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INHALED NITRIC OXIDE THERAPY IN ACUTE RESPIRATORY DISTRESS SYNDROME DUE TO ACUTE NECROTISING PANCREATITIS. CASE REPORT

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A b s t r a c t

A 17-year-old boy with respiratory failure due to acute necrotising pancreatitis was admitted to our intensive care unit. He successively developed severe septic shock and multiple organ failure with acute respiratory distress syndrome. Mechanical ventilation was instituted in addition to other therapy. Although he was on conventional pressure control ventilation, severe hypoxaemia and hypercapnia with high inspired oxygen fraction and pulmonary hypertension persisted and therefore inhaled nitric oxide therapy was started on day 8. The NO dose was increased up to a maximal value of 30 ppm and maintained for the following six days. This therapy enabled the patient to overcome the critical phase of respiratory failure. One year after illness, the patient was without any organ dysfunction, except for the presence of a pancreatic cyst.

K e y w o r d s

Acute necrotising pancreatitis, Acute respiratory distress syndrome, Pulmonary hypertension, Nitric oxide therapy

A b b r e v i a t i o n s u s e d

NO, nitric oxide; ARDS, acute respiratory distress syndrome; SaO_2 , saturation of oxygen; PAP, pulmonary artery pressure; FiO_2 , fractional concentration of oxygen in inspired gas; PaO_2 , partial pressure of oxygen in arterial blood; ppm, parts per million; PEEP, positive end-expiratory pressure; CO_2, carbon dioxide; O_2, oxygen

INTRODUCTION

Because NO improves pulmonary hypertension and hypoxaemia from ventilation-perfusion mismatching, it has been rapidly introduced in critical care medicine over the last ten years. Giving NO in the respiratory gas selectively dilates pulmonary vessels in ventilated lung regions by relaxation of vascular smooth muscle cells, mediated by cyclic guanosine monophosphate. Pulmonary hypertension with severe hypoxaemia may complicate the care of patients with diseases such as chronic pulmonary hypertension, ARDS, chronic respiratory failure or congenital heart disease. A rapid deterioration of pulmonary gas

exchange and a severe increase in venous admixture are typical features of ARDS. Inhaled NO can improve arterial oxygenation in ARDS patients by increasing the fraction of blood flow to lung regions with a normal ventilation-perfusion ratio (*1*).

CASE REPORT AND METHODS

A 17-year-old man, 96 kg in weight, was admitted to our Intensive Care Department. He presented with respiratory failure due to acute necrotising pancreatitis that developed five days after he had become ill. There was no other relevant medical history. He had been a smoker for the past three years. Because of severe hypoxaemia, hypercapnia and tachypnoea, it was decided to intubate the patient and institute pressure control ventilation. Electrocardiogram, SaO_2, artery pressure, PAP, pulmonary capillary wedge pressure, cardiac output (monitored by Vigilance, Edwards), urine output and temperature were monitored continually. In addition to parenteral and early enteral nutrition and therapy with a combination of antibiotics, somatostatinum and the inhibitor of C1 part of complement, open surgical intervention was performed (*2*). Severe septic shock and multiple organ failure with ARDS successively developed. The circulation was supported by a combination of norepinephrine (2 mcg/kg/min) and dobutamine (15 mcg/kg/min), because the volume expansion was not sufficient to compensate low peripheral resistance and hypotension. Due to lasting severe hypoxaemia, hypercapnia that existed in spite of high fraction of inspired O_2 achieved with conventional pressure control ventilation [PaO_2 47 mmHg; peak pressure, 30 cm H_2O; FiO_2, 1.0; PEEP, 7 cm H_2O; arterial oxygen tension/fractional inspired oxygen (PaO_2/ FiO_2) ratio, 47 mmHg] and pulmonary hypertension, we initiated NO administration, using a Pulmonox mini device (Messer, Austria) through an Y-piece, on day 8. The initial dose was gradually increased from 5 ppm NO to a maximal value of 30 ppm NO. This treatment was slowly discontinued six days later.

RESULTS

The NO inhalation therapy decreased pulmonary shunt, hypercapnia, pulmonary hypertension, and facilitated the lowering of peak pressure to 25 cm H_2O and FiO_2 to a value of 0.5. After six days of NO inhalation, the patient showed an improvement in pulmonary gas exchange with the PaO_2/ FiO_2 ratio of 138 mmHg. The results of arterial blood gas analysis during NO application are shown *Table 1*.

Table 1

Results of arterial blood gas analysis during nitric oxide therapy

Days of treatment	Blood pH value	CO_2 (mmHg)	O_2 (mmHg)	SaO_2 (%)	Pulmonary shunt (%)
1	7.44	52	47	86	38
3	7.48	45	58	92	28
6	7.43	38	69	94	19

Extubation was performed after another four weeks of mechanical ventilation. The patient was discharged from the Intensive Care Department four weeks later. One year after the illness, he was without any organ dysfunction, except for the presence of a pancreatic cyst.

DISCUSSION

The recent discovery of selective pulmonary vasodilating properties of inhaled NO has stimulated its administration in order to correct hypoxaemia or relieve pulmonary hypertension (*3*). Besides improving PaO_2 values, inhaled NO has been described to have anti-inflammatory effects in animal models and to induce a decrease in polymorphonuclear activation or the production of pro-inflammatory cytokines in patients with ARDS (*4,5,6*). However, inhaled NO may also worsen lung injury, especially when combined with high inspired oxygen fractions, via a rapid formation of toxic NO derivatives such as nitrogen dioxide or peroxynitrite (*7*). It is still unknown whether the apparent, short-term beneficial effects of inhaled NO on oxygenation and reduction of pulmonary hypertension are also associated with a positive effect on mortality, and no information exists on potential, long-term toxicity of NO (*8*). The short-term effect of NO on PaO_2 has been confirmed in studies, in which a response to inhaled NO was found in about 80 % of the patients with ARDS. On the contrary, some recent studies showed no significant long-term effect of inhaled NO on mortality and arterial oxygenation. In a randomised, controlled clinical trial, *Michael et al*. (*9*) compared PaO_2 in two groups, each consisting of 20 patients, in which the patients with severe ARDS were randomised to either an inhaled NO or a conventional therapy (*9*). Administration of 5 to 20 ppm of NO significantly increased PaO_2 during the first 24 h of the study period. However, after 24 h, there was no difference in arterial oxygenation between the two groups. The patients receiving NO had no sustained improvement in pulmonary gas exchange, sufficient to reduce inspired oxygen, in the three days after randomisation. *Troncy et al*. reported similar results (*10*). They compared conventional therapy with optimised doses of inhaled NO (0.5 to 40 ppm) in 30 patients with ARDS. NO improved PaO_2 and venous admixture in the first 24 h. Inhaled NO therapy had no significant effect on the percentage of patients who recovered and were weaned from mechanical ventilation 30 days after inclusion into the study (40%), as compared with the conventionally treated group (33.3%). It appears that NO consistently improves arterial oxygenation in about 60–80% of the patients with ARDS. However, the increase in PaO_2 is only temporary and does not influence the outcome. Our case of the young man with ARDS demonstrates the effectiveness of NO application as a rescue therapy for severe hypoxemia as well as pulmonary hypertension. Inhaled NO enabled the patient to overcome a critical phase of respiratory failure.

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LÉČBA AKUTNÍHO SYNDROMU DECHOVÉ TÍSNĚ PŘI AKUTNÍ NEKROTICKÉ PANKREATITIDĚ INHALOVANÝM OXIDEM DUSNATÝM. KAZUISTIKA

S o u h r n

Na jednotku intenzivní péče byl přijat 17 letý muž s respiračním selháním následkem akutní nekrotické pankreatitidy. Postupně došlo k rozvoji septického šoku a multiorgánového selhání s akutním syndromem dechové tísně. Kromě jiné léčby byla rovněž zahájena umělá plicní ventilace. Z důvodu trvající těžké hypoxémie a hyperkapnie přes vysokou inspirační frakci kyslíku při konvenční tlakově řízené ventilaci a plicní hypertenze byla 8. den započata inhalace oxidu dusnatého. Dávka byla postupně zvyšována až na hodnotu 30 ppm a udržována následujících šest dnů. Tato léčba umožnila překonat kritickou fázi respiračního selhání. Kromě pankreatické cysty nemá pacient jeden rok po nemoci jiná orgánová poškození.

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