INHALED NITRIC OXIDE IN A PRETERM NEWBORN WITH SEVERE HYPOXEMIC RESPIRATORY FAILURE

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Gülhane Tıp Dergisi 46 (3) : 255 - 257 (2004)

ÖZET

Ağır Hipoksemik Solunum Yetmezliği Olan Bir Prematür Yenidoğanda İnhale Nitrik Oksit Kullanımı

İnhale nitrik oksit oksijenizasyonu düzeltir, daha ileri tedavi modalitelerine ihtiyacı azaltır ve özellikle hipoksemik solunum yetmezliği olan term yenidoğanlarda persistan pulmoner hipertansiyonda yararlıdır. Her ne kadar birkaç çalışmada respiratuvar distres sendromlu prematür yenidoğanların oksijenizasyonunda akut iyileşme sağladığı gösterilmiş olsa da, hipoksemik solunum yetmezliği olan prematür yenidoğanlarda inhale nitrik oksitin etkinliği konusundaki rolü tartışmalıdır.

Konvansiyonel mekanik ventilasyon ve yüksek frekanslı ossilatuvar ventilasyona cevap vermeyen, şiddetli hipoksemik solunum yetmezlikli (oksijenizasyon indeksi >30 ve ortalama hava yolu basıncı=14 cmH_2O) ve gebelik yaşı 26 hafta olan 8 günlük bir prematür yenidoğan, 6 günlük inhale nitrik oksit (10-30 ppm) tedavisi gördü. Oksijenizasyon düzeldi, hasta tedaviye iyi yanıt verdi ve 28 günlükken ekstübe edildi.

Bu vakada düşük doz inhale nitrik oksit oksijenizasyonu düzeltip şiddetli hipoksemik solunum yetmezliğini tedavi etmiştir. Bu yüzden inhale nitrik oksit, şiddetli hipoksemik solunum yetmezliği olan prematür yenidoğanların kurtarma tedavilerinden biri olarak düşünülmelidir.

Anahtar Kelimeler: *Yenidoğan, Solunum Yetmezliği, Nitrik Oksit.*

SUMMARY

Inhaled nitric oxide improves oxygenation, lessens the need for further treatment modalities, and is especially useful in persistent pulmonary hypertension in term newborns with hypoxemic respiratory failure. The role of inhaled nitric oxide in premature newborns with hypoxemic respiratory failure is controversial as far as its efficacy is concerned, although a few studies have demonstrated acute improvement in oxygenation in premature newborns with respiratory distress syndrome.

An 8-day old 26 weeks' gestation premature newborn with severe hypoxemic respiratory failure (oxygenation index >30 and mean airway pressure=14 cmH_2O) unresponsive to conventional mechanical ventilation and high frequency oscillatory ventilation was treated with a 6-day-course of inhaled nitric oxide (10-30 ppm). Oxygenation improved, the patient responded well, and she was extubated on the 28th day of life.

Low-dose inhaled nitric oxide improved oxygenation and treated severe hypoxemic respiratory failure in the present case. Inhaled nitric oxide should, therefore, be considered as one of the rescue treatments of severe hypoxemic respiratory failure in premature newborns.

Key Words: *Newborn, Nitric Oxide, Respiratory Failure.*

BACKGROUND

Inhaled nitric oxide improves oxygenation, lessens the need for further treatment modalities and is especially useful in persistent pulmonary hypertension in term newborns with hypoxemic respiratory failure. The role of inhaled nitric oxide in premature newborns with hypoxemic respiratory failure is, however, controversial regarding efficacy although a few studies have demonstrated acute improvement in oxygenation in premature newborns with respiratory distress syndrome.

INTRODUCTION

Inhaled nitric oxide (INO) causes selective pulmonary vasodilation (1). It diffuses into vascular smooth-muscle cells in the lungs, where it increases concentrations of cyclic guanosine monophosphate, thus causing vasodilation. INO does not cause systemic hypotension when it diffuses into the intravascular space because it is inactivated by being avoided binding to hemoglobin.

Clinical studies suggest that INO reduces

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Kabul Tarihi: 30.6.2004

pulmonary hypertension in children with many forms of congenital heart disease (2), congenital diaphragmatic hernia (3), and in adults with primary pulmonary hypertension (4) or the acute respiratory distress syndrome (5,6). INO improves oxygenation, lessens the need for further treatment modalities and is especially useful in persistent pulmonary hypertension in term newborns with hypoxemic respiratory failure (7,8,9).

INO has additionally been used in chronic lung disease of the newborn (10). However its role in premature newborns with hypoxemic respiratory failure is controversial as far as its efficacy is concerned, although a few studies (11,12) have demonstrated acute improvement in oxygenation in premature newborns with acute respiratory distress syndrome.

We herein report a rescue use of INO in a premature newborn with severe hypoxemic respiratory failure who was unresponsive to vigorous conventional mechanical ventilation and high-frequency oscillatory ventilation.

CASE

A 26-week female infant of a twin gestation was born at 770 g. One- and five-minute Apgar scores were 3 and 7, respectively, and she was intubated and ventilated immediately because of respiratory distress after birth. The mother was treated with tocolytic drugs, and had no signs of intrauterine infection. The chest film showed respiratory distress syndrome, for which she was treated with two doses of surfactant and prophylactic antibiotics. On the 5th day, the need for additional oxygen progressively increased. The results of the search for a local or systemic infection, persistent ductus arteriosus, early signs of bronchopulmonary dysplasia and acute or adult respiratory distress syndrome were negative. However, the respiratory status of the patient deteriorated rapidly, and she was still severely hypoxemic (arterial partial oxygen pressure 25-40 mmHg) despite vigorous (peak inspiratory pressure 40-45 cm H_2O, positive end-expiratory pressure 5 cm H_2O, mean airway pressure 14-16 cm H_2O and FiO_2 100%) conventional mechanical ventilation. On the 8th day, INO (10-30 ppm) was started as described previously (13,14) because the patient also no longer responded to high-frequency oscillatory ventilation (mean airway pressure 16-20 cm H_2O and delta P 30-40). INO was performed with a time-cycled, pressure limited ventilator (SLE 2000, UK). INO was administered initially at 10 ppm. Arterial oxygen saturation was monitored by blood gases monitoring and pulse oxymetry during the treatment to ascertain response. During the first two days the dose was increased up to 30 ppm. FiO_2 was adjusted to keep oxygen saturation at 88-93%. After 48 hours of treatment the dose of INO was reduced to 20 ppm. The dose was further reduced every 12 hours by 2-3 ppm to a dose of 2 ppm as long as there was no worsening of oxygenation. The trial of cessation of INO was then undertaken and the treatment was discontinued after six days. Blood methemoglobin and inspired nitrogen dioxide were continually measured during the treatment.

DISCUSSION

INO has been reported as a rescue therapy based on short term trials in preterm infants with severe respiratory distress syndrome and hypoxemic respiratory failure (15,16). Van Meurs et al (15) and Kinsella et al (14) have tested the efficiency of nitric oxide in preterm infants beginning at 1-2 days of age with total treatment duration seven days in almost all infants. Subhedar et al (17) have treated 10 infants with respiratory distress syndrome from day 4th to day 7th with INO. The starting time of treatment in our patient is the rescue type, and the duration of treatment is also in accordance with the previous reports in premature newborns. Finer et al (18) have reviewed twelve randomized controlled studies and have stated that inhaled nitric oxide appears to improve outcome in hypoxemic term and near-term infants by reducing the incidence of the combined endpoint of death or need for ECMO. Desandes et al (19) have searched the response of oxygenation to INO therapy according to pulmonary blood flow in term or near term infants with hypoxemic respiratory failure and stated that INO therapy increases pulmonary blood flow in infants with low pulmonary blood flow and thus increases oxygenation. Barrington et al (20) have reviewed three randomized controlled trials of inhaled nitric oxide therapy in preterm infants and have stated that current republished evidence from randomized trials do not support the use of INO in preterm infants with hypoxic respiratory failure.

INO may either be administered with conventional mechanical ventilation (12,14) or high frequency oscillatory ventilation (13). The efficacy and superiority of these modalities remain to be determined. We used conventional mechanical ventilation in our patient.

In our patient low-dose INO improved oxygenation and treated severe hypoxemic respiratory failure. In accordance also with the previous reports, INO should, therefore, be considered as one of the rescue

treatments of severe hypoxemic respiratory failure in premature newborns.

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