Use of Nitric Oxide for Treatment of Pulmonary Hypertensive Crisis in a Child after Protamine Administration

H. Sakhai, A. Casta
Department of Anesthesiology, Children's Hospital of Pittsburgh and the University of Pittsburgh Medical Center, Pittsburgh, PA 15213

Introduction: Protamine is widely used to reverse heparin. However, protamine administration may cause systemic hypotension, pulmonary hypertension, anaphylactic shock, and cardiovascular collapse. (1) In one recent pediatric study, the only reaction seen was systemic hypotension. This was associated with small heparin dose, large protamine dose, and female gender with an incidence of 1.76%-2.88%. (2) We report a case of a child who developed pulmonary hypertensive crisis after protamine administration who was successfully treated with nitric oxide (NO).

Case Report: A 3-yr-old 12.6 kg nondysmorphic female with a history of atrial septal defect (ASD) and cleft mitral valve presented for repair. The patient had been full-term and was otherwise healthy without failure to thrive or cyanosis. Baseline blood pressure was 108/70 mmHg with a heart rate of 132 bpm. Cardiac exam showed a fixed split S2 and a systolic ejection murmur. Chest was clear bilaterally. A recent echocardiogram showed a large primum ASD, mild right ventricle (RV) dilation and hypertrophy, a left ventricular shortening fraction of 38%, increased flow across the main pulmonary artery (PA) with normal RV pressures, no patent ductus arteriosus, and a mitral valve cleft. With standard monitors in place, anesthesia was induced with sevoflurane in 70% N_2O. Pancuronium 0.15 mg/kg was given prior to an uneventful intubation, and cefazolin 500 mg and methylprednisolone 125 mg were administered. The patient remained stable throughout the pre-bypass period and anesthesia was maintained with isoflurane and intermittent fentanyl boluses. Cardiopulmonary bypass was maintained for 57 minutes. The patient tolerated weaning off bypass without inotropic support and good visual ventricular function was noted. Three minutes after an uneventful dose of cefazolin 500 mg, protamine 75 mg was administered via a peripheral vein over four minutes. Within five minutes of the protamine dose, there was a severe drop in blood pressure from an immediate post-bypass value of 90/70 to 60/30 mmHg. Epicardial ultrasound documented adequate repair, normal ventricular function, and an estimated RV pressure close to systemic. Central venous pressure rose from 9 to 15 mmHg. Heart rate decreased from 140 to 90 bpm and atrial pacing was initiated. Simultaneously it was noted that the RV and PA were significantly distended suggesting acute pulmonary hypertension. At this time PA pressures of 58/30 mmHg approximated systemic pressures. After administration of 2 doses of epinephrine, a dopamine infusion was started at 5 mcg/kg/min and titrated as needed. Concurrently, 5% albumin and packed red blood cells were administered. Along with hyperventilation to an end-tidal PCO_2 of 33 mmHg, the patient also received diphenhydramine 15 mg, sodium bicarbonate 10 meq, and calcium chloride 400 mg. Moreover, a higher peak inspiratory pressure was needed to achieve adequate tidal volumes after protamine administration. There was minimal improvement in the pulmonary pressures, so it was decided to administer inhaled NO. Starting at 40 ppm., a response to NO was seen within 7 minutes with repeat PA pressures normalizing to 24/5 mmHg at that time. The patient was transferred to the pediatric cardiothoracic ICU on dopamine and NO. She remained sedated, muscle relaxed, and mechanically ventilated for the next 18 hours. She was weaned off NO in 19 hours and the trachea was extubated without complications. Dopamine was discontinued shortly thereafter. Her subsequent hospital course remained uneventful and the patient was discharged home on postoperative day four.

Discussion: Pulmonary hypertension due to protamine administration is more common in adults. NO was used to treat protamine related pulmonary hypertension in a 75-yr-old male following coronary artery bypass graft surgery. (3) Post-operative use of NO, prostacycline, and high frequency oscillation ventilation have been described in a 6 week old full-term female following repair of ASD who developed cardiovascular collapse after protamine use. (4) Our patient responded successfully to NO in the operating room. NO should be readily available for the treatment of pulmonary hypertension unresponsive to the usual therapeutic interventions following protamine administration.

Refs:

1. Horrow JC et al., Anesth Analg, 1985
2. Seifert HA et al., Anesth Analg, 2003
3. Ralley FE, Anesth Analg, 1999
4. Boigner H et al., Pediatr Anesth, 2001