Nitric oxide does not prevent poor lung development or increase survival of preterm infants overall

21 July 2010

Administration of nitric oxide to preterm infants happens in some high-income countries to reduce rates of poor lung development (bronchopulmonary dysplasia) and improve survival in these children. But the EUNO study, published Online First and in an upcoming *Lancet*, shows that giving nitric oxide to these babies does not improve overall survival or their survival without poor lung development or brain injury. The Article is by Professor Jean-Christophe Mercier, Assistance Publique-Hopitaux de Paris and University of Paris, France, and colleagues.

This randomised controlled trial assessed 800 preterm infants with a gestational age at birth of between 24 weeks and 28 weeks plus 6 days (inclusive), who weighed at least 500g, and who required standard surfactant therapy or continuous positive airway pressure for respiratory distress syndrome within 24 h of birth. The babies were randomly assigned in a one-to-one ratio to inhaled nitric oxide (5 parts per million) or placebo gas (nitrogen gas) for a minimum of 7 days and a maximum of 21 days in the study, which took place in 36 centres in nine countries in the European Union. The primary outcome was survival without poor lung development at age 36 weeks.

Treatment with inhaled nitric oxide and placebo did not result in significant differences in survival of infants without poor lung development, survival at age 36 weeks, or in chances of poor lung development whether or not the child survived.

The authors note that ethnic origin affects susceptibility to chronic lung diseases. Some 82% of the children in this new study were white, and overall there was no effect of nitric oxide, but in those babies that were black the treatment effect was higher, with survival 10% higher in black babies. Other studies have reported clear benefits of nitric oxide treatment in black babies. The authors call for a new analysis of all relevant trials to show the relationship between ethnic origin of premature babies and response to nitric oxide.

The authors conclude: "Inhaled nitric oxide at 5 ppm, started within the first 24 h after birth and continued for a median of 3 weeks, does not improve survival without bronchopulmonary dysplasia in very preterm neonates with mild to moderate respiratory distress syndrome. Our negative results should alter practice by helping to eliminate the use of inhaled nitric oxide in preterm infants developing bronchopulmonary dysplasia."

In a linked Comment, Dr Ilene R S Sosenko and Dr Eduardo Bancalari, Department of Pediatrics, University of Miami Miller School of Medicine, Miami, FL, USA, say: "Can the clinician, with the availability of data now from six large-scale clinical trials, make an evidence-based decision about the use of inhaled nitric oxide in premature infants to improve their survival without bronchopulmonary dysplasia? The answer for now seems to be no. Although inhaled nitric oxide might be promising in specific subgroups of infants, more work is needed to define the optimum dose and duration, and the target population in terms of maturity, severity of illness, race, and age at enrolment at which the infant would potentially be most responsive to intervention with inhaled nitric oxide."

Provided by Lancet