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Oxygenation response to NO in newborns with severe pulmonary hypertension

Sir,

We read with interest the article by Turbow et al. in which a sub-group of infants (6 out of 13) with severe persistent pulmonary hypertension of the newborn (PPHN) presented an improvement in oxygenation beyond a 30 min exposure period to inhaled nitric oxide (NO). They suggested that the clinical challenge was to identify these infants, since the response time to NO inhalation is multifactorial and dependent on the disease process associated with PPHN (1).

Our protocol includes the evaluation of the response to NO at 6 h of therapy before considering other alternative treatments such as extracorporeal membrane oxygenation (ECMO). In 16 consecutive neonates (median gestational age 38 weeks, range 27–41; median birthweight 2530 g, range 550–4100) with PPHN, NO (mean 12.3 parts per million, range 5–40) caused an overall significant decrease in mean oxygenation index (OI), from 74 (range 27–131) to 42 (11–127); $p < 0.04$. However, the oxygenation improvement markedly varied in relation to the underlying disease associated with PPHN: in the group of patients with asphyxia or sepsis (n.6) mean OI significantly decreased, from 87 (40–131) to 16 (11–35) ($p < 0.03$); OI moderately improved in premature patients with hyaline membrane disease ($n = 6$), from 56 (27–72) to 40 (16–80) (p = NS); however, in newborn infants with pulmonary hypoplasia (congenital diaphragmatic hernia, $n = 3$, and oligohydramnios, $n = 1$) OI worsened from 83 (72–91) to 100 (62–127) and this group of patients also showed no response to NO inhalation 30 min after onset of therapy, three of them undergoing ECMO.

Since NO enhances oxygenation by a selective pulmonary vasodilation (2) and an improvement in ventilation-perfusion matching (3), we suggest that alveolar diseases, with collapsed and non-ventilated regions may limit inhaled NO to reach blood vessels in these terminal lung units, thus blunting its potential effect, whereas a scarce response to NO treatment in patients with severe bilateral hypoplastic lungs could be related to an early arrest in the development of their peripheral vascular and bronchial tree, associated with surfactant deficiency (4, 5).

In agreement with Turbow et al. we believe that some infants may benefit from a trial of NO therapy that exceeds 30 min since the response to NO treatment is multifactorial and dependent on the disease process. Nevertheless, infants with pulmonary hypoplasia could represent a distinct clinical sub-group of non-responders, early identifiable after onset of NO inhalation. In fact, in our series of early non-responders, 2 RDS infants out of 3 showed an OI improvement 6 h later, while the remaining 4 patients with PPHN secondary to hypoplastic lung persisted hypoxic.

The exact reasons for this lack of acute response are still controversial. However, our data suggest that the absence of an acute NO response in this specific structural pulmonary disease may be an early predictor of poor outcome, prompting alternative treatments.

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