CASE REPORT

Endotracheal tolazoline for severe persistent pulmonary hypertension of the newborn

Jennifer C Welch, John M Bridson, John L Gibbs

Barnsley District
General Hospital,
Barnsley
J C Welch
J M Bridson
Killingbeck Hospital,
Leeds
J L Gibbs

Correspondence to:
Dr J L Gibbs, Department
of Paediatric Cardiology,
Killingbeck Hospital,
York Road,
Leeds LS14 6UQ

Abstract

The condition of a neonate with severe persistent pulmonary hypertension who became severely hypoxic and acidotic despite intensive conventional treatment improved dramatically after endotracheal administration of tolazoline. This logical mode of administration of vasodilator therapy for this condition has not been reported before. It seemed to be life saving in this case and it warrants further clinical trial.

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Persistent pulmonary hypertension of the newborn is primarily a disease of term and post term neonates and is characterised by severe pulmonary hypertension with right to left shunting across the atrial septum and the arterial duct. This produces marked hypoxaemia with a metabolic acidosis that in itself may provoke a further increase in pulmonary vascular resistance. The reported mortality associated with the condition ranges from 10% to 60%.^{1,2} The vasodilator tolazoline, given intravenously, is a widely used treatment³ but when pulmonary blood flow is low the drug may fail to reach the pulmonary capillary bed in therapeutic concentration. The failure of intravenous tolazoline in a severely hypoxic and acidotic neonate with persistent pulmonary hypertension and the patient's apparently impending death led us to administer tolazoline directly into the bronchial tree via the endotracheal tube, a route of administration not previously reported.

CASE REPORT

A 2.9 kg boy was delivered vaginally at 38 weeks' gestation after an uneventful pregnancy. The Apgar scores were 7 and 9 at one and five minutes respectively. Three hours later the child was cyanosed and tachypnoeic and was treated with intravenous antibiotics and intermittent positive pressure ventilation. A chest radiograph showed pulmonary oligaemia but no other abnormality. During the first 24 hours he required increasing ventilatory support and when he was 30 hours old increasing hypoxaemia developed, with systemic hypotension and metabolic acidosis. He improved slightly after the acidosis was corrected with intravenous sodium bicarbonate and tolazoline was given intravenously (initial loading dose of 2 mg/kg followed by an infusion of 2 mg/kg/hour). At 40 hours of age he deteriorated and again became severely cyanosed despite the addition of a dopamine infusion. Echocardiography confirmed the diagnosis of severe pulmonary hypertension with right to left shunting across both the arterial duct and the atrial septum. He became increasingly acidotic (base deficit 14, pH 7.0) and hypoxic (arterial P_{O_2} 2.2 kPa with oxygen saturation of 11%) with an unrecordable blood pressure and appeared moribund despite continued intensive supportive

Oxygen saturation and arterial P_{O_2} (in kPa), pH, and P_{CO_2} (in kPa) plotted against the age of the child in hours. At 29 hours a loading dose of intravenous (IV) tolazoline was given, followed by an infusion. Further deterioration occurred despite the addition of dopamine. Endotracheal (ET) tolazoline was given at 41 hours of age (second arrow), producing a rapid rise in oxygen saturation and P_{O_2} . Two hours later the tolazoline infusion was changed to epoprostenol to minimise side effects of drug treatment.

treatment. At this stage we decided to attempt to deliver a vasodilator directly to the pulmonary bed. Because there was no nebuliser to use with the infant ventilator, we injected tolazoline (0.5 mg diluted in 1 ml of physiological saline) rapidly into the endotracheal tube with a 1 ml syringe and a 25 gauge needle. After this and a brief period of vigorous ventilation diffuse cutaneous flushing developed and, over the next few minutes, the arterial oxygen saturation increased to 72%, with a concomitant rise in systemic blood pressure and gradual resolution of the metabolic acidosis. Treatment was continued with intravenous tolazoline. One hour later the pH was 7.45, the arterial PO_2 was 8.8 kPa, and the oxygen saturation was 94%. The infusion was changed from tolazoline to epoprostenol (to minimise side effects) and this treatment was continued for a further 24 hours. When he was 48 hours old radiographic changes compatible with hyaline membrane disease developed but, after ventilatory support for 9 days and oxygen supplements until he was 30 days old, he recovered fully.

Discussion

Our patient with severe persistent pulmonary hypertension of the newborn had received optimum conventional treatment. The calculated alveolar/arterial oxygen differences at three hours and 40 hours of age were 80.5 and 85.6 kPa respectively and indicated that he was likely to die soon.^{2,4} He would have been a candidate for emergency extracorporeal membrane oxygenation had this been available.⁵ His haemodynamic state, his acidosis, and his alveolar/arterial oxygen difference improved promptly after endotracheal tolazoline was given. This improvement followed an abrupt appearance of widespread cutaneous flushing, which typically is associ-

ated with intravenous administration of the drug, suggesting that it was rapidly absorbed from the lungs and transmitted to the systemic circulation. The prompt improvement in oxygen saturation strongly suggests that the drug was absorbed by the pulmonary capillary bed and that this local administration of the drug resulted in lifesaving pulmonary vasodilation.

Despite the apparent initial lack of parenchymal lung disease, our patient required ventilatory support followed by oxygen therapy for a long time after his initial improvement. This need for prolonged ventilatory assistance is likely to have been related to lung barotrauma caused by vigorous ventilation, when peak inflation pressure was 40 mm water, during the period of severe hypoxia. Tolazoline, however, is acid in solution with pH of 4.0 and we cannot exclude the possibility that direct administration of an acid solution to the lungs might have caused some alveolar injury. Nonetheless, there appeared little doubt that endotracheal administration to tolazoline was highly effective in this case of life threatening persistent pulmonary hypertension of the newborn. The endotracheal route of administration of vasodilator therapy warrants further study.

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