Preemies still receive inhaled nitric oxide despite lack of supporting evidence and standards

March 12 2012

Many premature infants throughout the United States continue to receive inhaled nitric oxide (iNO) during their NICU stay, despite the lack of evidence to support its use. Whether or not a preemie will receive iNO treatment, when and for how long, varies greatly throughout the country, as its use in premature infants appears to be unstandardized. These are the findings of a Nationwide Children's Hospital study appearing in the journal *Pediatrics*.

Inhaled nitric oxide (iNO) is a selective pulmonary vasodilator approved for use in term and near-term infants with hypoxic respiratory failure. It has been hypothesized that iNO might help prevent complications of prematurity in infants born less than 34 weeks gestation. However, the National Institutes of Health (NIH) and the Agency for Healthcare Research and Quality (AHRQ) have concluded that there is no evidence to support the routine use of iNO in preterm infants who require respiratory support.

"Despite years of data unable to support its off-label use, iNO treatment in preterm infants remains common in U.S. children's hospital NICUs," said Michael R. Stenger, MD, Nationwide Children's neonatologist and lead study author. "It's important to determine how iNO is being used in this patient population, as we may need to implement evidence-based standards of care."

To help characterize variation in recent practice, Nationwide Children's faculty and members of the Ohio Perinatal Research Network (OPRN) performed a retrospective study using the Child Health Corporation of America's Pediatric Health Information Database. The study cohort included 22,699 premature infants born less than 34 weeks gestation admitted to NICUs in 37 U.S. children's hospitals during a three-and-a-half-year period. Documented care was delivered immediately before the aforementioned NIH and AHRQ statements.

Findings revealed that the use of inhaled nitric oxide in premature infants was variable, even when controlling for demographic characteristics and disease. There was substantial variation in the age of initiation of iNO treatment and the average number of days of use. Hospitals that used iNO in more patients also used iNO for a longer duration. Higher volume NICUs used less iNO and had lower mortality rates. Northeastern hospitals reported less use of iNO. Infants who received iNO were less likely to survive, suggesting that iNO is used in infants already at high risk of death.

"Overall, we found that there is a pervasive lack of standardization in iNO use across NICUs," said Dr. Stenger. "Adherence to National Institutes of Health consensus guidelines may decrease variation in iNO use."

Since this study's data are observational, investigators cannot be certain whether or not premature infants benefitted from iNO use. Yet, Dr. Stenger says that the findings suggest that the use of iNO in extremely low birth weight infants with the most severe forms of respiratory failure did not improve mortality rates.

"It is clear that there is a need for adherence to and further development of evidence-based protocols to standardize care to avoid unnecessary and costly treatment," said Dr. Stenger.

Provided by Nationwide Children's Hospital