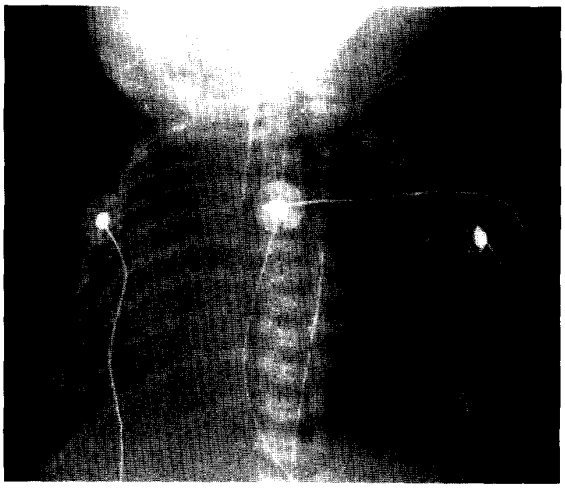

Fig 2. Chest roentgenogram taken immediately after birth showing the right hemithorax filled by a mass.

caval obstruction or cardiac compression from extreme mediastinal shift [4]. Although our fetus had no signs of hydrops, he was treated by serial thoracocenteses because of the massive mediastinal shift, to prevent pulmonary hypoplasia. According to the experience of Adzick [4], serial thoracocenteses are ineffective because of rapid reaccumulation of cyst fluid. Thoracoamniotic shunts seem to be more effective, but are difficult to place, can lead to premature rupture of membrane, and are prone to migration and occlusion [4].

Esophageal duplications present with different symptoms depending on localization, size, and mucosal characteristics. Large cysts usually present with respiratory distress. Small ones may be found as asymptomatic masses on chest roentgenograms. Peptic complications can occur if the mucosal lining of the esophageal duplication is gastric tissue. This is described in about one third of the cases [1]. The acid and pepsin secretions may digest the cyst's mucosal lining locally, causing peptic ulceration or producing mucosal necrosis. Among 81 cases of thoracic duplications collected by Ware and Conrad [2], peptic ulcers developed in 14, and 5 of these cases ended fatally. These ulcers may perforate into different organs: esophagus, tracheobronchial tree, and pleural space. Perforation into the esophagus causes hematemesis or melena [5, 6]. When the cyst ruptures into the tracheobronchial tree, hemoptysis becomes the prominent symptom [6, 7]. Fatal hemorrhage into the bronchial tree has been recorded [5], and partial pulmonary resection or pneumonectomy has been lifesaving in some cases [8]. Rupture into the pleural space causes chemical pleurisy, pneumothorax, or empyema [5].

Unlike unruptured esophageal duplication cysts, which should be easily identifiable mediastinal masses, ruptured cysts may be obscured by the adjacent pleural and pulmonary disease. The fluid content of the cyst may be partially evacuated and replaced by air, thus resembling a lung or mediastinal abscess [5, 7]. Peptic complications usually develop in newborns or infants [5]. Our case demonstrates that bleeding complications due to gastric mucosa in an esophageal duplication can occur even in the fetal period.

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Nitric Oxide Treatment for Pulmonary Hypertension After Neonatal Cardiac Operation

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This report describes a newborn with transposition of the great arteries who underwent a Blalock-Taussig shunt with transient improvement in oxygenation, but required emergent insertion of a central shunt later the same day due to progressive hypoxia and cardiac arrest. Two hours after central shunt insertion, sudden episodes of hypoxia and hypotension developed that were resistant to all pharmacologic therapy. Inhaled nitric oxide (25 ppm) was then administered with dramatic improvement in oxygenation and hemodynamics within minutes. The patient's condition stabilized after these measures, and nitric oxide therapy was discontinued after 2 days.

(Ann Thorac Surg 1995;60:1791–3)

Pulmonary hypertension after congenital cardiac operations in pediatric patients is a potentially fatal complication [1]. Therapy with vasodilators such as pros-

Accepted for publication May 31, 1995.

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0003-4975/95/$9.50
SSDI 0003-4975(95)00657-7

Ann Thorac Surg
1995;60:1791–3

tacyclin is often limited by systemic hypotension. Nitric oxide (NO) has been reported to cause selective pulmonary vasodilation without significant systemic effects when administered as an inhalational agent [2–5]. In a study of 11 patients with pulmonary hypertension undergoing cardiac catheterization at our institution (7 with idiopathic primary pulmonary hypertension, 4 with associated congenital heart disease), both inhaled NO (20 to 80 ppm) and prostacyclin were found to significantly reduce pulmonary arterial pressures [2]. However, unlike prostacyclin, which caused a significant reduction in mean arterial pressure, NO was not found to have any appreciable systemic effects.

A 3.5-kg full-term male infant with Apgar scores of 8 and 8 at 1 and 5 minutes was noted to be cyanotic at 2 hours of life. The O_2 saturation (SaO_2) was 80% on room air with arterial blood gas values as follows: pH, 7.37; carbon dioxide tension, 39 mm Hg; and oxygen tension, 42 mm Hg. Mechanical ventilation was initiated, and transthoracic echocardiography at another institution revealed transposition of the great arteries. Prostaglandin E ($0.2\ \mu g \cdot kg^{-1} \cdot min^{-1}$) and dopamine ($5\ \mu g \cdot kg^{-1} \cdot min^{-1}$) were given without significant improvement (SaO_2, 60% to 70% on an inspired oxygen fraction of 1.0), and the patient was transferred to Columbia-Presbyterian Medical Center for further treatment.

Echocardiography on arrival revealed transposition of the great arteries, subvalvular pulmonary stenosis with a 40 mm Hg gradient, a large ventricular septal defect, good ventricular function, and a patent ductus arteriosus. Balloon atrial septostomy with a 5F catheter was successfully performed, with the SaO_2 improving to 84% immediately after the procedure. A progressive decline in SaO_2 (SaO_2, 68% to 70%) and clinical condition necessitated placement of a right modified Blalock-Taussig shunt on the second day of life.

Intraoperative anesthetic management included the administration of high doses of fentanyl and ventilation with an inspired oxygen fraction of 1.0. The chest was entered through a right thoracotomy in the fourth intercostal space. Findings included a right-sided aortic arch, and a pulmonary artery of normal size. A 4-mm thin-walled Gore-Tex graft (W. L. Gore & Assoc, Flagstaff, AZ) was interposed between the origin of the right subclavian artery and the right pulmonary artery. The SaO_2 improved to 85%. The prostaglandin infusion was discontinued and the patient returned to the intensive care unit.

Approximately 1 hour postoperatively significant hypoxemia developed with an oxygen tension of 17 mm Hg. Prostaglandin E administration was reinstituted with no improvement in oxygenation. The Blalock-Taussig shunt could not be visualized by echocardiography. The patient was taken emergently to the operating suite for placement of another shunt. Cardiopulmonary arrest developed en route, and the patient was placed emergently on cardiopulmonary bypass during the arrest.

A 4-mm Gore-Tex graft was inserted from the right posterolateral aorta to the anterior aspect of the pulmonary artery using continuous 7-0 polypropylene suture. A small patent ductus arteriosus was ligated. Excellent flow was noted in the shunt, but initial attempts to wean the patient from cardiopulmonary bypass failed due to low O_2 saturations. Therefore, a 5-mm shunt was inserted in place of the 4-mm shunt using the same technique. There was excellent filling of the pulmonary vessels. Elevated pulmonary vascular resistance was suspected and treated by high-dose narcotic analgesia with fentanyl, sodium bicarbonate to correct an acid-base imbalance, and hyperventilation with an inspired oxygen fraction of 1.0. The patient was eventually weaned with difficulty from cardiopulmonary bypass. Despite this large central shunt the SaO_2 remained between 70% and 80%.

The patient was stable for approximately 2 hours postoperatively, but then the SaO_2 suddenly dropped to less than 30% and was treated with hand ventilation. Two additional sudden episodes of severe hypoxia developed, followed by bradycardia, hypotension, and near death. These hypoxic paroxysms were not temporally related to interventions by the physician or nursing staff such as repositioning or suctioning, and responded to resuscitative efforts, which included chest compressions, hand ventilation, epinephrine and dobutamine infusions, vasodilator therapy with tolazoline, and alkalinization of the blood. After three such paroxysms with marginal improvement after resuscitation, the patient remained hypotensive (systolic blood pressure, 30 to 40 mm Hg) and hypoxic (SaO_2 between 50% and 60%). Echocardiography revealed a right-to-left shunt across the atrial septum, moderate tricuspid regurgitation, no pericardial fluid collection, and slightly decreased ventricular function. The cardiopulmonary deterioration was attributed to severe pulmonary hypertension resulting in a right-to-left intracardiac shunt. Inhalational NO therapy was instituted during the third hypoxic paroxysm at a concentration of 25 ppm via the endotracheal tube. This resulted in almost immediate improvement in gas exchange and hemodynamics. The oxygen tension increased to approximately 35 to 40 mm Hg (SaO_2, 77% to 80%) and the systolic pressure increased to 60 to 65 mm Hg without additional inotropy. The patient's condition completely stabilized after NO infusion without further hypoxic paroxysms, and NO was decreased to 20 ppm within 2 hours. Both NO and nitrogen dioxide (NO_2) concentrations were measured continuously by chemiluminescence (model 42H; TEI Co, Franklin, MA) during inhalational NO therapy. The NO_2 concentration was measured to be less than 1 ppm throughout the treatment period (with the accepted toxic threshold being 5 ppm) [6]. Nitric oxide was administered as an investigational new drug under a research protocol approved by the Food and Drug Administration. Informed consent was obtained from the child's parents before initiation of NO therapy.

The patient remained hemodynamically stable, and NO administration was discontinued on the second postoperative day. The SaO_2 was between 80% and 90%. The methemoglobin level did not exceed 1.8% in this patient

during NO therapy. Inotropic support was discontinued, and the ventilator was weaned to continuous positive airway pressure on the fourth postoperative day. Echocardiography on the ninth day revealed good ventricular function with both shunts patent. The patient was weaned off all ventilatory support by the 11th day. The patient became tachypneic over the next several days (respiratory rate, 60 to 70 breaths/min) with radiographic evidence of pulmonary overcirculation. Therapy with digoxin and furosemide was instituted with moderate benefit. On the 27th postoperative day, the patient underwent right heart catheterization for attempted coil embolization of the Blalock-Taussig shunt. The pulmonary arterial pressure was 40/30 mm Hg (approximately half of the systemic pressure) and both shunts were patent. Stable catheter position for coil delivery was unable to be achieved, and embolization was not performed. On the 36th postoperative day the patient underwent operative ligation of the central shunt. The SaO_2 decreased from 96% to 92% on an inspired oxygen fraction of 0.4 after shunt ligation. The patient was extubated 1 day after central shunt ligation and discharged 13 days later.

Comment

Inhaled NO at a low concentration of 25 ppm caused rapid and complete reversal of paroxysmal pulmonary hypertensive crises in this newborn with complex congenital heart disease after central shunt insertion. Nitric oxide is believed to have benefited this patient by reducing pulmonary vascular resistance and reversing the right-to-left intracardiac shunt, resulting in more effective pulmonary blood flow with a probable reduction of ventilation-perfusion mismatch, and improved hemodynamics. Inotropic and ventilatory support were significantly reduced immediately after NO therapy. There was no clinical evidence of NO or NO_2 toxicity.

It is likely that the cardiopulmonary arrest suffered en route to the operating suite before central shunt insertion was due to an unrecognized pulmonary hypertensive crisis. At that time the cause of cardiopulmonary deterioration was thought to be secondary to Blalock-Taussig shunt occlusion. This error in diagnosis made by a team experienced in the management of congenital heart disease underscores the difficulty in detecting this condition in the postoperative setting after a palliative shunt procedure and stimulated the presentation of this case report.

We have reported previously the induction of selective pulmonary vasorelaxation without significant systemic effects by inhaled NO in patients evaluated for pulmonary hypertension [2]. Nitric oxide causes smooth muscle relaxation through a cyclic guanosine monophosphate–mediated mechanism, and may cause selective pulmonary vasorelaxation when administered as an inhalational agent by diffusing directly into the smooth muscle of the pulmonary vascular bed [7]. The inactivation of NO by binding to hemoproteins may account for its lack of appreciable systemic effects [7, 8].

Reversal of pulmonary hypertension with low-dose inhalational NO (20 ppm) has been reported in pediatric patients after operations for congenital heart disease [3, 9, 10]. In these reports, pulmonary hypertension was refractory to conventional therapeutic measures but responded to low-dose inhalational NO. Inhaled NO has been shown to cause selective reversal of acute and chronic pulmonary hypertension in large animal models and has also been reported to improve pulmonary hypertension in pediatric patients with idiopathic primary pulmonary hypertension and adult respiratory distress syndrome [4, 5, 11, 12].

Inhaled NO administered in low doses may play a critical role in improving gas exchange and hemodynamics in newborn surgical patients with refractory pulmonary hypertensive crises. Its administration may be less frequently associated with systemic hypotension, which can limit the use of other vasodilating agents.

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