Computer-based modeling improves outcomes for infants in drug withdrawal

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Computer-based modeling is helping to further reduce length of hospital stay and duration of treatment with opioids that are used therapeutically to wean babies born in withdrawal from drugs their mothers have taken. This condition is known as neonatal abstinence syndrome (NAS).

Using computers to represent pharmacokinetics (the movement of a drug from the moment it is administered up to the point at which it is completely eliminated from the body), researchers at Cincinnati Children's Hospital Medical Center reduced the duration of methadone treatment from 16.4 to 14.1 days and inpatient treatment from 21.7 to 18.3 days for infants with NAS.

"The incidence of neonatal abstinence syndrome after an infant's in utero exposure to opioids has risen dramatically in recent years," says Eric Hall, PhD, a researcher in the Perinatal Institute at Cincinnati Children's and lead author of the study. "Future protocol refinements may include personalized treatments, including strategies based on bedside pharmacogenetic analyses or individual opioid exposure profiles, which take into account individual genetic responses to drugs."

The study was conducted at six newborn nurseries in southwest Ohio between July 2014 and March 2015. It was based on an optimization to a standardized protocol previously developed by the Ohio Children's Hospital Neonatal Research Consortium, which has members from each of the six Ohio children's hospitals. In that study, Cincinnati Children's researchers not only found an improvement in length of stay and

duration of treatment, but also in adherence to the protocol, which increased from 87.9 percent to 96.7 percent.

The new study is published online in the *Journal of Pediatrics*.

A recent article in *The New England Journal of Medicine* noted an increase in the admission for NAS to newborn intensive care units from seven cases per 1,000 admissions to 27 per 1,000 admissions from 2004 through 2013. These infants are born in drug withdrawal - often in critical condition - having been exposed in utero to a range of opiates and opioids, from Percocet and Vicodin to heroin.

There is treatment for these babies, but only if they are detected before they go home. The problem is, symptoms do not occur for 48 hours, and many go home with their mothers just hours after birth with no one there to treat their withdrawal. They may end up failing to thrive, or in emergency departments with seizures.

This is why, in 2013, hospitals in the Cincinnati area became the first to begin widespread universal drug testing of all expectant mothers. Ohio law does not require notification of law enforcement if a maternal test is positive, unless there is suspicion of criminal behavior that directly affects the safety or well-being of the newborn. This diffuses the possibility of drug tests leading to criminal charges and increases the likelihood of expectant mothers agreeing to provide a urine sample.

"Prior to this program, one of four women using opioids went undetected. Today we are detecting nearly all," says Scott Wexelblatt, MD, a pediatrician at Cincinnati Children's who has spearheaded the universal drug testing method. Dr. Wexelblatt was a co-author of Dr. Hall's study, along with Jareen-Meinzen-Derr, PhD, a researcher in the division of Biostatistics and Epidemiology. Along with his position in the Perinatal Institute, Dr. Hall has a joint appointment in the division of

Biomedical Informatics at Cincinnati Children's.

Provided by Cincinnati Children's Hospital Medical Center