts TC, Swart M: Enteral drugs given through a central venous catheter. Anaesthesia 2007, 62:624–626.
18 Huddleston K, Creekmore P, Wood B: Administration of infant formula through the intravenous route: consequences and prevention. MCN Am J Matern Child Nurs 1994, 19:40–42.
19 Lopez Garcia MJ, Sorribes Monrabal I, Fernandez-Delgado Cerda R: Accidental intravenous administration of semi-elemental formula in an infant. Clin Pediatr 1992, 31:757–758.
20 ISMP Medication Safety Alert! Nurse Advise-ERR. Preventing accidental i.v. infusion of breast milk in neonates. Alta RN 2011, 67:22–23.
21 Kennelly C, Barnes S: Inadvertent i.v. administration of enteral formula causes adverse sequelae ranging from microembolism and hypersensitivity reactions to increased production of stool. Am J Crit Care 1998, 7:80.
22 Fechner G, Du Chesne A, Ortmann C, Brinkmann B: Death due to intravenous application of enteral feed. Int J Leg Med 2002, 116:354–356.
23 Malone M, Aftahi S, Howard L: Inadvertent intravenous administration of an elemental enteral nutrition formula. Ann Pharmacother 1993, 27:1187–1189.
24 Deckard GJ, Borkowski N, Diaz D, Sanchez C, Boisette SA: Improving timeliness and efficiency in the referral process for safety net providers: application of the Lean Six Sigma methodology. J Ambul Care Manage 2010, 33:124–130.
25 Szekendi MK, Barnard C, Creamer J, Noskin GA: Using patient safety morbidity and mortality conferences to promote transparency and a culture of safety. Jt Comm J Qual Patient Saf 2010, 36:3–9.

LMA Supreme for Neonatal Resuscitation: Study Protocol for a Randomized Controlled Trial

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Abstract

Background: The most important action in the resuscitation of a newborn in the delivery room is to establish effective assisted ventilation. The face mask and endotracheal tube are the devices used to achieve this goal. Laryngeal mask airways that fit over the laryngeal inlet have been shown to be effective for ventilating newborns at birth and should be considered as an alternative to facemask ventilation or endotracheal intubation among newborns weighing >2,000 g or delivered ≥34 weeks' gestation. A recent systematic review and meta-analysis of supraglottic airways in neonatal resuscitation reported the results of four randomized controlled trials (RCTs) stating that fewer infants in the group using laryngeal mask airways required endotracheal intubation (1.5%) compared to the group using face masks (12.0%). However, there were methodological concerns over all the RCTs including the fact that the majority of the operators in the trials were anesthesiologists. Our hypothesis is based on the assumption that ventilating newborns needing positive pressure ventilation with a laryngeal mask airway will be more effective than ventilating with a face mask in a setting where neonatal resuscitation is performed by midwives, nurses, and pediatricians. The primary aim of this study will be to assess the effectiveness of the laryngeal mask airway over the face mask in preventing the need for endotracheal intubation.

Methods/design: This will be an open, prospective, randomized, single center, clinical trial. In this study, 142 newborns weighing >1,500 g or delivered ≥34 weeks gestation needing positive pressure ventilation at birth will be randomized to be ventilated with a laryngeal mask airway (LMA SupremeTM, LMA Company, UK-intervention group) or with a face mask (control group). Primary outcome: Proportion of newborns needing endotracheal intubation. Secondary outcomes: Apgar score at 5 minutes, time to first breath, onset of the first cry, duration of resuscitation, death or moderate to severe hypoxicischemic encephalopathy within 7 days of life.

Background

The ability to maintain a patent airway and provide effective positive pressure ventilation (PPV) is the main objective of neonatal resuscitation [1,2]. This is currently achieved with the use of a face mask (FM) or an endotracheal tube (ETT). Both these devices have major limitations from a strictly anatomical point of view and require adequate operator skills. In certain situations, both FM ventilation and ETT intubation may prove difficult to establish an upper airway [3,4].

In 1981, Archie Brain designed the laryngeal mask airway (LMA) with the aim of producing an airway device that would be more practical than the FM and less invasive than the ETT [5].

In adults, the LMA is routinely used during anesthesiology procedures.

The potential advantages of the LMA over the FM include an easier insertion technique, less manipulation of the patient's head, neck, and jaw, a better airtight seal after positioning, and more effective PPV [6]. Ease of positioning and reduced invasiveness are the reported advantages of the LMA when compared to the tracheal tube [6].

A recent study including 11,910 anesthesia pediatric cases showed that only 102 cases (0.86%) experienced LMA failure. Common presenting features of LMA failures included leak (25%), obstruction (48%), and patient intolerance such as intractable coughing/bucking (11%) [7].

In the setting of the neonatal resuscitation, previous observational studies showed that, when used by teams with expertise (that is, anesthesiologists), the LMA provided effective PPV in most of the treated patients (range 95 to 99%) [8-10]. A 2005 Cochrane review concluded that there was no evidence to evaluate the safety or efficacy for the use of LMA versus FM ventilation in the resuscitation of newborn infants [11]. It suggested that a well-designed randomized controlled trial (RCT) comparing these two airway adjuncts was warranted [11]. In 2013, a systematic review and meta-analysis of supraglottic airways in neonatal resuscitation reported the results of four RCTs, stating that fewer infants in the LMA group required endotracheal intubation (1.5%) compared to the FM group (12.0%) [12]. There were however, methodological concerns over all the RCTs including the fact that the majority of the operators in the trials were anesthesiologists (who are less likely in most clinical settings to be present at neonatal resuscitation).

The LMA is used more often by anesthesiologists rather

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than pediatricians, nurses, and midwives. It is thus essential to demonstrate its effectiveness by those who will be more commonly involved in neonatal resuscitation in most clinical settings. Furthermore, it is important to thoroughly record any side effects, as in a case series of a comparison of LMA over FM in infants in the operating theatre, significantly more side effects were reported using the LMA over the FM [13,14].

Although previous studies showed that the LMA was effective also in preterm infants weighing less than 2,000 g [9,10], the last version of the International Guidelines for Neonatal Resuscitation state that "a LMA should be considered during resuscitation if FM ventilation is unsuccessful and tracheal intubation is unsuccessful or not feasible. The LMA may be considered as an alternative to a FM for PPV among newborns weighing >2,000 g or delivered ≥34 weeks' gestation" [1,2].

Despite this recommendation, it has not yet been shown in a well-conducted RCT whether or not LMA is more effective than FM in resuscitation of newborn infants.

Methods/design

Aim

The primary aim of this study will be to assess the effectiveness of LMA over FM ventilation in preventing the need for endotracheal intubation at birth.

Study design

This is a single center, prospective, unblinded, randomized clinical trial of LMA ventilation versus FM ventilation in infants weighing >1,500 g or delivered ≥34 weeks' gestation.

Inclusion criteria

Inborn infants satisfying the following inclusion criteria will be eligible to participate in the study:

1 gestational age ≥34 weeks (and)
2 expected birth weight >1,500 g [9,10] (and)
3 need for PPV at birth; the need for PPV will be determined by the presence of apnoea or gasping, or heart rate <100 beats per minute (bpm) after initial resuscitation measures (providing warmth, positioning, clearing the airway, drying and stimulation) over the first 30 seconds [1,2] (and)
4 parental consent; a written informed consent will be obtained by a member of the neonatal team involved in thestudy from aparent orguardian beforedelivery.

Exclusion criteria

1 Lethal anomalies.
2 Hydrops.
3 Major malformations of the respiratory system.
4 Congenital heart disease.
5 Stillbirths; a stillbirth will be diagnosed when a heart rate is never established.

Primary outcome measure

The primary outcome of this study will be the proportion of newborns needing endotracheal intubation.

Secondary outcome measures

1 Apgar score at 5 minutes.
2 Time to first breath, defined as the first respiratory effort.
3 Time to first cry, defined as the first audible cry spontaneously emitted by the infant.
4 Death or moderate to severe hypoxicischemic encephalopathy (HIE) within 7 days of life, according to a modification of Sarnat and Sarnat [15,16]. According to this classification, HIE grade I (mild) includes irritability, hyperalertness, mild hypotonia, and poor sucking; grade II (moderate) includes lethargy, seizures, marked abnormalities of tone, and requirement of tube feeding; grade III (severe) includes coma, prolonged seizures, severe hypotonia, and failure to maintain spontaneous respiration.
5 Complications secondary to the procedure.
6 Admission to NICU/normal nursery.

Other collected data

The following data will be collected during resuscitation: (1) Apgar score at 1 min after birth; (2) LMA insertion time, the rate of successful insertion at the first attempt, and the number of attempts required to insert the LMA successfully; (3) adverse effects during resuscitation.

Generalizability

The findings of this study will be important for other units/settings in high as well low resource countries where neonatal resuscitation is more often performed by pediatricians, midwives, or nurses. Based on the results of the present study, we could speculate whether a short-term educational program on the LMA use will be effective in the clinical practice; furthermore, we will be able to understand whether personnel involved in neonatal resuscitation should be trained to start resuscitation with an FM or with an LMA. Finally, potential complications and side effects due to the LMA will be strictly monitored and collected.

Sample size

It is estimated that 5% of newborns receive resuscitation with PPV [1,2]. Therefore, in C hospital, Hanoi, Vietnam with more than 20,000 deliveries per year, approximately 1,000 patients will require resuscitation. Of these, about 90% (900 neonates) are newborns weighing >1,500 g or delivered ≥34 weeks gestation. The sample size was based on a previous study in which the success rate of LMA and FM were 99% and 84%, respectively [17]. To obtain a 90% power at a 0.05 level of significance (one-sided), at least 58 subjects per group need to be enrolled. The number of patients was increased by 20% for each group considering the possibility of dropouts, leading to a final sample of 142 subjects.

Recruitment

Written and oral information will, whenever possible, be offered to parents prior to the birth of their child if the infant is likely to be eligible. Informed written consent will be signed by a parent or guardian. A senior investigator will be available at all times to discuss concerns raised by parents or clinicians during the course of the trial.

Randomization

Eligible infants will be assigned to the LMA or the FM group in a 1:1 ratio according to a computer-generated, randomized sequence. The randomized allocation will be concealed in double-enclosed, opaque, sealed, and sequentially numbered envelopes prepared at the University Hospital of Padua.

In the delivery room or operating room, the next sequential randomization envelope will be opened only when the infant will be considered to be eligible by the attending operator. The assigned procedure (PPV with LMA or FM) will then be performed. Multiple births will be separately randomized.

Blinding
Due to the characteristics of the intervention, neither caregivers nor outcome assessors will be masked to treatment allocation. To minimize bias, strict criteria and definitions will be maintained during the trial.

Guidelines for management
Before starting the study, all those involved in the neonatal resuscitation participated in a one-day theoretical and practical (manikin) course based on the Neonatal Resuscitation Program (NRP). During the course, one section was dedicated to the preparation and insertion of the size 1 Supreme LMA [18]. In November 2011, three courses were held by three certificated NRP teachers in collaboration with an expert in the LMA use (DT). A total of 44 participants (15 physicians and 29 nurses) were trained.

After the course, a period of 3 months was left to routinely introduce LMA use in the delivery rooms. Five successful LMA insertions in the manikin and three LMA insertions in the clinical setting were required to all participants before starting the study.

The American Heart Association and American Academy of Pediatrics Guidelines for Neonatal Resuscitation will be followed in this study [1,2]. After initial steps (warming, clearing airway, drying, stimulation), PPV with FM or LMA and bag will be initiated in the case of apnea and/or gasping and/or heart rate < 100 bpm. The neonate's trachea will be intubated if the heart rate does not rise or remains less than 60 bpm after 30 seconds of PPV with the LMA or FM. A maximum of three attempts for obtaining effective PPV with an LMA or an FM will be allowed.

Manual ventilation will be initiated in room air at a frequency of 40 to 60 breaths per minute [1,2]. The FiO2 will be increased to 1,0 (flow rate 6 to 8 L/min) in case of persistent cyanosis and/or heart rate <100 bpm after 90 seconds from the beginning of PPV. At least two trained people involved in the study will take part in the resuscitation of all enrolled patients.

Resuscitation will start immediately after delivery of the infant, when a stop watch will be switched on by one of the members of the resuscitation team.

The duration of resuscitation will be defined as the time period from starting resuscitation to the establishment of a spontaneous and sustained respiratory pattern of efficacious respiratory movements, which allowed the neonate to maintain adequate clinical parameters (heart and respiratory rate).

In this study, the last model of size 1 LMA Supreme (LMA Supreme, LMA Company, UK) will be used [18]. Previous studies conducted in adult patients showed the efficacy and the safety of the LMA Supreme [19,20]. The LMA Supreme is superior to the LMA Classic with regard to insertion time and oropharyngeal seal pressure [21]; a further advantage consists in the gastric access.

A previous neonatal manikin study confirmed these findings, including a higher level of satisfaction expressed by users [22].

Data collection
Data will be recorded from clinical records and from a data sheet designed for this study, where all the data obtained during resuscitation procedures will be collected by an observer not involved in the resuscitation maneuvers. Registered clinical information will be: eligibility, antenatal history, randomization, and all data above listed in the 'Primary outcome measure', 'Secondary outcome measures' and 'Other collected data' sections. Further information will be collected on expected serious adverse events (SAEs).

Statistical analysis
Categorical data will be expressed as number and percentage and compared using Fisher's test. Continuous data will be expressed as mean and standard deviation or median and interquartile range. The normality assumption of continuous variables will be evaluated using Shapiro-Wilk test. Continuous data will be compared using Student's t-test or the Mann-Whitney non-parametric test. Correlation between continuous data will be evaluated using the Pearson correlation coefficient or the Spearman correlation coefficient. A P-value less than 0.05 will be considered significant. Statistical analysis will be performed using the R 2.12 language [23].

Duration of study
In this study, 142 infants will be recruited. The trial will terminate when the last recruited infant is discharged from hospital, or dies.

Ethics committee approval
The C hospital, Hanoi, Vietnam Ethis Committees for Human Investigation approved the study (SO:901/QD-PSTW; Ha Noi, 9 August 2012).

Compliance to protocol
Compliance will be defined as full adherence to protocol. Compliance with the protocol will be ensured by two members of the project (TDC, NTTH) responsible for local data collection. They will weekly monitor the adherence to the study protocol and will input the patients' data in an Excel data sheet.

Safety
Safety measures will include incidence, severity, and causality of reported SAEs, represented by changes in occurrence of the expected common neonatal complications and the development of unexpected SAEs. All SAEs will be followed until complete resolution or until the clinician responsible for the care of the recruited patient considers the event to be chronic or the infant to be stable. If there is a reasonable suspected causal relationship with the intervention, SAEs will be reported to the Ethics Committee to guarantee the safety of the participants.

Discussion
There are unique features of this trial compared to prior studies on the use of the LMA during neonatal resuscitation. To our knowledge, three randomized controlled trials including 140 patients have been previously published [12]. Due to the limited number of enrolled patients, a final conclusion cannot be drawn. A further trial with a different study design (quasi-randomized controlled trial) showed that the LMA significantly reduced the need of intubation in the delivery room in comparison with FM ventilation [17]. All these studies were performed with a classic LMA. In this trial, we used, for the first time, a more advanced model of LMA, the LMA Supreme.

References
1 Perlman JM, Wyllie J, Kattwinkel J, Atkins DL, Chameides L, Goldsmith JP, Guinsburg R, Hazinski MF, Morley C,

Richmond S, Simon WM, Singhal N, Szyld E, Tamura M, Velaphi S, Neonatal Resuscitation Chapter Collaborators: International consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. Pediatrics 2010, 2010(126):e1319–e1344.
2 Kattwinkel J, Perlman JM, Aziz K, Colby C, Fairchild K, Gallagher J, Hazinski MF, Halamek LP, Kumar P, Little G, McGowan JE, Nightengale B, Ramirez MM, Ringer S, Simon WM, Weiner GM, Wyckoff M, Zaichkin J, American Heart Association: Neonatal resuscitation, American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Pediatrics 2010, 2010(126):e1400–e1413.
3 O'Donnell CP, Kamlin CO, Davis PG, Morley CJ: Endotracheal intubation attempts during neonatal resuscitation: success rates, duration, and adverse effects. Pediatrics 2006, 117:e16–e21.
4 Doglioni N, Cavallin F, Zanardo V, Trevisanuto D: Intubation training in neonatal patients: a review of one trainee's first 150 procedures. J Matern Fetal Neonatal Med 2012, 25:1302–1304.
5 AlB: The laryngeal mask—a new concept in airway management. Br J Anaesth 1983, 55:801–805.
6 Trevisanuto D, Micaglio M, Ferrarese P, Zanardo V: The laryngeal mask airway: potential application in neonates. Arch Dis Child Fetal Neonatal Ed 2004, 89:F485–F489.
7 Paterson SJ, Byrbe PJ, Molesky MG, Seal RF, Finucane BT: Neonatal resuscitation using the laryngeal mask airway. Anesthesiology 1994, 80:1248–1253.
8 Gandini D, Brimacombe JR: Neonatal resuscitation with the laryngeal mask airway in normal and low birth weight infants. Anesth Analg 1999, 89:642–643.
9 Trevisanuto D, Micaglio M, Pitton M, Magarotto M, Piva D, Zanardo V: Laryngeal mask airway: is the management of neonates requiring positive pressure ventilation at birth changing? Resuscitation 2004, 62:151–157.
10 Zanardo V, Weiner G, Micaglio M, Doglioni N, Buzzacchero R, Trevisanuto D: Delivery room resuscitation of near-term infants: role of the laryngeal mask airway. Resuscitation 2010, 81:327–330.
11 Grein AJ, Weiner GM: Laryngeal mask airway versus bag-mask ventilation or endotracheal intubation for neonatal resuscitation. Cochrane Database Syst Rev 2005, 2:CD003314.
12 Schmölzer GM, Agarwal M, Kamlin CO, Davis PG: Supraglottic airway devices during neonatal resuscitation: an historical perspective, systematic review and meta-analysis of available clinical trials. Resuscitation 2013, 84:722–730.
13 Harnett M, Kinirons B, Heffernan A, Motherway C, Casey W: Airway complications in infants: comparison of laryngeal mask airway and the facemask-oral airway. Can J Anaesth 2000, 47:315–318.
14 Mathis MR, Haydar B, Taylor EL, Morris M, Malviya SV, Christensen RE, Ramachandran SK, Kheterpal S: Failure of the Laryngeal Mask Airway Unique and Classic in the pediatric surgical patient: a study of clinical predictors and outcomes. Anesthesiology 2013, 119:1284–1295.
15 Levene MI, Kornberg J, Williams THC: The incidence of and severity of postasphyxial encephalopathy in full-term infants. Early Hum Dev 1985, 11:21–28.
16 Sarnat HB, Sarnat MS: Neonatal encephalopathy following fetal distress. A clinical and electroencephalographic study. Arch Neurol 1976, 33:696–705.
17 Zhu XY, Lin BC, Zhang QS, Ye HM, Yu RY: A prospective evaluation of the efficacy of the laryngeal mask airway during neonatal resuscitation. Resuscitation 2011, 82:1405–1409.
18 The LMA-Supreme: Instructions for Use. Jersey, UK: The Laryngeal Mask Company Limited, Teleflex Medical; 2013. http://www.lmaco.com/ catalogue_item.php?catID=5799&prodID=56350 (last access July, 15, 2014).
19 van Zundert A, Brimacombe J: The LMA Supreme—a pilot study. Anaesthesia 2008, 63:209–210.
20 Cook TM, Gatward JJ, Handel J, Hardy R, Thompson C, Srivastava R, Clarke PA: Evaluation of the LMA Supreme in 100 non-paralysed patients. Anaesthesia 2009, 64:555–562.
21 Wong DT, Yang JJ, Jagannathan N: Brief review: the LMA Supreme supraglottic airway. Can J Anaesth 2012, 59:483–493.
22 Trevisanuto D, Parotto M, Doglioni N, Ori C, Zanardo V, Micaglio M: The Supreme Laryngeal Mask Airway (LMA): a new neonatal supraglottic device: comparison with Classic and ProSeal LMA in a manikin. Resuscitation 2012, 83:97–100.
23 R Development Core Team: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2010. ISBN ISBN 3-900051-07-0.

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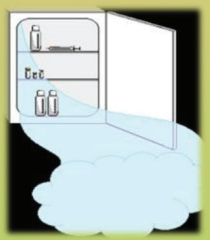

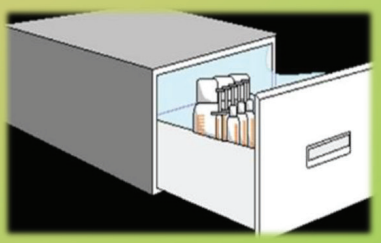

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