



Volume 12 / Issue 11
November 2017

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20th International Conference on Neonatology and Perinatology

Dec. 4-6, 2017; Madrid, Spain
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Hot Topics in Neonatology

Dec. 10-13, 2017; Washington, DC USA
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NeoPREP An Intensive Review and Update of Neonatal-Perinatal Medicine

Jan. 20-26, 2018; Atlanta, GA USA
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Feb. 22-25, 2018; Orlando, FL USA
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NEONATOLOGY TODAY

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ISSN: 1932-7137 (online)

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Editorial and Subscription Offices

16 Cove Rd., Ste. 200
Westerly, RI 02891 USA

www.NeonatologyToday.net

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Effect of Type of Feeding on Infants with Neonatal Abstinence Syndrome

By Ahmad Aboaziza, MD; Darshan Shah, MD; Jennifer Gibson MD; Des Bharti, MD

Methods

We conducted a retrospective chart review of 200 neonates admitted to a Level III Neonatal

Introduction

The incidence of Neonatal Abstinence Syndrome (NAS) continues to rise in the United States, as number of pregnant mother using opioids continues to grow.¹ As reported in recent literature, the incidence of NAS nearly tripled from year 2000 to 2009.^{2,3} With an increase in the incidence of infants diagnosed with Neonatal Abstinence Syndrome, hospitalization costs continue to significantly increase.^{1,4}

This study aims to explore the effect of feeding type (breast milk, formula, or both) on the Length of Stay (LOS), requirement of replacement therapy, and relapse rates in infants diagnosed with Neonatal Abstinence Syndrome.

“This study aims to explore the effect of feeding type (breast milk, formula, or both) on the Length of Stay (LOS), requirement of replacement therapy, and relapse rates in infants diagnosed with Neonatal Abstinence Syndrome.”

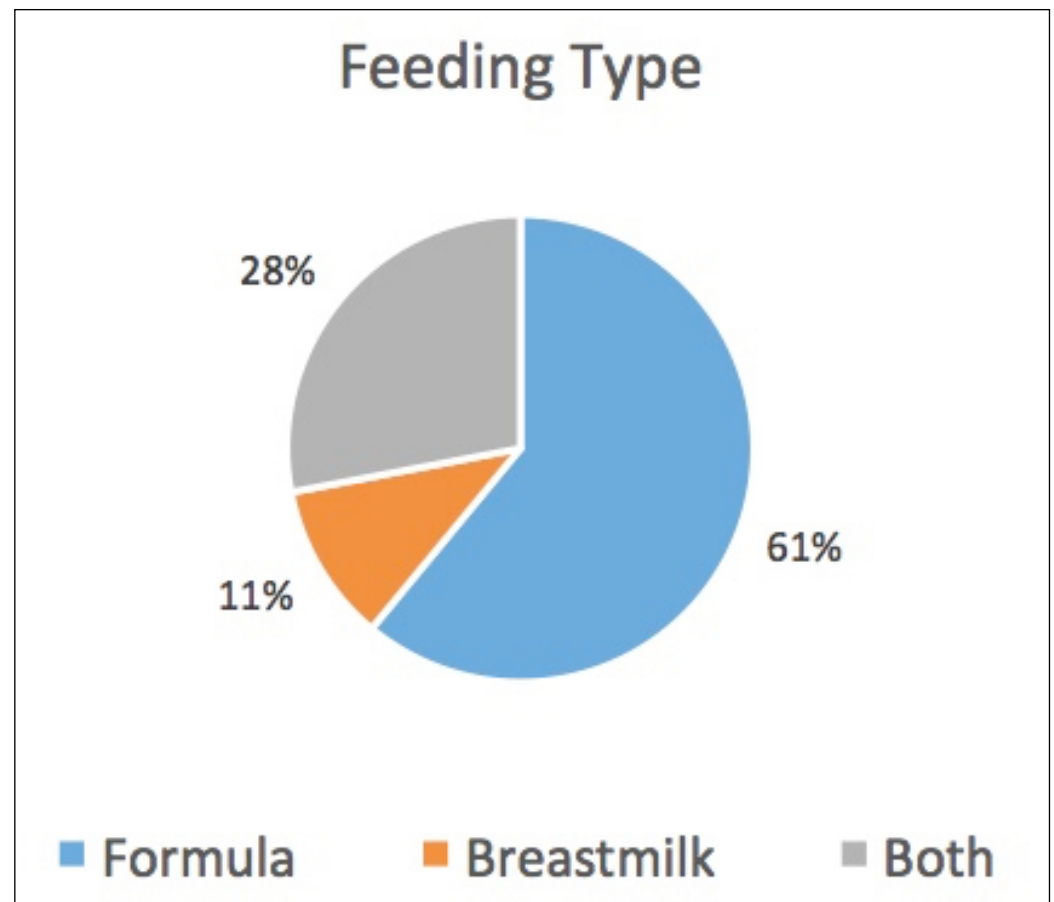


Figure 1: Pie chart shows the number of infants (in percentage) per feeding type received.

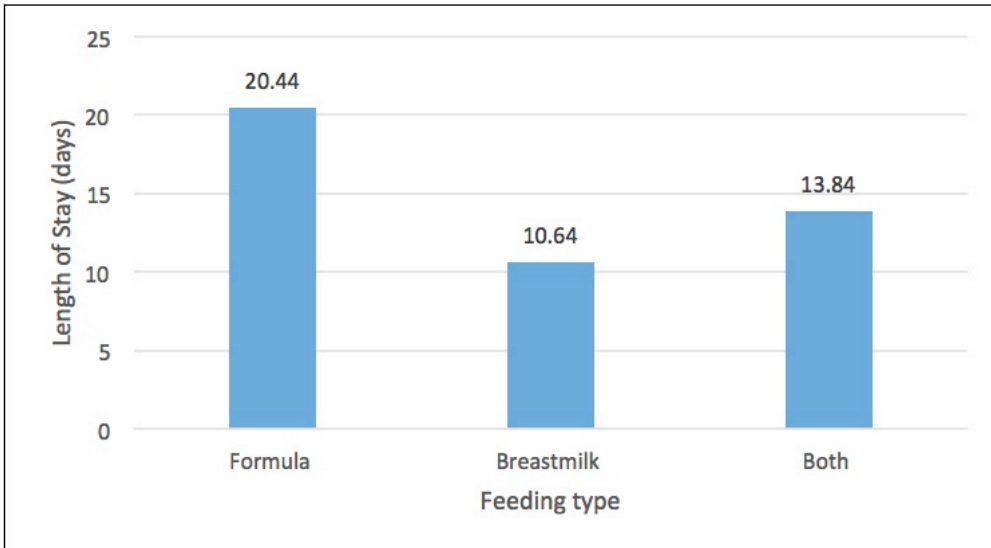


Figure 2: Bar graph comparing length of hospital stay (in days) to type of feeding among NAS babies.

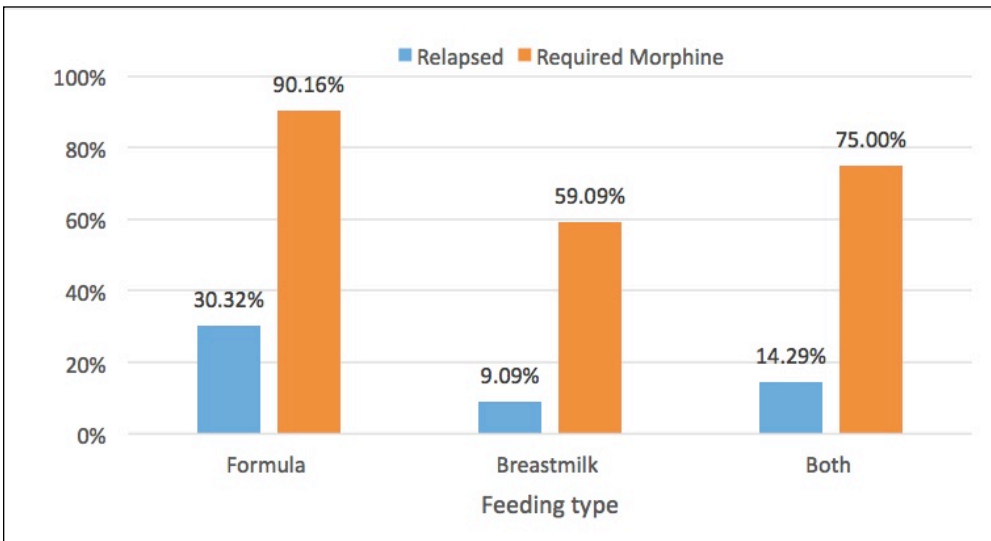


Figure 3: Bar graph showing per feeding type the number of NAS babies (in percentage) that received morphine treatment and percentage of NAS babies having relapsed after initial treatment.

Intensive Care Unit with a diagnosis of NAS, without comorbidity between August 2012 and August 2014. Approval for this study was obtained from the Institutional Review Board (IRB). During each infant's hospitalization, an institutionally-developed objective scoring tool was used to assess signs of NAS every 4 hours, and neonates were treated with opiate replacement therapy for two

consecutive scores >10. Patients were discharged when they had no increased scores for 48 hours after the morphine was discontinued. The information collected included gestational age, feeding type, LOS (measured in days), and requirement of opiate replacement therapy, as well as information about recurrence of NAS signs after weaning of replacement therapy or treatment

discontinuation. T-test, F-test, chi-square tests, and Fisher tests were used to compare the outcomes of the subgroups.

Results

In the study population, 22 babies (11%) were exclusively fed breast milk (BMB), 122 (61%) were exclusively fed formula (FFB), and 56 (28%) were fed both breast milk and formula (BFB) (Figure 1).

The LOS was significantly longer ($p < 0.0001$) in FFB (mean 20.4 days) than in either BMB (10.6 days) or BFB (13.8 days) regardless of gestational age (Figure 2).

Formula fed babies were significantly more likely ($p = 0.0004$) to require opiate replacement (90.2%) than BMB (59.1%) and BFB (75.0%). FFB were also significantly more likely ($p = 0.0153$) to experience relapse of NAS signs after discontinuation of opiate replacement and during the weaning process (30.3%) than BMB (9.1%) and BFB (14.3%) (Figure 3).

Conclusion

In this study, infants diagnosed with NAS who were fed exclusively formula had a

“This study brings awareness to the importance of breast milk for infants diagnosed with NAS. Feeding with breast milk should be recommended to all mothers of infants diagnosed with Neonatal Abstinence Syndrome to decrease the infants’ duration of stay, symptom severity, and risk for relapse.”

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Satyan Lakshminrusimha, MD
Chief, Division of Neonatology
Women and Children's
Hospital of Buffalo



Ashley Darcy Mahoney, PhD, NNP-BC
Neonatal Nurse Practitioner,
South Dade Neonatology
Assistant Professor,
Emory University School of Nursing

Indication

INOMAX is indicated to improve oxygenation and reduce the need for extracorporeal membrane oxygenation in term and near-term (>34 weeks gestation) neonates with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension in conjunction with ventilatory support and other appropriate agents.

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- INOMAX is contraindicated in the treatment of neonates dependent on right-to-left shunting of blood.
- Abrupt discontinuation of INOMAX may lead to increasing pulmonary artery pressure and worsening oxygenation.
- Methemoglobinemia and NO₂ 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 PaO₂, inspired NO₂, and methemoglobin during INOMAX administration.
- INOMAX must be administered using a calibrated INOMax DS_{IR}[®] Nitric Oxide Delivery System operated by trained personnel. Only validated ventilator systems should be used in conjunction with INOMAX.

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INOmax[®] (nitric oxide gas)

Brief Summary of Prescribing Information

INDICATIONS AND USAGE

Treatment of Hypoxic Respiratory Failure

INOmax[®] is indicated to improve oxygenation and reduce the need for extracorporeal membrane oxygenation in term and near-term (>34 weeks) neonates with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension in conjunction with ventilator support and other appropriate agents.

CONTRAINDICATIONS

INOmax is contraindicated in neonates 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 (NO₂) forms in gas mixtures containing NO and O₂. Nitrogen dioxide may cause airway inflammation and damage to lung tissues.

If there is an unexpected change in NO₂ concentration, or if the NO₂ concentration reaches 3 ppm 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 NO₂ analyzer should be recalibrated. The dose of INOmax and/or FiO₂ should be adjusted as appropriate.

Worsening 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.

DRUG INTERACTIONS

Nitric Oxide Donor Agents

Nitric oxide donor agents such as prilocaine, sodium nitroprusside and nitroglycerine may increase the risk of developing methemoglobinemia.

OVERDOSAGE

Overdosage with INOmax is manifest by elevations in methemoglobin and pulmonary toxicities associated with inspired NO₂. Elevated NO₂ may cause acute lung injury. Elevations in methemoglobin reduce the oxygen delivery capacity of the circulation. In clinical studies, NO₂ 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.

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significantly increased length of hospital stay and increased requirement for opiate replacement therapy. The exclusively formula-fed infants also had increased episodes of failed weaning of opiate replacement with relapses of NAS symptoms when compared with infants fed exclusively breast milk or a combination of breast milk and formula.

This study brings awareness to the importance of breast milk for infants diagnosed with NAS. Feeding with breast milk should be recommended to all mothers of infants diagnosed with Neonatal Abstinence Syndrome to decrease the infants' duration of stay, symptom severity, and risk for relapse.

Disclosure

The authors of this article have no conflict of interest to disclose.

Acknowledgements

We thank Yang Chen, MS, MPH, Sonica Sayam, and Claudia A. Kozinetz, PhD at the East Tennessee State University Statistics Department for their assistance with data analysis.

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Highlights of the First 99nicu Meetup

By Stefan Johansson; Francesco Cardona

Introduction

The 99nicu web community came online in 2006 (<https://99nicu.org>). Already from the start, the vision was to create a communication platform for neonatal staff around the world. We wanted to enable discussions about neonatal care with colleagues, not hindered by time zones and geographical boundaries. To date, we count 7,000 doctors, nurses, NNPs and other neonatal staff as members, and see about 200 daily visitors to 99nicu.org.

We are primarily a web-based community, but we felt that being online is not enough. Therefore, we created the “Meetup” format, an IRL event for bringing the neonatal community together, for staff sharing a passion to provide the best neonatal care. While our vision is to promote evidence-based neonatal care, and acknowledge the limitations thereof, we focus on the learning experience by creating a friendly and interactive context.

The 99nicu Meetup

The first 99nicu Meetup was held 12th-15th June 2017, in Stockholm, Sweden. The program was “crowd-

sourced,” by ideas and suggestions from community members. Unfortunately, the dates clashed with two other large neonatal conferences. Nevertheless, about 80 people from 17 different countries on three continents, came to this first Meetup!

The program included a wide range of topics. To mention a few examples, we

learned about: developmental hemostasis, probiotics, minimally invasive surfactant treatment, prevention of infections, and being a neonatologist in social media. One afternoon we had a





double session about family-centered care, also including a parent lecturing about his experience becoming a father of an extremely preterm daughter. Another breath-taking experience was the Syrian doctor who lectured on “How to Perform Neonatal Care in Aleppo.”

We originally planned to webcast all lectures, but due to budget shortcomings, we could only video-record sessions ourselves. However, despite the simple technical format, I believe you can

learn a lot from lectures, available for free on <https://99nicu.org/meetup2017/>

Thanks to dedicated delegates and faculty, we managed to create a friendly and welcoming atmosphere. Sessions, very interactive thanks to the smartphone app Sli.do (<https://sli.do>), were followed by vivid coffee break discussions.

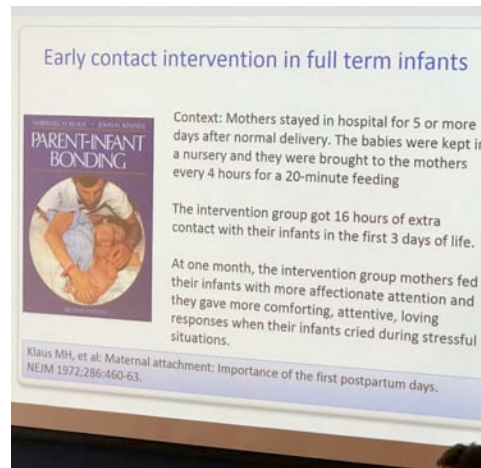
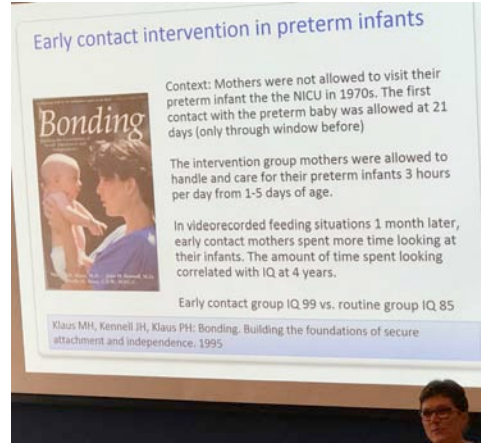
Next Meetup

Feedback from both delegates and faculty members were exceptionally good! Therefore, we feel committed to continue to arrange the 99nicu Meetups, the next being planned mid-April 2018, in Vienna, Austria. We are currently crowd-sourcing ideas. Without disclosing any details, we can promise there will be a

similarly great program for the 2018 Meetup!



With a “Young Lecturer Session” during the next Meetup, we also want to promote young neonatal staff who are passionate about teaching. Fellows, NNPs and other staff knowing how to frame and deliver take-home messages will be giving short lectures with high clinical relevance.



More information

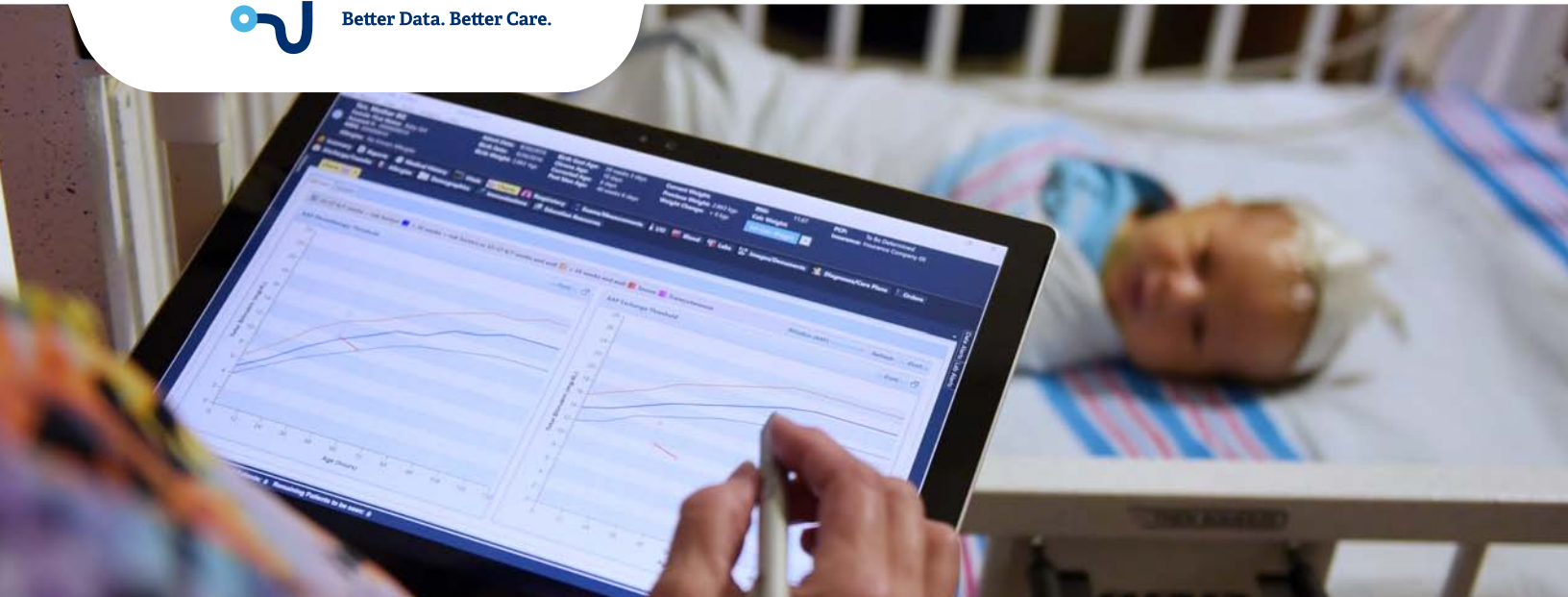
Stay updated about the 99nicu Meetup in 2018! Unless you are already a registered member, sign-up for a free membership on <https://99nicu.org/register>, and you will receive our bi-weekly newsletter. You can also subscribe to the Meetup Newsletter at: <https://99nicu.org/meetup/subscribe/>

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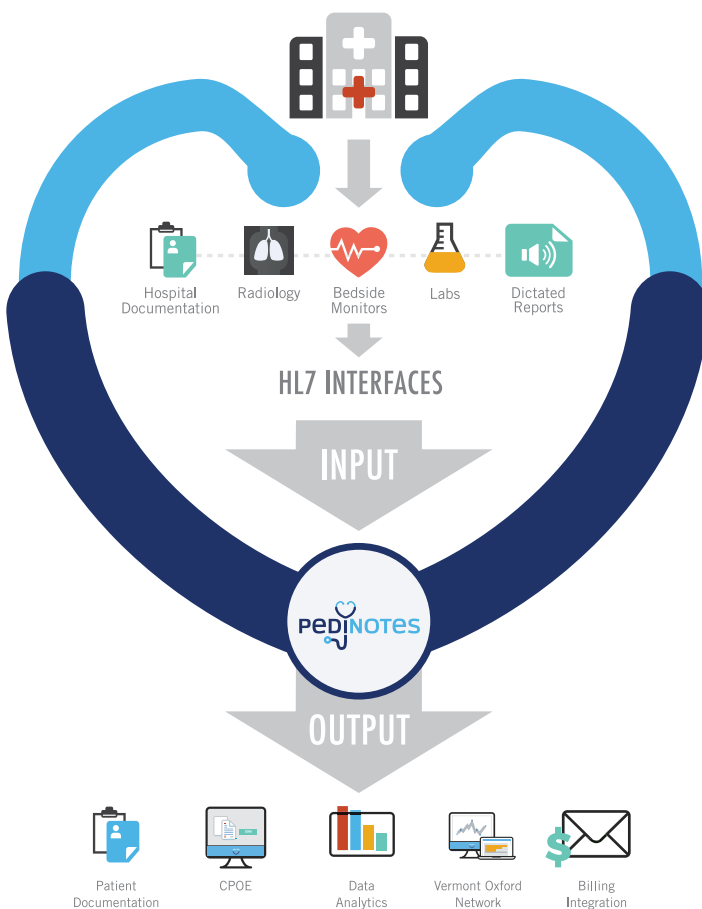
Stefan Johansson, Consultant Neonatologist, Associate Professor Sachs Children's Hospital Stockholm, Sweden Stefan.Johansson@ki.se

Francesco Cardona, Consultant Neonatologist, MSc Medical University of Vienna, Vienna Austria, Vienna



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Medical News, Products & Information

Compiled and Reviewed by Tony Carlson,
Senior Editor

Black Babies More Likely to Have Nursing Care Missed in Their NICU Stay

Newswise — Everybody wants a healthy life for their baby. Black babies are more likely to be born prematurely, which puts them at risk for death and developmental problems. In fact, a third of all infant deaths are preterm-related. The critical period in preterm babies' lives is when they are just born and are in the Neonatal Intensive Care Unit (NICU). The care they receive is vital to a healthy future.

NICU nurses are quite important because the babies are completely dependent, not fully developed, and require intensive treatments and monitoring. NICU nurses also teach and guide the parents of NICU infants, which is essential so the parents can care for the vulnerable babies when they go home.

Until now, we have not known whether nurses are able to complete all the care that is required for these complex infants. It is generally expected that a neonatal critical care unit is adequately staffed and that all required care is provided. Is it possible that nursing care is missed routinely in some NICUs?

A new study from University of Pennsylvania School of Nursing's Center for Health Outcomes and Policy Research (CHOPR) compared missed nursing care in NICUs caring for high and low fractions of black infants. Indeed, nurses in hospitals with one-third or more percent black infants missed 50% more nursing care than those in hospitals with less than one-tenth percent black infants. Additionally, nurses cared for a significantly higher number of babies in the hospitals with a high-black infant population. The predominant types of care missed, such as teaching and counseling parents, and preparation for discharge, address parents' capabilities and readiness for infant care at home. The



Eileen T. Lake, PhD, RN, FAAN, the Jessie M. Scott Endowed Term Chair in Nursing and Health Policy, and CHOPR Associate Director.

Source Newsroom: University of Pennsylvania School of Nursing

study is set for publication in an upcoming issue of *Health Services Research*, but is available now online first here.

"If I was a mom and my baby was being cared for in a NICU, I would be really worried about care being missed, as any parent would be. It is very distressing that black moms have more to worry about at an already stressful time," says lead-author Eileen T. Lake, PhD, RN, FAAN, the Jessie M. Scott Endowed Term Chair in Nursing and Health Policy, and CHOPR Associate Director.

The research team used survey data from more than 1,000 staff nurses in 134 NICUs in California, Florida, New Jersey, and Pennsylvania. Missed nursing care is a unique measure that reveals the clinical care process. Missed care is defined as required nursing care that is omitted or delayed in response to multiple demands or inadequate resources.

"Missed nursing care could affect the survival, growth, and development of these infants. Because we know that outcomes are so dependent on care processes," said Lake. "In hospitals where most black infants are born, inferior care from the point of birth could have lifetime consequences. Thus inadequate staffing levels and substandard work environments set nurses up for missing care. Hospitals need to fix their staffing levels and improve their environments so that nurses can do their jobs as they are dedicated to."

This study underscores the need for more supportive care environments in high-black NICUs to assure adequate staffing and that individual nurses are not overloaded.

In addition to Lake, co-authors included: Douglas Staiger, PhD, Dartmouth College, Erika Edwards, PhD, University of Vermont, Jeannette Rogowski, PhD, Rutgers University and postdoctoral fellow Jessica Smith, PhD, Penn Nursing.

The work was supported in part by grants to the Center for Health Outcomes and Policy Research from the National Institute of Nursing Research, National Institutes of Health (T32-NR-007104 and R01-NR-004513, L. Aiken, PI).

The University of Pennsylvania School of Nursing is one of the world's leading schools of nursing. For the second year in a row, it is ranked the #1 nursing school in the world by QS University, and has four graduate programs ranked number one by *U.S. News & World Report*, the most of any school in the United States. Penn Nursing is consistently among the nation's top recipients of nursing research funding from the National Institutes of Health. Penn Nursing prepares nurse scientists and nurse leaders to meet the health needs of a global society through research, education, and practice.

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The National Urea Cycle Disorders Foundation



The NUCDF is a non-profit organization dedicated to the identification, treatment and cure of urea cycle disorders. NUCDF is a nationally-recognized resource of information and education for families and healthcare professionals.

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Study Shows Probiotics Can Prevent Sepsis in Infants

Newswise — A research team at the University of Nebraska Medical Center College of Public Health has determined that a special mixture of good bacteria in the body reduced the incidence of sepsis in infants in India by 40% at a cost of only \$1 per infant. The findings are reported in the Aug. 16th issue of the journal *Nature*.

Pinaki Panigrahi, MD, PhD, Professor, Epidemiology and Pediatrics, Center for Global Health and Development, and his colleagues in the College of Public Health, led the international research team. The results reflect a culmination of 15 years of research and could seriously impact infant health worldwide.

The special mixture included a probiotic called *Lactobacillus plantarum* ATCC-202195 combined with fructo-oligosaccharide (FOS), an oral synbiotic preparation developed by Dr. Panigrahi.

Probiotics are live bacteria and yeasts that are good for your health, especially your digestive system. Synbiotics are combinations of probiotics with an FOS supplement that promotes growth and sustains colonization of the probiotic strain. FOS, naturally found in breast milk and such plants as onion, chicory, garlic, asparagus, banana, artichoke and others, is food for the probiotic bacteria.

Sepsis is a severe complication of bacterial infection that results in around one million infant deaths worldwide each year, mostly in developing countries. It occurs when the immune system stops fighting germs and begins to turn on itself and can lead to tissue damage, organ failure and death.

It is estimated that 40% of patients with severe sepsis in developing countries do not survive. When children and adults are included, the inpatient cost for managing patients with sepsis in U.S. hospitals is nearly \$24 billion each year.

“This is the largest clinical trial of probiotics in newborns funded by the National Institutes of Health,” Dr. Panigrahi said. The team enrolled more than 4,500 newborns from 149 villages in the Indian province of Odisha and followed them for their first 60 days, the most critical period when they get sick and die.

During their first days of life, the newborns were administered the oral preparation for seven days.

Results of the randomized, double-blind, placebo-controlled study showed that sepsis and deaths in the first two months of infancy were reduced by 40%, more than twice the anticipated reduction of 20%. The synbiotic treatment also lowered respiratory tract infections.

The effectiveness demonstrated in Dr. Panigrahi’s study was so successful the study was halted early.

The probiotic formula could be a “very cheap oral sepsis vaccine,” Dr. Panigrahi said.

Few trials on the use of probiotics to prevent sepsis have focused on newborns, whose largely naive immune system and less complex intestinal environment would allow the probiotic to grow.

“We were concerned when the data safety and monitoring board stopped the study prematurely. We had enrolled just about half of our proposed subjects. Typically, a study is stopped when something is wrong.

Family Centered Care is trendy, but are providers really meeting parents needs in the NICU?

Consider the following:

Surveys show hospital support groups are being widely underutilized by parents.



And only 10% of NICUs surveyed connect parents with non-hospital support.

Graham's Foundation, the global support organization for parents going through the journey of prematurity, set out to find the missing piece that would ensure all parents have real access to the support they need.

See what they found by emailing info@grahamsfoundation.org to request a free copy of the 2017 whitepaper, “Reaching Preemie Parents Today” (*Heather McKinnis, Director, Preemie Parent Mentor Program, Graham's Foundation*).

You may be surprised to see what NICUs are doing right and where their efforts are clearly falling short.

Graham's Foundation empowers parents of premature babies through support, advocacy and research to improve outcomes for their preemies and themselves.



Visit www.GrahamsFoundation.org to learn more.

“But, it was a moment of superlative thrill when we learned it was stopped due to early efficacy. We were surprised a second time when the complete data analysis showed that respiratory

tract infections also were reduced – something we did not anticipate in our population,” Dr. Panigrahi said.

What's Next?

A country's health is measured by its infant mortality.

India has one of the highest rates of infant mortality in the world. Of the one million newborns who die at birth worldwide, India accounts for 700,000 such deaths, according to UNICEF. For every 1,000 live births in India, 40 babies die.

By comparison, the infant mortality rate in Sri Lanka, Nepal, and Bangladesh are 9, 29, and 33, respectively, according to the World Health Organization (WHO).

Dr. Panigrahi wants to bring these numbers down and the results of his study are a big first step.

“This study has to be replicated in different countries and under different circumstances. We maintained tight controls on the administration of the synbiotic, and conducted a rigorous follow-up which will not be available in real life,” he said.

“We have to find out why respiratory infections went down. How does this treatment affect the lungs?”

The intestinal system is the largest immune organ in the body, Dr. Panigrahi said. “If you took it apart and spread out the villi – small, finger-like projections that extend into the small intestine – it would cover a tennis court. And, it's loaded with lymphoid cells. So, if you want to stimulate the body's immunity, go to the intestine.”

About Sepsis

Also known as “blood infection,” sepsis is a global health care problem that is more common than heart attack and claims more lives than any cancer. In the least developed countries, it is a leading cause of death.

In the developing world, sepsis accounts for 40% of all neonatal lives lost per year and more than 100,000 women contract sepsis in the course of pregnancy and childbirth.

In children and adults, sepsis occurs when the body's attempt to fight an infection results in the immune system damaging tissues and organs. This chaotic response, designed to protect us, causes widespread inflammation, leaky blood vessels and abnormal blood clotting, resulting in organ damage. In severe cases, blood pressure drops, multiple organ failures ensue and the patient can die rapidly from septic shock.

Perinatal Substance Use:

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Dr. Pinaki Panigrahi monitors a baby's progress in a clinical trial in India.

The Team

The study's team from UNMC included: Pinaki Panigrahi, MD, PhD, Professor and Principal Investigator; Lorena Baccaglini, DDS, PhD, Associate Professor, Epidemiology; and Dinesh Chandel, PhD, Research Assistant Professor, Environmental, Agricultural & Occupational Health, Center for Global Health and Development in the College of Public Health.

Other collaborators on the study were:

- Sailajanandan Parida, SCB Medical College, Cuttack, Odisha, India.
- Nimai Nanda, Ispat General Hospital, Rourkela, Odisha, India.
- Radhanath Satpathy, Arjit Mohapatra, Pravas Misra, Asian Institute of Public Health, Bhubaneswar, Odisha, India.
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- Judith Johnson, J. Glenn Morris Jr, Emerging Pathogens Institute, University of Florida, Gainesville.
- Nigel Paneth, Epidemiology, Pediatrics & Human Development;
- and Ira Gewolb, Neonatology, College of Human Medicine, Michigan State University, East Lansing.

The study was funded by a \$3 million, five-year grant from the National Institutes of Health - Eunice Kennedy Shriver National

Institute of Child Health and Human Development. An earlier \$4.5 million grant awarded to Dr. Panigrahi provided funds to build the field sites, clinical trial setup, labs and data management infrastructures at two sites in India. Funding also was provided by the Bill & Melinda Gates Foundation.

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Preemies' Separation from Mom + Physical Stress May Increase Health Risks in Adulthood

Newswise — A new study suggests that physiological stress in premature infants combined with separation from their mothers may have lasting effects into adulthood. In clinical studies, these factors have been found to increase the risk of obesity and insulin resistance, leading to metabolic disorders such as Metabolic Syndrome and Type 2 Diabetes Mellitus. The study was published ahead of print in the *American Journal of Physiology—Regulatory, Integrative and Comparative Physiology*.

Researchers from Aurora St. Luke's Medical Center/Aurora Research Institute in Milwaukee and the Medical College of Wisconsin studied groups of newborn rats in varying situations that simulated the experience of premature infants separated from their mothers for the purposes of clinical care:

- Low oxygen levels that spontaneously led to low body temperature;
- Normal oxygen levels and induced low body temperature;
- Low oxygen levels and steady (normal) body temperature (to mimic incubator care); and
- Normal oxygen and temperature levels (control group).

The control group with normal oxygen and temperature levels was compared to a group of neonatal rat pups staying with their mother (unseparated).

When the rat pups reached adulthood, the research team measured levels of insulin, glucose and hormones in the blood that are associated with appetite, body weight and insulin resistance.

Male and female adult rats that were separated from their mothers as newborns weighed more than the control group. Male rats separated from their mothers had higher levels of leptin, a hormone linked to increased appetite and obesity. This may contribute to the development of Metabolic Syndrome and Type 2 Diabetes Mellitus. Adult male rats that had been exposed to low oxygen with steady (normal) body temperature as neonates also had lower testosterone levels.

The researchers wrote that because touch between the caregiver and the separated newborn can weaken some of these effects, "we feel that continued mechanistic studies in our

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rat model will prove useful to develop new approaches to the management of the premature human infant to mitigate the long-term effects."

Read the full article, "Insulin sensitivity, leptin, adiponectin, resistin, and testosterone in adult male and female rats after maternal-neonatal separation and environmental stress" in the American Journal of Physiology—Regulatory, Integrative and Comparative Physiology at: (<http://ajpregu.physiology.org/content/early/2017/09/01/ajpregu.00271.2017>)

Electrical Grounding Technique May Improve Health Outcomes of NICU Babies

A technique called "electrical grounding" may moderate preterm infants' electromagnetic exposure in the Neonatal Intensive Care Unit (NICU) and improve their health outcomes, according to Penn State College of Medicine researchers.

Equipment in the NICU produces low-frequency electromagnetic fields that can have subtle, yet measurable effects on the autonomic nervous system, the system that regulates involuntary body functions. Preterm infants may be especially vulnerable to these effects.

Previous research in adults has shown that exposure to electromagnetic fields can affect the vagus nerve, a key component of the autonomic nervous system that regulates the body's internal organs during rest. Previous research also has shown that electrical grounding, which reduces the electrical charge to the body, can improve the functioning of the autonomic nervous system and the vagus nerve, producing improved vagal tone.

Vagal tone, which is measured by analyzing heart rate variability between inhalation and exhalation, is a valuable indicator of health. An earlier study performed with colleagues at Penn State found that low vagal tone in preterm infants is a marker of vulnerability to stress and a risk factor for developing necrotizing enterocolitis, an intestinal disorder that can have severe consequences. Strengthening vagal tone may reduce inflammation, guard against the development of necrotizing enterocolitis and offer protection from a variety of other conditions that can affect preterm infants.

Additionally, a separate study involving preterm infants in the NICU revealed that when the incubator's power was switched off, thereby eliminating the electromagnetic source, the vagal tone of the infants improved. But until this Penn State study, published in a recent issue of *Neonatology*, no other research had directly evaluated the effect of electrical grounding on vagal tone in preterm infants in the NICU.

To evaluate the connection between electrical grounding and vagal tone in preterm infants, the researchers conducted a prospective observational study that included a total of 26 preterm infants who were between six and 60 days old and in

the NICU at Penn State Health Milton S. Hershey Medical Center between October 2012 and January 2014.

"Preterm babies in the NICU have a lot of health challenges due to the immaturity of their lungs, of their bowel and of all their organs, so we decided to look at how electrical grounding could help improve vagal tone and mitigate some of those challenges," said Dr. Charles Palmer, Professor of Pediatrics and Chief of Newborn Medicine at Penn State Children's Hospital. "Anything we might do to improve the babies' resilience would be good."

After measuring the environmental electromagnetic levels in and around the incubators, the researchers electrically grounded the babies by connecting an electrode wire from the infants' incubators or open cribs to the ground. Twenty of the 26 infants were measured for both skin voltage -- the voltage measured between the patient's skin and electrical ground -- and heart rate variability -- to assess vagal tone, before, during and after grounding. Six of the infants were measured only for skin voltage.

"When we looked at the signal on the skin, it was an oscillating signal going out at 60 hertz, which is exactly the frequency of our electrical power. When we connected the baby to the ground, the skin voltage dropped by about 95% and vagal tone increased by 67%," Palmer said. After grounding, vagal tone returned to the pre-grounding level.

"What we can conclude is that a baby's autonomic nervous system is able to sense the electrical environment and it seems as though a baby is more relaxed when grounded," Palmer said. "When tied to our previous work, which found that vagal tone was an important risk factor for necrotizing enterocolitis, this new finding may offer an opportunity to protect babies even further."

A limitation of this study is the sample size, and further research is needed, said Palmer.

"If more research confirms our results, it could mean, for example, redesigning incubators to ground babies and cancel out the electrical field," he said.

Palmer also said that more study is needed to evaluate the long-term effects on preterm infants of exposure to low-frequency electromagnetic fields in the NICU.

Other researchers on this project were: Dr. Rohit Passi, Fellow in Neonatal Perinatal Medicine and Dr. Kim K. Doheny, both at Penn State Children's Hospital, Division of Newborn Medicine; Yuri Gordin, medical student, Penn State College of Medicine; and Hans Hinssen, Penn State Department of Clinical Engineering and College of Medicine.

This research study received no specific funding.

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How Reliable Are Capillary Refill and Blood Pressure in Determination of Hemodynamic Compromise?

Michael Narvey, MD

Originally Published on:

All Things Neonatal

<http://www.allthingsneonatal.com>

July 19, 2017; Republished here with permission.



When I think back to my early days as a medical student, one of the first lessons on the physical exam involves checking central and peripheral perfusion as part of the cardiac exam. In the newborn to assess the hemodynamic status, I have often taught that while the blood pressure is a nice number to have, it is important to remember that it is a number that is the product of two important factors: resistance and flow. It is possible then, that a newborn with a low blood pressure, could have good flow, but poor vascular tone (warm shock) or poor flow and increased vascular tone (cardiogenic shock or hypovolemia). Similarly, a baby with good perfusion could be in septic shock, and be vasodilated with good flow. In other words, the use of capillary and blood pressure may not tell you what you really want to know.

Is There a Better Way?

As I have written about previously, point-of-care ultrasound is on the rise in Neonatology. As more trainees are being taught the skill,

and equipment more readily available, opportunities abound for testing various hypotheses about the benefit of such technology. In addition to my role as a clinical Neonatologist, I am also the Medical Director of the Child Health Transport Team, and have pondered about a future where ultrasound is taken on retrievals to enhance patient assessment. I was delighted, therefore, to see a small, but interesting study published on this very topic in July 2017. Browning Carmo KB and colleagues shared their experience in retrieving 44 infants in their paper, "Feasibility and utility of portable ultrasound during retrieval of sick preterm infants." The study amounted to a proof of concept, and took 7 years to complete, in large part, due to the rare availability of staff who were trained in ultrasound to retrieve patients. These were mostly small higher-risk patients (median birthweight, 1130 g (680–1960 g) and median gestation, 27 weeks (23–30). Availability of a laptop-based ultrasound device made this study possible now that there are nearly palm-sized and tablet-based ultrasound units. This study would be even more feasible now (sometimes they were unable to send a three person team due to weight reasons when factoring in the ultrasound equipment). Without going into great detail, the measurements included: cardiac (structural and hemodynamic) & head ultrasounds. Bringing things full circle, it is the hemodynamic assessment that I found the most interesting.

Can We Rely on Capillary Refill?

From previous work normal values for SVC flow are >50 ml/kg/min and for right ventricular output >150 ml/kg/min. These thresholds, if not met, have been correlated with adverse long-term outcomes and in the short-term need for inotropic support. In the absence of these ultrasound measurements, one would use capillary refill and blood pressure to determine the clinical status. But how accurate is it?

First of all, out of the 44 patients retrieved, assessment in the field demonstrated 27 (61%) had evidence using these parameters of low systemic blood flow. After admission to the NICU, eight had persistent low systemic blood flow with the patients shown below in the table. The striking finding (at least to me), is that six out of eight had capillary refill times <2 seconds. With respect to blood pressure, 5/8 had mean blood pressures that would be considered

Table. Observations and Metabolic Status at Time of NUIt and Low Systemic Blood Flow

Case #	GA	Axillary Temp.	HR	MBP	CRT	pH	Lactate	SVC Flow	RVO Flow	Comments/HUSS
1	25	37	176	44	<2 sec.	7.34	NA	34	49	Grade IV IVH*
2	29	35.5	150	27	<2 sec.	7.21	3.7	41	92	HUSS normal
3	26	33.2	144	29	<2 sec.	7.27	4.9	39	91	HUSS normal
4	26	33.3	114	28	<2 sec.	7.6	5.8	29	108	HUSS normal
5	25	36.7	141	18	4 sec.	7.21	12.5	NA	79	Decreased filling of heart; HUSS normal*
6	28	35.3	135	27	<2 sec.	7.18	NA	43	133	HUSS normal
7	25	37	168	27	4 sec.	6.97	NA	10	104	HUSS normal*
8	29	36.4	162	54	<2 sec.	6.58	20	NA	36	Inotropes targeted so flow was visible on admission; HUSS normal

GA = Completed wks. of gestation at birth; HR = heart rate - beats per minute; MAP = mean arterial pressure - mmHg; CRT = capillary refill time; SVC = superior vena cave in mL/kg/min; RVO = right ventricular output in mL/kg/min; NA = not available; HUSS = head ultrasound scan; *Death within 72 hrs. of birth

normal or even elevated, despite clearly compromised systemic blood flow. I think the answer is that capillary refill, and I would also add blood pressure, are not telling you the whole story. I suspect in these patients the numbers were masking the true status of the patient.

How Safe is Transport?

One other aspect of the study which I hope would provide some relief to those of us who transport patients long distance, is that the head ultrasound findings before and after transport were unchanged. Transport with all of its movement to and fro and vibrations would not seem to put babies at risk of intracranial bleeding.

Where Do We Go from Here?

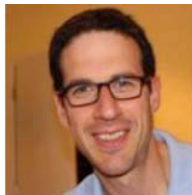
Before we all jump on the bandwagon and spend a great deal of money buying such equipment, it needs to be said "larger studies are needed" looking at such things as IVH. Although it is reassuring that patients with IVH did not have extension of such bleeding after transport, it needs to be recognized that

"Before we all jump on the bandwagon and spend a great deal of money buying such equipment, it needs to be said "larger studies are needed" looking at such things as IVH. Although it is reassuring that patients with IVH did not have extension of such bleeding after transport, it needs to be recognized that with such a small study, I am not comfortable saying that the case is closed."

with such a small study, I am not comfortable saying that the case is closed. What I am concerned about though, is the lack of correlation between SVC and RVO measurements and the findings, which we have used for ages to estimate hemodynamic status in patients.

There will be those who resist such change, as it does require effort to acquire a new set of skills. I do see this happening though, as we move forward, if we want to have the most accurate assessment of clinical status in our patients. As equipment with high resolution becomes increasingly available at lower price points, how long can we afford not to adapt?

NT



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NEONATOLOGY TODAY

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ISSN: 1932-7137 (digital).
Published monthly. All rights reserved.

Company offices:
11502 Elk Horn Dr., Ste. 201
Clarksburg, MD 20871 USA
www.NeonatologyToday.net

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