Inhaled nitric oxide can cause severe systemic hypotension

To the Editor:

Inhaled nitric oxide (NO) is a promising and now widely used pulmonary vasodilator for neonates with persistent pulmonary hypertension of the newborn (PPHN) because of its alleged lack of systemic hypotensive side effects.[1] We describe a term baby with PPHN and left ventricular dysfunction caused by birth asphyxia, in whom marked systemic hypotension developed after exposure to NO. The condition reversed when NO therapy was discontinued.

The baby, born at 38 weeks of gestation, was referred to our institution at 5 hours of age for cardiac assessment to exclude cyanotic heart disease. An echocardiogram showed a structurally normal heart, severe left ventricular dysfunction, and a patent ductus arteriosus (PDA) with bidirectional flow. This suggested that the systemic perfusion was dependent on the right-to-left shunt through the PDA, and therefore the prostaglandin E_2 infusion, started at the referring hospital, was continued to maintain ductal patency. A dobutamine infusion was commenced to provide inotropic support to the left ventricle.

The baby was given a trial of NO 6 hours later because of worsening hypoxemia (saturation of arterial oxygen intermittently falling to 50%). Exposure to NO (20 ppm) resulted in an immediate fall in the mean systemic arterial blood pressure from 48 to 35 mm Hg, which reversed when NO therapy was discontinued. This hypotensive episode was thought to have been caused by the NO's reversing the right-to-left shunt through the PDA on which the systemic circulation depended.

Thirty hours later, after recovery of left ventricular function (clinically and on echocardiography), a second trial of NO (20 ppm for 30 minutes) resulted in a marked improvement in oxygenation, from an arterial oxygen tension of 16 to 420 mm Hg without a change in the systemic arterial blood pressure. The baby was successfully weaned from NO during a period of 30 hours, and extubation was successful 2 days later.

This case demonstrates that although NO is a selective pulmonary vasodilator, it can nonetheless cause severe systemic hypotension in babies with PPHN associated with severe left ventricular dysfunction. NO should therefore be administered with caution to such babies.

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Neurodevelopmental outcome in extracorporeal membrane oxygenation survivors

To the Editor:

The long-term outcome for critically ill neonates requiring extracorporeal membrane oxygenation (ECMO) reflects not only the inherent risk of the procedure but also the underlying disease state, the aggressive conventional therapy required, and the child's family/home environment. The recent article by Glass et al.[1] has been helpful in delineating the 5-year neurodevelopmental outcome for ECMO-treated survivors. However, these 103 ECMO-treated subjects include 61% of discharged survivors, leaving an almost 40% of loss–to–follow-up rate, particularly among those requiring extended travel, and hence raising the possibility of selection bias along urban/rural or near/distant lines. Comparison subjects numbered less than one third of study subjects and were not adequately matched for a case-control study; notably they had a significantly longer gestation with a narrower standard deviation, suggesting that the ECMO-treated children had a greater range of gestational age. This is particularly important because the authors previously suggested a possible association between gestational age and outcome.[2] Nonetheless, the report of 42% of nonretarded ECMO-treated children at risk of school failure is clinically very important.[1] The proportion of reported behavioral concern in this Washington population is high and requires further evaluation. In view of recent reports of undetected neurosensory hearing loss after infancy in both ECMO survivors and children with persistent pulmonary hypertension[3, 4] and the link of undetected hearing loss with poor neurobehavioral performance and school failure, further evaluation of childhood hearing should be carried out in this population.

We ask the authors of this article, if at all possible, to reanalyze their data for the ECMO-treated study group, using family/home environment and underlying respiratory diagnostic variables to predict the risk of academic failure. In view of the complexity of insults of ECMO-treated survivors, it is strongly recommended that subsequent comparisons use a comparable "control" group of critically ill infants not treated with ECMO to assess the safety and effectiveness of ECMO therapy. Because most nontreated ECMO candidates do not survive, the choice of control groups is not ideal; however, those with documented hypoxemia are preferable to healthy children as control subjects.

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