



Sham feeding in post-operative neonates may enhance oral development, decrease maternal stress levels

Sham feeding may enhance oral skill development in neonates after bowel surgery and decrease stress levels in mothers, says research published by Le Bonheur Neonatologist Mark Weems, MD, in the *American Journal of Perinatology*. This research marks the first time that sham feeding post-operative neonates has been described in published literature. The research is a result of a pilot study developed to test whether sham feeding would be feasible in this population, identify any safety hazards and assess the impact on mothers.



The novel sham feeding protocol used in the study was developed collaboratively between Le Bonheur's neonatology and pediatric surgery divisions. Sham feeding is the process of offering an oral feeding followed by removal of the feed before digestion. In the study, all 15 infants enrolled were able to sham feed with just four infants experiencing minor complications. Mothers reported a decrease in stress and 100% satisfaction with sham feeding.

"Neonates who have abdominal surgery often have a considerable delay until they are able to initiate oral feeding," said Weems. "This delay during a critical time for development of oral skills is further complicated by negative oral feeding stimuli, such as prolonged airway management and nasogastric tubes, which may negatively impact long-term outcomes."

The mothers of these children can also suffer from psychological morbidity from the stress of their stay in the Neonatal Intensive Care Unit (NICU), which can interfere with infant bonding and breastmilk supply and lead to longer NICU stays. Furthermore, mothers who cannot feed their babies often begin to feel helpless, said Weems. Le Bonheur neonatologists introduced sham feeding to attempt to mitigate these negative effects.

"Post-operative delay in enteral feeding contributes to prolonged hospital stay, prolonged exposure to parenteral nutrition and increased risk of infection," said Weems. "Sham feeding is one place where we may be able to offer an intervention for better outcomes."

In the pilot study, 15 patients admitted to the Le Bonheur NICU were enrolled for sham feeding after assessment for feeding readiness by a speech therapist. Infants were sham fed first by bottle and then at the mother's breast. Gastrointestinal suction remained on for the duration of the feed and for five minutes after the feed ended. An eight-question survey was administered to mothers in the study to assess maternal stress and satisfaction with sham feeding.

Of the 15 patients, all were able to safely sham feed after surgery with a total of 312 sham feeds. After the satisfaction survey, all mothers reported a reduction in stress with sham feeding, and 86% reported that sham feeding improved the mother-infant relationship. All reported that they would recommend sham feeding.

"Our study demonstrates that sham feeding in neonates after abdominal surgery is feasible," said Weems. "Ultimately we may be able to improve long-term outcomes for both the mother and infant."



Pediatric Onco-Nephrology: Time to Spread the Word



The need for pediatric nephrologists to develop a special expertise in the onco-nephrology field is increasingly important as childhood cancer rates have been on the rise and new therapy protocols are advancing, according to a *Pediatric Nephrology* article published by Le Bonheur Nephrologist Arwa Nada, MD. Nada also serves as a consulting nephrologist at St. Jude Children's Research Hospital. The first of a two-part educational summary, Nada provides an overview of how pediatric cancer and its therapies can impact kidney function and the increasing need for involvement of pediatric nephrologists as an integral part of the care team for children with cancer.

"Children diagnosed with malignancy can experience unique and complicated forms of kidney injury at any stage of therapy and afterwards," said Nada. "The pediatric nephrologist is an increasingly important member of the care team to mitigate and manage acute kidney involvement or injury during pediatric cancer treatment."

Cancer and kidney disease have numerous interconnections. Historically, pediatric nephrologists have treated the kidney complications occurring during cancer therapy, such as acute kidney injury (AKI), fluid and electrolyte disturbances, tumor lysis syndrome (TLS), hypertension and chronic kidney disease. However, advances in treatments in the field of pediatric cancer, specifically the introduction of CD19-targeted chimeric antigen receptor T cell (CAR-T) therapy, now require more specialized knowledge and expertise in the field.

The review explores 11 unique consult scenarios in the field of pediatric onco-nephrology to highlight the role of the pediatric nephrologist during pediatric cancer therapy:

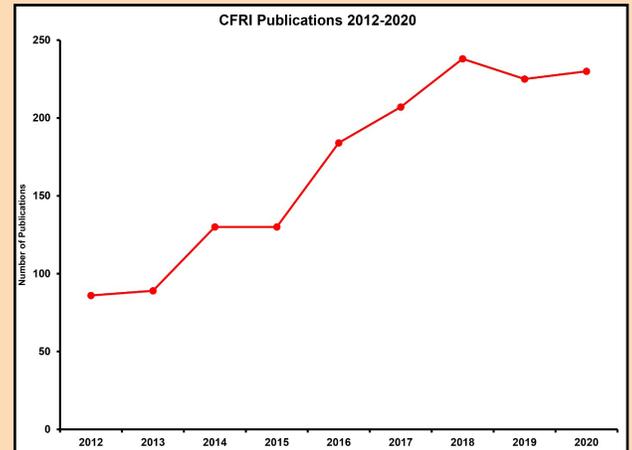
1. "I have a child with a kidney tumor."
2. "I have a child with rising creatine."
3. "I have a child receiving potentially nephrotoxic medications."
4. "I think my patient has TLS."
5. "I'm sending my patient to get CT with intravenous contrast. What is the risk?"
6. "My patient with refractory leukemia is receiving CAR-T therapy."
7. "My patient is getting a stem cell transplant."
8. "My patient has developed thrombotic microangiopathy (TMA)."
9. "I need help with electrolyte and acid base management."
10. "I am seeing a child with proteinuria."
11. "I have a child with a kidney infection."

Nada shows that kidney involvement in pediatric cancer is not uncommon and can be encountered in myriad ways. Pediatric nephrologists must be involved in the care of children with cancer from diagnosis to help prevent kidney complications and improve outcomes, she said.

"We have preventive measures that can help decrease the risk of AKI and other kidney complications in this population," said Nada. "Due to the improved survival of children with cancer and long-term effects of interventions on kidney function, the role of the pediatric nephrologist is now expanded to include management of kidney health in pediatric cancer survivors."

CFRI investigators publish more than 200 manuscripts for 4 years in a row

Despite the difficulties posed by the COVID-19 pandemic, CFRI researchers produced 230 publications in 2020. These publications appeared in 156 peer-reviewed and indexed journals with an average 2019 CiteScore of 7.4. These journals are also highly respected within their specific fields, with 61% of these journals ranked in the top 25% of their first category.



New Faces in the CFRI



Sherlonda Allen
Project Facilitator



Rhondalind Barcus
Clinical Research Coordinator



Sarah Barve, RN, BSN
Neurology Clinical Research Coordinator



Kenishia Guy
Clinical Research Coordinator



Nicholas Leal, MS
Clinical Research Coordinator



Katherine Newsom
Research Data Specialist



Danny Self, PhD
Clinical Research Coordinator

Molecular biology of brain tumors impacts prognosis, treatment of pediatric brain tumors

Understanding the molecular biology of brain tumors is key to prognosis and treatment, said Le Bonheur Neuroscience Institute Co-Director Frederick Boop, MD, in his presentation “How Molecular Biology Impacts Clinical Practice” at the International Society for Pediatric Neurosurgery (ISPN) 2020 Virtual Meeting.

“Historically we have depended on what we see under a microscope to differentiate tumor types and determine prognosis and therapy,” said Boop. “We know now that what we see doesn’t necessarily predict how these tumors are going to behave.”

Physicians are able to send a piece of a child’s tumor to FoundationOne, an FDA-approved tissue-based broad companion diagnostic (CDx) for solid tumors, which provides the genomic alterations of that particular tumor. This explanation of the genetic aberrations includes its significance, best available treatment with mechanism of action and studies open for enrollment.

Manipulation of tumors based on molecular genetics began more than 35 years ago with shrinking prolactinomas before turning to neurosurgery. Boop and his team now use a molecular biological approach with medulloblastomas, low-grade gliomas, congenital glioblastomas and many more



Co-Director of the Neuroscience Institute Frederick Boop, MD, presented on the molecular biology of brain tumors at the International Society for Pediatric Neurosurgery 2020 Virtual Meeting.

types of brain tumors. Closer study of molecular genetics has revealed different variants within each type of tumor, each with a different treatment approach and prognosis based on the genetic variant. Further study is needed into treatment side effects and long-term consequences for some of these therapies.

“As neurosurgeons, it is important for us to get tissue to the lab in every instance for us to understand what’s going on so that these children can have a chance,” said Boop.

For tumors that can’t be removed surgically but tissue is needed for diagnostics,

biopsies provide better understanding and treatment of the tumor. Previously, neurosurgeons avoided these biopsies because it was believed that the cells required were closest to necrotic areas that could cause catastrophic complications. Better understanding of tumors means that the tumor can be biopsied in a safer area in order to obtain the molecular profile of the tumor.

“Molecular genetics has completely changed our field and will continue to do so,” said Boop. “There may come a time when the role for surgeons is much less than it is today.”

IN BRIEF

CFRI labs achieve high score in safety, compliance

The National Institutes of Health (NIH) and governmental regulatory agencies require that research laboratories be inspected for safety and compliance with applicable regulations. The Office of Research Safety Affairs at UTHSC performs annual inspections of CFRI research laboratories. CFRI laboratories scored 99/100 for the second year in a row, demonstrating CFRI’s dedication to maintaining a safe environment in laboratory spaces. These high scores would not have been possible without Billie Masek, CFRI’s research laboratory manager, whose continued support has allowed all investigators and laboratory staff in CFRI to remain in compliance.

CFRI receives Assisi Foundation grant renewal

The CFRI received a renewal award from the Assisi Foundation of \$1.25 million in five years to support research infrastructure. The Assisi Foundation of Memphis supports nonprofit organizations that work to improve Memphis and the Mid-South. This award will support Le Bonheur and CFRI’s mission to prevent, treat and eliminate pediatric disease.

2021 Le Bonheur research grants accepted through April

Applications are currently being accepted for the Le Bonheur Research Grants program. This program supports clinical and basic research at Le Bonheur Children’s Hospital. While the program prioritizes studies by junior faculty members, all investigators initiating new lines of research will be considered.

Le Bonheur medical staff, nursing staff and investigators in the CFRI are eligible to apply for grant support. Junior faculty (fewer than five years out of training) are eligible for junior faculty grants up to \$25,000, while all other applicants are eligible for grants up to \$5,000. The application deadline is noon on Friday, April 30, 2021. Applications and instructions are available at lebonheur.org/research/investigator-resources.

Samarasinghe receives American Lung Association award

Le Bonheur Researcher Amali Samarasinghe, PhD, was awarded the Charles and Amelia Gould Innovation award amounting to \$75,000 in two years through the American Lung Association’s Awards and Grants Program. Samarasinghe’s research is focused on eosinophils and how they respond to influenza virus and *Streptococcus pneumoniae* bacteria.

Early PDA closure may improve outcomes in preterm infants

Le Bonheur cardiologists evaluate the benefits of PDA closure prior to 4 weeks of age

Extremely low birth weight (ELBW) infants with moderate to large patent ductus arteriosus (PDA) may benefit from transcatheter PDA closure (TCPC) in the first four weeks of life, according to research published by Le Bonheur Cardiologist Ranjit Philip, MD, and Medical Director of Interventional Cardiac Imaging and Interventional Catheterization Laboratory Shyam Sathanandam, MD. Early PDA closure may prevent early onset pulmonary vascular disease, promote growth and facilitate faster weaning off supplemental oxygen and ventilator support.

“The primary objective of this study was to describe changes in hemodynamics, respiratory support and growth associated with TCPC in ELBW infants,” said Philip. “We also wanted to describe clinical outcomes in early versus delayed PDA closures to identify factors associated with worse clinical outcomes.”

The study followed 100 infants with a hemodynamically significant PDA (hsPDA) who were born at less than 27 weeks gestation, weighed less than 1 kg at birth and were referred for possible TCPC. The infants were separated by age into those who underwent TCPC at younger than 4 weeks (group 1), 4-8 weeks (group 2) and older than 8 weeks of age (group 3).

A hemodynamic assessment was completed as part of the procedure and included baseline pulmonary to system flow ratio, pulmonary artery systolic pressure (PASP), degree of shunting and pulmonary vascular resistance. To assess respiratory outcomes of these infants, a respiratory severity score (RSS) was calculated by a product of the mean airway pressure and the fractional inspired oxygen with a lower score denoting less respiratory support.

“The presence of moderate to large PDA in ELBW preterm infants is associated with poor respiratory outcomes and an increased mortality,” said Philip. “Our study aimed to determine if early PDA closure demonstrated a reduction in these adverse outcomes.”

While all infants were on mechanical ventilator support at the time of TCPC, baseline RSS was highest for infants in group 3. Although younger and smaller, infants in group 1 were able to extubate sooner compared to group 3 and reach an RSS of less than two (denoting minimal support) significantly faster than those with late PDA closure.

Pulmonary hypertension (PHT) also influenced RSS. Those with PHT were referred for PDA closure later and consequently had a higher pre-procedure RSS. This group took a longer time to return to baseline RSS following TCPC in comparison to infants without PHT. Finally, age at PDA closure affected weight gain for these infants. Specifically between four and eight weeks,



weight gain was much more rapid for infants in group 1 than for those in group 3 who still had the PDA at this age.

The study's results raise questions regarding when, how and whether a PDA should be closed in ELBW infants. Based on this study, benefits of early closure in ELBW include rapid improvement of respiratory status and normal weight gain. Delayed PDA closure and PHT are risk factors for worse respiratory outcomes.

In terms of how closure is performed, the study shows that TCPC can be performed with good success with no significant adverse events while also obtaining invaluable information on hemodynamic significance. And finally, this is the first-time published study of PDA closure whose hemodynamics were measured prior to closure.

“When we first started offering this novel procedure, the infants were usually older and more critical. Since January 2016, with our growing experience in TCPC, younger and smaller infants are being referred,” said Philip. “As our team has gotten more comfortable with the procedure and post-procedure care, ELBW infants are referred for TCPC between the second and third week of life.”

Philip and the Le Bonheur cardiologists work closely with neonatology teams at Le Bonheur and referring centers in order to provide excellent care for ELBW infants with hsPDAs and determine the best course of treatment for each patient.

The study concluded that it may be beneficial to close hsPDAs in the first four weeks of life before the onset of elevated pulmonary vascular resistance in ELBW infants with the additional benefits of faster weaning off ventilator and oxygen support and better weight gain. Researchers concluded that additional RCTs are needed to examine the short- and long-term benefits for ELBW infants, evaluating no intervention versus TCPC and long-term neurodevelopmental outcomes.