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Leading the Way

Baby TAPE Looks to Fill a Major Gap in Infant Health Care

Weight is the foremost marker of health and health outcomes in infants. A weighing scale remains the universal gold standard for obtaining weight in children and is highlighted by the World Health Organization as one of four essential pieces of equipment needed when caring for newborns. However, the vast majority of healthcare providers in remote, resource-constrained settings simply do not have access to functional, calibrated scales with the precision necessary to accurately determine weight. Many critically ill newborns in the U.S. suffer similar challenges when it comes to weight assessment. For infants receiving care in a neonatal intensive care unit, it can be nearly impossible to remove or account for the weight of life-sustaining medical equipment prior to obtaining a scale-based weight. The relative error introduced by such equipment can significantly affect the safety profile of the medicines these infants receive.

Importantly, there is no other patient population for whom more calculation and manipulation of drug doses occurs than in the newborn—from prescribing and transcribing the dose to diluting, compounding, dispensing, and administering the final formulation. Dosing errors represent the most common type of medication errors and receive a fair amount of attention when implementing improvements in the drug delivery process. However, if the infant's weight is captured incorrectly, improvements in the process become irrelevant. If the child's weight is unavailable, the process, as a whole, is rendered useless.

In response to similar issues for older children, the PTN, under the leadership of Dr. Susan Abdel-Rahman at Children's Mercy Hospital in Kansas City, recently validated the Mercy TAPE—an anthropometric-based device developed by Dr. Abdel-Rahman that predicts weight in children 2 months through 16 years of age. The critical gap that remains unaddressed by the Mercy TAPE and other weight estimation strategies, is the newborn period. The Baby TAPE study intends to collect the necessary anthropometric data in children under the age of 3 months so that we can develop, design, and validate a similar weight estimation tool for newborns and young infants. Anthropometric data on length and girth surrogates will be collected in 2000 infants at approximately 5–10 study sites. Visit the **PTN website** for more details about the study as it progresses.

A Message from the Lead Principal Investigator

Danny Benjamin, MD, PhD, MPH

Welcome to the eleventh issue of the *PTN Post*, your quarterly source for information about the work of the Pediatric Trials Network (PTN).

As you will see from this newsletter, the PTN is moving full steam ahead. Of note, data from several earlier PTN studies are in the process of being submitted to the Food and Drug Administration, along with proposed label changes to improve dosing, safety, and efficacy of therapeutics in children. Drugs included among these submissions are **meropenem**, **ampicillin**, **fluconazole**, **hydroxyurea**, and **lisinopril**. Data concerning the **Mercy TAPE** (mentioned elsewhere in this newsletter) have also been presented for approval as a new device. We will keep you updated on the progress of these submissions in future issues.

As always, we welcome your input about topics of interest for future issues. Please contact us with your suggestions via the PTN website (**https://pediatrictrials.org/contact-info**).

The Clindamycin Obesity Study Wraps Up Enrollment

The **Safety and Pharmacokinetics of Multiple-dose Intravenous and Oral Clindamycin in Obese Children** study recently completed enrollment, with a total of 22 participants recruited. Principal investigator Michael J. Smith, MD, of the University of Louisville led the way in enrollment, with assistance from the site teams at Lurie Children's Hospital of Chicago, Children's Mercy Hospital of Kansas City, Akron Children's Hospital, and the University of Maryland Hospital.

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a leading cause of hospitalization among children and adolescents in the United States. Although infection may remain confined to the skin, it can also spread throughout the body, causing potentially life-threatening infections in bones, joints, and the cardiovascular system. Antimicrobial agents such as clindamycin are often employed as first-line therapies for the treatment of MRSA: use of clindamycin among children hospitalized with this disease increased from 21% in 1999 to 63% in 2008.

Over the same time span, rates of childhood obesity have also increased. National estimates suggest that one out of every five children in the United States is obese. These children are more likely to develop *Staphylococcus aureus* infections and to suffer from complications related to such infections. All too often, however, this population is excluded from pediatric trials of drugs used to treat this and a host of other diseases.

We know from studies in adults that the PK of drugs commonly used in the obese can be markedly different than that of their lean peers; as such, specific dosing recommendations for

(continues on page 2)

Best Practices: Lurie Children's Shows Communication Is Key

For an example of an outstanding PTN site, look no further than Ann & Robert H. Lurie Children's Hospital of Chicago. The top enrolling site for the POPS study, Lurie Children's has enrolled 279 patients as of October 22. To put this number into perspective, the second highest enrolling POPS site has recruited 153 patients, and the third highest 119 patients. Lurie Children's is also a leader in the clindamycin obesity trial, enrolling almost one third of the patients needed to complete the study. A nimble team of 6 individuals makes it all happen, under the direction of Dr. Ram Yogev, site PI and professor in Pediatrics–Infectious Diseases at Northwestern University Feinberg School of Medicine.

Dr. Yogev attributes his site's success to communication and dedication. Site team members participate in a mandatory weekly meeting to review study progress over the preceding week and to identify and troubleshoot any problems that may have arisen. This combination of accountability and collaboration helps to ensure that everyone keeps invested in the team's success.

The Lurie Children's team (from left to right): Rohit Kalra, Brize Morales, Ram Yogev, Laura Fearn, Kathy Rosa, and Mayra Gomez

But, Dr. Yogev is careful to note, communication must extend beyond the confines of the site team to ensure optimal conduct of a study. To this end, he devotes a great deal of time nurturing relationships in other departments at his institution to facilitate understanding of study goals and to bank good will with people who can help make reaching those goals possible. Dr. Yogev observes, "You can't rely on the hierarchy to make things happen; it's personal relationships that create a willingness to help."

For example, one study of a drug with a very short half-life required sampling at 3 time points within a half hour. To ensure coverage for those draws, non-study personnel in relevant departments had to be enlisted and reminded to alert the site team of when eligible patients would be available. Such teamwork would be difficult to foster had those individuals not been approached and befriended by Dr. Yogev. "Thanks to this study, I have more friends than I had before," he jests.

Much of what drives Dr. Yogev to go the extra mile in this regard is the desire to be an example to his team. "If your people see that you are dedicated," he observes, "they will try to match or even beat that dedication." In fact, he admits that he is in friendly competition with his study coordinator, Laura Fearn, to be the best at what they do (and she usually wins, he notes). Other team members who routinely go above and beyond include Jannie Stewart (site phlebotomist), Kathy Rosa (regulatory specialist), and Mayra Gomez (data entry coordinator).

When asked about why he decided to become involved with the Pediatric Trial Network, Dr. Yogev highlights the critical lack of knowledge to inform dosing of the vast majority of drugs used in kids. Collaboration between government, academia, and industry, he notes, is a positive way to make crucial changes — "I only wish I had come up with the idea myself!"

The Clindamycin Obesity Study Wraps Up Enrollment (from page 1)

this population are often required. Similarly, clindamycin dosing guidelines based on weight may not be appropriate for obese children because the physiologic changes related to excess weight can alter the way that a child's body uses and excretes the drug. As a result, obese children are at greater risk of being over-dosed or under-dosed than their non-obese counterparts. This is concerning not only because it risks the health of the child but also because sub-therapeutic drug concentrations may increase the development of clindamycin-resistant MRSA organisms.

To date, no PK data exist to guide clindamycin dosing in obese pediatric patients. To fill this gap, this PTN study is evaluating the safety and PK of clindamycin in obese pediatric patients ages 2 – <18 years. Preliminary results are expected in early 2015. For more information about this study, visit ClinicalTrials.gov.

The Pediatric Trials Network (PTN) is made possible by the Best Pharmaceuticals for Children Act (BPCA). The BPCA, first enacted in 2002, provides mechanisms for studying on- and off-patent drugs in children. Visit us on the web at www.pediatrictrials.org.

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