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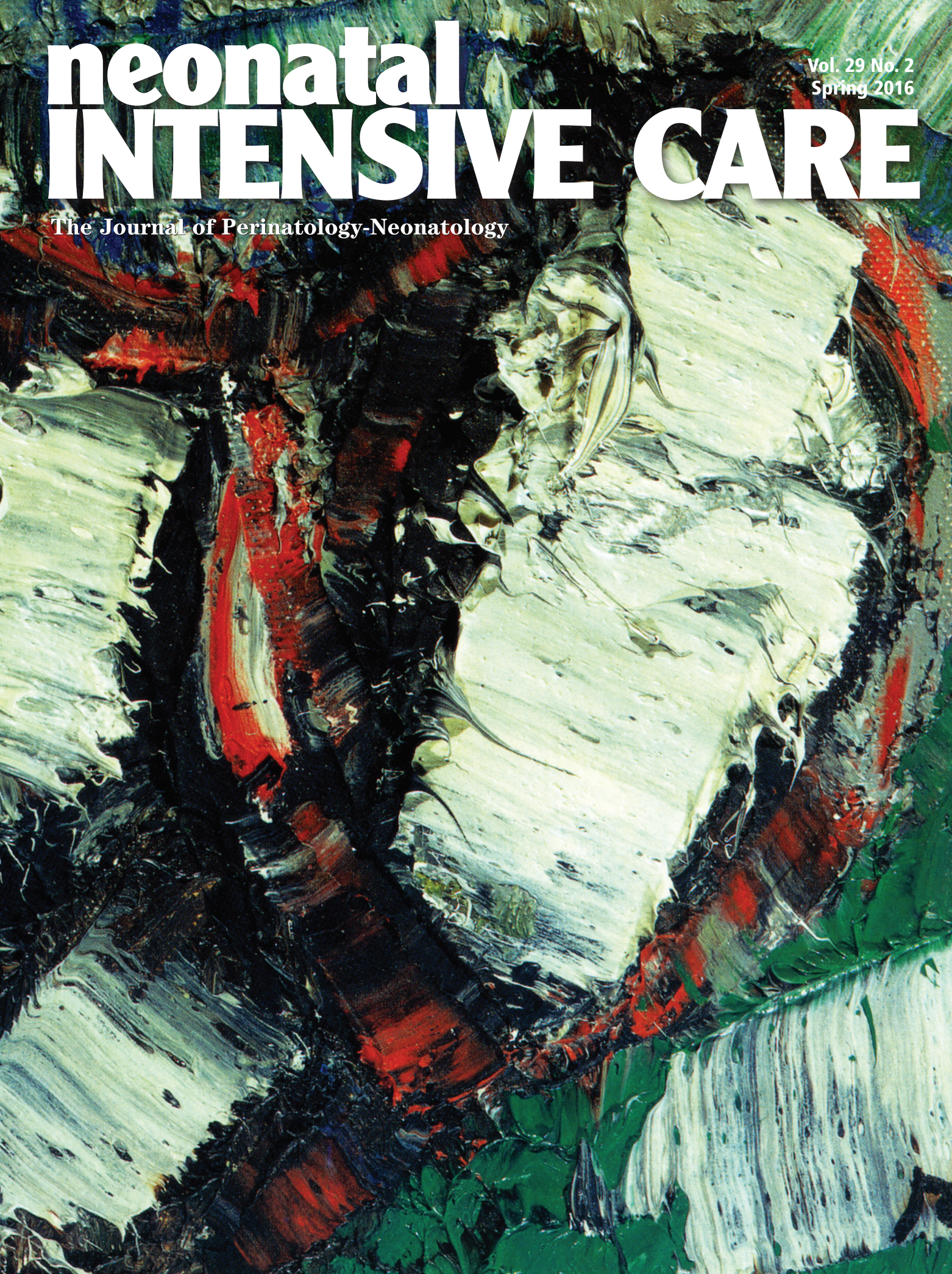

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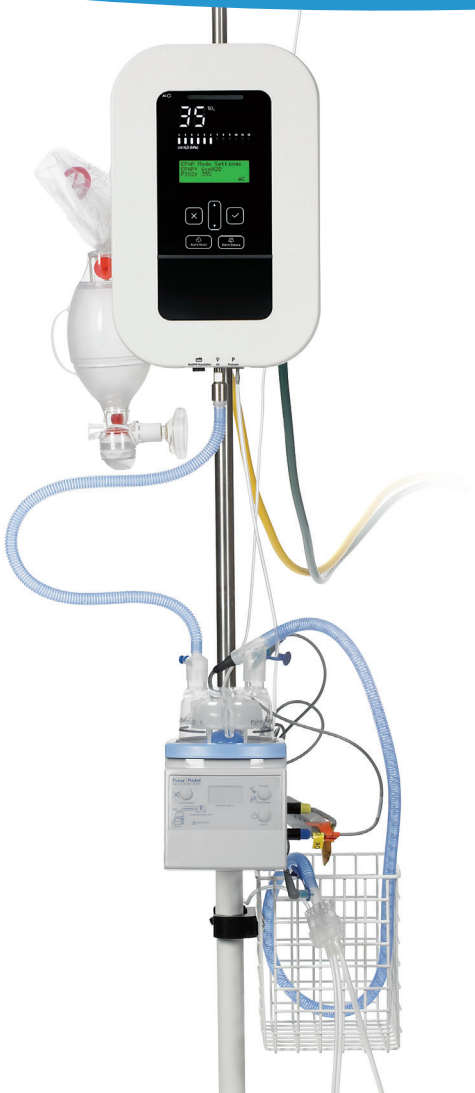

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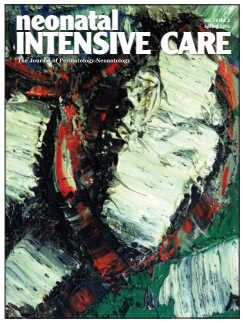

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Editorial Advisory Board

Human milk makes all the difference

The American Academy of Pediatrics' (AAP) policy recommends the use of human milk for all preterm infants, whether mother's own milk (MOM) or pasteurized donor human milk when mother's own milk is unavailable.[1]

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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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News

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NX Prenatal Preterm Birth Risk Biomarker Data Presented

NX Prenatal Inc, a US-based molecular diagnostics company utilizing its proprietary NeXosome technology for early warning of adverse pregnancy outcomes, announced the presentation of its most recent study by Dr Thomas McElrath of Brigham & Women's Hospital at the Society for Maternal Fetal Medicine's (SMFM) annual meeting held in Atlanta. The presentation reported initial positive top-line results regarding the development and continued validation of NX Prenatal's NeXosome Preterm Birth Risk Assay. In a blinded peer-reviewed process, SMFM selected this study entitled "Circulating microparticles as an effective means to stratify the risk of spontaneous preterm birth" for oral presentation during its annual meeting. This new collaborative study of 75 pregnant moms was designed to identify functional proteomic biomarkers that are already unique in their expression profiles at 10-12 weeks gestation among women who go on to deliver spontaneously at less than 34 weeks. In pregnancy, the analysis of the protein content of circulating microparticles, such as exosomes, is of revolutionary potential as it represents a non-invasive 'biopsy' of active gestational tissues. "The NeXosome platform offers a unique opportunity to assess biomarkers related to the network of inter-related systems of the mom and baby that must stay in balance during pregnancy," commented Dr McElrath. "Interestingly, our findings suggest that we can find irregularities in these networks long before eventual spontaneous preterm birth from a maternal blood sample."

C-Sections Made More Like Natural Births

New approaches are being looked at by hospitals delivering babies by caesarean section that make them more like natural births. Surgeons who just delivered an infant by C-section almost immediately might hand it off to be placed on the mother's chest, as often occurs after vaginal deliveries. Breast-feeding might be encouraged while mother and infant are still in the operating room. And clamping of the umbilical cord may be delayed, as is increasingly common in vaginal births. Some hospitals are going further, aiming to make caesarean delivery more like a birthing experience than an operation. Mothers get to choose options such as dim overhead lighting, soothing music and watching through a clear surgical drape, rather than the usual opaque curtain, as the baby emerges. In a traditional C-section, the baby is immediately placed in a warmer to be assessed by the pediatrics team before being handed to the mother up to an hour later in postoperative recovery. The practice was founded on the need to quickly determine which newborns require assistance breathing and to maintain sterility during the operation. Doctors say the new approach, typically offered only for nonemergency C-sections, adopts some practices of vaginal deliveries that have been found to bring health benefits to the mother and child, such as skin-to-skin contact and early breast-feeding. Often called family-centered caesareans or gentle caesareans, the approach also aims to make the C-section birth experience more rewarding for families, they say. Some doctors are concerned the new approach could make caesarean births more attractive, at a time when U.S. hospitals are under pressure to reduce the rate of C-sections.

Home Births Come With More Risks

Home births are gaining in popularity, but is that a good thing given the current state of care? In Britain, about 10 percent of births don't happen in a hospital. The Centers for Disease Control and Prevention estimates that in 2012, more than 53,000 births took place out of the hospital in the United States. More than 35,000 took place at home, the rest at dedicated birth centers. Out-of-hospital births are a small percentage of overall deliveries, about 1.36 percent, but the rate has been increasing since 2004, when they were about 0.8 percent. In some states, like Alaska (6 percent), Montana (3.9 percent) and Oregon (3.8 percent), out-of-hospital births are even more common. In Oregon, data is recorded on birth certificates that allows researchers to know which births were planned for the home and which were planned for the hospital. They can compare outcomes. In 2012 and 2013, researchers found

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In term and near-term neonates with hypoxic respiratory failure (HRF)...

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Indication

INOMAX® is a vasodilator, which, in conjunction with ventilatory support and other appropriate agents, is indicated for the treatment of term and near-term (>34 weeks) neonates with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension, where it improves oxygenation and reduces the need for extracorporeal membrane oxygenation.

Utilize additional therapies to maximize oxygen delivery with validated ventilation systems.

Important Safety Information

- INOMAX is contraindicated in the treatment of neonates known to be dependent on right-to-left shunting of blood.
- Abrupt discontinuation of INOMAX may lead to increasing pulmonary artery pressure and worsening oxygenation even in neonates with no apparent response to nitric oxide for inhalation.
- Methemoglobinemia and NO_2 levels are dose dependent. Nitric oxide donor compounds may have an additive effect with INOMAX on the risk of developing methemoglobinemia. Nitrogen dioxide may cause airway inflammation and damage to lung tissues.
- In patients with pre-existing left ventricular dysfunction, INOMAX may increase pulmonary capillary wedge pressure leading to pulmonary edema.
- Monitor for PaO_2, methemoglobin, and inspired NO_2 during INOMAX administration.
- Use only with an INOmax DS_{IR}®, INOmax® DS, or INOvent® operated by trained personnel.

Please see Brief Summary of Prescribing Information on adjacent page.

References: 1. INOMAX [package insert]. Hampton, NJ: Ikaria, Inc.; 2013. **2.** González A, Fabres J, D'Apremont I, et al. Randomized controlled trial of early compared with delayed use of inhaled nitric oxide in newborns with a moderate respiratory failure and pulmonary hypertension. *J Perinatol*. 2010;30(6):420-424.

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Brief Summary of Prescribing Information

INDICATIONS AND USAGE

Treatment of Hypoxic Respiratory Failure
INOMAX® is a vasodilator, which, in conjunction with ventilatory support and other appropriate agents, is indicated for the treatment of term and near-term (>34 weeks) neonates with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension, where it improves oxygenation and reduces the need for extracorporeal membrane oxygenation.

Utilize additional therapies to maximize oxygen delivery with validated ventilation systems. In patients with collapsed alveoli, additional therapies might include surfactant and high-frequency oscillatory ventilation.

The safety and effectiveness of INOMAX have been established in a population receiving other therapies for hypoxic respiratory failure, including vasodilators, intravenous fluids, bicarbonate therapy, and mechanical ventilation. Different dose regimens for nitric oxide were used in the clinical studies.

Monitor for PaO_2, methemoglobin, and inspired NO_2 during INOMAX administration.

CONTRAINDICATIONS
INOMAX is contraindicated in the treatment of neonates known to be dependent on right-to-left shunting of blood.

WARNINGS AND PRECAUTIONS

Rebound Pulmonary Hypertension Syndrome following Abrupt Discontinuation
Wean from INOMAX. Abrupt discontinuation of INOMAX may lead to worsening oxygenation and increasing pulmonary artery pressure, i.e., Rebound Pulmonary Hypertension Syndrome. Signs and symptoms of Rebound Pulmonary Hypertension Syndrome include hypoxemia, systemic hypotension, bradycardia, and decreased cardiac output. If Rebound Pulmonary Hypertension occurs, reinstate INOMAX therapy immediately.

Hypoxemia from Methemoglobinemia
Nitric oxide combines with hemoglobin to form methemoglobin, which does not transport oxygen. Methemoglobin levels increase with the dose of INOMAX; it can take 8 hours or more before steady-state methemoglobin levels are attained. Monitor methemoglobin and adjust the dose of INOMAX to optimize oxygenation.

If methemoglobin levels do not resolve with decrease in dose or discontinuation of INOMAX, additional therapy may be warranted to treat methemoglobinemia.

Airway Injury from Nitrogen Dioxide
Nitrogen dioxide (NO_2) forms in gas mixtures containing NO and O_2. Nitrogen dioxide may cause airway inflammation and damage to lung tissues. If the concentration of NO_2 in the breathing circuit exceeds 0.5 ppm, decrease the dose of INOMAX.

If there is an unexpected change in NO_2 concentration, when measured in the breathing circuit, then the delivery system should be assessed in accordance with the Nitric Oxide Delivery System O&M Manual troubleshooting section, and the NO_2 analyzer should be recalibrated. The dose of INOMAX and/or FiO_2 should be adjusted as appropriate.

Heart Failure
Patients with left ventricular dysfunction treated with INOMAX may experience pulmonary edema, increased pulmonary capillary wedge pressure, worsening of left ventricular dysfunction, systemic hypotension, bradycardia and cardiac arrest. Discontinue INOMAX while providing symptomatic care.

ADVERSE REACTIONS
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The adverse reaction information from the clinical studies does, however, provide a basis for identifying the adverse events that appear to be related to drug use and for approximating rates.

Controlled studies have included 325 patients on INOMAX doses of 5 to 80 ppm and 251 patients on placebo. Total mortality in the pooled trials was 11% on placebo and 9% on INOMAX, a result adequate to exclude INOMAX mortality being more than 40% worse than placebo.

In both the NINOS and CINRGI studies, the duration of hospitalization was similar in INOMAX and placebo-treated groups.

From all controlled studies, at least 6 months of follow-up is available for 278 patients who received INOMAX and 212 patients who received placebo. Among these patients, there was no evidence of an adverse effect of treatment on the need for rehospitalization, special medical services, pulmonary disease, or neurological sequelae.

In the NINOS study, treatment groups were similar with respect to the incidence and severity of intracranial hemorrhage, Grade IV hemorrhage, periventricular leukomalacia, cerebral infarction, seizures requiring anticonvulsant therapy, pulmonary hemorrhage, or gastrointestinal hemorrhage.

In CINRGI, the only adverse reaction (>2% higher incidence on INOMAX than on placebo) was hypotension (14% vs. 11%).

Based upon post-marketing experience, accidental exposure to nitric oxide for inhalation in hospital staff has been associated with chest discomfort, dizziness, dry throat, dyspnea, and headache.

OVERDOSAGE
Overdosage with INOMAX will be manifest by elevations in methemoglobin and pulmonary toxicities associated with inspired NO_2. Elevated NO_2 may cause acute lung injury. Elevations in methemoglobin reduce the oxygen delivery capacity of the circulation. In clinical studies, NO_2 levels >3 ppm or methemoglobin levels >7% were treated by reducing the dose of, or discontinuing, INOMAX.

Methemoglobinemia that does not resolve after reduction or discontinuation of therapy can be treated with intravenous vitamin C, intravenous methylene blue, or blood transfusion, based upon the clinical situation.

DRUG INTERACTIONS
No formal drug-interaction studies have been performed, and a clinically significant interaction with other medications used in the treatment of hypoxic respiratory failure cannot be excluded based on the available data. INOMAX has been administered with dopamine, dobutamine, steroids, surfactant, and high-frequency ventilation. Although there are no study data to evaluate the possibility, nitric oxide donor compounds, including sodium nitroprusside and nitroglycerin, may have an additive effect with INOMAX on the risk of developing methemoglobinemia. An association between prilocaine and an increased risk of methemoglobinemia, particularly in infants, has specifically been described in a literature case report. This risk is present whether the drugs are administered as oral, parenteral, or topical formulations.

that the rate of perinatal death was significantly higher for births planned at home: 3.9 versus 1.8 per 1,000. That would be an additional death for each 500 births at home. At-home births were also associated with an increased risk of neonatal seizures. However, the risk of admission to an intensive care unit was significantly lower for those born at home. More than 30 percent of women with planned in-hospital births had labor induced, versus 1.5 percent of those with planned at-home births. Almost 25 percent of those who planned to deliver in the hospital had a cesarean section versus 5.3 percent of those who planned to deliver at home. The rates of severe morbidity (permanent harm or significant temporary harm) and death in women are 27 per 1,000 for planned (or "low-risk") C-section deliveries versus 9 per 1,000 for planned vaginal deliveries. C-sections are probably more common in the United States than they need to be, and being in the hospital increases your chance of getting one, and the risks that come with it. Thchoice of birth location has become a charged debate in this country. In Britain, on the other hand, the medical system seems to have been adopting a more holistic view. The National Institute for Health and Care Excellence (NICE) released guidelines just over a year ago that recommended that health care providers explain to women at low risk of complications that home birth is a safe and acceptable option. n fact, for British women who have given birth before and are at low risk, NICE recommends that providers explain that birth out of the hospital carries no differences in risk and is associated with higher rates of normal vaginal deliveries and lower rates of intervention. In addition, there are "protocols and mechanisms" in place to coordinate care between home births and the hospital. An editorial in the New England Journal of Medicine last year noted that almost half of first-time mothers in Britain who intend to give birth out of the hospital wind up doing so in the hospital — and that this might be looked at as a sign of systemic success, not failure. If things don't go well at home, everyone is prepared and ready to make the transfer because home and hospital delivery systems work closely together. The British safety net works.

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Finding the Right Oxygen Saturation Targets

An oxygen saturation target of 85% to 89%, rather than 91% to 95%, may increase the risk for death or disability at 2 years' corrected age in infants born before age 28 weeks, according to pooled results from the UK and Australian Benefits of Oxygen Saturation Targeting (BOOST) II trials. he trials form part of a larger collaboration of five trials called the Neonatal Oxygen Prospective Meta-analysis (NeOProM), conducted in the United States, Canada, Australia, New Zealand, and the United Kingdom. Results from observational studies sparked NeOProM by suggesting that targeting an oxygen saturation range of 85% to 89% might improve retinopathy of prematurity without any negative effects on death or disability, Dr Tarnow-Mordi explained. n 2010, however, results from the American Surfactant, Positive Pressure, and Oxygenation Trial (SUPPORT) showed a reduction in retinopathy, but also increased mortality, with the lower oxygen saturation targets. That led investigators from the NeOProM trials to request interim analyses from their data and monitoring committees. Pooled analyses from the British, Australian, and New Zealand studies suggested increased mortality with lower oxygen saturation targets and prompted an early end to enrolment according to a prespecified protocol. The Australian trial ended enrolment at 1135 infants, and the UK trial ended enrolment at 973 infants. Both studies had planned to enrol 1200 patients. The studies enrolled infants born before 28 weeks' gestation and randomly assigned them to either lower (85% - 89%) or higher (91% - 95%) oxygen saturation.

Vaginal Progesterone and Preterm Births

In women with high-risk pregnancies, including those with a short cervix, vaginal progesterone does not protect against preterm birth, according to disconcerting results from the

OPPTIMUM study. "We saw no significant effect of vaginal progesterone on obstetrical, neonatal, or childhood outcomes," reported Jane Norman, MD, from the University of Edinburgh in the United Kingdom. This was true even for women with a cervix of 25 mm or less, and "we found no evidence of benefit in any identifiable subgroups," she said here at the Society for Maternal-Fetal Medicine 2016 Pregnancy Meeting. The use of progesterone — both the vaginal form and 17-hydroxyprogesterone, the intramuscular form — was assessed in a Cochrane meta-analysis of women who had previously delivered a preterm child (Cochrane Database Syst Rev. 2013;7:CD004947). Progesterone was shown to prevent preterm births, reduce perinatal mortality, reduce the incidence of birthweight below 2500 g, and reduce neonatal deaths. In women with a short cervix, progesterone was shown to reduce preterm births, but did not affect the other parameters.

Stress and its Impact on Pregnancies

Mothers who have a higher level of perceived stress in their second trimester are more likely to have elevated second-trimester hair cortisol concentration as well as decreased gestational age at delivery. The results thus correlate a physiologic measure of maternal stress (cortisol) with preterm birth. M. Camille Hoffman, MD, from the University of Colorado School of Medicine in Denver, and colleagues published the results of their prospective cohort study in the March issue of Obstetrics & Gynecology. Their cohort of 92 women had a prematurity rate (12%) that was consistent with state and national norms. The study was unique in that the investigators attempted to evaluate how physiologic stress relates to psychological stress and how the two, together, are related to gestational age at delivery and preterm birth. The researchers measured stress with the Average Perceived Stress Scale, State-Trait-Anxiety Inventory, State version, and Center for Epidemiologic Studies-Depression Scale. Stress was scored at 16, 22, 28, 34, and 40 weeks of gestation. The researchers also measured hair cortisol levels and found that they rose over the course of pregnancy and were significantly higher in the third trimester than the first and second trimesters. Moreover, perceived stress at 16 weeks of gestation correlated with second-trimester cortisol concentration ($r = 0.28$; $P = .007$), as well as earlier gestational age at delivery ($r = -0.30$; $P < .01$). In addition, gestational age at delivery was negatively correlated with cortisol concentration in the second trimester ($r = -0.25$; $P = .02$).

Pregnant Women Able to Lose Weight

Obese nondiabetic women randomly assigned to receive metformin during pregnancy gained less weight than those who did not take the drug, but they were no less likely to have large-for-gestational-age (LGA) neonates, a study published in the February 4 issue of the New England Journal of Medicine shows. Because metformin improves insulin sensitivity and has been shown to reduce weight gain in pregnant patients with gestational diabetes, Argyro Syngelaki, PhD, from the Harris Birthright Research Centre for Fetal Medicine, King's College Hospital, London, United Kingdom, and colleagues hypothesized the drug might lead to a lower median neonatal birth weight z score when given to nondiabetic pregnant women with a body mass index of more than 35 kg/m2. To test the hypothesis, the researchers enrolled 450 obese pregnant women without diabetes in the double-blind, placebo-controlled Metformin in Obese Nondiabetic Pregnant Women (MOP) trial. Of the 450 women, 225 were randomly assigned to receive a maximum of 3.0 g metformin per day from 12 to 18 weeks of gestation through delivery, and 225 were assigned to receive a placebo. A total of 50 women withdrew consent during the trial, which left 202 women in the metformin group and 198 in the placebo group, the study authors report. Specifically, the median neonatal birth weight z score was 0.05 in the metformin group and 0.17 in the placebo group ($P = .66$). Similarly, the proportion of LGA infants, defined as those whose weight was higher than the 90th percentile, was 16.8% and 15.4% in the two groups, respectively ($P = .79$). There were, however, differences in maternal outcomes, including median maternal gestational weight gain (4.6 vs 6.3 kg; $P < .001$), and in the incidence of preeclampsia (3.0% vs 11.3%; $P < .001$), both of which were lower in the metformin group.

Intestinal Microbiome in Infants

The intestinal microbiome in 6-week-old infants was the same in babies who were exclusively formula fed and babies who were fed with both formula and breast milk, according to a new study. Babies who were exclusively breast-fed had an intestinal microbiome that was distinctly different from those who were fed only formula or a combination of formula and breast milk. However, mode of delivery appeared to be a more important factor in microbiome development than feeding practices. Juliette C Madan, MD, from the Division of Neonatology, Department of Pediatrics, Children's Hospital at Dartmouth, Lebanon, and the Children's Environmental Health and Disease Prevention Research Center at Dartmouth, Hanover, New Hampshire, and coauthors report their findings. "To our knowledge, our study was the first to examine the contribution of delivery mode to infant intestinal microbiome composition in association with that of another important predictor of

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microbiome composition, infant diet," the researchers write. "We found that delivery mode was more strongly associated with infant microbiome composition than was diet at 6 weeks." The researchers reviewed the medical records of 102 infants who were followed up as part of the New Hampshire Birth Cohort Study to determine delivery mode and ascertained feeding information from telephone questionnaires. They analyzed the infants' stool samples at 6 weeks for microbiome composition and determined associations among birth type, feeding method, and intestinal microbiome. The average gestational age of the infants was close to 40 weeks; 70 newborns were delivered vaginally, and 32 underwent cesarean delivery. During the first 6 weeks of life, 70 infants were breast-fed exclusively, 26 were fed with both breast milk and formula, and six were fed only formula.

Vaginal Microbes Restored

Vaginal microbes can be at least partially restored to infants who are delivered by cesarean delivery, according to the results of a pilot study. However, the long-term health consequences of the results remain unclear, researchers caution. Maria G Dominguez-Bello, PhD, from New York University in New York City, and colleagues published the results of their pilot study online February 1 in Nature Medicine. The researchers tracked four infants delivered by cesarean delivery who were exposed to maternal vaginal fluids at birth. The researchers determined the composition of their microbiota over time, using more than 1500 samples from anal, oral, and skin sites of infants and mothers in this group and comparator groups during the first month of life. The investigators found that exposing infants delivered by cesarean delivery to maternal vaginal microbiota results in in bacterial communities that resemble those found on vaginally delivered babies.

Benefits of Antenatal Steroids

A National Institutes of Health study has shown that infants born at 34 to 36 weeks of gestation can benefit from antenatal steroids in much the same way that younger preemies do. In a study of 2831 women, the use of antenatal betamethasone reduced the chance of respiratory complications in "late" preterm infants, who constitute about 8% of all deliveries. "Our results indicate that prenatal steroid therapy for women delivering late preterm infants could greatly reduce the rate of serious respiratory complications," said Uma Reddy, MD, from the Eunice Kennedy Shriver National Institute of Child Health and Human Development in Bethesda, Maryland. "Betamethasone is the standard of care for women delivering at 34 weeks and earlier, but we have not had data for those born at 34 to 37 weeks. The conventional thinking is that these babies do so well that it's not necessary, but it turns out that they also have increased risk for respiratory problems and admission to the neonatal intensive care unit," Dr Reddy explained. "The study was undertaken to determine whether steroids help in this age group," she said.

Almond Milk Use Linked to Scurvy

Plant-based beverages like almond milk can't be used to replace breast milk or infant formula, a new report warns. The authors of the report describe an infant in Spain who was fed only almond beverages or almond flour-based formulations from age two months to 11 months and developed fractures and failure to thrive due to scurvy. Scurvy is a serious condition caused by lack of vitamin C in the diet. Once the scourge of sailors

who did not have access to sources of vitamin C during many months at sea, scurvy is rare today. Dr Isidro Vitoria of the Hospital Universitario y Politecnico La Fe in Valencia, Spain, and coauthors report the case of a male baby who was born at term, vaccinated according to Spanish guidelines, and fed with a cow's milk based formula for the first two and a half months of life. When he developed skin inflammation, a medical doctor recommended he be switched to daily intake of a prepared mixture including almond drink, almond flour, sesame powder, brown rice malt, brown rice, millet and a sachet of probiotics and prebiotics marketed in Spain. From age six months onward, his mother offered him pureed fruits and vegetables that he would not eat. At 11 months of age, the baby was tired, irritable, had failed to thrive and refused to support his legs on a solid surface, crying even when an adult moved his legs for him. He had abnormal levels of zinc, vitamin D, thyroid stimulating hormone and ascorbic acid, or vitamin C. X-rays revealed fractures in his legs and back and thinning bones. The almond formula was stopped and replaced with infant formula, cereals, meat, fruits and vegetables supplemented with vitamin C and D replacement therapy. One month later his X-rays had improved. Soon afterward, his vitamin C and D levels had normalized. Two months after stopping the almond formula he started walking, the authors reported. In the first year of life, babies should consume 50 to 60 milligrams of vitamin C every day, the authors say. On average, 8 ounces (240 ml) of breast milk contains about 11 milligrams of vitamin C. Infant formulas should contain 10 to 30 milligrams per 100 calorie serving, the authors write. The American Academy of Pediatrics recommends that infants be exclusively breastfed for about the first six months of life, and then solid foods can be introduced.

Preemies Weaker as Adults: Study

Young adults who were born prematurely may have weaker muscles than their peers born at full term, a Finnish study suggests. These young adults born preterm also considered themselves less physically fit, even though the study didn't find their cardiorespiratory fitness levels to be much different than people who weren't born early. Pregnancy normally lasts about 40 weeks, and babies born after 37 weeks are considered full term. In the weeks immediately after birth, preemies often have difficulty breathing and digesting food. Some premature infants also encounter longer-term challenges such as impaired vision, hearing, and cognitive skills as well as social and behavioral problems. Previous research has also found that the tiniest and most immature preemies may have poor muscular fitness. But the current study is important because it suggests that this problem may extend to all pre-term babies, even those who are only slightly early or a little bit underweight, said lead author Dr Marjaana Tikanmaki of the National Institute for Health and Welfare and University of Oulu in Finland. To see how the timing of birth might impact fitness later in life, the researchers studied 139 young adults born before 34 weeks gestation, which is considered early preterm, as well as 247 people born from 34 to 36 weeks, or late preterm. They compared these individuals to a control group of 352 full term individuals. On average, the participants were around 23 years old. Researchers assessed muscular fitness based on the number of modified push-ups performed in 40 seconds, a test that measures short-term endurance capacity of the upper body and the ability to stabilize the trunk. On average, women did about 10 push-ups and men managed about 14. But the people who were born preterm typically did about one less push-up than their full-term peers. In another assessment of muscular fitness, researchers also examined grip strength based on how hard people could squeeze a force-measuring device with their dominant hand. With this test, people born early preterm didn't do as well as those born late preterm or full term.

Progesterone Questioned

A therapy widely recommended in the UK to prevent babies from being born too soon is ineffective, according to a new study. A research team led by the University of Edinburgh says that although the treatment does not appear to pose any harm to mother or infant, it has no effect on preventing an early birth.

They say the findings should lead to a review of the practice and give fresh impetus to the search for alternative treatments for preventing babies being born too early. The latest trial involved 1,228 women assessed to be at risk of having a premature birth because they had either had a premature birth previously or had lost a baby later on in pregnancy. The women, from 65 UK hospitals, were randomly assigned to receive either progesterone or a dummy pill with no therapeutic value. The researchers report that, although the therapy appeared safe, it did not reduce the risk of giving birth early and there were no notable health benefits either to the mother or the child. They conclude that the findings "should prompt a major review of the use of progesterone for preterm birth prophylaxis, a search to identify specific women who might specifically benefit, and a redoubling of efforts to find alternative strategies to prevent preterm birth in women at risk".

Impacts of Sedation on Preterms

Children born preterm who receive sedation or anesthesia for procedures outside of the operating room are almost twice as likely to experience adverse events compared with those born at term, and these risks persist into adulthood, according to a new study. Ronald S Litman, DO, from the Department of Anesthesiology and Critical Care, The Children's Hospital of Philadelphia, Perelman School of Medicine at the University of Pennsylvania, reiterated that point in an accompanying commentary. "This novel (but not surprising) finding that prematurely born children have an increased risk of sedation-related respiratory complications throughout all ages of childhood should now influence the way in which sedation practitioners and anesthesiologists approach risk management in this population." The researchers analyzed data from 57,628 children from birth through age 22 years who were part of the Pediatric Sedation Research Consortium, which has been collecting data on sedation and anesthesia safety and effectiveness since 2003. The researchers categorized children born at less than 37 weeks' gestational age as preterm children and children born at 37 weeks' gestational age or older as term children. In the preterm children, the most frequent procedures requiring sedation or anesthesia were magnetic resonance imaging scans (57.5%), auditory brainstem response testing (7.7%), and upper endoscopy (7.5%). In term children, the most frequent procedures requiring sedation or anesthesia included magnetic resonance imaging scans (41.7%), lumbar puncture for chemotherapy administration (14.7%), and upper endoscopy (6.6%). In all, 8.6% of the children had an adverse sedation/anesthesia event, which occurred most frequently in children younger than 6 months. The most frequently reported adverse events included airway obstruction (2.0%), coughing (2.0%), snoring (1.7%), and oxygen desaturation (1.8%), defined as oxygen saturation lower than 90% for longer than 30 seconds. No children died in the study.

Impacts of Lupus Before Diagnosis

Pregnancy complications and poor fetal outcomes are known to be more common among women with systemic lupus erythematosus (SLE) during pregnancy. Now researchers report that the risk is also elevated among women who had subclinical SLE during pregnancy but were diagnosed within 5 years postpartum. "Our study supports the idea that the underlying immunologic profile of subclinical SLE may be associated with higher likelihood of adverse maternal and fetal outcomes," write Elizabeth V Arkema, PhD, and colleagues. The data from the prospective cohort study confirm what was already known about pregnancy with SLE: increased risk for preeclampsia, preterm birth, and small-for-gestational-weight infants, says Sara K Tedeschi, MD, rheumatology fellow at Brigham and Women's Hospital, Boston, Massachusetts. "What is new is that prior studies have not specifically evaluated pregnancy outcomes among women who were later diagnosed with SLE compared to outcomes among healthy women," Dr Tedeschi told Medscape Medical News. "In this study, women who were diagnosed with SLE within 2 years after delivery had a higher proportion of adverse pregnancy outcomes compared to women with prevalent SLE and women without SLE, although whether these differences were statistically significant was not reported." The researchers identified women with first singleton pregnancies registered in the Swedish Lupus Linkage database and in the Swedish Medical Birth Register, including 551 women with prevalent SLE, 65 with pre-SLE diagnosed within 0 to 2 years after pregnancy, and 133 with pre-SLE diagnosed within 2 to 5 years. Maternal and fetal outcomes in these women were compared with those of a randomly selected matched sample from the general population in the Swedish Medical Birth Register (n = 12,847). The authors found that diagnosed SLE or pre-SLE was associated with an increased risk for Cesarean delivery, preterm birth, preeclampsia, serious infection during pregnancy, hypothyroidism, and postpartum stroke. Risk was highest in women with prevalent SLE and in those diagnosed with SLE 0 to 2 years after their first pregnancy. Risk was lower for women diagnosed with SLE 2 to 5 years postpartum but was still higher than in the general population.

Impact of Probiotics on Preterm Babies

Giving preterm babies probiotics reduces the risk of late-onset sepsis (LOS), according to a new meta-analysis of 37 studies. LOS is a major cause of illness and death in preterm infants and new strategies to reduce LOS are "urgently needed," the authors note in their paper, online February 12 in Pediatrics. One possible strategy is probiotic supplementation. "Animal research and in vitro studies have shown that probiotics improve gut barrier function, inhibit gut colonization with pathogenic bacteria, improve colonization with healthy commensals, protect from enteropathogenic infection through production of acetate, enhance innate immunity, and increase maturation of the enteric nervous system, all of which have the potential to decrease the risk of LOS in preterm infants," Dr Shripada Rao, from Prince Margaret Hospital for Children, Perth, Western Australia and colleagues point out. Yet, two recent meta-analyses — one a Cochrane analysis of 19 studies and the other of 17 studies — failed to show a statistically significant reduction in LOS in preterm infants given probiotics. The analysis by Dr Rao's group included 37 studies and did show a benefit of probiotics (versus placebo or no probiotic) on LOS. "Ours is the largest meta-analysis on this topic so far. In fact, to our knowledge, it is the largest meta-analysis of randomized trials in neonatal medicine. For the first time, probiotics have been shown to reduce the incidence of LOS in preterm neonates in a meta-analysis," Dr Rao told Reuters Health by email. Pooled results from all 37 studies (9,416 infants) gave a relative risk of LOS with probiotics of 0.86, with a number needed to treat of 44. There were 675 cases of LOS in 4,852 preterm infants who received probiotics (13.9%) versus 744 cases in 4,564 infants who received placebo/no probiotic (16.3%). "The results were significant even after excluding studies with high risk of bias," the authors say in their paper. "The results were also significant in studies that included only infants with gestational age <32 weeks or birth weight <1500 g (24 studies, sample size 7175), studies where

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Bifidobacterium was part of the supplementation (22 studies, sample size 6069), studies where Lactobacillus was part of the supplementation (21 studies, sample size 4608), studies where single-strain probiotics were used (23 studies, sample size 5961), and studies where multiple-strain supplements were used (14 studies, sample size 3455)," they note. The most likely reason for the difference between the current meta-analysis and the previous ones is the sample size, the researchers say. "Our findings are not against the Cochrane 2014 analysis; they take it one step forward," Dr Rao told Reuters Health. "The Cochrane analysis had shown a 'trend' towards benefits of probiotic supplementation in reducing LOS. Its small sample size was probably not sufficient to detect a small, but statistically and clinically significant benefit of probiotic supplementation. The sample size of our meta-analysis is 9,416, which is 4,078 more than the Cochrane analysis for this outcome." The researchers say a limitation of their analysis is that LOS was a secondary outcome of interest in most of the studies. Also, they lacked information from 14 studies and minimal information was available on extremely preterm or extremely low birth weight babies. They also weren't able to objectively assess the effect of variables such as dosage and duration of supplementation on LOS — "highly important questions" that need to be addressed in controlled trials, they say.

Firms Team Up for Transport Incubator

International Biomedical and Hamilton Medical have teamed up. The Airborne Voyager and Aviator products are the most versatile transport incubators on the market. The flexible platforms allow you to customize your incubators to fit your team's individual needs. Whether you transport by air, ground, or both, the Voyager and Aviator are adaptable to any mission. With the addition of the fully featured ICU ventilator HAMILTON T-1, a variety of neonatal ventilation modes and sophisticated monitoring capabilities reliably manage the smallest and most fragile patients. "For the HAMILTON-T1 and the Airborne products to team up to provide an integrated solution for neonatal critical care transport teams – on the ground and in the air – was inevitable. With the T-1 it is possible to carry a fully functioning ventilator on transport. The product's capabilities provide the same level of respiratory support as that provided in a Neonatal Intensive Care Unit", said Greg Will, International Biomedical's Vice President of Sales and Marketing. "Another benefit is that the transport team does not need to carry air cylinders with them. The integrated air compressor provides the ability to adjust the oxygen level to meet the baby's needs without additional gas tanks."

Cells Found Recovered in Urine

Highly potent kidney stem/progenitor cells (KSPCs) can be recovered from the urine of preterm neonates, researchers report. "The most surprising result is that urine contains cells at very early stages of kidney development that can be differentiated ex vivo into functional renal cells," Dr Elena Levtchenko from Katholieke Universiteit Leuven in Leuven, Belgium, said. Researchers have already shown that urinary sediment can serve as a noninvasive source of cells of different parts of the nephron, and recently renal progenitor-like cells were isolated from amniotic fluid, which is composed mainly of fetal urine. Dr Levtchenko's team hypothesized that urinary cells from preterm neonates (born before completion of nephrogenesis) might be a potent source of progenitors with higher potential compared with adult cells. They collected urine from preterm neonates born at 31-36 weeks' gestational age. Half (51%) of the samples gave rise to growing clonal colonies, compared with all samples of amniotic fluid collected at weeks 15-22 and three of seven urine samples from adult women and none of the samples from adult men. Clonal cells from preterm urine and amniotic fluid were positive for kidney progenitor genes SIX2, CITED1 and Vimentin, and showed expression of cell surface antigen markers of mesenchymal stem cells. Adult progenitor cells were negative for SIX2. Co-staining of SIX2/FOXD1 in neonatal KSPCs using flow cytometry analysis and immunofluorescence confirmed the expression of these markers in single cells at the protein level, the researchers report in the Journal of the American Society of Nephrology. Podocytes derived from these progenitor cells acquired arborized morphology and became bi- or multinucleated, resembling conditionally immortalized podocytes isolated from human kidney. When cultured in proximal tubule cell (PTEC)-specific medium, neonatal KSPCs showed a significant upregulation of PTEC-specific genes, including significant increased expression of p-glycoprotein.

NICU Transmission Risks Studied

In neonatal intensive care units (NICU), bloodstream infection (BSI) of one infant with Pseudomonas aeruginosa or Serratia spp poses an elevated risk of spreading to others, according to German researchers. In a March 8 online paper in Pediatrics, Dr Buhrer of Charite Medical University Berlin and colleagues noted that nosocomial outbreaks tend to cluster and can be devastating but nothing has been known of pathogen-specific transmission probabilities. To investigate, the team examined German NICU surveillance data from 2000 to 2011 on more than 44,000 infants below 1500 g birth weight being cared for in 229 hospitals. After excluding BSIs due to relatively benign coagulase-negative staphylococci, there were a total of 2004 culture-positive infections. Among the most common pathogens were methicillin-sensitive S aureus in 407 cases, Enterobacter spp in 246 and vancomycin-sensitive Enterococcus spp in 243. The corresponding relative risks of another infant in the same unit having a same-pathogen BSI were similar at 9.5, 7.9 and 4.3. This was also true of other common pathogens. However, although there were only 58 cases of Serratia spp, the relative risk was 77.5. For Pseudomonas aeruginosa with 38 cases, the relative risk was 64.5. Rates of BSI per 100 exposed infants ranged between 2.21 for Enterococcus to 8.15 for Serratia.

Early-term Elective Delivery Studied

Infants born electively at 37 to 38 weeks' gestation are not at increased risk for neonatal morbidity or infant mortality compared with infants who are expectantly managed and born at 39 weeks' gestation or older, according to a population-based retrospective cohort study of more than 600,000 infants through the Baylor College of Medicine. However, the researchers did see elevated rates for adverse outcomes among the subset of infants delivered by elective cesarean. The study findings run counter to current recommendations from the American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine. A joint committee opinion specifies, "Although there are specific indications for delivery before 39 weeks of gestation, a nonmedically indicated early-term delivery is not appropriate." "In contrast to the current dogma, we found that when a methodologically appropriate comparison group was used, elective induction before 39 weeks of gestation was not associated with an increased likelihood of adverse outcomes," the researchers write. The researchers classified the infants into either a control group born at 39 to 40 weeks of gestation

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after expectant management or one of four early-term (37 - 38 weeks' gestation) delivery groups: infants who were born by electively induced delivery, elective cesarean delivery without a trial of labor, spontaneous delivery, and medically indicated delivery. Most of the infants (64.6%) were born full-term. Among the babies born early-term, 50% were born after spontaneous onset of labor (n = 112,846) and 40% were delivered after elective induction (n = 33,213) or cesarean birth (n = 55,515). Overall, 51,846 (8.2%) infants experienced an adverse outcome, the most prevalent of which was respiratory morbidity (5.98%; 95% confidence interval [CI], 5.92% - 6.04%). The neonatal intensive care unit (NICU) admission rate was 2.61% (95% CI, 2.57% - 2.65%). The infant mortality rate was 1.46 per 1000 live births (95% CI, 1.37 - 1.56), with 928 infant deaths. Neonatal sepsis (1.34%; 95% CI, 1.31% - 1.37%) and feeding difficulties (1.26%; 95% CI, 1.23% - 1.29%) occurred at approximately the same rate.

Curbing Lung Problems Via Late Surfactant

Giving a second surfactant treatment two weeks after birth to very preterm infants with prolonged respiratory distress may reduce respiratory morbidity during the first year of life, according to a small randomized trial. However, duration of mechanical ventilation for infants given late surfactant was no shorter than it was for controls. Surfactant treatment given at birth significantly improves mortality and morbidity in preterm infants, but some of them do not respond. The study involved 118 infants born at less than 33 weeks' gestation who still required ventilation on day 14 with fraction of inspired oxygen (FiO2) of more than 0.30. After randomization, they received either 200 mg/kg of poractant alfa (surfactant) or the same volume of air. There was early respiratory improvement, as reflected in a decrease in FiO2 requirements, in the group receiving surfactant but not in controls (0.36 versus 0.43, $p<0.005$). But this effect waned after 24 hours, the researchers reported. Duration of ventilation (the mean age at first successful extubation), the primary outcome, was similar for the two groups (35.7 days versus 38.3 days for surfactant and control groups, respectively). Similarly, for the combined outcome of death or bronchopulmonary dysplasia (BPD) at 33 weeks' postmenstrual age, infants receiving late surfactant did not fare significantly better than those in the control group (27.1% versus 35.6%, $p=0.32$). Nevertheless, "clinical status of the infants at discharge suggests a difference in illness severity between the groups," the authors wrote. Surfactant infants had significantly less necrotizing enterocolitis (8% versus 25%) and earlier full enteral feeding (98% versus 85% receiving full feeds on day 28) than control infants.

Curbing Adverse Mental Health Outcomes

Children born extremely preterm but without severe neurodevelopmental disorders nevertheless have higher rates of adverse mental health outcomes, researchers from Norway report. Children born extremely preterm and with extremely low birth weight (EP/ELBW) have increased rates of neurodevelopmental disabilities and increased risk of autistic symptoms, inattention, hyperactivity, and emotional symptoms when they reach school age. Whether EP/ELBW children without neurodevelopmental disabilities have the same increased risk of adverse mental health outcomes remains unclear. Dr Silje Katrine Elgen Fevang from University of Bergen and colleagues compared the prevalence and gender characteristics indicative of mental health problems in 216 11-year-old EP/ELBW children born without intellectual disability, blindness, deafness, or nonambulatory cerebral palsy in Norway between 1999 and 2000 with those of an unselected population of 1882 11-year-old children in the Bergen Child Study. Significantly more EP/ELBW children (18%) than reference children (3.2%) scored above the 98th percentile of autism spectrum disorder symptoms. EP/ELBW children were two to eight times more likely than reference children to have symptoms of inattention and hyperactivity/impulsivity, anxiety, or obsessive-compulsive disorder. More than a third of parents (37%) and teachers (36%) reported at least one mental health problem in the EP/ELBW children, compared with 16% and 9%, respectively, in the reference group. EP/ELBW children were 4.5 times as likely as reference children to have at least one mental health problem reported by a parent or teacher. These outcomes did not appear to differ by gender.

COMPANY PROFILE

Capnia

Capnia, Inc. is a diversified healthcare company that develops innovative diagnostics, devices and therapeutics addressing unmet medical needs. Capnia's first commercially-available product in the US is the CoSense® End-Tidal Carbon Monoxide Monitor, an FDA-cleared device that uses the Sensalyze™ Breath Technology Platform. CoSense is a portable, non-invasive device that rapidly and accurately measures carbon monoxide (CO) in exhaled breath. CoSense is used for the monitoring of CO from internal sources (such as hemolysis, a dangerous condition in which red blood cells degrade rapidly), as well as external sources (such as CO poisoning and smoke inhalation).

The initial clinical application for CoSense is newborns with jaundice who are at risk for hemolysis, comprising approximately three million births in the US and Europe. Understanding the rate of hemolysis, and whether that rate is normal or abnormal, is a critical part of understanding the cause of jaundice and hyperbilirubinemia in newborns.

Neonatal jaundice is a very common condition worldwide, occurring in up to 60% of term and 80% of preterm newborns in the first week of life.[1] Jaundice may be the result of problems with bilirubin excretion, conjugation or production. Newborns with both jaundice and an underlying hemolytic condition are at high risk for adverse neurodevelopmental outcomes.[2,3]

The tests that are currently used to diagnose hemolysis (eg, Coombs/DAT, retic count, CBC) are not always accurate in newborns and do not provide a direct measure of hemolysis.[4] The American Academy of Pediatrics' 2004 guidelines on the management of hyperbilirubinemia in newborns ≥35 weeks of gestation states that testing End-Tidal Carbon Monoxide (ETCO) is the only way to directly measure bilirubin production and confirm the presence or absence of hemolysis.[5]

In addition, many hospitals only perform hemolysis testing on a subset of newborns who are at risk of having a hemolytic condition. As a result, many babies with underlying hemolytic conditions may not be identified during their initial hospital stay, placing them at risk. Newborns at higher risk for hemolysis include those with Rh incompatibilities, early-onset jaundice, mothers who have diabetes, and newborns with certain ethnic backgrounds. Our device, the CoSense ETCO

Monitor, allows physicians to rapidly, accurately and non-invasively measure the rate of hemolysis in newborns at the bedside.[6]

CoSense is uniquely capable of automatically collecting and analyzing an end-tidal breath sample to determine the rate of CO production and identify the risk of hyperbilirubinemia in a newborn. Traditional breath measurement devices require a patient who is mature and compliant enough to perform breathing maneuvers. However, CoSense uses a patented approach to automatically collect an end-tidal breath sample without the need for breathing maneuvers, making it an ideal technology for newborns.

With the correct information about ETCO and the rate of hemolysis, physicians have the opportunity to appropriately manage the care of a newborn with a hemolytic condition, including decisions regarding treatment and discharge. A recently-published study demonstrated that newborns with elevated bilirubin levels who received a CoSense test were less likely to be readmitted to the hospital for jaundice treatment than newborns with hyperbilirubinemia who did not receive a CoSense test.[7] With an average cost of $4,500 per readmission for hyperbilirubinemia,[8] the use of CoSense to appropriately manage newborns at risk for hyperbilirubinemia could provide significant clinical and financial benefits for newborns, families, and hospitals.

With the recent acquisition of NeoForce Group, Capnia has further committed to leveraging technology to address unmet medical needs in infant pulmonology. The NeoForce Group's neonatology-focused product line includes innovative pulmonary resuscitation solutions including the NeoPIP™ Infant T-Piece Resuscitator and Universal T-Piece Circuit that fits seamlessly with the most commonly-used infant resuscitation systems.

Capnia is dedicated to bringing innovative solutions to the market to address unmet medical needs, particularly those for neonates. The Sensalyze™ technology platform allows for breath monitoring of neonates, unlike other technologies. CoSense is the first product to be approved using this technology—and Capnia is developing other devices to detect analytes such as hydrogen (for malabsorption), nitric oxide (for asthma), ammonia (for urea cycle disorders) and carbon dioxide (for infants with respiratory distress).

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In this feature, Neonatal Intensive Care interviews clinicians and healthcare providers about the actual application of specific products and therapies. This interview is with Scott Horowitz, Senior Product Manager at Mercury Medical.

Neonatal Intensive Care: How has the Neo-Tee Infant T-Piece been accepted in the market?
Scott Horowitz: The Neo-Tee Infant T-Piece Resuscitator is truly Mercury's Flagship NICU product. As the world's only disposable Infant T-Piece resuscitator, it has gained worldwide acceptance for providing consistent infant ventilation around the globe. Neo-Tee has offered hospitals a burden relief of capital equipment spending for similar devices. Many hospitals don't have an adequate budget to put capital equipment at every bedside, or where it's needed most, now Neo-Tee affords these facilities the opportunity to have a device at every bedside, whether it is in the L&D, NICU, ER or transport. This way, these precious infant patients all consistently and equally get the best care available, resulting in optimized patient outcomes.

Neo-Tee has been widely accepted not only in actual clinical use; but more and more clinicians we hear from are using the device and share their success when we meet them at conventions, such as the American Academy of Pediatrics and the recent Neo 2016 meeting. Excitingly for us, last year the Neo-Tee was a product contest finalist (2nd place) for the European Respiratory Society's "Product of Outstanding Interest Award." Furthermore, the Neo-Tee is now mentioned in the S.T.A.B.L.E. manual as a recommended product to have on the product requirements list for the delivery room, nursery and emergency department.

NIC: How does it work?
SH: As a typical user would explain, it's very easy to set-up and connects simply to a flowmeter/blender and/or O_2 tank nipple. The desired PIP and PEEP pressures are set and monitored on the colorcoded manometer that is easily visible on the Tee. This enables the eyes to watch chest rise, rather than needing to look up at an external manometer. We do recommend, however, reviewing the Neo-Tee DFU and our on-line in-service video prior to use at www.mercurymed.com.

NIC: Are there special features that make it stand out in the market?
SH: There is no other disposable T-piece Resuscitator on the market today for neonates. More importantly, when compared with other products/technologies that are available for resuscitating, such as CPR bags, (BVM's – bag, valve, masks), you do not get consistent PIP and PEEP pressures, and some CPR bags do not come with manometers or PEEP valves. The Neo-Tee comes standard with a manometer and PEEP valve. Best of all, the product is very lightweight and ideal for transport. Recently at the Neo 2016 in Orlando, a couple of physicians had seen a demonstration between a hyperinflation bag (flow-inflating), which their facility typically uses vs. the Neo-Tee. Once the Neo-Tee benefits were clearly seen during ventilation, they wanted an in-service as soon as possible.

Additionally, there are two other "ONLY ONE" products that Mercury Medical offers that work with the Neo-Tee and create a great combination. One is the airQ®SP, size 1.0, Laryngeal Mask Airway (LMA), which is an alternative to ET intubation and is very easy to insert. Most importantly, a Laryngeal Mask Airway is mentioned in the AHA Guidelines, "a laryngeal mask should be considered during resuscitation if face mask ventilation is unsuccessful and tracheal intubation is unsuccessful or not feasible." And, there was a recent abstract published in the Journal of Perinatology, "that an LMA shows promising results in surfactant delivery and helps to prevent the need for mechanical ventilation with pre-term neonates with RDS."

Another product, the Neo-StatCO_2 <kg® is the "ONLY ONE" colorimetric CO_2 device that can be used for tiny babies for weight ranges of 0.25kg to 6 kgs.

NIC: In the course of product evolution, have there been recent enhancements made on the Neo-Tee?
SH: Absolutely. Receiving feedback from our customer base helps keep us on course for ongoing, continuous quality improvements. We recently introduced a product line extension of the Neo-Tee with a Red Override Button. This enables the clinician to be able to deliver airway pressure above 40 cm H_2O in certain emergency situations. The new PIP knob design is also larger for easier turning and maneuverability. The PEEP knob on this product line extension utilizes a different spring and offers a tighter tolerance — keeping PEEP settings intact. Along with this model, we've introduced a new style Manometer that has larger numbers so that it is easier to read in the NICU under dim lighting conditions. Last, since babies are hooked-up to many lines, the O_2 tubing is green so it can be quickly identified among the other lines/connections. This newer offering is, without a doubt, the "Deluxe" T-Piece model.

NIC: Can you describe the ease-of-use for clinicians? Is there any special training that has to be completed before using it?
SH: The Neo-Tee product is very easy to set pressures and use. A

Input on questions was provided by 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.

brief in-service on the product is really all that is needed. When RT students visit our booth at conventions, they try the CPR and hyperinflation bags, but when they demonstrate the Neo-Tee, they see first-hand how easy a T-piece is to set up — and it's much less intimidating for them; also, they realize how safe it is to use.

NIC: Are there cost-savings associated with the device for clinicians, patients or payers?
SH: The savings could be realized in a variety of situations. For example, many CPR bags (BVM's) do not come with masks, manometers and PEEP valves, resulting in extra costs to purchase these items and then, it can be cumbersome to add/use them. While the Neo-Tee® may come with or without a mask, the Manometer and PEEP valve are standard and are integrated into the product design. As mentioned, there is no capital cost with the Neo-Tee. Other devices require both capital equipment and disposable spending, (mask, O_2 tubing, circuit, etc.)

NIC: What do you think the next generation of Neo-Tee will look like?
SH: Funny…that's like asking Hyundai what the next evolution of their Sonata Hybrid will look like. I'm sure it will be impressive, but you'll just have to wait for it to be introduced.

Agenesis of the Corpus Callosum

B Petrikovsky, MD PhD, D Cohen, MD, S Pavlakis, MD

Definition

The corpus callosum is part of the brain consisting of neurofibers, which connect both cerebral hemispheres. Agenesis of the corpus callosum (ACC) is a failure to develop these neurofibers.

Prevalence

3.5 per 1000 live births

Etiology

Corpus callosum formation completes by 18 to 20 weeks of pregnancy and manifests by the presence of commissural neurons with axons crossing the midline bilaterally. The causes of ACC are multiple and includes genetic factors as well as teratogens, e.g. alcohol. The majority of fetuses with ACC do not have a known genetic syndrome. The following are most common conditions associated with ACC:

- Aneuploidy
- Mutations in the ARX, L1CAM, and KCC3 genes
- Alcohol, anti-epileptic medication, and cocaine
- Viral infections, e.g. rubella
- Miscellaneous

Classification

ACC may be complete or partial.

Major principles of diagnosis

Sonographic diagnosis of ACC may be difficult: 10 to 15% of ACC is missed in patients who underwent two or more ultrasound examinations during pregnancy. Ultrasound signs of ACC include increased separation of the frontal horns of the lateral ventricles. The posterior horns of the ventricles exhibit so called "tear drop" appearance. Indirect signs of agenesis of the corpus callosum include, difficulty to identify cavum septum pellucidum, mild ventriculomegaly, disproportional enlargement of the occipital horns, displacement of the third ventricle, and occasional visualization of midline cysts and lipomas. The cavum septum pellucidum appears as two parallel lines separated by cerebrospinal fluid after 14 weeks in the BPD plane. The development of the septum pellucidum is related to the corpus callosum. The septum pellucidum is absent in complete agenesis of the corpus callosum. Demonstration of the cavum septum pellucidum excludes complete agenesis of the corpus callosum. When the septum pellucidum is absent and when the atria and occipital horns of the lateral ventricles are dilated, the differential diagnosis includes lobar holoprosencephaly and agenesis of the corpus callosum. On ultrasound, non-normalization of the cavum septum pelucidum and/or mild ventriculomegaly are the most common indications for fetal brain MRI. By 22 weeks of pregnancy, MR can detect the full range of callosal dysmorpholgy including agenesis, partial agenesis, diffuse hypoplasia, and short/thick patterns as well as co-morbid associations — septooptic dysplasia, neuromigrational disorders and brainstem kinking (ponto-mesencephalic dysmorphology.) These imaging attributes are essential in establishing a syndromic differential diagnoses and are necessary to complete and optimize prognostication and patient counseling.

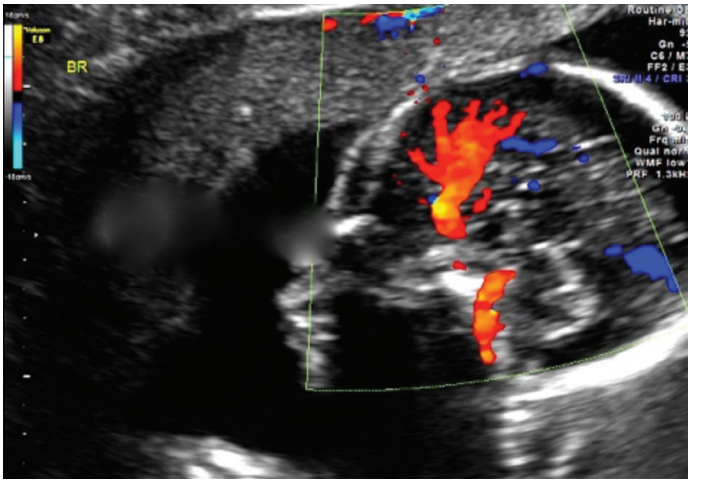

Figure 1. Sonographic appearance of absent corpus callosum: Please note that the abnormal branching of the anterior cerebral artery is due to the absence of the pericallosal arteries. (Courtesy of D Cohen, MD)

Early presentation

Since the development of corpus callosum is completed at 18-20 weeks of pregnancy, first trimester diagnosis is not available.

MRI diagnosis

MRI will consistently visualize the normal and abnormal corpus callosum after 22 weeks and in the majority of cases between 20-22 weeks.

Prenatal management

The algorithm of prenatal management includes:

- Search for associated anomalies

B Petrikovsky is with Fetal Research Fund, Inc; D Cohen is with Hudson Valley Radiology Associates; S Pavlakis is with Maimonides Medical Center.

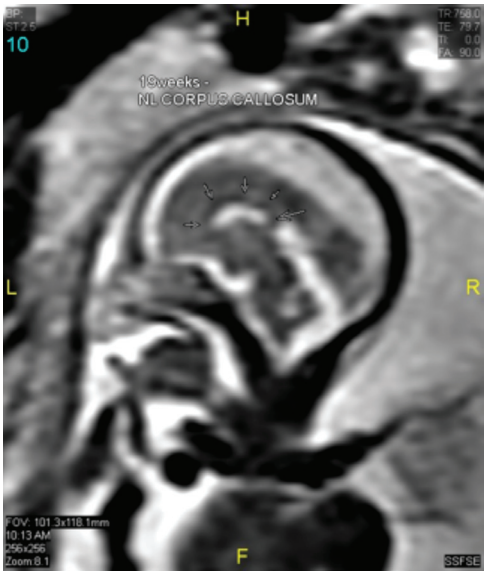

Figure 2. Normal MRI appearance of corpus callosum (MRI image courtesy of D Cohen, MD)

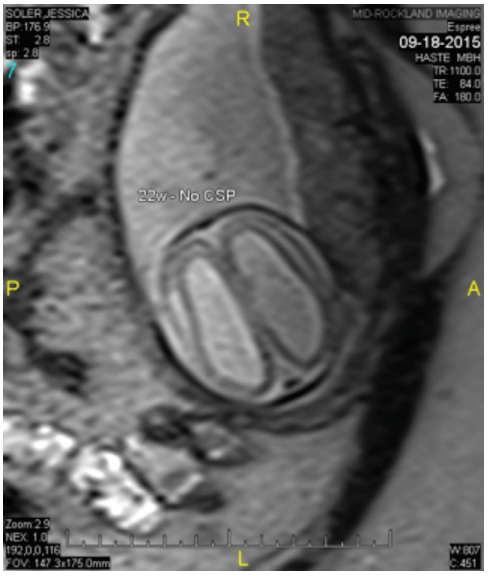

Figure 3. Absent corpus callosum (MRI image courtesy of D Cohen, MD)

- Karyotyping, microarray analysis
- Counseling by a pediatric neurologist
- Serial ultrasound assessment searching for progressive ventriculomegaly

Prognosis

Over 60% of children with isolated ACC will have mild behavioral problems. The type of ACC (partial vs. complete) has no bearing on the prognosis. Patients with ACC also show difficulties with expressive language and have impaired social skills. Recurrence rate depends on etiology and usually ranges between 2 to 4%.

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Many Face Masks for Preterm Infants Just Don't Measure Up

Chris Campbell

A common complaint when adults are fitted with a continuous positive airway pressure (CPAP) mask so they can sleep better is that it doesn't fit right. The mask feels awkward and that makes them not want to keep it on, even if there are positive benefits. That's a matter of comfort. But for a newborn, it's not about how comfortable they feel—no, the impacts of a mask that is too big are obstructions or leaks between the infant's face and the mask, with far deadlier consequences than comfort. Studies that have investigated delivery rooms have found that mask intermittent positive pressure ventilation (IPPV) can be frequently disrupted through such obstructions and leaks—made even worse by the fact that such problems are often not even noticed by delivery room staff.[1-5]

The solution is to find masks that are the perfect fit—with an optimal seal—for the tiniest of patients, but that is far more complicated to achieve than it sounds if most of the masks being produced by manufacturers aren't in the size range needed by babies. According to a study funded by the Department of Newborn Research, Royal Women's Hospital, in Australia, that an issue affecting neonatal health care—to the detriment of preterm infants. What O'Shea et al concluded was that the "smallest size of some brands of mask is too large for many preterm infants."

Why A Study?

International recommendations out of the UK, US and Australia emphasize the importance of a well-fitting face mask,[6-8] and O'Donnell et al9 found that round face masks were used 85% of the time and anatomically shaped masks were used the other 15%. But as far as the type or size of rounds masks commonly used, that hasn't been established by surveys.[10-12]

The researchers in Australia, Ireland and Scotland were curious to delve more into the size of masks for preterm infants or how their faces change as they get older.

"There are no data available regarding the size of preterm infants' faces or how their facial dimensions change in the weeks following preterm birth. The aims of this study were to (1) measure the dimensions of preterm infants' faces across a range of gestational ages at birth and over the first weeks of life, (2) compare these results with the dimensions of commonly available round masks and (3) make recommendations regarding appropriate mask size for preterm infants."

Chris Campbell is the Senior Editor of Neonatal Intensive Care.

The Study

One issue faced by O'Shea et al was that this was the first study of its kind, with no data available to base a sample size calculation. That meant a lot of photographs were needed for the study. Researchers completed a cohort of 107 infants ranging between 24 and 33 weeks' gestational age, including at least 10 babies per week of gestation. No significant differences were discovered when gender was examined.

"Each infant was photographed while supine with their head in the neutral position and their jaw neutral, that is, the position in which they would be placed to receive mask IPPV. A plastic scale was placed next to and level with the infant's face and included in the photograph … Infants were photographed within 72 h after birth and weekly until they reached 33+6 weeks' postmenstrual age or were discharged or transferred to another hospital. Measurements were combined to determine (i) measurements of newborns (<72 h of age)—presented as mean (SD) distance in millimetres for each completed week of gestation and by birth weight divided into 250 g cohorts; and (ii) measurements of growing infants—presented as mean (SD) distance in millimetres for each completed corrected week of gestation and by weight divided into 250 g cohorts."

The researchers write that the strengths of their study include being the first to measure the dimensions of preterm infants' faces and to compare the results with those of commonly available masks. After all, if babies need a certain size of masks, hospitals need to know which company has those masks available. Researchers also said their study found interesting results in the area of masks in relation to how the faces of infants change in the first few weeks. "The results have demonstrated that postnatal growth in these infants' facial measurements closely resembles growth in utero. The study cohort was evenly distributed across the range of gestational ages allowing for good representation of the extremely low birthweight infants. This is important because even though the extremely low birthweight infants make up a small proportion of the entire preterm population, they are the group most likely to require respiratory support."

An Issue Of Size

In the conclusion section of the study, the researchers highlighted two issues regarding the size of masks that should be used for infants, and what brands are available to hospitals. As it turns out, the most commonly available mask—50 mm—didn't fare well when tested. "This study shows that a mask with an

Infant Resuscitation Masks | FEATURES

The Fisher & Paykel Healthcare Infant Resuscitation Masks are available in a range of sizes providing an anatomical seal.

Range Of Sizes

The infant resuscitation masks are available in five sizes. The range includes extra small sizes for micro-premature neonates to larger sizes for term infants and pediatric patients. This ensures there is a match for a wider patient range. A mask sizing chart is available in the starter kit to assist with mask selection for each patient.

Anatomical Seal

The extended edge of the mask is soft and pliable, easily creating a comfortable anatomical seal around the infant's mouth and nose. To achieve a good seal, it is recommended to gently roll the mask onto the face from the chin and to apply the C-Hold hand positioning.

1. Anatomical Seal

- Soft and pliable extended rim
- Firm sides provide support

2. Visibility

- Transparent surface
- Allows clear observation of breath condensate

3. Versatile Connection

- 15 mm conical male ISO 5356-1:2004
- Connects to common resuscitation devices

4. Range of Sizes

- Extra small mask sizes suitable for premature neonates
  35 mm pictured left at actual size

INFANT RESUSCITATION MASKS

	RD803-10 Micro-Premature (XS)	RD804-10 Premature (S)	RD805-10 Neonatal (M)	RD806-10 Infant (L)	RD807-10 Pediatric (XL)
Diameter	35 mm (1.38")	42 mm (1.65")	50 mm (1.97")	60 mm (2.36")	72 mm (2.83")
Suggested Weight Range	400 g - 1 kg (0.88 - 2.2 lb)	‹1.5 kg (‹3.3 lb)	‹2.5 kg (‹5.5 lb)	‹5 kg (‹11 lb)	‹10 kg (‹22 lb)
	Extremely Low Birth Weight (ELBW)	Very Low Birth Weight (VLBW)	Low Birth Weight (LBW)	Term	Pediatric
Material	Thermoplastic Elastomer (The product does not contain any latex or DEHP plasticizer).				
Cleaning and Disposal	Single patient use - supplied clean, not sterile. Discard according to hospital protocol.				

There is a range of kit options for the Infant Resuscitation Masks, including a Mask Starter Kit (RD900-EN). These options are included in the Neopuff Product Catalog.

external diameter of 50 mm may be too large for infants <34 weeks' postmenstrual age. A 35 mm mask fits infants <29 weeks' postmenstrual age. For babies born at 27-28 weeks' gestational age, having both 35 and 42 mm masks available allows clinicians to choose the best-fitting mask for a particular baby. The 42 mm mask is appropriate for infants up to 33 weeks' postmenstrual age. However, having the 42 and 50 mm masks available may help select the best one for babies born at 32-33 weeks' gestational age."

The researchers added that: "there are many brands of round neonatal masks available in a range of sizes. Most brands start with smallest external diameter around 50 mm. To our knowledge, there is only one brand of smaller mask available — Infant Resuscitation Masks (Fisher & Paykel Healthcare, Auckland, New Zealand), sizes small (premature mask) and extra small (micro-premature mask), with external diameters of 42 and 35 mm, respectively."

In the end, O'Shea et al recommended further studies regarding the effectiveness of different-sized masks in preterm infants, including a focus on clinical use on different-sized infants.

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Initiation and Ongoing Clinical Management of an Infant Supported by Volume Guarantee

Robert DiBlasi RRT-NPS, FAARC

The patient is a premature female infant born at 25 4/7 weeks, weighing 452 grams, following premature rupture of membranes at a community hospital. She was supported briefly in the delivery room with CPAP following surfactant administration, and was transferred to a level IV NICU for further care on the second day of life. The infant arrived at the hospital with the neonatal transport team on CPAP with a pressure of 8 cm H_2O and a set FiO_2 of 0.7. The infant was in distress and presented with the following: nasal flaring, intercostal and substernal retractions, and occasional apneic episodes that responded to intermittent tactile stimulation. The chest X-ray showed diffuse bilateral infiltrates and profound hypoinflation, consistent with Respiratory Distress Syndrome (RDS).

Due to the patient's deteriorating respiratory status on high CPAP settings, Non-Invasive Ventilation (NIV) was initiated using the Dräger Babylog VN500.

Initial Settings

Application Mode	NIV
Mode	PC-CMV
PIP	20 cm H_2O
PEEP	6 cm H_2O
Respiratory Rate	20/min
Ti	0.4 s
FiO_2	0.6

Initial arterial blood gas via Umbilical Artery Catheter

pH	7.28
$PaCO_2$	55 mmHG
PaO_2	55 mmHG
HCO_3	19 mmHG

NIV resulted in reduced work of breathing and avoided intubation for this patient. The patient was initially asynchronous with the non-invasive PC-CMV[1] breaths, so the respiratory rate (RR) was adjusted to match every other spontaneous effort being made by the patient (Figure 1).

Robert DiBlasi is Manager of Clinical Diagnostics and Research in the Respiratory Care Department at the Seattle Children's.

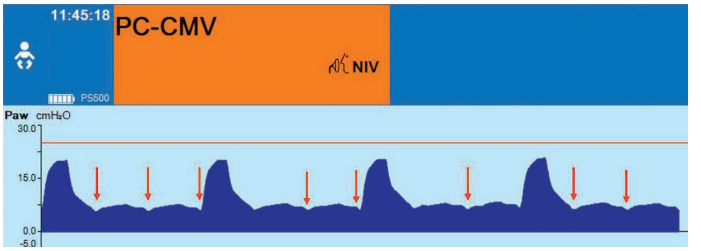

Figure 1. Graphical representation of airway pressure in the patient during NIV with the Babylog VN500

The red arrows in Figure 1 indicate small depressions in the baseline pressure where the patient is making an inspiratory effort. Adjusting the rate to provide fully supported breaths on every other spontaneous effort was useful for improving synchrony in this patient.

The patient failed NIV after 10 hours due to apnea, desaturations, and bradycardia. The chest X-ray (Figure 2) after intubation revealed diffuse bilateral infiltrates consistent with RDS. The patient was given 2 mL/kg Curosurf for poor compliance (0.5 mL/cm H_2O), refractory hypoxemia, and radiographic evidence of pulmonary atelectasis.

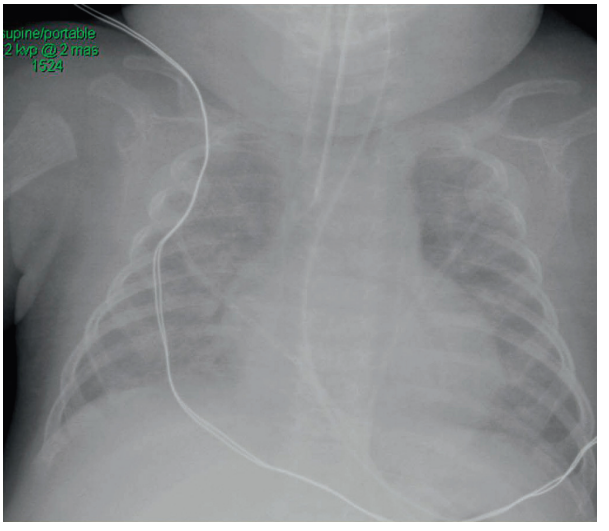

Figure 2. X-ray after intubation

The application mode was changed to "tube" for invasive ventilation. The physician ordered PC-AC[2] with Volume Guarantee (VG) with the following settings: tidal volume (VT) of

4 mL/kg, PEEP of 8 cm H_2O, an inspiratory time (Ti) of 0.3 s, RR 50/min. The patient was spontaneously assisting all breaths and was breathing at a rate of 70/min. The transcutaneous CO_2 levels were 75 mmHg and these values correlated well with the arterial CO_2 levels observed with the last blood gas on nasal CPAP. Upon the physician's request, the Respiratory Therapist (RT) increased the VT to 5 mL/kg to account for the instrumental deadspace of the flow sensor and ET tube. The respiratory rate and CO_2 levels decreased in response to this change and the patient appeared comfortable.

Following this change, an audible ET tube leak could be heard . The ventilator was registering a 50-60 percent leak and an alarm on the ventilator began reading "VT low". This problem was remedied by changing the Pmax setting from 25 to 30 cm H_2O in order to provide enough pressure to allow the tidal volume to be delivered.

Twenty-four hours later, the patient's lung mechanics improved as reflected by lower Peak Inspiratory Pressure (PIP) values. However, the bedside Registered Nurse (RN) expressed concerns that the patient appeared tachypneic and had low PIP values. The bedside RT assured the nurse that this was related to the nursing care and usually the PIP values returned to normal after care was rendered. The RT presented a trend of the pressures and volumes (Figure 3) to the RN. She was then assured that this was a normal function of the ventilator and may be appropriate so that the patient isn't receiving too much pressure and volume during periods of anxiety.

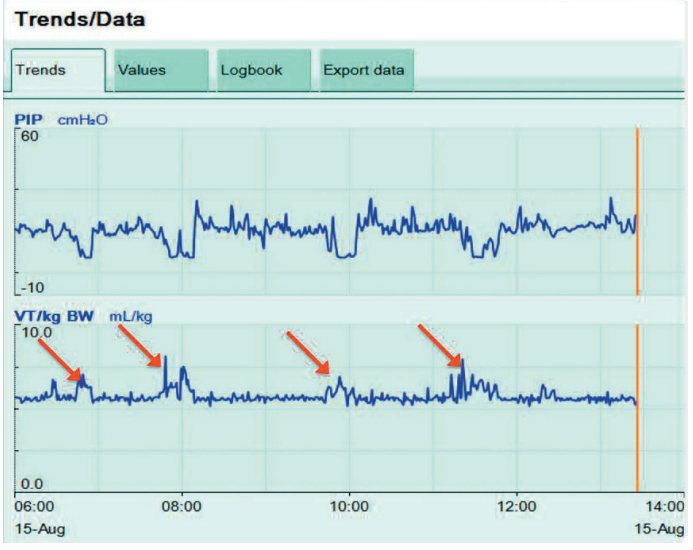

Figure 3. Trend of tidal volume and airway pressure

The trending of pressure and volume show reduced inspiratory pressures due to increased volumes during periods of nursing care (red arrows). The patient's efforts are reduced after nursing care, resulting in smaller volumes and higher PIP values.

A month later, the infant was still supported with the Babylog VN500 in the PC-AC mode with Volume Guarantee activated. The infant gradually started showing signs of increased work of breathing on the ventilator and increased FiO_2 requirement following upsizing of the ET tube.

Settings

Application Mode	Tube
Mode	PC-AC with VG
PIP	7 cm H_2O
Vt	14.4 mL (set)
	17.5 mL (measured)
PEEP	6 cm H_2O
Respiratory Rate	20/min
Ti	0.30 s
FiO_2	0.29

Venous Blood Gas

pH	**7.23**
$PaCO_2$	**68 mmHG**
PaO_2	**23 mmHG**
HCO_3	**29 mmHG**

Airway graphics revealed consistently low PIP values with tidal volumes greater than that set on the ventilator (Figure 4A). The chest X-ray showed low lung volumes with increasing atelectasis and air bronchograms (Figure 4B) from the previous exam. The patient developed retractions, nasal flaring, and SpO_2 78-89 percent. Breath sounds were reduced in the bases with fine inspiratory crackles throughout.

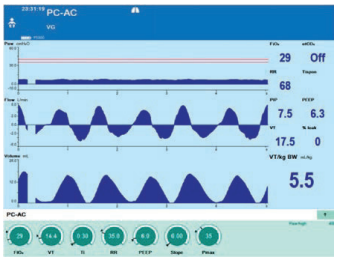

Figure 4A. Inadequate support during PC-AC

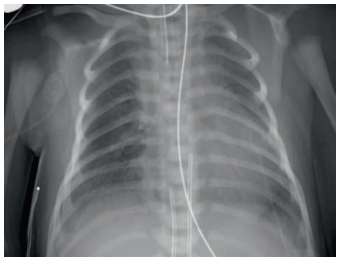

Figure 4B. Strong infiltration constant with atelectasis

Based on the clinical deterioration, the RT chose to assess the appropriateness of the tidal volume setting. The attending neonatologist wanted to place the patient in PC-AC without Volume Guarantee, so that the patient could get a higher level of support. During this time, the NICU team discovered that the dose-calculated weight in the ventilator hadn't been updated in over a month. When the new weight was entered, it became obvious that the patient was only receiving a tidal volume ~3.5 mL/kg. This prompted the team to increase the set tidal volume targeted from 14 to 19 mL. This resulted in an immediate

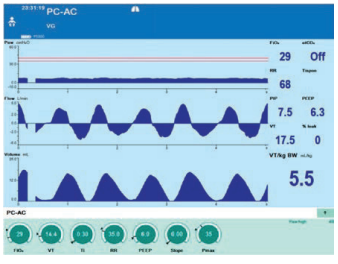

Figure 5A. Airway graphic following setting change

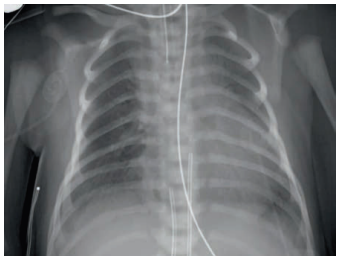

Figure 5B. X-ray following setting change

reduction in the observed high levels of work of breathing and increased in PIP values (Figure 5A) as well as radiographic improvement in lung inflation (Figure 5B).

A week later the PIP values were again reduced to only 1 cm H_2O above the PEEP level during PC-AC with Volume Guarentee. However, with the exception of this time, the patient had normal breathing and acceptable gas exchange. Based on this, the patient was extubated to non-invasive CPAP. Subsequently, five days later, the patient was transferred home utilizing oxygen therapy at 0.5 L/min via nasal cannula.

Rob is a Principle Investigator for the Center for Developmental Therapeutics at the Seattle Children's Hospital Research Institute. His research interests include: neonatal pulmonary mechanics monitoring, patient/ventilator interaction, ventilator induced lung injury, neonatal lung protective strategies, mechanical ventilator performance, and aerosolization of respiratory medications. Rob is an inventor for multiple life support devices designed for use in resource limited settings, receiving much of the funding for implementing these devices in the clinical setting from the Bill and Melinda Gates Foundation. He has authored 25 peer reviewed papers, 12 textbook chapters on neonatal and pediatric mechanical ventilation, and co-editor for the 4th edition of Perinatal/Pediatric Respiratory Care Textbook. He also serves on the Editorial Board for RESPIRATORY CARE journal. He is also a fellow of the American Association for Respiratory Care.

Footnotes

1 Pressure Control - Continuous Mandatory Ventilation
2 Pressure Control - Assist Control

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Changes in Cerebral Oxygenation During Early Postnatal Adaptation in Newborns Delivered by Vacuum Extraction Measured By Near-Infrared Spectroscopy

Tanja Karen, Martin Wolf, Rahel Nef, Daniel Haensse, Hans Ulrich Bucher, Gabriele Schulz and Jean-Claude Fauchère*

Abstract

Background: Newborns delivered by vacuum extraction quite often show clinical signs of a hemodynamic compromise, which is difficult to assess in terms of severity. The conventional means to measure the hemodynamic status are not sensitive enough to appreciate the severity of general, and more specifically of cerebral circulatory imbalance. The aim was to study cerebral tissue oxygenation during postnatal adaptation in these infants using near-infrared spectroscopy.

Methods: The tissue hemoglobin index (THI), tissue oxygenation index (TOI), arterial oxygen saturation (pre-ductal SaO2) and heart rate (HR) were recorded immediately after birth, and again after 12-24 hours of life in 15 newborns delivered by vacuum extraction due to fetal distress. A comparison with 19 healthy newborns delivered by elective cesarean section was performed.

Results: Newborns delivered by vacuum extraction had significantly higher THI 10-15 minutes after birth. TOI and HR were significantly higher in the first 5 min and SaO2 in the first 10 minutes but then did not differ from those after cesarean section.

Conclusion: Infants delivered by vacuum extraction following fetal distress show transient deviations in cerebral oxygenation and perfusion after birth which were not detectable after 24 hours.

Background

The transition from fetal to extra-uterine life is characterized by a number of unique physiological changes within the first minutes to hours, or even days after birth. There is a substantial body of literature concerning the changes in arterial oxygen and carbon dioxide content, in pulmonary and systemic blood flow, the closure of the intra- and extra-cardiac shunts, and the changes in oxygen saturation immediately after birth [1-5]. These changes, together with the compression of the skull during delivery followed by decompression at the moment of birth, may be assumed to play important parts in the cerebral circulatory adaptation to neonatal life [1]. The mechanisms, which regulate the postnatal adaptation of cerebral blood flow are poorly understood [6-8]. Data about these changes, especially immediately after birth, are scarce [9-17]. Furthermore, data are lacking in infants, in whom the postnatal adaptation of the circulatory and respiratory systems do not occur smoothly. Because of the possibility of permanent central nervous damage, the assessment of cerebral circulation and oxygenation dynamics is essential during this critical phase. Abnormal labor, instrumental vaginal delivery or emergency cesarean section for fetal distress, have been associated with an increased risk of low Apgar scores, fetal acidosis, and moderate to severe neonatal encephalopathy [18-21]. The conventional means to assess the hemodynamic status in these infants such as heart rate, capillary refilling, pulse quality and non-invasive blood-pressure are not sensitive enough to accurately assess the magnitude of a hemodynamic imbalance. For instance, arterial blood pressure can remain normal in a situation of impaired cardiac output due to compensatory vasoconstriction and considering a mean arterial blood pressure equal to gestational age as a normal blood pressure within the first 24-48 hours of life.

Our true interest, however, is to obtain more precise information concerning cerebral tissue oxygenation, and even more important to assess the severity of cerebral hemodynamic compromise, and thereby to help the clinician to decide if a baby requires a therapeutic intervention. Near-infrared spectroscopy (NIRS) is a validated tool to assess changes in oxygenated (O2Hb) and deoxygenated hemoglobin (HHb) in the brain, and thereby it directly measures cerebral tissue oxygenation. This tool has been extensively evaluated in preterm and term neonates undergoing intensive care, and it has been shown that NIRS is able to monitor cerebral hemodynamics in critically ill term and preterm infants [22,23].

The aim of this study was to determine the effect of vacuum extraction assisted vaginal delivery on the changes in cerebral perfusion and oxygenation in the first fifteen minutes of life and at 24 hours of life measured by near-infrared spectroscopy.

Methods

Setting and patients

15 newborn infants born at the University Hospital Zurich who were delivered by vacuum extraction due to fetal distress (abnormal cardiotocogram, meconium stained amniotic fluid) were eligible for this study. The exclusion criteria were a

All of the authors contributed to the study planning, discussion and interpretation of data. All the authors read and approved the final manuscript. TK was the principle investigator for this work. She wrote the first draft of the manuscript. The data collection and data management were performed by TK and RN. MW performed the statistical analysis.

Table 1 Clinical characteristics of the study group

	Vacuum (n = 15)		C-section (n = 19)	
	Median	Range	Median	Range
Gestational age (wk)	40	38-41	38	37-40
Birth weight (g)	3390	2480-4200	3130	2520-4190
APGAR 1 minute	8	1–9	8	7–9
5 minutes	9	6-10	9	8-10
Umbilical artery pH	7.23	7.12 - 7.31	7.28	7.2-7.38
BE	−6.53	-11.3-(−3.0)	−0.2	-2.2-2.4
Lactat (mmol/l)	5.33	3.4-7.8		
Hospitalization on NICU (n)	4		1	

genetically defined syndrome, a congenital malformation, and absence of parental consent or poor quality NIRS signals. At our perinatal center, neonates born by vacuum extraction are routinely under the supervision of a neonatologist for the first 10-15 minutes after birth. The neonatal resuscitation was performed according to a standard protocol [24].

Immediately after birth the infants were placed on a resuscitation table under a radiant warmer and taken care of by a neonatologist. The head and the right arm were cleansed. Using a pulse oximeter (Covidien-Nellcor N-395, Boulder, Colorado, USA) attached to the right hand or wrist, both the arterial oxygen saturation (tcSaO2) and heart rate (HR) were recorded. When measured on the right hand or wrist, SaO2 is representative of the oxygen saturation reaching the brain. At the same time a near-infrared sensor (NIRO-300TM Hamamatsu Photonics, Hamamatsu, Japan) was placed over the right forehead of the infant and the measurements of oxygenated (O2Hb) and deoxygenated hemoglobin (HHb), tissue oxygenation index (TOI) and tissued hemoglobin index (THI) were performed until 15 minutes after birth. THI, which is calculated as the sum of O2Hb and HHb corresponds to cerebral blood volume (CBV) provided that the hematocrit remains constant [25]. The optodes were kept in place by an elastic bandage, and covered by a light-occluding cloth to prevent contamination of the near-infrared signal by external light. The NIRS sensor contains one light emitter with 775, 810, 850 and 910 nm wavelengths and one detector with 3 segments (SI-photo-diodes). The pre-calibrated emitter and detector optodes were fixed in a probe holder to ensure the inter-optode distance of 50 mm. The chosen path-length of the NIRO was 19 cm, and the optical path-length factor was 3.8 [26]. All measured data were stored electronically at a sample time of 2 seconds (0.5 Hz) for subsequent analysis, while demographic data were noted. The measurements were performed by trained study personnel who were not involved in the care of the newborns in the delivery room.

After 12-24 hours of life, a second measurement was performed over 15 minutes on the maternity ward or in the neonatal intensive care unit (NICU).

Ethics

The study design was approved by the hospital's Ethic Committee (Centre of Ethics, University of Zurich). Due to the emergency situation leading to perform vacuum delivery due to fetal distress, oral consent was obtained by the present father for the first measurement and a formal written parental consent was obtained thereafter for the second measurement. All parents asked for permission agreed.

Statistical analysis

Mean values for THI, TOI, pre-ductal tcSaO2 and HR were calculated for the first 0-5, 5-10 and 10-15 minutes, and for the measurement at 12-24 hours of life. These mean values were compared by Wilcoxon Mann Whitney test with those of 19 healthy newborns delivered by elective cesarean section [13]. The analysis was performed by using IBM SPSS, Version 18, Inc, Chicago, IL.and Matlab, the mathworks, version 7.7, Natick, MA.

A sample size of 15 in the vacuum group was calculated based on the hypothesis that a control group included 19 infants born after elective cesarean section without fetal distress [13] and there was an effect size of 1, i.e. the difference in TOI between the two groups was the same or larger than the standard deviation within the groups (Power 80%, alpha 5%).

Results

The clinical data of the 15 newborn infants delivered by vacuum extraction and of the 19 infants born by uncomplicated elective cesarean section are shown in Table 1. There was no statistically significant difference between the groups regarding gestational age, birth weight, and Apgar scores. Infants after vacuum extraction had a significantly lower pH in the umbilical arterial blood and showed a tendency for low base excess values and high lactate levels. In the vacuum group, 4 infants required supplemental oxygen due to persisting cyanosis with a FiO2 of 0.25 during the first 10 minutes, and one infant needed intermittent bag and mask ventilation for the first 2 minutes of life. No infant in the cesarean section group required supplemental oxygen or bag and mask ventilation. Four infants were admitted to NICU after vacuum delivery due to respiratory distress (RDS), hypothermia, hypoglycemia or feeding difficulties and none after cesarean section.

The median age at start of NIRS measurements was 2 minutes after birth (range 0 to 4 minutes), and SpO2 measurements were reliable within 1 minute after the sensor was placed. The values of TOI, THI, SaO2 and HR for the first 0-5, 5-10 and 10-15 minutes and for the measurement at 12-24 hours (median 21 hours) of life are given in Table 2 and Figure 1. Four out of 15 measurements in the vacuum group were omitted due to movement artifacts. The mean values of TOI in the vacuum group (vs. cesarean section) rose from 65% at 0-5 minute, to 69% at 5-10 minute, and reached a steady state at 15 minutes (Figure 1a). TOI was significantly lower (54%) at 0-5 min and lower at 5-10 min (66%) in the section group and reached the same level as the vacuum group at 10-15 min and at 21 hours. THI was around 55 µM during the whole measuring period and significantly higher at 10-15 minutes than in the section group (Figure 1b). The SaO2 level in the first 10 min and the HR in the first 5 minutes were significantly higher in the vacuum group (Figure 1c and d).

Discussion

This study shows a higher THI in infants delivered by vacuum after fetal distress than control infants delivered by cesarean section without fetal distress, but this difference was only significant after 10-15 minutes after birth. We also found a higher TOI and SaO2 for the first 10 minutes in the vacuum group compared to the control group.

This finding is in contrast to previously published studies that did not show a difference in TOI nor THI between infants after elective cesarean section and vaginal delivery [11,12,15].

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Table 2 Mean values ± SEM of HR, SaO2, TOI and THI during the first 15 minutes (min) and 12–24 hours (mean 21 h) after birth, mean difference, 95% confidence interval (CI) of the difference p-value (significant p < .05 by Mann–Whitney *U* test)

		0-5 min			5-10 min			10-15 min			21 h		
		Mean ± SEM	95% CI	P-value	Mean ± SEM	95% CI	P-value	Mean ± SEM	95% CI	P-value	Mean ± SEM	95% CI	P-value
TOI (%)	Vacuum	65 ± 3			69 ± 8			68 ± 3			67 ± 6		
	C-section	53 ± 3			67 ± 3			69 ± 4			68 ± 2		
	Difference	11.6 ± 6.3	−1.4 to 24.9	**0.03**	2.4 ± 4.6	−7.1 to 11.9	0.35	−0.5 ± 5	−10.7 to 9.8	0.99	−0.5 ±4.4	−9.8 to 9	0.67
THI (µM)	Vacuum	55 ± 10			56 ± 9			56 ± 9			52 ± 7		
	C-section	47 ± 9			42 ± 7			34 ± 5			36 ± 7		
	Difference	8.6 ± 16	−25.1 to 42.4	0.27	13.7 ± 11.8	−10.5 to 37.8	0.17	22.1 ± 9.3	−2.9 to 41.2	**0.04**	16.8 ± 10.2	−5.1 to 38.6	0.11
HR (/min)	Vacuum	169 ± 4			166 ± 18			158 ± 7			118 ± 5		
	C-section	155 ± 5			152 ± 3			157 ± 4			114 ± 16		
	Difference	14.1 ± 9.1	−5.2 to 33.3	0.19	13.9 ± 6.4	−0.7 to 27.1	0.06	−0.4 ± 7.1	−14.2 to 15	0.83	3.9 ± 12.4	−24.3 to 32.0	0.69
SaO_2(%)	Vacuum	95 ± 1			95 ± 2			95 ± 1			94 ± 1		
	C-section	70 ± 4			87 ± 2			93 ± 1			97 ± 2		
	Difference	24.4 ± 828	6.9 to 41.8	**0.001**	9.7 ± 2.6	3.3 to 14.1	**0.002**	2.6 ± 1.7	−0.9 to 6.1	0.18	−3.0 ± 1.7	−6.8 to 0.8	0.19

Few studies have investigated changes in cerebral oxygenation and hemodynamics in neonates immediately after birth, and during the first hours of life [6,7,9-17,27]. NIRS studies in the immediate postpartum period showed a rapid increase in cerebral oxygenation after birth with a decrease after few hours, but the influence of the mode of delivery on these changes has been discussed controversially [9-12,15].

Dani et al performed a study looking at changes between two to five hours after birth. They found that, independently of the delivery mode, O2Hb and CBV decreased approximately at four and five hours of life. They found a decrease in CBV of about 10% at the fifth hour of life, and they attributed this decrease to a reduction of cardiac output after delivery, and also to the increase of the left-to-right-shunt through the arterial duct, which progressively increases in the first hours of life with decreasing pulmonary resistance. The values of mixed cerebral oxygenation ranged from 64% to 72% in infants born by vaginal delivery, and from 64% to 70% in infants born by cesarean section [12]. Urlesberger et al. published two studies about cerebral oxygen saturation during birth transition in term infants [14,15], one comparing vaginal with elective cesarean delivery [15]. They reported TOI (oxygenated/ total haemoglobin) increasing from 50% at 3 minutes after birth to 80% at 8 minutes not depending on the mode of delivery. These values are considerably higher than ours which is most likely due to different instrumentation using different hardware and different algorithms.

The higher THI and TOI after vacuum extraction in our study can be explained by several factors. The indication for vacuum extraction was fetal distress and therefore these infants are a selection of highly stressed infants with high catecholamine levels which lead to accelerated heart rate, increased cerebral perfusion and increased tissue oxygenation. Other factors may be local forces by the vacuum, pain and instrumental design.

It has been shown that in vaginally delivered neonates the catecholamine surge was significantly different compared to neonates delivered by cesarean section, with higher serum epinephrine and norepinephrine concentrations in the vaginally delivered group [28]. These concentrations were found to be very high at the moment of birth, and to fall during next 2-4 hours after an uncomplicated vaginal delivery [27,29-32]. Isobe et al. speculated that in a vaginal delivery, many catecholamines are released and act to constrict the peripheral vessels, and to initially increase CBF. Later on, the arterioles remain dilated for a relatively long time due to this effect, which may be the reason for continued high levels of TOI after vaginal delivery [11]. However, norepinephrine is able both to constrict (via alpha-receptors) and to dilate (via beta-receptors) cerebral vessels [33]. This could also explain the higher THI values we observed in the group of infants delivered by vacuum extraction. It is known, that NIRS is particularly sensitive to small blood vessels and that the TOI represents the oxygen saturation of all the haemoglobin in these vessels. Approximately 70-75% of this haemoglobin is in the venous, approximately 20-25% in the arterial and the rest in the capillary compartment [34-36]. If only the arterioles remain dilated, this would consequently account for only a small increase in THI. But a dilation of the arterioles also means that the resistance of the vessels is reduced. Consequently the blood flow is increased, which explains the high TOI values (washout effect) and since this also leads to a higher pressure within capillaries and veins, i.e. all the vessels will open up, not only the arterioles, this leads to a significantly increased THI.

The mode of delivery has also a transitory effect on cerebral vascular resistance [8,32]. A study in which peripheral blood vessel resistance was measured reported that peripheral constriction remained higher for up to 2 hours after birth in infants delivered vaginally when compared to a cesarean section group [32]. The cerebral vascular resistance showed higher values 1 hour after birth in newborns after cesarean section, but after 24 hours of life the values were equal for the vaginally delivered group [30]. In a recent study in healthy term neonates Noori et al. speculated, that the reduction in cerebral blood flow (CBF) 8 minutes after normal vaginal delivery is likely due to an increase in arterial O2 content, Patent ductus arteriosus (PDA) shunting or both [16]. The authors concluded that the offset of the left-to-right PDA shunt and the full compensatory increase in left-ventricular output might not yet be in place soon after birth in this group of healthy term newborns after vaginal delivery [16]. Assuming this as a physiologic response with a consecutive drop or plateau in cerebral blood flow after approximately 8 minutes after birth found by several groups [11-16], we can only speculate whether an earlier onset and longer persistent increased left ventricular output in infants after vacuum delivery is responsible for the remaining high THI values. The other explanation for higher THI values could also be fetal distress during labor. Towner et al suggested, that a substantial proportion of the morbidity associated with operative vaginal delivery may be due to an underlying abnormality of labor [18]. Nevertheless, although there seems to be no differences in the

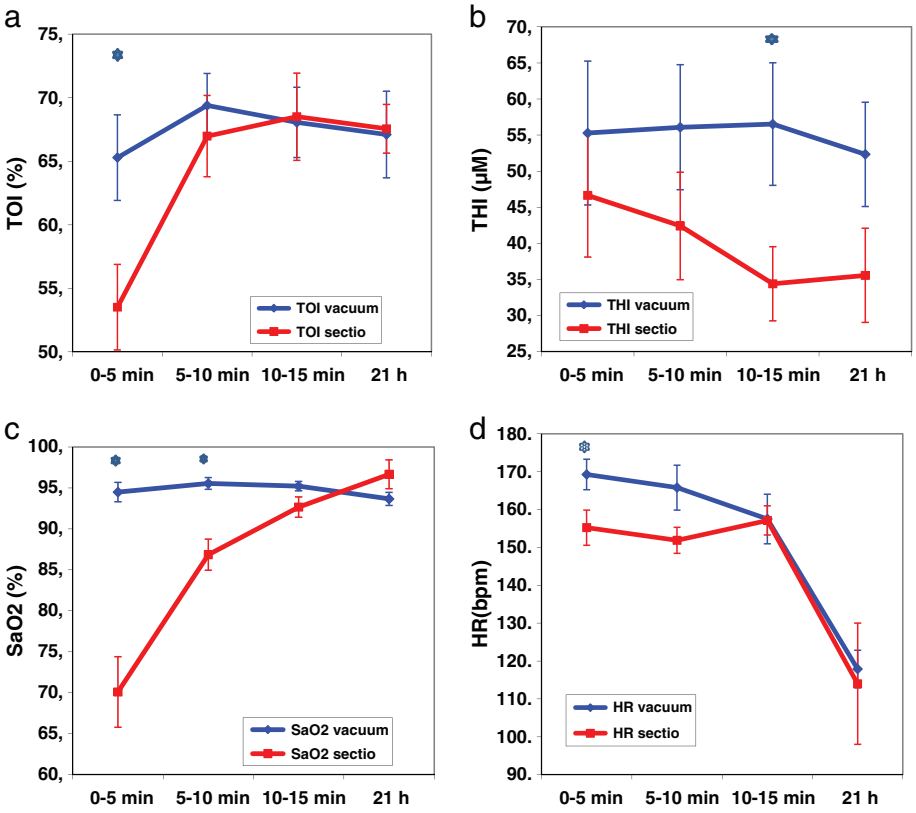

Figure 1. a) TOI b) THI c) SaO2 and d) HR, during the first 15 minutes (min) and 12–24 hours (mean 21 hrs) after birth (mean values ±SEM) for the vacuum group (blue) vs sectio (red); * markes significant differences.

long-term cognitive development , the clinician must be aware of short-term morbidities such as pain, feeding difficulties or jaundice after vacuum extraction, which can occur within the first 10 hours of life [37,38] or more serious morbidities such as subgaleal hematomas or intracranial haemorrhage [18,19].

Although the infants of the vacuum group were born after fetal distress, this distress had only a short effect on cerebral hemodynamics lasting less than 24 hours when compared to healthy infants born after elective cesarean section. There was still a trend for higher THI after 24 hours, but this oberservation was not statistically significant. This finding is important as from the clinical point of view many of these studied infants born after vacuum delivery showed a prolonged postnatal adaptation, and 4 infants had to be admitted to NICU. Furthermore, infants in our vacuum group showed a lower cord blood pH, a tendency for low base excess values and high lactate levels, a phenomenon, which was also shown in a study by Salamalekis et al. [37].

We found higher SaO2 levels in the vacuum group during the first 5 minutes compared to the control group born by cesarean section, which can also explain higher TOI and THI in the first 10 minutes. This difference in SaO2 immediately after birth is in agreement with the published [2,4,5]. Harris et al speculated that the difference was due to the increased amount of lung fluid after caesarean section [2]. 4 infants in our study group required intermittend oxygen during the first 10 minutes. The initial decision on whether to initiate oxygen supplementation was based on clinical evaluation only due to persisting cyanosis. But interestingly there was no difference between these infants with or without oxygen in reaching SaO2 levels > 90% in the first 5 minutes. This finding is in accordance with previous studies in asphyxiated newborns with no difference in time to reach SaO2 levels > 90% between the groups receiving oxygen or room air for resuscitation [39,40]. A limitation of the present study is that our study group is very small with 11 infants and we therefore could miss some more differences in our parameters. We did not measure the haematocrit values in our newborns, which may influence cerebral oxygenation. Another question could be if the differences between our groups are due to vacuum extraction by itself or due to fetal distress. Vacuum extraction is often associated with caput succedaneum (edema of the scalp) or with a cephalhematoma [18-21]. In both situations there is a potential for significant volume trapping which is not available for cardiac output, and therefore also not for cerebral perfusion. The physicians taking care of these babies in the delivery room may balance reasons about whether a particular newborn with or without clinical signs of hypovolemia needs a volume therapy or not. NIRS may be useful for guiding volume therapy in these infants at risk.

Since the light of NIRS penetrates the skin and skull before it reaches the brain, one potential issue may be that the TOI and THI are influenced by these superficial tissues. In particular this may be a problem in case of a haematoma below the NIRS sensor. Therefore, we always placed the NIRS sensor on the right forehead, where there never was a haematoma. The NIRO 300 that we have employed as NIRS instrument has two modes of operation: 1) the approach based on the modified Lambert Beer law, which provides relative changes in the concentration of O2Hb and HHb, which are known to be affected by superficial tissue. For this reason, these data have not been presented here. 2) The other approach is based on spatially resolved spectroscopy [25], which measures the decrease in intensity with

the source detector distance and which was demonstrated by Franceschini [41] to remove the influence of superficial tissue. The TOI and THI values are calculated according to spatially resolved spectroscopy and consequently reflect oxygenation and blood volume of the brain unaffected by superficial tissue. TOI is the NIRO 300's most reliable parameter, because it is a ratio and hence the absolute value of the scattering coefficient, which cannot be measured by the NIRO 300, and other factors reducing the reliability cancel out. By assuming a reasonable value of the scattering coefficient, the total haemoglobin concentration (THI) can be determined as an absolute value. Since this parameter requires an assumption, it is less reliable than the TOI. On the basis of measurements in single subjects, an error in the assumption will propagate directly to the THI value. Unless there are factors affecting the scattering coefficient systematically and differently for the two groups, for a group of subjects in average as for any statistical mean, the error should average out or at least be substantially reduced. Consequently when a difference in THI is found between two groups, this is probably a fairly reliable result."

Conclusion

In summary, our study shows that the cerebral oxygenation and perfusion in newborns delivered by vacuum extraction following fetal distress is disturbed in the first 15 minutes compared to newborns delivered by elective cesarean section.

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Initiating Breast Milk Expression in the NICU: How NICU Clinicians Can Assist Mothers

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Undeniably, human milk is the preferred nutrition for all infants. This is especially true for fragile, premature infants in the NICU as human milk provides protection from multiple prematurity specific morbidities. Evidence demonstrates greater protection to the infant with the delivery of exclusive mother's own milk. (Meinzen-Derr 2009; Sisk 2008; Vohr 2006; Vohr 2007). However, infant prematurity poses many challenges that prohibit direct feeding at the breast. Mothers choosing to provide milk for their infants face an often uexpected reality of breast pump dependence.

Lactation best practices are changing to reflect scientific evidence related to optimal milk production outcomes with increasing attention to lactation initiation practices and technologies.

Nurses in labor and delivery, on other baby units and in special care nurseries are critical to mothers' lactation success because they support, educate and assist new mothers with breastmilk expression from the first minutes after birth until both mother and infant are discharged home. The following practice guidelines summarize evidence-based practices to best assist pump dependent mothers with milk expression.

Practice Guidelines	Rationale
1. Assess mother's intention to provide human milk for her infant.	1. A mother may have questions about providing pumped milk for her infant. The provision of scientific information regarding the value of human milk allows the mother to make an informed decision regarding pumping milk for her infant (Spatz 2012).
2. Educate mother on the importance of early initiation of pumping.	2. In the absence of effective infant sucking, mechanical methods of milk expression should be employed to provide appropriate and adequate mammary gland stimulation and milk drainage. Without sufficient stimulation, milk volumes may be affected (Neville 2001; Chapman 2001).
3. Assist mother to initiate pumping as soon as possible after delivery preferably within one hour of delivery.	3. Early breast expression increases early and long-term milk volumes (Hill 2001; Parker 2012, 2015). Pumping within one hour (compared to 1-6 hours) of delivery was found to significantly increase maternal milk output at different time points from in the first few days after birth through six weeks postpartum. Average milk volumes were increased by approximately 100% (Parker 2012).
4. Provide a hospital-grade (multi-user), double electric breast pump with Initiation Technology™.	4. Initiation Technology™ mimics sucking patterns of healthy term infants during the colostral phase of lactation. In a randomized controlled trial, pumping mothers of preterm babies produced on average 43% more milk by day four and 67% more milk by day seven. Milk increases were sustained throughout the study with women pumping 124 fewer minutes during the first two weeks (Meier 2011). Similar results were found in other studies regardless of infants' gestational age (Torowicz 2015; Post 2016; Meier 2016).
5. Demonstrate the set-up and instructions of the breast pump.	5. Patients should have clear, specific operating instructions when using a medical device (Swayze 2011).
6. Instruct mother to double pump.	6. Research demonstrates double or simultaneous pumping is more efficient, increases volumes of milk expressed and produces milk that is higher in fat than sequential pumping (Prime 2012).

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7. Teach mother how to pump using Maximum Comfort Vacuum™	7. Maximum Comfort Vacuum™ is the mother's highest, yet comfortable vacuum setting used while pumping. Use of Maximum Comfort Vacuum enhances milk flow rate and milk yield (Kent 2008).
8. Assist mother to initially pump a minimum of 8 times daily.	8. Mothers should be instructed to pump at the same frequency healthy term infants would normally breasfeed (Walker 2010). Frequent breast/nipple stimulation causes prolactin and oxytocin release while emptying the breast stimulates ongoing milk production (Kent 2012).
9. Inform mother she may need to initially include a night time pumping session.	9. Around the clock pumping sessions provide necessary mammary gland stimulation, simulate the normal feeding patterns of term infants, and help to prevent a decline in milk volumes (Kent 2013; Spatz 2004).
10. Once milk volumes increase, instruct mother to pump for 2 minutes after the last droplets are noted.	10. Ensures all available milk and high fat milk has been removed. Well drained breasts will produce more milk than breasts that are only partially drained (Meier 2010; Daly 1996).
11. Provide mother with appropriate size containers to collect milk.	11. The healthy, term infant ingests minimal amounts of colostrum in the first twenty-four hours-approximately 15ml. Providing small containers to collect colostrum and subsequent milk sets realistic expectations for the mother. Large containers may intimidate the mother to think her milk production is abnormal (Santoro 2010; Spatz 2012).
12. Encourage mother to keep a daily journal documenting her pumping sessions and milk volumes.	12. A milk journal enables mothers and clinicians to identify milk volume issues early so that interventions can be implemented (Spatz 2004; Meier 2010; Wu 2015).
13. Provide pumping target volumes.	13. Providing target volumes helps set expectations of the volume of milk the mother should be producing. Ideal target volumes should reach 750-1000 milliliters within the first two weeks post birth. This volume of expressed milk is aligned with meeting the breast milk intake for the infant over the entire NICU stay (Meier 2010).
14. Assess for risk factors associated with delayed lactogenesis.	14. Multiple risk factors have been identified that may significantly impact the onset of copious milk production (Secretory Activation). These include; diabetes mellitus, preterm labor, pregnancy induced hypertension, excessive maternal blood loss, prolonged bed rest, maternal stress during labor and delivery, an unscheduled Cesarean delivery, obesity, and the use of selective serotonin re-uptake inhibitors (SSRIs). Many mothers have more than one risk factor and should be carefully followed for a delay in lactogenesis (Nommsen-Rivers 2010; Marshall 2010; Hurst 2007).
15. Assess breast shield fit daily during the first two weeks after birth.	15. Mothers' breasts undergo multiple changes in the early post birth period. A too large or too small breast shield may cause physical discomfort and/or injury. An ill-fitting breast shield can also impact milk removal and lead to milk volume issues (Meier 2010).
16. Support bedside pumping.	16. Pumping at the infant's bedside provides the mother the opportunity to visit her infant while she pumps. It also allows staff to correct any incorrect pumping techniques. Providing a bedside pump in L & D and for each mother on post-partum facilitates pumping. Staff should not have to spend valuable time searching for a pump when needed (Meier 2007; Spatz 2011).
17. Provide frequently opportunities for skin to skin holding.	17. Studies have demonstrated mothers are able to express significantly more milk after a skin to skin session (Furman 2002; Hurst 1997; Spatz 2004; Meier 2007). Skin to skin care results in improved breastfeeding, milk production, parental satisfaction and bonding (Baley 2015).
18. Assist with the transition for the infant to begin tasting breast milk.	18. Nonnutritive sucking can be initiated once the infant is no longer intubated and has demonstrated improvement in the transition to direct breastfeeding and longer breastfeeding rates (Narayanan 1991; Briere 2015; Wilson 2015).

The process of initiating and maintaining adequate volumes of human milk for premature infants requires dedication from mothers and commitment from clinicians. Bedside nurses can have a significant impact on pumping experiences of pump dependent mothers by integrating lactation best practices — starting with milk expression initiation- into their care and unit policies. With the encouragement, guidance and support of clinicians, pump dependent mothers can successfully initiate and maintain milk supplies for their infants.

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Kangaroo Care: the Nurturing Right of Every Mother and Neonate

Yamile Jackson, PhD, PE, PMP and Jasmine LaCoursiere, MS

Kangaroo Care (KC) is a skin-to-skin method of holding and caring for infants. The KC holding technique encourages caregivers to hold their infants chest-to-chest to maximize ventral contact (Figure 1). Bare-skinned chest-to-chest holding reacquaints the infant with the familiar sounds, smells, and sensory stimulation experienced in utero. It also provides a safe base for the child to take in novel environments. The reputable Zero to Three organization finds that Kangaroo Care: (1) decreases psychological and physical stress in both mother and child, (2) increases mother's milk production, (3) promotes organized sleep patterns, better oxygenation and temperature regulation in infants via physiological co-regulation, and (4) increases parent-child psychological and physiological connection. This article will explore the benefits of KC holding practices by discussing a host of relevant research findings.

In the 1980s, it was a commonly held belief that infants do not experience pain because the central nervous system is not fully developed (Eckstein Grunau, 2013). Due to the speculative belief that infants are unable to experience pain, medical interventions were often administered without anesthesia or appropriate pain reducing interventions. The Center on the Developing Child at Harvard University (2016) states the release of cortisol is a crucial physiological response to pain and stress, but prolonged cortisol release early in life can negatively impact long-term development. Cortisol is a hormone that enables the body to react and recover from short-lived stressful experiences. Prolonged activation of the physiological stress response may become toxic to the developing infant and lead to emotional or developmental psychopathologies (Center on the Developing Child, 2016). Ruth Eckstein Grunau from the Department of Pediatrics at the University of British Columbia reviewed clinical research that investigated the long-term effects of pain-related stress on brain development of premature infants receiving medical interventions in the NICU. She explains preterm infants are more sensitive to pain and stress in comparison to full-term infants because preterm infants hospitalized in the NICU often respond to routine handling as if it were an invasive medical procedure. Finding interventions that mitigate the negative effects of pain on infant brain development are crucial for aiding more positive infant developmental outcomes (Eckstein Grunau, 2013).

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Understanding the impacts pain and stress have on brain development are essential because maternal separation and brain immaturity increase the risk of disturbances in the programming and development of the hypothalamic-pituitary-adrenal (HPA) axis (Mörelius et al, 2015). The HPA axis controls the physiological stress response and regulates many biological processes including but not limited to digestion, immune response, and emotions. When a child experiences severe pain or stress, hormone levels of cortisol increase and immature neurons in the HPA axis may become over stimulated. Over

Figure 1. Mother nurturing her babies during kangaroo care. Photo courtesy of Capturing Hopes Photography. Kangaroo Zak offered by Nurtured by Design.

stimulation of HPA axis neurons may lead to cell death and abnormal axis structure in the brain. Brain structure changes caused by pain and stress may become permanent if the stress response is prolonged during early development. The risks of long-term effects magnify the need for non-pharmacological parent-led interventions to help protect the developing brain (Eckstein Grunau, 2013).

The Nurture Science Program at Columbia University Medical Center directed by Dr Martha G Welch and Dr Michael M Myers, researches the impact of Family Nurture Intervention on the quality of maternal caregiving behavior (MCB) in the neonatal intensive care unit (NICU). The Nurture Science Program conducted a randomized controlled trial in the Morgan Stanley Children's Hospital NICU in 2008 to study the effects of facilitated emotional connection on premature infant developmental outcomes (Hane et al, 2015). Family Nurture Intervention facilitated mother-child emotional connection by supporting developmental care practices like scent cloth exchange, vocal soothing and emotion expression, eye contact, kangaroo care and clothed holding, along with family-based support sessions while the child was hospitalized in the NICU. Relative to mothers receiving standard care, mothers that received Family Nurture Intervention showed significantly higher quality MCB, which remained significant when controlling for birth order, twin status, maternal depression, and maternal anxiety (Hane et al, 2015). This study highlights the benefits of instituting high nurture based care practices in the NICU and acknowledges the benefits of developmentally friendly interventions.

Correspondingly, a study by Mörelius, Örtenstrand, Theodorsson, and Frostell (2015) investigated the effects of KC and standard hospital care on mother and infant cortisol levels. This study analyzed salivary cortisol levels from preterm infants and their mothers after the dyad received an average of 19 hours of KC per day during the first week of life. Parent-child dyads were randomized into the KC and standard hospital care groups, eliminating the risk of parent self-selection. Mörelius and colleagues found lower cortisol levels in the KC group; concluding that continuous close parental contact and human touch buffer the effects of infant stress and pain. Mother's partaking in KC had lower cortisol levels and exhibited higher rates of breastfeeding upon discharge compared to the standard care group.

Research studies described above highlight parent and child benefits from receiving KC. KC is correlated with decreased pain perception, enhanced physiological co-regulation, and increased maternal milk production and sensitive maternal caregiving behaviors. Overall, KC is more than a practice that helps strengthen the emotional connection between a parent and the infant; it empowers parents to provide a humane and nurturing environment that is proven to enhance healthcare outcomes, decrease length of stay, and improve staff/patient/parent satisfaction as documented by the Sobreviver Project (2015). The Sobreviver Project describes Mary Coughlin's efforts in implementing an effective kangaroo care device and training program to create a sustainable kangaroo care practice for every baby in multiple NICUs in Portugal.

The absence of nurturing care in the NICU has long-term repercussions. A former preemie, Amber Nicole Brown, posted about her experience in the Kangaroo Mother Care's Facebook page (www.facebook.com/kangaroomothercare): "It was an aha moment for me, when I became aware of kangaroo care for preemies. I began to understand some of my own problems with intense fear of abandonment and rejection…"

Additional personal accounts are featured on the Kangaroo Mother Care Facebook page.

The International Kangaroo Care Awareness Day is celebrating its 5th anniversary on May 15, 2016. This day was created by Nurtured by Design on behalf of Zachary Jackson to raise global awareness, promote education, improve the implementation of nurturing interventions, and help translate KC evidence into practice. To learn about stories, events, suggestions, and friendly competitions among hospitals, staff, and parents please visit http://tinyurl.com/kangaroocareday. Additionally, please contact kangaroo@nurturedbydesign.com for more information about Kangaroo Care, the International Kangaroo Care Awareness Day, the ergonomic Kangaroo Zak, and recommendations.

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From Surviving to Thriving: The Impact of Cranial Deformation and Pressure Ulcers in the Hospitalized Infant

George Hutchinson, PhD and Richard Wayne, MD

Abstract
Neonatal and pediatric patients often experience significant periods with minimal movement which can be even more pronounced in the NICU and PICU settings due to therapeutic equipment, external monitoring, or an otherwise fragile patient. Over time, this can lead to periods of prolonged pressure especially in the cranial area.

Increased pressure is linked to the development of pressure ulcers and positional plagiocephaly, both of which are drivers for increased healthcare expenditures. In the case of positional plagiocephaly, evidence continues to accumulate that cranial deformations can negatively impact long-term quality of life, including serious implications of alterations in appearance, the inappropriate neuronal mapping secondary to anatomical anomalies, or delayed developmental milestones.

Hospital acquired pressure ulcers, in addition to increasing healthcare costs, can result in litigation, government penalties, and impact hospital metrics. The 2011 Institute for Healthcare Improvement's "How-to Guide: Prevent Pressure Ulcers" states that "Redistribution of pressure, especially over bony prominences, is of primary concern. Patients with limited mobility are especially at risk for the development of pressure ulcers. Every effort should be made to redistribute the pressure on the skin, either by repositioning or by utilizing pressure-redistribution surfaces."

A prevention strategy of providing continuous reduction in the peak pressure applied to the cranium represents a wise investment for a high reliability organization on a journey to eliminate preventable harm. This is true whether the infant has restricted mobility or has sufficient strength to move its head and neck.

Pressure Ulcers

Prolonged exposure to pressure must be managed at all hours, regardless of staffing levels, fatigue, or other emergent and acute conditions. In the PICU and NICU, the current standard of care calls for frequent checks, for instance, to ensure that the infant has not rolled off a positioning aid, and then to reposition the head after a prescribed period of time. In some hospital protocols, this procedure must also be entered in the medical record which is often completed outside of the normal shift as mandatory overtime. Despite best efforts and enhanced protocols, pressure ulcer occurrence in the PICU and NICU continues to be a concern for providers.

Pediatric pressure ulcer prevalence rates vary greatly throughout the hospital with published reports ranging from less than 1% to nearly 30%, with higher rates occurring in intensive care units.[1-3] Pressure ulcers are also more prevalent in younger pediatric patients and patients with limited mobility which places patients in the NICU and the youngest in the PICU at risk.[4-6] In a multi-center prospective cohort study across three PICUs, a total of 199 pressure ulcers developed in 86 of the 322 enrolled patients (27%).[7] A later study of PICUs in nine institutions found the average incidence rate per 100 admissions was 10.2.[8]

The cranium is of particular concern for pressure ulcer development due to its weight relative to the body in young patients and the presence of bony prominences that can be exposed to prolonged pressure.[1,4,9] Patients lacking the strength to move their head or having impaired mobility have a further increased risk.[6,10] In Curley's study of 322 PICU patients, 33% of the pressure ulcers were located on the head with 19% on the occiput and 14% on the ears.[7] Baldwin's questionnaire-based study echoed these difficulties with 17.4% of pressure ulcers occurring on the occiput of hospitalized children.[1] Groeneveld et al found among hospitalized children that over 50% of pressure ulcers occurred on the occiput or ears (19.0% and 33.3%, respectively).[4] Curley et al[7] also report marked increases in the risk of pressure ulcers in the presence of concomitant therapies as follows (odds ratios reported):

- Use of mechanical ventilation = 7.8
- Use of high frequency oscillation vent = 7.3
- Use of chemical paralysis = 4.6
- Total parenteral nutrition = 3.0.

Pressure ulcers in neonatal and pediatric patients have also been linked to complications brought on by medical devices affixed to the patient[7,11] such as extracorporeal membrane oxygenation (ECMO) cannula, nasogastric tubes, and EEG leads. Providing a cushioned boundary between these medical devices and the patient's skin may prevent or reduce the severity of the hospital acquired pressure ulcers.

The impact of pressure ulcers on the hospitalized infant to a healthcare organization is profound. A review of over 500,000 patient discharges in the National Inpatient Sample Dataset

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from 2009 to 2011 identified cases of pressure ulcers in patients between 1 and 4 years of age. These cases were matched to controls via propensity scoring in order to assess differences in treatment costs and length of stay in patients with otherwise comparable medical conditions. In this sample, the authors estimated the average impact associated with the development of pressure ulcers was $86,000 and 14 additional days stay.[5] Aggressively moving on even Stage I or II pressure ulcers is a prudent part of a patient safety program. Brilli et al describe this as a preoccupation with failure in which a small error is a major event waiting to happen.[12]

While less easily quantifiable, an important financial impact of hospital acquired pressure ulcers can be felt through Medicaid reimbursement. The Centers for Medicare & Medicaid Services (CMMS) can withhold a hospital's Medicaid reimbursement based on their quality performance, 30% of which is based on the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey. The occurrence of a pressure ulcer may negatively impact families' satisfaction with the care of their infant. Finally, providing nurses with tools to help prevent pressure ulcers can improve job satisfaction and employee retention. The cost of replacing a nurse can be twice the annual salary of that nurse.[13]

Pressure ulcers are a significant concern for children in the PICU and NICU due to their stage of development and the likelihood of impaired mobility in an environment that must continually assess myriad competing risks. Evidence suggests there may be substantial impact on the resulting treatment costs and length of stay in this especially vulnerable population. Patients with known risks for pressure ulcers or patients with existing Stage I pressure ulcers may warrant focused preventive measures.

Positional Plagiocephaly

Positional plagiocephaly is another known risk associated with prolonged exposure to extracranial pressure in infants. A 2011 clinical report by the American Academy of Pediatrics indicates that the prevalence of cranial asymmetry has markedly increased since the inception of the "back to sleep" campaign urging parents to have infants sleep on their backs.[14] This increased prevalence is found in healthy and hospitalized infants alike.

In a prospective cohort study of 380 healthy consecutively born neonates, a total of 84 (22%) were found to have "severe skull deformity." Of these, 75 (89%) did not have plagiocephaly at birth which suggests environmental factors result in cranial deformation.[15] These findings mirror earlier data collected by Hutchison et al where the prevalence of plagiocephaly or brachycephaly was found to be 19.7% at four months of age, dropping off with increasing age.[16] Very pre-term infants have been found to have an even greater incidence of plagiocephaly with one study showing an incidence of 38% for very preterm infants as opposed to 23% across all births.[17]

Collett et al provide a review of the impact of plagiocephaly on quality of life concerns and note that "…children's overall attractiveness may be compromised by plagiocephalic head shape. Parents frequently report being afraid that their child will be 'teased, embarrassed, or otherwise stigmatized because of the condition'."[18] Numerous studies highlight the nature and extent of the distinct cranial deformities that can occur, ranging from facial asymmetry, visual field constriction, astigmatism, malocclusion of the jaw, otitis media, and malposition of ears

Figure 1. GELShield on patient

to statistically significant dimensional differences measured by MRI.[19-26] In a study of auditory evoked potentials in infants with and without deformational plagiocephaly, differences were detected in amplitudes of certain components of the evoked potential.[27] The authors opine that this might indicate "an auditory processing dysfunction, as a possible result of the delayed or disturbed maturation of the auditory pathways." The decrease in the evoked potential amplitude was focused in the region of the skull that was deformed. To the extent that visual or auditory acuity is adversely affected, the development of neuronal networks may also be affected during this vulnerable period of brain development.

Purzycki et al (2009) studied the occurrence of otitis media in patients with deformational plagiocephaly and the associated hearing problems. They concluded, "Considering the time that otitis media presents, the loss of hearing causes real concerns for language, speech, and cognitive developments."[24]

The 2011 Clinical Report by the American Academy of Pediatrics[14] indicated that sufficient evidence did not yet exist associating plagiocephaly with developmental issues; however, more recent published studies indicate that there may in fact be such an association:

- A 2016 study of malocclusion in children with and without positional plagiocephaly found that "the prevalence of orthodontic abnormalities is increased in children with former positional plagiocephaly" when compared to a control group of normal children.[23]
- A 2011 longitudinal study indicated increased relative risks for Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III) score categorized as "delayed" when compared to children without plagiocephaly in the areas of adaptive behavior, motor, language and cognitive. Language and cognitive differences were still present at 36 months.[28,29] In addition, 37% of children with previously diagnosed plagiocephaly participated in some form of developmental intervention, such as physical or occupational therapy or speech-language therapy vs 6% without a prior diagnosis.
- Published 2012 results of an 80 patient survey indicated parent-reported developmental delay occurred frequently, distributed as 21% having language difficulties, 28% having motor difficulties, and 15% requiring special education. This exceeded the population averages for developmental delay, which occurs in 5-6% of children.[30]

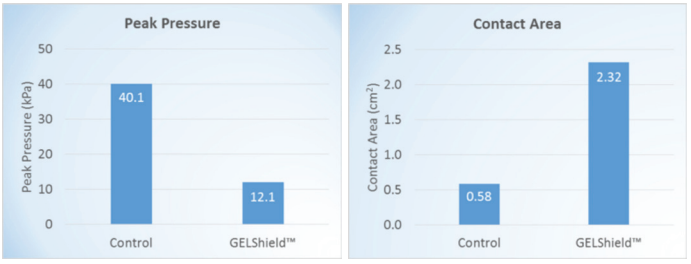

Figure 2. Pressure reduction and increase in contact area

Litigation in cases of plagiocephaly has become a significant threat for providers as well, with one plaintiff's attorney noting that the "expert psychiatrist contended that the child will probably suffer significant emotional turmoil because of the deficits as he goes through elementary school."[31] Multiple seven figure verdicts have been reported.[31-33]

The standard treatment for moderate and severe cases of plagiocephaly is cranial helmet therapy.[19] In general, cranial helmets are prescribed to be worn about 23.5 hours per day and are reported to cost between $2,000 and $4,000 per device with more than one device often needed during the course of treatment as the child grows; this cost is not generally covered by insurance.[34] Despite its routine use, there is a paucity of Class I literature actually supporting the use of cranial helmet therapy in plagiocephalic patients and helmet use has been associated with complications including skin erosions and infections.[35-37]

Prolonged pressure is known to affect cranial shape in the very young and can lead to more serious deformities that are associated with significant treatment costs. Additionally, emerging evidence continues to indicate that the effects may substantially impact quality of life, cognition, and development. Given the acute concerns of pressure ulcers and long term consequences of cranial deformity, there is an emerging need for an easy-to-use device to help reduce cranial pressure in hospitalized infants and children.

The Invictus Medical GELShield with its Pressure Relief System is a device that fits securely to an infant's head and provides a continuous reduction in the peak pressure applied to the cranium of a recumbent infant (Figure 1). This device reduces the peak pressure experienced by the head by dispersing the force of the head over a larger area. In this manner, manually repositioning the infant's head may become less time-critical since the device absorbs much of the pressure that the head experiences.

The Association of Women's Health, Obstetric and Neonatal Nurses (AWOHNN) for pressure ulcer prevention in neonates of less than 32 weeks of gestation recommends gel pads placed behind the ears and occiput.[38] The GELShield addresses this recommendation by placing a foam encapsulated hydrogel pack directly behind the occiput and a padded strap above the ear so that the device is able to move with the patient during normal activity. Figure 2 details the results of bench testing on the pressure reduction and increase in contact area achieved with GELShield.

Cost and potential impact

Review of ICU data shows that the average length of stay for preterm infants is 21 days at an average cost of stay for preterm infants of $121,000 ($5,600/day) with lower gestational ages costing more.[39] The cost of devices to alleviate these enumerated problems need to be evaluated in light of these per-day costs. From another point of view, the costs associated with pressure ulcers are straightforward. The prevalence of pressure ulcers in the PICU is well documented,[1-8] many of these occur on the occiput or around the ears,[1,4,7] and they can result in an increased length of stay and costs.[5] Pressure ulcers would likely have a negative impact on CMMS reimbursement secondary to poor HCAHPS scores.

The costs of deformational plagiocephaly affect the healthcare institution less directly than that of pressure ulcers. The costs to the larger healthcare delivery system are real nonetheless. The cost of orthotic helmets are generally borne by the family directly. And while physical therapy has shown some positive effect on the degree of cranial molding,[40] this can involve many months of physical therapy with return visits to a plagiocephaly clinic. These families are obligated to make return visits to the clinic, in some cases arranging for transportation and obtaining time off work. These can be a significant financial burden on many families.

Clinical approaches that can positively impact risk mitigation, cost control, patient satisfaction, and staff satisfaction, especially those approaches that are easy to implement, should be explored.

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Giant Congenital Melanocytic Nevus with Neurocutaneous Melanosis

Tarik Zahouani, Farranaz Alvarez, Sunanda Kandi, Benamanahalli Rajegowda

Introduction

Giant congenital melanocytic nevus (GCMN) is a benign proliferative tumor characterized by an abnormally dark skin patch (nevus) composed of pigment-producing cells (melanocytes). GCMN is usually rare but its incidence is reported to be close to 1 in 20000 newborns.[1] Infants with GCMN are at increased risk of social and behavioral problems in addition to malignant changes of the lesion.[2] The other major medical concern with GCMN is the risk of neurocutaneous melanosis (NCM) which is the proliferation of melanocytes in the central nervous system (CNS).[3] We present the case of a Giant congenital melanocytic nevus with neurocutaneous melanosis.

Case Presentation

We performed an assessment of a newborn girl with birth weight of 3670 g, head circumference of 35 cm, chest circumference of 34 cm, abdominal circumference of 33.5 cm and length of 50 cm. The Apgar scores were 9 and 9 at one and five minutes of life respectively. The infant was born to a 25 year old mother with gestational age of 41 weeks. The prenatal course was unremarkable. Mother had 7 prenatal visits and fetal sonogram at 14, 21 and 27 weeks with no evidence of anatomical anomalies. The family history was negative for congenital nevi or melanoma.

The physical examination was remarkable for an adequate for gestational age infant whose skin had multiple brown papules and plaques scattered all over the body but sparing the face, with satellite lesions varying from 2 to 20 cm, some with coarse hair, on the scalp, trunk, back and limbs. They mostly have well-defined borders except the large extensive plaque involving the occiput, posterior neck and mid upper back (Figures 1-4). That lesion has a thick, rough and irregular skin with scaly texture, some papules and hemangioma-like lesions in the nape area. No other abnormalities were detected. Dermatology and Neurology consultation concluded that the lesions represented GCMN with NCM warranting imaging of the CNS due to the risk of leptomeningeal involvement. Brain, cervical, thoracic and lumbar spine magnetic resonance imaging (MRI) were performed and reported as normal as was the infant's neurological examination. The infant passed the newborn hearing screen test and the newborn metabolic and genetic screening test were performed and the results were reported normal.

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Discussion

GCMN is a melanocytic lesion present at birth that will reach a diameter ≥ 20 cm in adulthood. Its incidence approximates 1 in 20000 newborns, with rates slightly higher in females than males with ratios ranging from 1.17:1 to 1.46:1.[4] Congenital melanocytic nevus originates between the 5th and 24th week of gestation from a morphological error in the neuroectoderm that leads to aberrant growth of melanoblasts, the precursor cells of melanocytes.[5]

GCMN presents as hyperpigmented lesions with clear-cut edges and a papular, roughed, warty or cerebriform surface. These lesions can undergo color variegation, hypertrichosis, nodular formation and ulceration. Their most frequent location is the trunk, limbs, head and neck. There are often smaller satellite lesions scattered over the body in up to 78% of the cases. They can be associated with pruritus, ulceration and infection.[4,5]

GCMN lesions can undergo malignant transformation with a rate between 1-5%. These patients have a 5-10% lifetime risk for malignant melanoma. About half of melanomas occur in the first 5 years of life and arise deep in the skin or residual fatty tissues of GCMN, making an early detection difficult. Clinical follow-up of GCMN is crucial, given the tendency of the surface of the lesion to have irregularities and nodules, and often a darken coloration and hypertrichosis. Therefore, patients and their parents should be instructed to perform regular self-examination of the skin. During the periodic examination, it is important to perform palpation of the lesion and lymph nodes. Serial photographs facilitate the monitoring of the evolution of GCMN.[4] Because malignancy rates increase with age, many surgeons stress the importance of early and complete excision of melanomas.[5]

GCMN can also be associated with NCM which is the proliferation of melanocytes within the leptommeninges and brain parenchyma. NCM can affect the amygdala, cerebrum, cerebellum, pons, medulla, and spinal cord. Patients with neuromelanosis may be symptomatic or asymptomatic. There seem to be two peak ages for presentation of complications from NCM. The first peak, which represents the majority of patients, occurs before 3 years of age and those who become symptomatic are associated with increased intracranial pressure which can lead to seizures, hydrocephalus, cranial nerve palsy, hemiparesis, and developmental delays. The other peak occurs during the second to third decades of life. Delayed presentation in older children, adolescents, and adults has

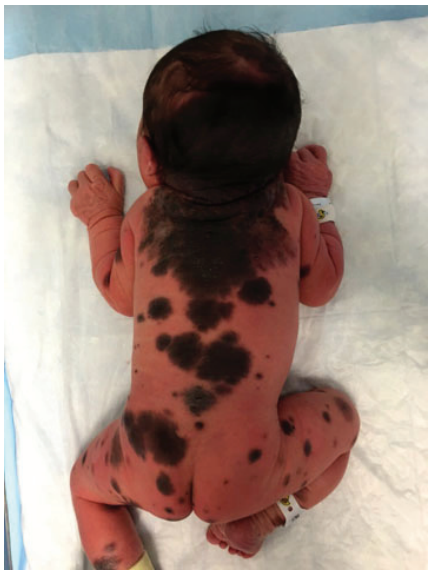

Figure 1. Lesions on the back

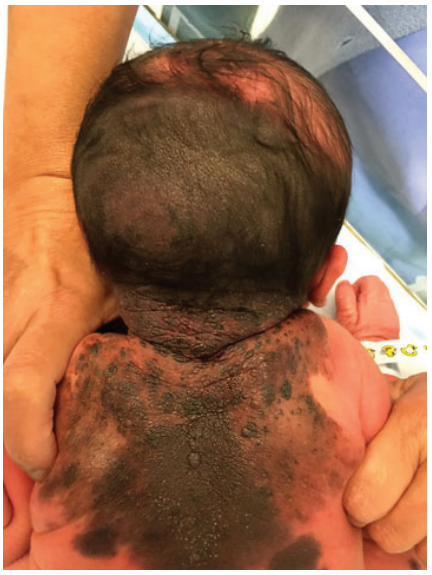

Figure 2. Lesions with extension on the occipital area

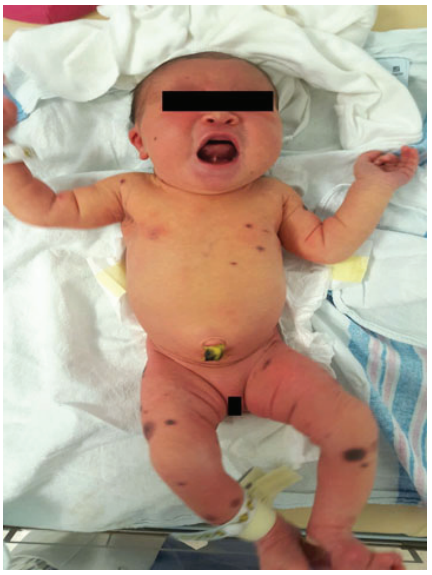

Figure 3. Satellite lesions on the periphery

also been reported, usually with symptoms such as headaches or neuropsychiatric manifestations.[6] Risk factors for NCM are midline nevi and the presence of more than 20 satellite nevi. Although absent in our patient, tethered spinal cord, syringomyelia, and structural abnormalities, particularly Dandy Walker malformation, encephalocele, arachnoid cysts, and Chiari type 1 malformation have been reported to be associated with NCM.[7]

Prognosis is poor in symptomatic patients, even in the absence of malignant transformation, with death usually occurring within 2 to 3 years of diagnosis. MRI of the brain with intravenous administration of the contrast agent should be performed in all patients with GCMN to confirm or rule out NCM, especially it's most severe and lethal form, one with leptomeningeal contrast enhancement. However imaging neither predicts which patients will become symptomatic nor identifies those who might benefit from a proven therapy.[6] Our patient did not present any neurological symptoms and brain, cervical, thoracic and lumbar spine MRI were normal. However, the normal appearance of the brain will not rule out later complications that require close follow up.

Koot et al studied the psychosocial sequelae in 29 children with GCMN and found that 30% of the patients had social problems and 25.9% had behavioral and emotional problems, with mothers suffering considerable psychological impact due to their child's condition.[2]

Conclusion

Giant congenital melanocytic nevus is a rare condition associated with severe complications including malignant melanoma, neurocutaneous melanosis and major psychosocial impact on the patient and his family. MRI of the brain is necessary in each patient with GCMN to confirm or rule out NCM. A multidisciplinary approach to these high-risk patients is imperative. Treatment of GCMN remains a challenge and should be tailored individually for each case. Lifelong, regular follow-up, with a pediatrician for neurodevelopmental assessment and a dermatologist for skin examinations is crucial to detect any malignancy in its earliest stages, even for patients whose nevus was completely removed.

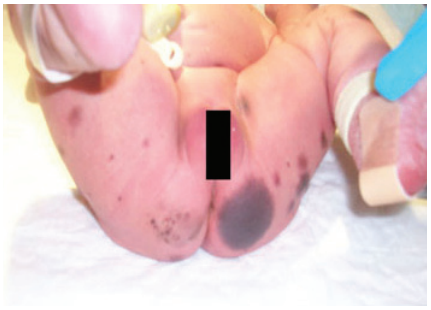

Figure 4. Lesion on the gluteal area

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Does Cultural Practice Affect Neonatal Survival–A Case Control Study Among Low Birth Weight Babies in Aceh Province, Indonesia

Rosnah Sutan[1] and Satrinawati Berkat[2]

Abstract

Background: Cultural practice have often overlooked when providing maternal and child health care services. Low birth weight is the second cause of neonatal mortality in the world but it is a major factor in a developing country such as Indonesia. The purpose of this study is to predict the neonatal mortality among low birth weight babies in Aceh Province Indonesia.

Methods: Unmatched case control study was conducted using data from year 2010 to 2012 in 8 selected districts of Aceh Province Indonesia. A total of 500 samples were obtained. There were 250 of the samples died in neonatal period (case group) and 250 who were alive (control group). There were 26 variables studied and were grouped into 4 factors: neonatal factor, maternal factor, maternal and child health services and neonatal care practices. The data was analysed using bivariate logistic regression and multivariate logistic regression.

Results: There were 13 out of 26 variables found as determinant factors of neonatal mortality among low birth weight babies in Aceh Province. The predictors found in this study were: boy (aOR1.80, 95% CI: 1.09-2.96), moderate low birth weight (aOR17.84, 95% CI: 6.20-51.35), preterm (aOR1.84, 95% CI: 1.07-3.17), presence of maternal illnesses (aOR1.87, 95% CI: 1.06-3.30), too short or too long birth interval (aOR1.80, 95% CI: 1.20-2.91), inappropriate antenatal care (aOR2.29, 95% CI: 1.34-3.91), inappropriate neonatal visit (aOR7.04, 95% CI: 3.67-13.49), not practicing kangaroo mother care (aOR15.32, 95% CI: 2.85-82.56), not using warm bottle padding (aOR20.70, 95% CI: 6.32-67.80), not practicing 'didaring' (aOR4.33, 95% CI: 1.83-10.19), late initiation of breastfeeding (aOR2.03, 95% CI: 1.09-3.80), discard colostrums (aOR3.53, 95% CI: 1.93-6.43) and not practicing exclusive breastfeeding (aOR5.58, 95% CI: 2.89-10.77).

Conclusions: Cultural practices are strongly seen among Acehnese. Inappropriate antenatal care and neonatal care, late initiation of breastfeeding, discarding colostrums and not practicing exclusive breastfeeding were related to cultural practices. Improving knowledge heat preservation to prevent hypothermia using Kangaroo mother care, warm bottle padding and 'didaring' were proven methods to reduce neonatal mortality. Strengthening of health services in screening for high risk cases and anticipate intervention tailored to cultural practices are important to decrease neonatal mortality among low birth weight.

Background

Cultural practice is one of the important factors that the healthcare workers need to focus when providing maternal and child health care services. It involved the management of most illnesses at any stages for an individual who lives in society with strong cultural beliefs. Many studies done earlier had shown the association between cultural practice, its shared beliefs and norms that influence family behaviours in obtaining maternal and child health care [1-3]. Modern healthcare practice is not well accepted or utilized if family awareness and knowledge level is inadequate for them to make good decision. Even though the young are not keen to practice cultural practice, they have no choice but to follow since they live with their family and especially when the bonding as part of extended family is strong. They do that for the purpose of not offending their parents or society. Scarce researches are available focusing on neonatal health and cultural practice. Many cultural practices are still commonly practice without knowing its existing health benefits or potential harm. The common reasons for cultural practicing were due to self-belief, convenience, family pressure and to please the elders [1,4].

Developing countries are rich with cultural practice for healing of diseases and care of mothers and their newborns [4-9]. A mother who has just delivered her baby is considered as entering into 'cold' period and she is vulnerable to infections and exposed to diseases. The mother strongly needs to have adequate rest after delivery and early clinic appointment given is commonly not routinely followed. If the healthcare worker visits her at her house, the family will appreciate. However, they will not bring the mother or baby out of the house during the 'cold' period. The healthcare worker needs to inform and educate them the dangerous situation when the baby is especially born with low birth weight. This depended on the capability of healthcare services to provide enough manpower to do routine postnatal visit.

Many babies were reported dead when born with low birth weight [10,11]. Early neonatal deaths account for 75% of all

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Table 1 Distribution of neonatal deaths among low birth weight in 8 districts

District	Number of Live Birth (2009–2010)	Estimation of LBW (11.1%)	Number of neonatal deaths due to LBW (2009–2010)	Distance from capital province to capital district (Km)	Road to capital district and sub district
Aceh Besar	16,708	1,854	43	80	Very good
Pidie	18,628	2,067	21	120	Very good
Lhoksumawe	3,189	353	14	280	Very good
Aceh Utara	6,037	670	12	380	Very good
Aceh Timur	8,376	930	35	450	Very good
Aceh Tamiang	3,703	411	32	500	Very good
Bener Meriah	5,127	569	25	300	Under construction
Aceh Tengah	8,376	930	6	320	Under construction
TOTAL	70,142	7,784	188		

Source: Aceh Province Health Office, 2010 & 2011.

neonatal deaths, and preventing these depends on the attention to the causes of death that are unique to the first week of life, particularly birth asphyxia and prematurity [12]. World health organization estimates 18 million babies will be born with low birth weights every year with majority in South Asia [12-14]. The fourth Millennium Development Goal (MDG4) has put a target to reduce less than 5 year mortality and its main effort is to focus on preventing neonatal deaths [10-14]. Low birth weight babies survived poorly compared to normal weight babies. Low birth weight (LBW) is defined as a baby born with a birth weight of less than 2500 grams. Even though LBW is not the immediate causes of mortality, it is a major contributor and may jeopardize the newborn's chance of survival [12-19]. The prevalence rate of LBW worldwide between 2007 and 2011 was 15% of all live births [10]. The highest neonatal mortality among the South East Asian countries is Indonesia [10]. The percentage of LBW in Indonesia in 2010 was 11.1% of live births [20]. A large number of LBW babies contribute to higher neonatal mortality rate (NMR). Among the causes of neonatal mortality around the world between 2007 and 2011 were: preterm birth complications (35%), complications during birth (23%), infection (sepsis, meningitis, tetanus) (15%), pneumonia (11%), congenital abnormalities (9%), diarrhea (2%) and other condition (6%) [10]. NMR in Indonesia in year 2011 was 15/ 1000 live births [20]. The LBW was the second main causes of early neonatal mortality in Indonesia, after respiratory disorders [21-23]. In Indonesia, Aceh Province has reported high prevalence of neonatal deaths especially among the low birth weight babies [20-23]. Aceh province has recorded 40 per 1000 live births which are above the Indonesia national average [24].

LBW babies are vulnerable to risk and there are many health problems related to LBW as compared to baby born with normal weight. Effort in reduction of maternal mortality and morbidity has shown improvement of child survival. Extra effort to improve feeding, attention to warmth and early treatment of infection was noted effective in neonatal death reduction [25-30]. Babies whose mothers died during the first six weeks of their lives have lesser chance of survival [25]. Health disparity is one of important factors that determine neonatal survival [26,27]. A three delay model described by Thaddeus and Maine [31] for maternal deaths can be applied to prevent neonatal death. It covers delay in recognition of illness, delay in seeking and accessing care, and delay in the provision of care once at a health facility. A study has reported that more than 90% of post-neonatal children with pneumonia were taken for outside care, whereas only 60% of newborn babies with severe infection were taken out of the home for care [30]. Neonatal period is a vulnerable time and should merit the highest-priority attention when responsible governments are making decisions about laws, policies, programs and money [32,33].

In order to achieve the MDG4 target in reduction under 5 year child mortality, efforts are planned to improve care at neonatal period. Attempts to reduce the proportion of babies born with low birth weights at the population level, in general, have been met with little success [32-35]. However, most deaths in moderately preterm babies and in those born at term but whose growth have been restricted in utero can be prevented with extra attention to warmth, feeding, and prevention or early treatment of infections [26,27]. Therefore, community practices in neonatal care must be explored further before initiating any intervention plan. Information related to healthcare acceptance and barrier during neonatal period is not routinely collected. There are many factors associated with mortality among the LBW and it can be grouped into maternal factors, nutritional factors, social factors, environmental factors, medical factors, lifestyle, cultural practice and health care factor. Therefore the purpose of this study is to predict the neonatal mortality among low birth weight babies in Aceh Province Indonesia by focusing on its cultural practices and other factors such as maternal, neonatal, healthcare services and homecare practice.

Methods

An unmatched case control retrospective study was conducted in Aceh Province. Aceh Province is one of 33 provinces in Indonesia. Aceh province is approximately 58,375.63 Km^2, consists of 23 regencies/districts, 276 sub district and 6455 villages. Population density in Aceh Province is 74 inhabitants/ Km[23]. The total population of Aceh province, is about 4.5 millions with the rate of population growth is 1.46% per years. Aceh province has same common health problems with other provinces in Indonesia with high maternal mortality rate, high infant mortality rate, malnutrition problems in infants and pregnant women and chronic and acute infection diseases [20]. Aceh is a multicultural province. Variety ethnic groups with cultural diversity created non homogenous complex cultural of Acehnese. With regard to inheritance practices that women inherit the house while men inherit the land [36]. Ideally, the houses of women and their daughters are located next to each other like matrilineal clusters.

The number of neonatal deaths in Aceh Province in 2010 was 735 of 99,924 live births (0.73% of total live births), neonatal mortality

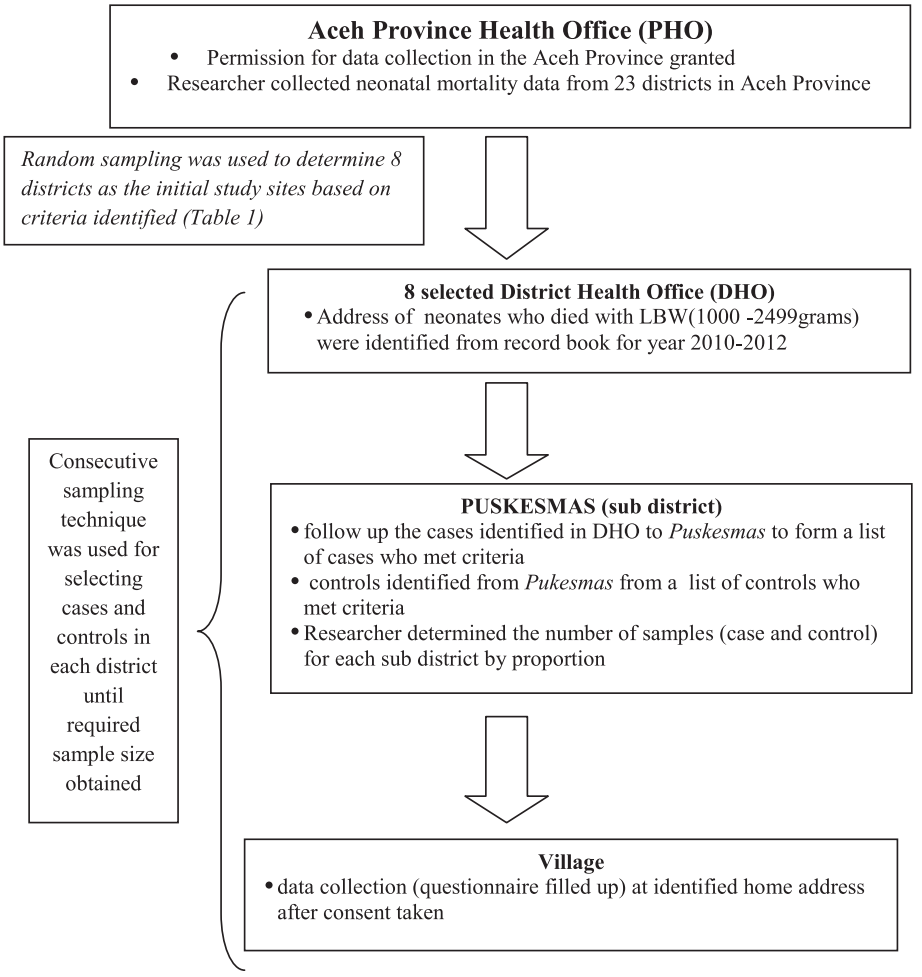

Figure 1 Flowchart of sampling frame.

rate 7.3 / 1,000 live birth and the number of neonatal death due to LBW is 217 or 29.5% of all neonatal death [21]. There are 292 community healthcare centres (Puskesmas) serving at sub district level. The community midwives (Bidides) who are responsible for MCH service in the village was 4,477 out of 6,265 villages (71.4%). There are 26 government hospitals, 21 private hospitals and a thousand small private delivery clinics [20].

Selection of study sites depended on several basic criteria: high level of neonatal mortality, geographical accessibility and security. Eight districts were selected randomly from a list of districts with high level of neonatal mortality (Table 1). High level of neonatal mortality among low birth weight babies was calculated based on Aceh province estimation of 11.1%. Geographical accessibility and security is defined as availability of road for transportation and safe accommodation to be reach by the researchers. The target population of this study was low birth weights babies who were born alive between 2010 and 2012 regardless they survived or died during neonatal period. The inclusion criterion was babies born alive with birth weight between 1,000 and 2,499 grams, in the period of 2010-2012, in study sites and living with biological mother during neonatal period. The exclusion criteria was the presence of congenital abnormalities, multiple birth, delivery by traditional birth attendant and the baby who did not received neonatal visit by health care worker in neonatal period and baby which was hospitalized during neonatal periods (hospitalized more than 14 days in neonatal period) and were adopted baby.

The sample size was determined based on the previous study [37], which was related to neonatal mortality among LBW. It was calculated by Power and Sample Size 2 (PS2) based on Fleiss JL formulae [38]. The calculation used the value of alpha = 0.05, power = 0.08, probability of exposure in the control ($P_0 = 44$), probability of exposure in case ($P_1 = 56$) and the ratio of controls to cases as 1:1. The total sample size needed was 518 and was divided into two groups for case and control group. The case group was low birth weight babies who died in neonatal period and the control group was the low birth weight babies who survived in neonatal period.

Descriptive and analytical statistics were computed using Statistical Package for Social Sciences version 20.0. Frequency distribution of each variable studied was conducted to check for missing data and normality. Crude odds ratio with 95% confidence interval was performed to assess the association between socio demographic factor, neonatal factor, maternal factor, maternal and child health services factor and neonatal care practices and the neonatal deaths. The association was set as $p < 0.05$. All explanatory variables that were found associated ($p < 0.05$) in the bivariate analysis were included in the multivariable logistic analysis. In multivariable logistic regression analysis, variables with p-value <0.05 were identified as predictors of neonatal deaths. The enter method was used in analysis and the –2 log-likelihood ratio test was used to test the overall significance of the predictive equation. Enter method was used referring to the method in SPSS in multiple regression of

Table 2 Results of regression analysis on neonatal and maternal factors of neonatal mortality among low birth weight

Variables	Case N = 250 (%)	Control N = 250 (%)	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Neonatal factors						
Sex						
boy	149 (59.6)	110 (44.0)	1.87 (1.31-2.67)	<0.01	1.80 (1.09-2.96)	0.02
girl	101 (40.4)	140 (56.0)	1		1	
Birth weight (g)						
1001–1499	79 (31.6)	7 (2.8)	16.00 (7.22-35.5)	<0.01	17.84 (6.20-51.35)	<0.01
1500-2499	171 (68.4)	243 (87.2)	1		1	
Gestational age						
Pre term	206 (82.4)	147 (58.8)	3.28 (2.17-4.95)	<0.01	1.84 (1.07-3.17)	0.03
Full term	44 (17.6)	103 (41.2)	1		1	
Maternal factors						
Maternal death						
Mother dead	0 (0.0)	2 (0.8)		Cannot be estimated		
Mother alive	250 (100.0)	248 (99.2)				
Maternal illness						
present	87 (34.8)	39 (15.6)	2.88 (1.87- 4.43)	<0.01	1.87 (1.06-3.30)	0.03
absent	163 (65.2)	211 (84.4)	1		1	
Maternal age (years)						
<20 or >35	68 (27.2)	39 (15.6)	2.0 (1.30- 3.14)	<0.01	1.5 (0.92- 2.45)	0.10
20 - 35	182 (72.8)	211 (84.4)	1		1	
Birth Interval (years)						
<2 or >4	85 (34.0)	49 (19.6)	2.11 (1.40- 3.17)	<0.01	1.8 (1.20- 2.91)	<0.01
2 - 4	165 (66.0)	201 (80.4)	1		1	
Parity						
Para 1 or >5	116 (46.4)	103 (41.2)	1.23 (0.86- 1.76)	0.24	1.1 (0.75- 1.67)	0.56
Para 2-4	134 (53.6)	147 (58.8)	1		1	
Maternal education level						
primary	221 (88.4)	214 (85.6)	1.28 (0.75- 2.16)	0.35	1.12 (0.43-3.41)	0.54
≥secondary	29 (13.6)	36 (14.4)	1		1	
Antenatal care						
Appropriate	140 (56.0)1	205 (82.0)4	1	<0.01	1	<0.01
Inappropriate	10 (44.0)	5 (18.0)	3.57 (2.38-5.38)		2.29 (1.34-3.91)	
Place of delivery						
Non health facilities	105 (42.0)	80 (32.0)	1.53 (1.03-2.21)	0.02	1.03 (0.87-1.98)	0.08
Health facilities	145 (58.0)	170 (68.0)	1		1	
Birth attendant						
TBA	22 (8.8)	8 (3.2)	2.91 (1.27-6.68)	0.11	1.23 (0.86-1.76)	0.26
Trained personnel	228 (91.2)	242 (96.8)	1		1	
Mode of delivery						
Assisted or LSCS	37 (14.8)	42 (16.8)	0.92 (0.57-1.47)	0.86	0.69 (0.21-2.25)	0.54
Normal delivery	213 (85.2)	208 (83.2)	1		1	

entering all variables together regardless of significance levels. Confidence interval (CI) and crude odds ratio (OR) was stated. Adjusted odds ratio (aOR) was adjusted with all variables used in this study.

The significance of the variables in the model was assessed by the Wald χtest and CIs. The fit of the model was assessed by the Hosmer-Lemeshow goodness of fit χtest. Variables that were significantly associated with the outcome in bivariable analysis, but not in multivariable analysis were presented together for comparison. Ethical clearance was obtained from UniversitI Kebangsaan Malaysia research and innovation ethic committee. Formal letter of permission was written to Ministry of Health Aceh province, Indonesia before conducting the study. Respondents who gave oral consent were witnesses by the healthcare worker who accompanied the researchers. The witnesses signed the consent form in front of the respondent after explanation given and verbal approval obtained. Most

Table 3 Results of regression analysis on maternal-child services and neonatal care practice factors of neonatal mortality among low birth weight

Variables	Case n = 250 (%)	Control n = 250 (%)	Crude OR 95% CI	p-value	Adjusted OR 95% CI	p-value
Maternal-child health services						
Referral						
Appropriate	155 (62.0)	101 (40.4)	1	0.67	1	0.77
Inappropriate	95 (38.0)	149 (59.6)	0.86 (0.69-1.23)		0.93 (0.02-5.92)	
Neonatal visit						
Appropriate	198 (79.2)	239 (95.6)	1	<0.01	1	<0.01
Inappropriate	52 (20.8)	11 (4.4)	10.15 (5.47-18.84)		7.04 (3.67-13.49)	
Neonatal care practice						
Time of first bath						
Immediately	16 (6.4)	5 (2.0)	3.35 (1.21-9.29)	0.02	2.03 (0.24-16.96)	0.51
Delay (≥12 hours)	234 (93.6)	245 (98.0)	1		1	
Bath twice a day						
No	246 (98.4)	237 (94.8)	1	0.04	1	0.65
Yes	4 (1.6)	13 (5.2)	0.30 (0.09-0.92)		1.55 (0.23-10.45)	
Kangaroo mother care (KMC)						
Not practice	248 (99.2)	206 (82.4)	26.49 (6.35-110.57)	<0.01	15.32 (2.85-82.56)	0.01
Practice	2 (0.8)	44 (17.6)	1		1	
Use warm bottle pack						
Not practice	241 (96.4)	140 (56.0)	21.04 (10.34-2.83)	<0.01	20.70 (6.32-67.80)	<0.01
Practice	9 (3.6)	110 (44.0)	1		1	
Use lamp bulb						
Not practice	241 (96.4)	211 (84.4)	3.33 (0.97-11.42)	0.06	0.42 (0.10-1.70)	0.23
Practice	9 (3.6)	39 (15.6)	1		1	
Use '*didaring*'						
Not practice	225 (90.0)	147 (58.8)	3.32 (2.00-5.50)	<0.01	4.33 (1.83-10.19)	<0.01
Practice	25 (10.0)	103 (41.2)	1		1	
Umbilical cord care						
Appropriate	230 (92.0)	228 (91.2)	1	1.00	1	1.00
Inappropriate	20 (8.0)	22 (8.8)	0.99		0.99	
Hand wash before touch baby						
No	247 (98.8)	238 (95.2)	4.51 (1.16-14.89)	0.06	6.62 (0.16-28.41)	0.32
Yes	3 (1.2)	12 (4.8)	1		1	
Initiation of breastfeeding						
Late (>1 hour)	219 (87.6)	131 (52.4)	6.42 (4.09-10.07)	<0.01	2.03 (1.09-3.80)	0.03
Early	31 (12.4)	119 (47.6)	1		1	
Discard colostrums						
No	119 (47.6)	224 (89.6)	1	<0.01	1	<0.01
Yes	131 (52.4)	26 (10.4)	9.48 (5.89-15.27)		3.53 (1.93-6.43)	
Exclusive breastfeeding (n = 462)						
No	195 (92.0)	117 (46.8)	13.0 (7.8-22.0)	<0.01	5.58 (2.89-10.77)	<0.01
Yes	17 (8.0)	133 (53.2)	1		1	

respondents (97%) gave written consent to participate in this study and the rest gave verbal consents as they are not good in writing and reading.

Inappropriate antenatal care in this study means a mother who received antenatal care visit less than 4 times during her antenatal period [39]. Inappropriate referral was defined as a baby delivered at home or in a nonhealth facility and was not referred to health facilities for identified risk health condition. In appropriate neonatal visit means a neonate born alive but did not obtain minimum standard of scheduled neonatal visit for health examination by the healthcare worker. Inappropriate umbilical cord care is defined as care of umbilical stump using unhygienic ways such as applying traditional ingredients or alcohol. Delay

time of first bath is defined as bathe within less than 12 hours after birth. Late initiation of breastfeeding means the baby was breastfed after 1 hour delivery.

Data collection was carried out from June 2012-Feb 2013. Cases were universally selected from a list of neonatal deaths recorded in the health districts office chosen (Figure 1). The selected cases health records were tracked down from health clinics. Cases who met the criteria were chosen for follow up at clinic visit to reach the mother or do house visit to complete the questionnaire after consented. Controls were chosen from child health clinic visits. Recall bias on specific information were overcome by checking mother and baby record. Information for practices done during neonatal period were reassess using open ended question to check for consistency in answer given. There were 2 interviewers were trained to ask respondents and completed the questionnaire. Both interviewers were assigned to specific 4 districts each and have to collect for both cases and controls. The questionnaire used was in bilingual English and Indonesia language and were validated during pre-test. The value of cronbach's alpha obtained was between 0.70-0.79. In reporting this study, guidelines from Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) group were followed (Additional file 1).

Results

There were 250 cases of low birth weight babies died during neonatal period and 250 cases for control group who survived during neonatal period. Both group were comparable for family income ($p > 0.05$) and distance from home to capital province or district ($p > 0.05$). There were 4 components on determinant factors used as independent variables: neonatal factor, maternal factor, maternal-child health services and neonatal care practice. Results were tabulated as shown in Tables 2 and 3. Neonatal factor were assessed using sex, birth weight and gestational age at delivery. Majority of cases were baby boys (59.6%) compared to controls (44.0%). There were 31.6% of cases and 2.8% of control were born with weight between 1001 g and 1499 g (moderate low birth weight). There were 82.4% of cases and 58.8% of control were born as pre term with gestational week less than 37 weeks.

There were 6 variables grouped under maternal factor: maternal death, maternal illness, maternal age, birth interval, parity and maternal education level. None of the cases had maternal death and only 2 controls had maternal deaths (0.8%). There were 34.8% cases with maternal illnesses compared to 15.6% controls. Maternal illness was defined as a mother who was ill by any cause (during antenatal or postnatal) and could not care for her neonate. Young mother (<20 years old) and older mother (>35 years old) group was higher among cases (27.2%) compared to controls (15.6%). Birth interval of less than 2 years or more than 4 years was noted higher among cases (34.0%) compared to controls (19.6%). There is not much different in assessment of parity for both groups (46.4% vs 41.2%). Percentages of low maternal education (primary) were not much differing between the cases and controls (88.4% vs 85.6%). Percentage of inappropriate antenatal care of less than 4 times [39] was higher in case group (44.0%) compared to control group (18.0%). Higher percentages of cases were delivered in non-health facilities (42.0%) compared to controls (32.0%). Non health facilities were referred to either home or at village health post volunteer (Posyandu) [40]. Number of babies delivered by traditional birth attendance (TBA) was higher in case group (8.8%) compared to controls (3.2%). Not much difference noted for mode of delivery. There was 85.2% cases had normal delivery compared to 83.2% controls.

Maternal and child health services received by respondents were assessed based on 2 items: referral and neonatal visit. Referral in this study means a case who was delivered at home or village health post volunteer (Posyandu) should be referred to health facilities or hospital for further screening or management [41]. Among the babies born at home, 14.3% cases and 43.7% controls were referred to hospital. Assessment on the level of neonatal visit showed that a percentage of inappropriate neonatal visits for cases were 4.4% compared to controls 20.8%. Inappropriate was defined as neonate who was delivered at home or village health post volunteer (Posyandu) but did not get the number of neonatal visit as scheduled during life period [42,43].

Neonatal home care practice factor was evaluated using 11 items. There were 6.4% of cases had baby's first bath immediately after delivery compared to only 2.0% of controls. Very few in both cases (1.6%) and controls (5.2%) practice neonatal bath twice a day. Higher percentages of cases (17.6%) compared to controls (0.8%) practiced Kangaroo Mother Care (KMC) during neonatal period. To warm the baby, only 3.6% of cases and 44.0% of control group used warm bottle pack. Other method of warming the baby is by using bulb lamp. This study noted that only 3.6% of cases and 15.6% of controls used bulb lamp. These practices were not popular among the cases. However, higher percentages of cases (41.2%) practice 'didaring' to warm up baby as compared to controls (10.0%). 'Didaring' is referred to activity conducted by highland population sitting near fire to warm themselves. Normally mothers after delivery will hold their babies together while sitting near the fire. Majority of both cases and controls did not apply traditional ingredients or alcohol for umbilical cord care. Both groups showed low percentage of hand washing practice before touching the babies. Late initiation of breastfeeding was higher among cases (87.6%) compared to controls (52.4%). Majority of cases (52.4%) discard the colostrums compared to controls (10.4%). There were 15.2% of cases died before starting feeding. Only 8% of cases practiced exclusive breastfeeding as compared to controls (53.2%).

Bivariate logistic regression analysis found that all 3 items under neonatal factors (sex, birth weight and gestational age) were significantly associated between neonatal mortality among LBW ($p < 0.05$). There were 5 items out of 10 items studied under maternal factors (maternal illness, maternal age, birth interval, antenatal care, and place of delivery) were found as significant factors for neonatal deaths. Only neonatal visit was associated with neonatal mortality under maternal and child health services. There were 8 out 11 items under neonatal care practices found associated with neonatal care (time of 1st bath, bathing twice a day, KMC, the use of warm bottle pack, the use of 'didaring', initiation of breastfeeding, discarding practice of colostrums and exclusive breastfeeding). Multivariate logistic regression was conducted to predict the final model for determinant of neonatal mortality. The model showed Cox and Snell squared test was 0.439 and Nagelkerke R Square test was 0.586. Thus it can be interpret as 44% of predictors contributing to neonatal death are explained by logistic model. There were 17 associated factors found using bivariate analysis but only 13 showed continuously significant association as predictors: sex, birth weight, gestational age, maternal illness, birth interval, antenatal care, neonatal visit, KMC, use of warm bottle pack, use of 'didaring'

initiation of breastfeeding, the practice of discarding colostrums and exclusive breastfeeding. Being a boy faced 1.8 times higher risk of neonatal death than girl. Born with very low birth weight had 18 times higher risk of neonatal deaths. Preterm baby faced 1.8 times risk of mortality compared to term baby. The presence of maternal illnesses was 1.9 times risk of neonatal death (aOR 1.87(95% CI: 1.06-3.30). The birth interval showed that mothers with birth intervals less than 2 years or more that 4 years from the previous delivery faced 1.8 times high risk of having neonatal deaths (aOR 1.80, 95% CI:1.20-2.91). Inappropriate antenatal care was 2.3 times risk for neonatal mortality (aOR 2.29, 95% CI: 1.34-3.91). Having an inappropriate neonatal visit showed 7 times risk of mortality (aOR 7.04, 95% CI: 3.67-13.49). Practicing kangaroo mother care was shown as beneficial practice for low birth weight baby (aOR 15.32, 95% CI: 2.85-82.56). Those not practicing padding their babies with warm water bottle showed 21 times risk of neonatal mortality (aOR 20.7, 95% CI: 6.32-67.8). Another method found useful was using 'didaring'. Those not practicing 'didaring' to warm their babies faced 4.3 times risky of neonatal mortality (aOR 4.33, 95% CI: 1.83-10.19).

'Didaring' is a method used by Acehnese people who stayed in highland to warm their body. Late initiation of breastfeeding was twice risky for neonatal mortality (aOR 2.03, 95% CI: 1.09-3.80). It is common among Acehnese to discard colostrums and this practice was 3.5 times predisposed the baby to death (aOR 3.53, 95% CI: 1.93-6.43). Not practicing exclusive breastfeeding was noted 5.6 times having the risk of neonatal mortality (aOR5.58, 95% CI: 2.89-10.77).

Discussion

Neonatal period is crucial in determining a child's health. Cultural health beliefs and practices are still strongly practiced especially among developing countries on mother and child care. Asian population practice postpartum traditional cultural practice to restore the balance in the body elements i.e. soil, water, wind and fire. It aims to restore general wellbeing after delivery process back to normal state [42]. Healthcare workers need to be sensitive with cultural practice among population they served. Some may be harmful and some may be beneficial to prevent mortality especially among the low birth weight baby. This study has shown that neonatal factor, maternal factor, healthcare services and neonatal care practice were determinants of neonatal mortality among low birth weight babies in Aceh. In relation to neonatal factor, the sex, birth weight group and gestational age were found significant in this study and they were similar with previous findings [10-12].

The maternal factors have a great effect on neonatal health. It is considered as direct cause of neonatal mortality [12,30,32,34,37,43]. Maternal health refers to the health of women during pregnancy, childbirth and the postpartum period. The major direct causes of maternal illnesses include postpartum haemorrhage, maternal infection such as malaria, high blood pressure, and obstructed labour [44-47]. Therefore, the newborn's health is closely tied to maternal health, because it is highly dependent on its mother for living. The social culture of Aceh province still put a mother as the primary caregiver at home, especially within first 40 days after birth. The father or family members are only a replacement caregiver if the mother is tired or unwell. All the baby basic needs are provided by mother for 24 hours a day, including feeding, bathing and changing diapers. If the mother is unwell or cannot care for her baby, this would affect the baby healthy or even lead to death.

After adjusting with other confounders in the multivariate logistic regression analysis, there were three variables grouped under maternal factor found as determinants of neonatal mortality among LBW: present of maternal illnesses, poor birth interval and inappropriate antenatal care. Birth interval was a determinant factor of neonatal mortality among LBW. A study done earlier in Indonesia using population data showed a strong association between short birth intervals and neonatal death [45]. Short inter pregnancy interval may result in inadequate replenishment of maternal nutrient stores and reduce foetal growth. The short inter pregnancy interval can lead to increase stress to the mother and it affects care given to her child. Shorter birth space increases the chances for a mother to develop chronic disease such as hypertension, diabetes and poor nutrition. A study done in Ethiopia showed that birth interval was strong predictor and had beneficial effects for health of mother and child [47].

Inappropriate antenatal care was found strongly associated with neonatal mortality in Aceh. According to the health system in Indonesia, all mothers in Aceh should get a minimum of 4 antenatal checks up: 1 in first trimester, 1 in second trimester and 2 in 3 trimesters. Measurement of body weight, blood pressure, symphysis fundus height tetanus toxoid vaccination and iron folic acid supplementation are minimum standard required [47]. However, 2007 IDHS documented only 84% of mothers in West Java Province attended at least 4 antenatal services [47].

In relation to maternal and child health services, it was found that inappropriate neonatal visit is seven times riskier for neonatal death. Neonatal visit is important in checking the baby's health status and identify the risk of danger for appropriate management. According to Aceh healthcare system practice, it is recommended to have at least 2 adequate health care checks within 0-7 days and another 2 health checks around 8–28 days after delivery [47]. There are many factors that may affect the level of care in Aceh. Demographic and health survey done in Indonesia earlier has shown that poverty, poor education level, living in rural area are the reasons of having poor antenatal and postnatal health services utilization [43,47-49].

Neonatal hypothermia is common among neonates and challenges for newborn survival. A systematic review study done earlier showed lack of thermal protection contributes to a substantial proportion of neonatal mortality globally mostly as co-morbidity of severe neonatal infection, pre term birth and asphyxia [7]. Low birth weight babies are at risk of losing body heat after delivery because of immature thermal regulation and hypoglycaemia [7]. Breastfeeding helps to warm-up the baby and giving easily digested food to replenish newborn's need of glucose level. Early bathing has shown significantly increase of incidence of hypothermia and should be postponed until at least after 6 hour of life [50,51]. Cultural practice of immediately bathing neonate after delivery is link with belief of 'ritual pollution' [52] reducing body odour in later life and helping the baby sleep and clean [53]. Using warm bottle pack helps to preserve the environment temperature. Using cultural practice 'didaring' is found beneficial in this current study among Acehnese to prevent hypothermia. It is cheap and can be used for the whole family to warm their room. This cultural practice is common among Acehnese staying in highland area. Resting near the fire may give heat to warm up but it expose to air pollution and it may affect the baby's respiratory system.

Skin to skin care is helpful in reducing morbidity and mortality among preterm infants [54]. Practicing kangaroo mother care is shown beneficial practice to prevent neonatal deaths among Acehnese but very few of them are practicing kangaroo mother care. Awareness on its importance should be highlighted by the healthcare provider.

Improving knowledge of parent and community on neonatal care especially for low birth weight baby is very important and should be emphasised. Many cultural practices which are shared and believed to be ideal for a group of people should be tackled with caution. They need to be well informed about the danger of practicing them unless proven beneficial. Cultural practices which have been deeply rooted need to be address carefully if we are aiming on their behaviour change. Relation of cultural practice with other poor pregnancy outcome was noted in many literatures [32,49,55,56].

Early initiation of breastfeeding and exclusive breastfeeding are proven evidence of protecting babies from ill and death. This study support earlier research finding on its effectiveness in neonatal survival [33]. Many studies found that cultural practice of discarding colostrums will lead to late initiation of breastfeeding [57-60]. However, once they discard the colostrums normally for 2 days only then they continue to breastfeed their baby exclusively. During the first 2 days they may start with pre lacteal feeding. Discarding colostrums is still common in Acehnese and it is significantly associated with neonatal mortality. Previous literatures have stated that this practice is performed because of believing it will cause harmful to the baby's health. Therefore they start breastfeeding late and normally after 2 days [61-64].

In Aceh, community partnership program has been initiated since 1998 and known as 'Desa Siaga'. This program helps pregnant women within their own society by arranging transports, fund and social support [47]. However, monitoring and evaluation of this program activity need to be enhanced. Harmful cultural practice should be informed for the community to recognize and prevent health problems. Ensuring appropriate health care seeking behaviour such as avoiding harmful cultural practices are important and need to be strengthened. Advocacy and dissemination of information to the community by healthcare workers will help empower their knowledge. Community based education targeting high socio cultural practices population may help to improve their awareness on obtaining appropriate antenatal and neonatal care. Each antenatal mother needs to be informed about the importance of colostrums, early initiation of breast breastfeeding and practicing exclusive breastfeeding. Lack of understanding on the important of antenatal and neonatal care may affect the neonatal survival.

Harmful cultural practice needs to be addressed as major public health priority. Any active intervention to reduce neonatal death should start at maternal health program which provides appropriate antenatal care and the child health program which provides appropriate neonatal care. Emphasising continuum of care from maternal to child health will lead to better acceptance for good health seeking behaviour. Establishing rapport with the healthcare workers will improve the community trust on changing their bad practices. The three-delays model described two decades ago can be applied in the averting neonatal death intervention strategy: early in recognition of illness, early in seeking and accessing care, and early in the provision of care once at a health facility [31]. The cost effectiveness intervention has been documented in an article published by Lancet [33]. However, cultural practice in a resilient community may affect the success of any intervention adopted. Care for mothers and neonates after birth has received little emphasis in public health programmes and, typically, has neither been monitored in demographic and health surveys nor included among key programme indicators [33]. To scale up neonatal care, two interlinked processes are required: a systematic, data-driven decision-making process and a participatory, rights-based policy process [65]. Even though Aceh has low resources, strengthening health system through proper monitoring of routine services and specific program for maternal and child health will help identifying problem to be raise up for further planning. Strategies like intervention through facility-based such as community healthcare centre (Pukesmas), population outreach such as village health post volunteer (Posyandu) and family-community partnership program (Desa Siaga) need to be monitored closely in term of its achievement coverage, quality, equity of services and sensitivity of cultural practice when providing services to targeted population. Involvement of men during antenatal check up, delivery and postnatal check up may open up their mind toward better decision making. Many cultural practices are implemented because of the man or their superior like mother, grandmother or strong relatives think it should be done as it is been done through their experience and this act as barrier for good health seeking behaviour [66-70].

This study has limitation in excessive accurate data on the causes of deaths, very low birth weight babies of less than 1000 g because some of them could be under reporting. Therefore, to limit incomplete information this study has focussed only moderate to low birth weight babies and causes of deaths was not included in the analysis.

KMC is not popular among Aceh and it has proven effective in prevention of neonatal deaths as found in this study and stated in the systematic review [33]. Having a group of women during antenatal care visit will allow them to learn more than they may get during individual care. They will get social support and broaden their understanding and empowered them to act positive health seeking behaviour as suggested by a study done in Canada [69]. It should be emphasized on proper healthcare provider-client communication and cultural sensitive care in order to promote usage of healthcare services as result shown in a study conducted in Ethiopia [70].

This study has its limitation as it been conducted as unmatched case control. It is well known that sex, birth weight, gestational ages and presence of maternal illnesses are determinants for neonatal mortality among the low birth weight neonates. After adjusted in the multivariate analysis, these variables persistently showed significant. Cultural beliefs and practices contribute to determinant of low birth weight in this study was inappropriate antenatal care, short birth interval, inappropriate antenatal visit, not practicing KMC, not practicing warm bottle padding, not practicing 'didaring' late initiation of breastfeeding, discard colostrums and not practicing exclusive breastfeeding. Both case and control group were comparable for family income ($p > 0.05$) and distance from home to capital province or district ($p > 0.05$). These 2 factors are important to assess to determine inappropriate of antenatal care neonatal visit received. Future explorative qualitative study should be carried out to identify

gap of knowledge on people influencing neonatal care behaviour related to cultural practices.

Conclusions

A cultural practice in this study using 'didaring' has been shown effective in preventing mortality among low birth weight in Aceh population stay in highland where source of electricity is scarce. Inappropriate neonatal visit, not practicing KMC, not practicing warm bottle pack, late initiating of breastfeeding, discarding colostrum and not practicing exclusive breastfeeding have been shown bad cultural practice that need urgent action to reduce neonatal mortality among low birth weight in Aceh population. Cultural practices affect population health seeking behaviour. Promoting good knowledge among the population and awareness on existing healthcare facilities services provided should be carried out continuously. Sensitivity to cultural practice is a key to attract population closer and practice good health behaviour. Knowledge on care of newborn especially the low birth weight baby need to be deliver to mother and family earlier during antenatal care. Healthcare workers need to conduct regular neonatal home visit to screen and identify health problem of the newborn. Existing intervention strategies should be monitored and evaluate regularly to assess its effectiveness.

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Comparative Performances Analysis of Neonatal Ventilators

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Abstract

Background: Mechanical ventilation is a therapeutic action for newborns with respiratory diseases but may have side effects. Correct equipment knowledge and training may limit human errors. We aimed to test different neonatal mechanical ventilators' performances by an acquisition module (a commercial pressure sensor plus an isolated chamber and a dedicated software).

Methods: The differences (ΔP) between peak pressure values and end-expiration pressure were investigated for each ventilator. We focused on discrepancies among measured and imposed pressure data. A statistical analysis was performed.

Results: We investigated the measured/imposed ΔP relation. The ΔP do not reveal univocal trends related to ventilation setting parameters and the data distributions were non-Gaussian.

Conclusions: Measured ΔP represent a significant parameter in newborns' ventilation, due to the typical small volumes. The investigated ventilators showed different tendencies. Therefore, a deep specific knowledge of the intensive care devices is mandatory for caregivers to correctly exploit their operating principles.

Background

Respiratory diseases are among the main causes of morbidity and mortality for preterm newborns and infants. A proper and focused mechanical ventilation can be decisive for the survival of such patients in some cases. Assisted ventilation of newborns remains a great challenge for technical staff, especially considering the wide variety of infants (eg weight varying from 500 g to 3-4 kg, so Vt varying from 3 to 24 ml). Based on this, the outcome of ventilation process is affected by the risk of side effects and complications, in particular because of the sensitivity of lung tissues and the smallness of volumes involved [1,2].

Given the complexity of the application domain, a continuous education program is necessary to train neonatologists and nurses, in order to give them adequate practical knowledge and experience to face hindrances.

High fidelity training is the best way to reach this aim, since it represents a completely interactive training system based on innovative strategies in a realistic clinical scenario [3-5].

In this framework, we are actively involved in a national research project (MERESSINA project, founded by the Italian national Commission for the Education and Training) about the design, development and testing of a neonatal pulmonary simulator able to represent lungs physiological features in a high fidelity model. In more detail, the simulator has been designed to reproduce infants' breathing patterns, in both cases of controlled and assisted ventilation, and it is based on a multi-compartment model composed of five autonomous units replicating the anatomy of the human lobes [6,7].

In order to ensure the adaptability of the designed simulator to the wide range of ventilation conditions that can be set during a real training session, a study of the performances of different Intensive Care Units (ICUs) neonatal ventilators was carried out as similarly reported in the literature [8]. Our study was focused on the pressure values delivered at the Pressure Inspiratory Peak (PIP) and at the end of the expiratory phase — the Positive End Expiratory Pressure (PEEP), and in particular, on the pressure values difference (ΔP). ΔP is related to the tidal volume (V_T), which expands lungs at each respiratory act, by lungs compliance (C, ml/cmH_2O) according to eq. 1:

$$V_T = C\Delta P = C(PIP - PEEP) \quad (1)$$

Being the control on ΔP, and hence on V_T, a crucial feature of mechanical ventilation, especially considering the tiny lung volumes in newborn affected by pulmonary pathologies, neonatologists have to take great care of this aspect [9,10]: inaccuracies and errors in comparison to actual set values can appear paltry in an absolute sense, but they risk becoming significant if related to small volumes. V_T which results in less than the desired value can determine insufficient oxygenation, while an excessive volume can lead to stress and tissue damage.

In order to assess the correspondence between the imposed ΔP and the value measured downstream the ventilation circuit, acquisitions of the pressure signals delivered from different ICUs infant ventilators were performed with an appropriate experimental set up. In particular, the study was focused on the

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Table 1 Major performances of 3 infant ventilators

Ventilator	Ventilation modalities	Time cycling	Flow cycling	Minimal pressure variation	Minimal flow variation	Loops and waves	Flow sensor calibration	Pressure working range
Bear Cub 750 PSV	AC, AC-CF, SIMV/IMV, SIMV/PSV, SIMV-CF	YES	YES	1 cmH_2O	0,5 L/min	YES	NO	0-72 cm H_2O
Leoni Plus	IPPV/IMV, SIPPV,SIMV, PSV-SIPPV, PSV-SIMV	YES	YES	0,1 cmH_2O	0.1 L/min	YES	YES	6-60 cmH_2O
Babylog 8000 Plus	IPPV/IMV, SIPPV,SIMV, PSV	YES	YES	0,1 cmH_2O	0,1 L/min	Only waves	YES	10-80 cm H_2O

AC = Assisted Controlled, CF = Cycled Flow, SIMV = Synchronized Intermittent Mandatory Ventilation, IMV = Intermittent Mandatory Ventilation, PSV = Pressure Support Ventilation, SIPPV = Synchronized Intermittent Positive Pressure Ventilation, IPPV = Intermittent Positive Pressure Ventilation.

possible connection between delivered ΔP and other parameters of the controlled ventilation setting, eg inspiratory time and breathing frequency. We focused on pressure values because this parameter may be responsible for lung damage (so called barotrauma) in a volume-control ventilation modality, that is generally set on the modern neonatal ventilators.

Methods

Experimental set up

The tested medical devices are:

- n.3 Bear Cub 750 PSV Infant Ventilator (Bear Medical, Inc., CA, USA),
- n.1 Leoni Plus (Bomimed, Canada)
- n.1 Babylog 8000 Plus (Draeger Medical, Inc, USA).

The technical characteristics of the infant ventilators involved in the proposed analysis are reported (Table 1).

The same ventilation circuit was used for every device and it was adapted for making it compatible with a glass and sealed measurement chamber. The chamber was connected to the ventilation circuit thought an endotracheal tube (3.0 mm). During the tests we used 0.21 FiO_2 and did not use the humidifier chamber.

The pressure delivered by the ventilator was revealed inside the chamber thanks to an analogic pressure sensor (MS147105GT, Measurement Specialties, Hampton, USA) able to cover the measurement range of 0-34.5 kPa[a] which results adequate for the required ventilator working range (equal to 0-5.5 kPa) based on physiological data of a preterm infant. Finally, the pressure signals were acquired by a data acquisition hardware (Multifunction DAQ System NI USB-6218, USA) and treated with a Labview (LabVIEW, NI, USA) software for amplification and filtering (Figure 1a). The same Labview software, equipped with a custom Graphic User Interface — GUI (Figure 1b), was employed to extrapolate the specific parameters of the pressure wave in the fully controlled modalities.

Pressure levels corresponding to imposed PIP and PEEP values were obtained searching for local maxima and minima of the calibrated function; the period (T) is the time distance between two sequent maxima. In order to obtain the inspiration time (t_i), pressure signals were derived to obtain the flow curve and time intervals were detected from the positive segment of the flow wave.

Expiratory times (t_e), respiratory frequency (fr) and mean airway pressure (MAP) are revealed according to eq.2 and eq.3:

$$T = t_i + t_e = 60/f_r \quad (2)$$

$$MAP = \frac{(t_i \times PIP) + (t_e \times PEEP)}{T} \quad (3)$$

Setting a fictional value for the C parameter (for newborn affected by neonatal respiratory distress syndrome, C varies from 0.5-1 cm H_2O [10]), V_T, flow trends (Q) and minute volume (VM) (eq.1, eq.4 and eq.5) are detectable for every respiratory period:

$$Q = \frac{dV_T}{dt} = C\frac{d(PIP - PEEP)}{dt} \quad (4)$$

$$VM = V_T \times f_r \quad (5)$$

Testing protocol

The pressure wave delivered from each infant ventilator was recorded. For each investigated device, the relation between measured ΔP (mΔP , mean ± SD) and imposed ΔP (iΔP) was investigated in two different working conditions: i) fixed fr, we varyed t_i; ii) fixed t_i we imposed variation of fr. A critical analysis of the results, considering every combination of the parameters, was carried out.

Acquisition protocol was defined according to medical specifications: basal flow, inspiratory flow and PEEP values were fixed, varying PIP, fr and ti coefficients. Data acquisitions were performed according to the procedural settings described here:

Fixed parameters:
Basal flow: 10 L/min;
Inspiratory flow: 20 L/min;
PEEP: the minimum value reachable for each device (0 cmH_2O for BEARs, 2.2 cmH_2O for Leoni and 2.45 cmH_2O for Babylog)
Variable parameters:
PIP: 10, 20, 30, 40 cmH_2O
fr: 10, 50, 90 rpm
t_i: 0.1, 0.3, 0.5, 0.9 s

Based on the clinical experience and considering the functional principles of the ventilators, some combinations of the chosen parameters are incompatible:

- by fixing t_i equal to 0.1 s, the maximum PIP value reachable by the ventilator is 20 cmH_2O
- in case of 90 rpm, ti equal to 0.1 s and 0.3 s are the solely time values admissible in the procedure, being fr and t_i mathematically related by the inspiratory-expiratory times ratio (I:E) according to eq.6:

Data analysis

Pressure wave, delivered for the 34 possible combina- tions of

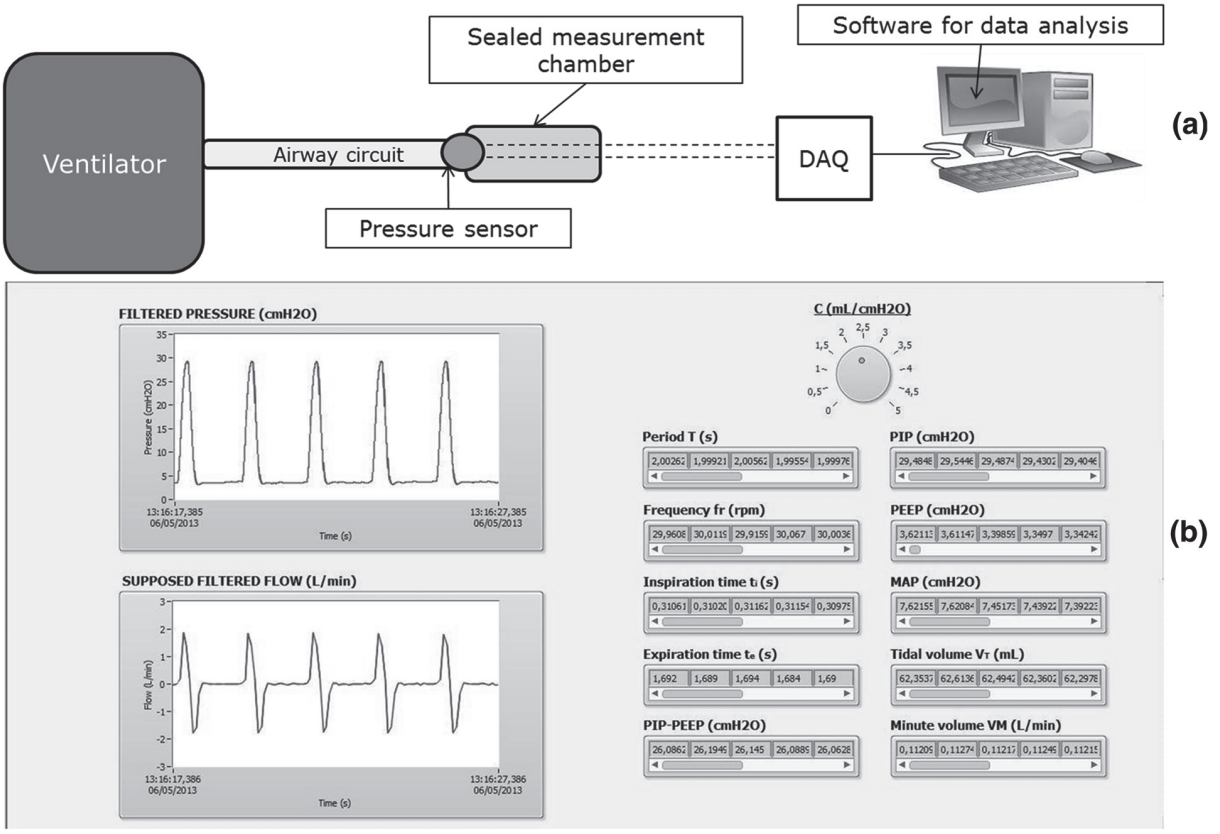

Figure 1. Experimental set up. (a) Simplified scheme of set up applied to test ventilators. (b) Labview GUI for extrapolating parameters from the pressure wave delivered from ventilators: on the left the acquired pressure curve is shown in real time and the related air flow -Q- is reported below, according to the fictional C range imposed by the user; on the right, the pressure wave features that are extrapolated by the software are shown: T, fr , t_i and t_e, PIP, PEEP and ΔP, MAP, supposed V_T and VM.

parameters described above, was acquired for three minutes for each ventilator. Thanks to the cus- tom software, ΔP values were extrapolated and aver- aged (mean ± SD values were reported). Measured ΔP and comparison between the mean and the imposed values were related to the chosen ΔP by varying both fr and t_i (Figure 2a).

The distribution of the set of differences between measured and imposed ΔP was studied for each ventilator (Table 2). The study was then expanded to the selection of ΔP obtained just with settings owing to clinical practice. For the 3 Bear Cub ventilators, we focus on intra- device variability as well. Finally, statistical analysis of the data was carried out (Table 3 and Figure 2b).

Results

Each ventilator showed a markedly linear trend (R^2 >0.99) and there were no tendencies introduced by either fr or t_i (Figure 2a).

Differences between measured ΔP (mΔP) and imposed ΔP (iΔP), do not reveal univocal trends related to PIP, fr or ti. Basically, as reported in Figure 2a for the Bear Cub ventilator, the mΔP – iΔP value increases applying high PIP values in case of low ti (eg ti:0,1 s), because such limited time is insufficient to practice the required pressure impulse.

Table 2 Statistic features of mΔP - iΔP distributions for the 3 ICUs infant ventilators under investigation

	mean (mΔP - iΔP) (cmH_2O)	std dev (cmH_2O)	max (cmH_2O)	min (cmH_2O)
LEONI	0,08	0,29	1,17	−0,57
BABYLOG	1,62	0,46	3,46	−0,13
BEAR	0,09	0,43	1,61	−1,03

Ideally, Mean and SD values should tend to 0.

mΔP – iΔP was studied for each ventilator, revealing the features resumed in Table 2.

The presence of significant divergences between mΔP and iΔP induced a further analysis, taking into account the results obtained in case of setting parameters usually employed in clinical practice. This choice allowed us to understand if such unexpected results, not entirely negli- gible, are related just to unusual settings.

In particular, the detection of optimal functioning pa- rameters range had been possible based on guidelines of medical practice [10]:

- 5 ≤ imposed ΔP ≤ 30 cmH_2O;
- ti range: 0.3-0.5 s;
- I:E = 1:2-1:3.

The last two conditions imply 40 rpm as minimal fr (considering the worst working conditions: ti equal to 0.3 s and I:E equal to 1:2) and 100 rpm as maximal fr (ti: 0.5 s and I:E:1:3). Based on this, data acquisitions were carried out by imposing:

fr: 50 rpm, ti: 0.3 and 0.5 s;
fr: 90 rpm and ti: 0.3 s.

In these working conditions, the parameters derived from data analysis are clearly improved (Table 3).

Table 3 Comparison among results from all mechanical ventilators, after the implemented tests (i.e. with settings owing to clinical practice)

Statistic features for the 3 ICUs infant ventilators				
	Mean (mΔP- iΔP) (cmH_2O)	SD (cmH_2O)	max (cmH_2O)	min (cmH_2O)
LEONI	0,05	0,99	2,90	−6,59
BABYLOG	1,47	0,77	3,56	−3,30
BEAR	0,12	0,68	2,95	−1,83
BEAR Ventilator: INTRA-VARIABILITY of the Results				
BEAR n.1	0,78	0,77	3,18	−2,49
BEAR n.2	−0,26	0,71	2,19	−1,70
BEAR n.3	−0,17	0,56	3,46	−1,29

For each ventilator (n.3 BEAR, n.1 Leoni, n.1 Babylog), the set of the selected differences is presented in histograms (Figure 2b) and their distribution was studied with the D'Agostino-Pearson normality test, revealing, in each case, a markedly non-Gaussian behavior ($P < 0.01$).

Since sampling distributions are quite numerous (284 at least), original data populations are likely Non-Gaussian distributions, therefore a comparison among the five samples was carried out with the non-parametric Kruskall-Wallis test. This analysis revealed some sets have significantly different results. ($P < 0.01$).

The Kruskall-Wallis test was used also to compare data from the 3 BEAR CUB ventilators, showing significant divergences ($P < 0.01$). In case of difference, we per- formed Dunn's test using multiple, stepdown comparisons (Kruskall-Wallis analysis): each couple of ventilator differs significantly ($P < 0.01$) from the other one, also from the couples composed of devices of the same brand.

Discussion

We tested the performances of three most largely used ICUs infant ventilators in Italy and Europe, by using a simple testing workbench. For the Bear Cub 750 PSV Infant Ventilator, three devices were tested in order to investigate the performances of different ventilators of the same brand and to underline the intra-variability of the results. This choice allowed us to compare not only devices of different brands, but also ventilators of the same trademark.

The working ranges of the parameters were intentionally chosen wider in comparison to the ones actually employed in clinical practice in order to test the ventilator performances at the working limits, which are rarely used into the NICUs, but still guaranteed by the head offices. Moreover, being a comparative study about the ventilator performances with the ultimate goal to design and develop an innovative simulator for medical training, we need to replicate the entire range of operation, to allow us to fully investigate the consequences of extreme choices during mechanical ventilation. In more detail, the imposed flows are higher than values employed in clinical practice because they allow reaching desired PIP for every device.

Pressure data show a relevant discrepancy between peak values set on the ventilators and the measured ones. These differences become even larger when setting extreme ventilation parameters (ie ΔP values of −6.59 or +3.56 cmH_2O). On the contrary, in conditions more similar to physiological settings, such differences tend to be reduced. Minimum discrepancies are negligible in children and adult patients, but may be important in newborns. Indeed, extremely low birth weight preterms need very small V_T (eg a newborn having a weight of 500 g requires a 2-3 ml gas exchange volume + 2.5 ml dead space) and it is possible that even small changes in the PIP can affect delivered volume. For instance, with a given compliance of 1 ml/cmH_2O the discrepancy of 6 cmH_2O between set PIP and measured PIP causes a variation of 6 ml in V_T. Considering a 2000-grams-weightened newborn, who has a theoretical tidal volume of 10 ml, the variation is more than 50% of the desired value.

Moreover, we cannot exclude that also in non-conventional ventilation techniques, such as in volume-target ventilation, differences between set volumes and delivered volumes could occur. Consequently, developing lungs can be damaged by excess of volume and/or pressure, since acceptable values range is actually small. Indeed, it is well known that injury induced by mechanical ventilation is a major co-factor of BPD.

Our study was carried out in optimal ventilation conditions, hardly reproducible in vivo, for example, no losses through endotracheal tube, no secretion, compliance and resistance being constant during each single breath. Therefore, it is possible that during a real ventilation of infants, which involves all the variables mentioned above, differences may be even higher.

A limitation of our study can be due to the ventilators age: in fact, the Bear and Babylog are older than 15 years. Anyway, some discrepancies, even if less important (basing on the mean (mΔP – iΔP) value), have been also found with the Leoni plus ventilator, that is about 2 years old.

Finally, we have to underline that measures among ventilators of the same brand can vary.

For all these reasons, it is mandatory to have adequate education and a correct knowledge of the equipment, in order to predict and limit the margin of error during mechanical ventilation and to minimize the possible iatrogenic damage to newborns.

It is worth to mention that in our opinion the knowledge about the accuracy limitations of commercial ventilators could be very important during a simulation program. However, our study was an only in vitro analysis, and additional surveys about the benefit for training sessions will be further investigated.

In conclusions, we analyzed three different ICUs neonatal ventilators performances, comparing inter- and intra-devices variations. We focused on the difference pressure values (ΔP) between the inspiration peak data and the pressure delivered at end of the expiratory phase. Indeed, ΔP is one of the most important features of ventilation modalities because it is related to the V_T, which is responsible for lungs expansion at every respiratory act.

It has to be specified that the Bear Cub ventilators measure airway pressure at the patient connection while the Draeger ventilators (Babylog) use internal inspiratory and expiratory pressure sensors to compute airway pressure based in the known pressure drop in the patient circuit. Even if it is not a very plausible hypothesis since the ventilation circuit is closed, we

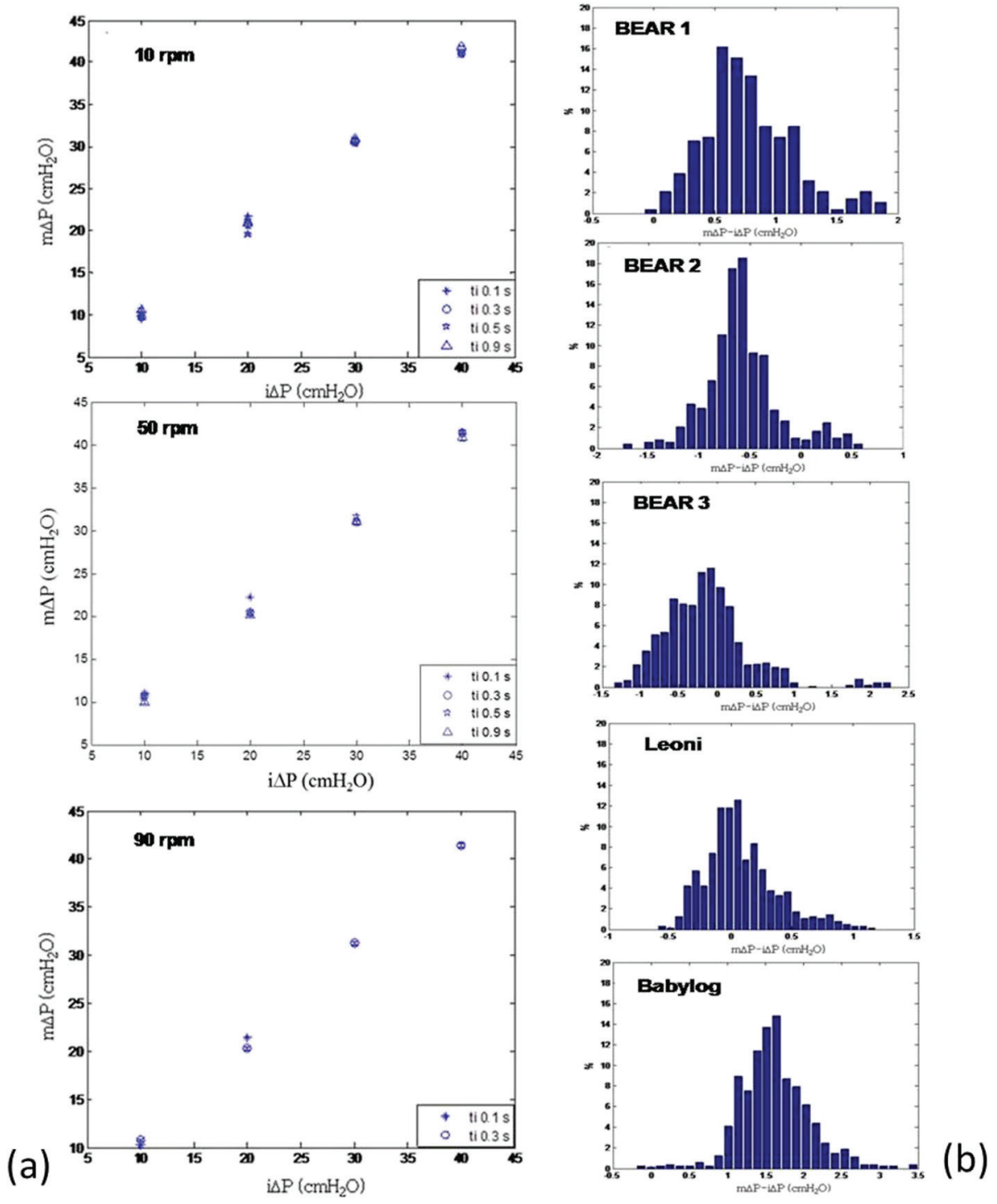

Figure 2. ΔP experimental evaluation. (a) Trend of measured ΔP vs imposed ΔP values by using the BEAR CUB n.1 ventilator by varying ti values. (b) Histograms of mΔP-iΔP distributions for the 3 ventilators (n.3 BEAR, n.1 Leoni, n.1 Babylog), by using setting parameters used in clinical practice.

cannot certainly exclude that this aspect could account for the different performances of the ventilators found in our study.

Our study underlines that the pressure differences reported represent a negligible discrepancy for children and adult patients, but they may be significant in newborns, due to the small volumes involved. In addition, during a real ventilation procedure, the optimal working conditions used in the analysis are not easily reproducible; therefore, these differences may be even higher.

Based on these, even if in clinical practice the use of Vt monitoring, the use of optimal PCO_2 and PO_2 target values, and the transcutaneous PCO_2 and PO_2 monitoring should guide the ventilator management of the more vulnerable infants, nevertheless staff are required to get a correct and deep knowledge also of the equipment and to undergo adequate training, in order to limit the margin of error during mechanical ventilation and minimize the induced damages to newborns' lungs.

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