CASE REPORT

Sildenafil as a pulmonary vasodilator after repair of congenital heart disease

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Abstract

We describe successful use of enteral sildenafil following surgery for congenital heart disease in three cases. One infant after repair of ventricular septal defect and aortic coarctation had pulmonary hypertension non-responsive to nitric oxide, another infant and 3.5 year child following palliative surgery for congenital heart disease with univentricular physiology were treated with inhaled nitric oxide and had severe systemic desaturations associated with endotracheal suctioning. Therapy with sildenafil reduced pulmonary arterial pressure, prevented episodes of arterial desaturations and allowed weaning from nitric oxide *(Ref. 7)*. Full Text (Free, PDF) *www.bmj.sk*
Key words: congenital heart disease, pulmonary vascular resistance, postoperative care.

Elevated pulmonary vascular resistance (PVR) may complicate postoperative course in children after cardiac surgery. Inhaled nitric oxide (iNO) has a potential to improve management of these patients (1) but there are nonresponders and a rebound pulmonary hypertension on withdrawal can occur in patients who respond to iNO.

Sildenafil, a type 5 phosphodiesterase inhibitor has been shown to act as a pulmonary vasodilatator; single or multiple doses of sildenafil augmented and prolonged the pulmonary vasodilator effect of iNO in children in whom NO withdrawal had previously failed (2–4). Studies assessing the effects of intravenous sildenafil showed that phosphodiesterase-5 inhibition potentiated response to iNO during cardiac catheterization and after open-heart surgery in patients with biventricular physiology (5, 6). One case of administration of sildenafil to a patient after Bidirectional cavopulmonary shunt after withdrawal of iNO, was reported (7).

We present a successful use of enteral sildenafil in three children early after cardiac surgery; in one patient with biventricular and two patients with univentricular physiology.

Case reports

A 4.5-month-old girl with ventricular septal defect and coarctation of aorta with echocardiographic signs of severe pulmonary hypertension underwent corrective surgery foramen ovale was left open to decompress right ventricle. Postoperative therapy included infusion of dopamine, milrinone, sufentanyl and atracurium and controlled hyperventilation. Arterial oxygen saturation (SaO_2) ranged between 80 and 85 % and did not change with an increase of inspired oxygen fraction (FiO_2) to 1.0. Systemic blood pressure (SAP) was 95/50/70 mmHg, pulmonary artery pressure (PAP) 70/45/55 mmHg. Despite the improvement of cardiac output the infant was not weaned from muscle relaxation and sedation because of persistent arterial desaturation and acute increases in PAP to systemic pressure. On postoperative day (POD) 3 therapy with iNO at 20 pm was initiated but did not produce any effect. On 4th day after the surgery sildenafil (Viagra, Pfizer Laboratories) through nasogastric tube was started at dose 0.33 mg/kg every 4 hours. Within the same day reactivity to endotracheal suctioning subsided, PAP/SAP ratio decreased from 0.7–0.85 to 0.5 and SaO_2 increased to 90 %. Patient was extubated on POD9 with PAP/SAP ratio of 0.4, and sildenafil was discontinued uneventfully on POD11.

The second patient was a 3.5 year-old girl with heterotaxy, double outlet right ventricle and mitral atresia who underwent pulmonary artery banding in infancy. Later, progression of cardiac decompensation and cyanosis have been observed, however the second stage of univentricular repair was delayed due to

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recurrent respiratory infections and missed outpatient and hospital visits. Patient underwent three cathetrizations; the latter was performed in 3 years of age and showed SaO_2 of 68 %, PAP 28/17/23 mmHg, atrial pressure 10 mmHg, Qp/Qs 0.52, and PVR 3.4 j/m^2. The patient was indicated for surgery as a high-risk candidate. During surgery pulmonary artery band was removed and bilateral bidirectional cavopulmonary anastomosis was created. The patient was weaned from cardiopulmonary bypass with superior vena cava pressure 20 mmHg, atrial pressure 5 mmHg and resulting transpulmonary gradient 15 mmHg. The SaO_2 was 83 % on FiO_2 of 1.0.

Postoperatively, the patient was on infusion of dopamine having SaO_2 of 80 % on FiO_2 0.5. Following endotracheal suctioning, pulmonary hypertensive episode with arterial desaturation to 55–60 % and systemic hypotension, occurred. Therapy with sufentanyl, atracrium, and iNO was initiated, however decreases in SaO_2 followed every endotracheal suctioning and required an increase of FiO_2 and iNO from 0.5 to 1.0 and from 10 ppm to 30 ppm, respectively. On POD2 therapy with enteral sildenafil at dose 0.35 mg/kg every 6 hour was initiated. The SaO_2 stabilized and iNO was stopped on POD4. On POD7 patient was extubated with SaO_2 of 80–85 %. Therapy with sildenafil was continued during the period of oxygen dependency and lasted 20 days.

The third patient, an infant with double outlet right ventricle and mitral atresia underwent pulmonary artery banding at the age of 10 days; cardiac type of total anomalous pulmonary vein drainage was unobstructive and was not corrected. At 6 months of age, the infant became severely cyanotic; echocardiography and cathetrization revealed obstruction to pulmonary venous drainage with pressure gradient of 22 mmHg. At operation pulmonary artery band was removed and pulmonary venous confluence was anastomosed to the atrium. SaO_2 was 75–80 % on FiO_2 1.0, SAP 74/48/58 mmHg, PAP 54/32/43 mmHg. Postoperative therapy included infusion of dopamine, sufentanyl and atracurium and controlled hyperventilation. Patient was hemodynamically stable with SaO_2 of 80% on FiO_2 0.5. On POD2 pulmonary hypertensive episode occurred; the SaO_2 dropped to 60 %, PAP exceeded SAP by 10–15 mmHg. Therapy with iNO at 20 ppm was started. On POD 3 following further two episodes of severe arterial desaturation associated with endotracheal suctioning, therapy with enteral sildenafil at dose 0.35 mg/kg every 6 hour was initiated. The SaO_2 stabilized, iNO was discontinued on POD4, and the patient underwent pulmonary artery banding on POD7. After extubation on POD11, therapy with sildenafil was discontinued uneventfully.

Discussion

We report the use of enteral sildenafil in one patient following aortic coarctation and ventricular septal defect repair in whom pulmonary hypertension failed to respond to iNO. Favorable response to sildenafil suggests that in some patients overactivity of cGMP-degrading phosphodiesterase-5 may be more important risk factor for postoperative pulmonary hypertension than a decreased endogenous nitric oxide production.

We also report the use of enteral sildenafil in two patients with single ventricle physiology. Both patients had elevated PVR and thus were high risk candidates for surgery. In the early postoperative period elevations of PVR resulted in a severe impairment of pulmonary perfusion. Episodes of arterial desaturation were nitric oxide reversible however, enteral sildenafil prevented further episodes and allowed weaning from iNO. We can also speculate whether preoperative administration of sildenafil to our high-risk patients would have improved pulmonary vascular hemodynamics and reduced the risk of pulmonary hyperreactivity in postoperative period.

There have been concerns regarding adverse effects of intravenous sildenafil on gas exchange and systemic hemodynamics (5, 6). No adverse effects were observed, even when enteral sildenafil was used concomitantly with iNO. Furthermore, enteral administration allowed continued therapy following extubation.

Conclusion

Our experience suggests that enteral sildenafil either alone or in combination with nitric oxide may improve pulmonary hemodynamics and prevent hypertensive episodes in children undergoing biventricular as well as univentricular repair of congenital heart disease.

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