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EDITORIAL

Measurement of Nasal Nitric Oxide in Neonates

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Nitric oxide (NO) is a biological messenger produced by numerous mammalian cells with many important biological functions such as the regulation of blood flow, platelet function, immunity and neurotransmission. NO is synthesized by the enzyme NO synthase acting on the amino acid L-arginine.[1] The presence of NO in the exhaled breath of humans was first demonstrated by Gustafsson et al in 1991.[2] NO found in exhaled air essentially originates from the upper airways with only a minor contribution from the lower respiratory tract and the lungs.[3] The exact origin of the NO found in nasal air and the relative contribution from different sources within the nasal airways is an area of controversy. Some evidence support the notion that the paranasal sinuses rather than the mucosa of the nasal cavity may act as a major source of nasal NO in healthy adult humans.[4] However, the paranasal sinuses in infants are only partially pneumatized. Haight et al found that blocking the sinus ostium resulted in only a 12% decrease in the overall nasal NO concentration and suggested that the main source of NO is the nasal mucosa.[5]

The exact role of nasal NO remains unclear. The potential effects of various diseases on nasal NO levels that have been reported in children include Kartageners' syndrome, cystic fibrosis, allergic rhinitis, and acute sinusitis.[6–11] However, nasal NO is known to have a clear diagnostic value only in primary ciliary dyskinesia.[12] High local nasal NO concentrations in the nasal airway suggest that NO may be involved in local host defense in the upper airway, the regulation of ciliary motility, acting as an airborne messenger to the lungs, and regulation of pulmonary functions.[12,13] Learning more about the respiratory physiology of NO in neonates is of great interest to physicians, especially as NO inhalation therapy is widely studied in neonates with respiratory failure.[14–17] Early use of inhaled NO as rescue therapy for mildly sick, preterm infants seems to decrease the risk of severe brain injury and may improve rates of survival without chronic lung disease. However, inhaled NO as a rescue therapy for very ill preterm infants with assisted ventilation does not seem to be effective and may put them at risk of severe intracranial hemorrhage. In addition, inhaled NO therapy does not seem to be effective in preventing chronic lung disease.[18]

In this issue of *Pediatr Neonatol*, Chang et al developed a modified method of measuring NO concentrations in the upper airways of neonates with a bead instead of an olive.[19] Nasal NO levels measurements are attractive since they are non-invasive and can easily be performed, even in neonates. This simple test may provide information for the diagnosis and treatment monitoring in neonatal respiratory disorders. The potentially different factors that may affect nasal NO levels remain to be verified.[20] Nasal NO production and absorption can be modified by alternation in nasal blood flow and/or volume and by alternation in nasal cavity volume. In addition, the passage of NO from the sinus to the nasal cavity may be blocked due to swelling of the mucosa or by secretions.[12] Nasal NO levels have been reported to be different between term and preterm infants.[21,22] Williams et al reported, that care must be taken to avoid contamination with nasal NO in preterm infants examined in the first

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postnatal days, if lower airway levels are to be accurately assessed.[22] In this study, Chang et al recruited 109 healthy term infants with normal birth weights.[19] They concluded that NO concentrations increases with postnatal age in the first 3 days and there is no significant difference in nasal nitric oxide between sexes, gestational age, birth weight or the left or right nostril. However, the conclusions of no difference in nasal NO levels between term and preterm infants need to be clarified because of the recruitment of the cases only involve the term infants in their study. It is important in further study, to develop a standardized and reliable technique to evaluate fully the potential of nasal NO measurements in a clinical setting. The other issue concerns the possibly of limited diagnostic value of nasal NO levels in neonates with various respiratory diseases.

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