Use of prostaglandin E₂ in management of transposition of great arteries before balloon atrial septostomy

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SUMMARY Fifteen infants with transposition of the great arteries and severe hypoxaemia were treated with prostaglandin E₂ infusions before atrial septostomy was performed. Twelve patients had simple transposition and three had small ventricular septal defects. The infusion resulted in a highly significant increase of P_aO₂ from 22±3 mmHg to 37±5 mmHg within one to two hours. Only one patient did not respond to treatment. P_aO₂ remained constantly above 30 mmHg throughout prostaglandin infusion. After balloon atrial septostomy prostaglandin administration was stopped. Only two patients required reinfusion within 24 hours after septostomy because of a decrease of P_aO₂ below 25 mmHg. At angiocardiology before balloon septostomy the ductus was of aortic size in eight, and of about half the aortic diameter in six patients. In one infant the ductus was closed. One infant had to undergo early ductus ligation because of heart failure. In 10 of 11 infants who have undergone total correction the initially large ductus had closed spontaneously.

Many patients with transposition of the great arteries are admitted to cardiac units in a state of hypoxia and acidosis within their first days of life and have to undergo emergency catheterisation.

Even with technically adequate septostomy some patients show a poor rise in their oxygen saturation and have to undergo early corrective or palliative surgery.¹⁻³ Recently, however, prostaglandin E₁ has been shown in a number of these cases to be effective in increasing P_aO₂ after balloon septostomy.^{1,2,4} This is because of ductal enlargement and perhaps a decrease in pulmonary vascular resistance.^{1,2}

As it is not possible in our small unit to proceed with emergency catheterisation within hours after admission we tried to avoid prolonged severe hypoxia before catheterisation and balloon atrial septostomy by infusing prostaglandins.

This report gives our experiences with a group of 15 patients with haemodynamically simple transposition who were infused with prostaglandin E₂ (Upjohn) before creation of an atrial septal defect.

Subjects and methods

From April 1980 to November 1981, 18 newborn babies in whom the provisional diagnosis of transposi-

tion of the great arteries was made were admitted to the Children's Hospital, University of Graz. Out of this group, 15 infants were severely hypoxic (P_aO₂ below 25 mmHg) and acidotic (pH below 7.30). Ages at admission varied from 3 to 38 hours (mean 15 hours). Twelve of them had transposition with intact ventricular septum and three had small ventricular septal defects in addition. Mean birthweight was 3200 g and mean gestational age was 40 weeks.

All were treated with prostaglandin infusion before catheterisation. Prostaglandin E₂ was initially infused at 0.1 µg/kg per min in 5% dextrose solution into a large peripheral vein. P_aO₂ samples were taken from right or left radial artery punctures at hourly intervals. As soon as P_aO₂ values over 30 mmHg were found, prostaglandin E₂ was reduced to 0.05 µg/kg per min and later to 0.025 µg/kg per min. After termination of the infusion blood gases were checked using capillary PO₂.⁵ The two-tailed Student's *t* test was used for statistical analysis.

During prostaglandin infusion, heart rate, respiratory rate, blood pressure, and temperature were continuously monitored, and apnoeic spells, flushing, or muscle twitching were noted. All patients were paralysed, intubated, and ventilated (F_iO₂ 50%) throughout catheterisation. They received a premedication of 1 mg/kg of pethidine and 0.01 mg/kg of atropine.

Accepted for publication 30 November 1982

During catheterisation pressure recordings were made using a Siemens-Elema Mingograf 82 and oximetry was done using a Micro Reflection Oximeter (American Optical Co.). All babies had at least a right and left ventricular contrast medium injection using Renografin 60%. We tried to estimate the ductal size and quantity of aortic to pulmonary artery shunting angiographically. Oximetry was used to detect the presence of any shunt at atrial level. If oxygen saturation values of ascending aorta (Ao), a pulmonary vein (PV), and superior vena cava (SVC) were available we tried to calculate the anatomical left to right shunt using the formula: $(Ao-SVC)/(PV-SVC) \times 100 = \% Q_s$.⁶ After oximetry and pressure recordings a balloon atrial septostomy was performed through a right femoral venous cutdown using a 5 French Edwards septostomy balloon catheter filled with 3 ml diluted contrast medium.

Prostaglandin E_2 infusions were stopped immediately after balloon septostomy and were only started again if capillary PO_2 dropped below 30 mmHg. Clinical signs of persistence of the ductus were carefully noted after prostaglandin withdrawal. PO_2 was measured after balloon septostomy up to the time of corrective surgery at regular intervals.

Results

On admission all babies had an arterial oxygen tension of between 17 and 25 (mean 22 ± 3) mmHg. The ages at cardiac catheterisation ranged from 6 to 50 hours (mean 28 hours). The duration of prostaglandin infusion before catheterisation and balloon septostomy was four to 24 hours (mean 11 hours) including the time of cardiac catheterisation.

Within one to two hours after initiation of prostaglandin E_2 the arterial P_{aO_2} rose significantly ($p < 0.001$) up to between 30 and 48 (mean 37 ± 5) mmHg (Fig. 1). Only one patient did not respond to treatment and his P_{aO_2} remained below or at 25 mmHg. Fourteen patients developed signs of a haemodynamically significant ductus with murmurs and bounding pulses. Side effects of prostaglandin application were episodes of apnoea in four, muscle twitching in two, and a generalised flush and fever in one patient. These side effects were easily controlled by stopping prostaglandin E_2 for 15 minutes and then reducing the rate of administration. In two patients prolonged patency of the ductus with heart failure required medical treatment. One of them had to undergo ductus ligation at the age of 5 days while in the other one the ductus closed spontaneously at the age of 3 weeks. Two patients who initially had responded well to prostaglandin E_2 infusion had to be reinfused because of a gradual decrease in PO_2 values after septostomy. Weaning from prostaglandins was

Fig. 1 P_{aO_2} values before and after intravenous infusion of prostaglandin E_2 .

possible after 11 and 16 days, respectively.

At cardiac catheterisation left atrial pressures varied from 5 to 22 mmHg (mean 13 ± 6 mmHg). Gradients of greater than 3 mmHg between left and right atrium were found in 11 of 15 patients. Gradients from these patients ranged from 5 to 10 mmHg (mean 7 mm). By oximetry a left to right interatrial shunt was calculated in 12 of 15 patients. Values ranged from 25 to 79% (mean 58 ± 18) of systemic blood flow. Fig. 2 shows the interatrial pressure gradients plotted against the left to right atrial shunt volume in 12 patients in whom shunt calculations were possible. On angiography using lateral projections during right ventricular

Fig. 2 Relation between left to right shunts at atrial level and interatrial pressure gradients.

or aortic contrast medium injections the ductus was of aortic size in eight patients and was half the aortic size in another six patients at the point of central constriction. In all these 14 patients angiography showed a large aorta to pulmonary artery shunt.

Discussion

The use of prostaglandins in transposition of the great arteries has been reported.^{1-3 7-11} Some authors however^{7 8} who present large numbers of cases do not state whether prostaglandins were infused before or after balloon septostomy. All our patients were treated with intravenous prostaglandin E₂ before balloon septostomy was performed.

In transposition with intact interventricular septum any increase in pulmonary blood flow increases pulmonary venous return, left atrial pressure, and left to right interatrial shunt in the presence of an adequate interatrial communication.^{6 12 13} As the total left to right and right to left shunts have to be equal in transposition, a ductal shunt from aorta to pulmonary artery increases the interatrial left to right shunt by the same amount, thereby increasing arterial oxygen saturation.^{2 6}

The principle of increasing arterial oxygen saturation by ductus dilatation has been applied to hypoxic newborns with simple transposition after balloon septostomy.^{1-4 9-11 14} All of these patients probably had adequate interatrial communications and open ducts. While most patients initially responded excellently to prostaglandin infusions, weaning from prostaglandins was only possible in a small number of patients.^{1 3 14} If early operation can be performed within the first weeks the patient will benefit from this treatment. Failure to raise arterial PO₂ in spite of a dilated ductus and an atrial septal defect can be attributed to persistence of high pulmonary vascular resistance.^{1 3 15}

We administered prostaglandin E₂ to our patients with transposition because we had to defer catheterisation and balloon septostomy for a mean of 13 hours after admission. The use of prostaglandins for hypoxia in transposition before septostomy has so far only been reported twice.^{10 11} Our patients with simple transposition showed a significant ($p < 0.001$) rise of P_aO₂ within one to two hours after prostaglandins were started. While prostaglandin infusion continued, oximetry and angiography showed a moderate to large aortic/pulmonary shunt via the ductus and a left to right shunt at atrial level. Pressure recordings showed high left atrial pressures and interatrial gradients, with a mean of 7 mmHg in the majority of patients. In the presence of high interatrial gradients any left to right interatrial shunt is probably via a regurgitant valve of foramen ovale.¹⁶

The site of prostaglandin infusion does not seem to

affect its action upon the ductus.^{1 10 11} Administration via umbilical arterial or venous catheters^{1 3 4} should be avoided to prevent infection and late portal vein occlusion. Side effects of prostaglandins seem mainly to be related to dosage.¹¹ Heart failure resulting from prolonged ductus patency can be a rare complication and it occurred in two of our patients. Both required medical treatment for heart failure and one had to undergo ligation.

In conclusion, prostaglandin E₂ can be used safely to treat hypoxic patients with simple transposition before balloon atrial septostomy. This could be especially helpful for smaller units which have to defer catheterisation and during the transport of sick neonates.

The statement that prostaglandin can only produce an adequate rise of P_aO₂ in the presence of a large interatrial communication^{1 3} cannot therefore be correct. Heart failure caused by ductus patency may be a complication of prostaglandin treatment. We further recommend a trial of prolonged low dose treatment after balloon septostomy if adequate P_aO₂ levels cannot be achieved immediately.

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