EDITORIAL CORRESPONDENCE

Inhaled nitric oxide can cause severe systemic hypotension

To the Editor:

We read with interest the case report presented by Henrichsen et al.[1] in a letter to the Editor of The Journal, illustrating the risk of systemic hypotension with inhaled nitric oxide (iNO) therapy in patients with left ventricular (LV) dysfunction. Though we do entirely support their statement, we believe that other mechanisms than those described may explain the observed hypotensive effect of iNO.

A structurally normal heart with severe LV dysfunction and a bidirectional shunt through a patent ductus arteriosus does not suggest that systemic perfusion is duct dependent, inasmuch as the shunt is not exclusively unidirectional right to left. Bidirectional shunting usually is explained by a high, near systemic, total pulmonary vascular resistance resulting from maladaptation of the pulmonary circulation to the extrauterine life, and perhaps also by reflex pulmonary vasoconstriction induced by severe LV dysfunction.

In patients with increased pulmonary venous pressure caused by LV dysfunction and elevated left atrial pressure, a decrease in pulmonary vascular resistance (induced by iNO) will lead to an increase in pulmonary venous return and hence to an increase in left atrial and LV filling pressure.[2, 3] This increase may not be assumed by a failing left ventricle that is working on the flat portion of the Frank-Starling curve. Accordingly, we believe that, in the patient described, massive vasodilation induced by iNO resulted in further LV failure.

Inhaled nitric oxide should be administered with caution to babies with LV dysfunction because pulmonary vasoconstriction may act as a protective mechanism of LV overfilling.

Maurice Beghetti, MD
Michel Berner, MD
Peter C. Rimensberger, MD
Pediatric Cardiology Unit
Pediatric Intensive Care Unit
Hôpital des Enfants, University Hospital of Geneva
Geneva 14, Switzerland
9/35/80533

REFERENCES

1. Henrichsen T, Goldman AP, Macrae DJ. Inhaled nitric oxide can cause severe systemic hypotension. J Pediatr 1996;129:183.
2. Loh E, Stamler JS, Hare JM, Loscalzo J, Colucci WS. Cardiovascular effects of inhaled nitric oxide in patients with left ventricular dysfunction. Circulation 1994;90:2780-5.
3. Adatia I, Perry S, Landzberg M, Moore P, Thompson JE, Wessel DL. Inhaled nitric oxide and hemodynamic evaluation of patients with pulmonary hypertension before transplantation. J Am Coll Cardiol 1995;25:1656-64.

Granulocyte colony-stimulating factor and neonatal infection

To the Editor:

I read with interest the article "Granulocyte Colony-stimulating Factor as a Marker for Bacterial Infection of Neonates," by Kennon et al.[1] The authors stressed the specificity of granulocyte colony-stimulating factor (G-CSF) for neonatal infection and concluded that G-CSF can be used as an early marker of neonatal infection. However, I disagree with this view, especially as it pertains to the first few days after birth.

In the early neonatal period, especially in the first few days after birth, data on various kinds of laboratory values (i.e., hormones, biochemical parameters, immunologic products, and cytokines) vary considerably, and their average "normal" values differ from those measured in later periods. Some of these differences are due to direct stress on the baby during the perinatal period or to maladaptation to the extrauterine environment, causing the activation or suppression of the production of certain substances. Creatine kinase and thyroid-stimulating hormone are in this category. Other variations are due to influx from the placenta. Small molecular materials that cross the placenta raise their concentrations in the infants toward the levels in the mother. Immunoglobulin G is in this category. G-CSF is also one of these factors that can cross the placenta.[2]

The placenta is an organ that produces various cytokines. Under conditions that stimulate production of cytokines, such as chorioamnionitis or labor, the placenta produces large amounts of cytokines and raises their concentration in cord blood, which results in high values of these cytokines in the neonates. High cytokine levels have been observed in the healthy neonate with no evidence of clinical infection.[3] Ikeno[4] reported that cord blood G-CSF levels in neonates may be increased in response not only to infection but also to stressed states such as fetal distress and neonatal asphyxia. The elevated level of G-CSF in cord blood persists in the neonate's peripheral blood for several days. This also seems likely for other cytokines.

The data contained in the article do not include the G-CSF value in the early neonatal period. The authors did not refer to this point in the discussion, either. The investigators should reconsider the sensitivity of G-CSF to infection in the early neonatal period, when infants are relatively susceptible to infection.

Seiji Mizuno, MD
Department of Neonatology
Toyota Memorial Hospital
Toyota, Aichi 471 Japan
9/35/80532