Pulmonary artery growth during treatment with oral prostaglandin E₂ in ductus dependent cyanotic congenital heart disease

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SUMMARY Growth of the pulmonary arteries was assessed in 11 patients with cyanotic congenital heart disease treated with oral prostaglandin E₂. Each patient was dependent on patency of the ductus arteriosus for maintenance of the pulmonary circulation. Measurements were made initially from angiographic data obtained in the neonatal period. Subsequent assessments were made at the time of surgery after an interval of 2-8 months, during which time all the infants had gained weight normally. Comparisons were made with data obtained from 13 normal necropsy specimens. In only 4 of the 11 patients had the pulmonary arteries grown appreciably during the treatment period. In 2 patients no growth occurred, while in 5 patients the pulmonary arteries had actually become smaller. It had been hoped that the pulmonary arteries would grow in all 11 patients during this period, facilitating later surgical intervention. In patients with ductus-dependent cyanotic congenital heart disease, the prolonged use of oral prostaglandin E₂ should be restricted to patients in whom the pulmonary arteries are too small to allow a palliative operation to be performed initially.

The mortality rate for infants with cyanotic congenital heart disease associated with reduced pulmonary blood flow remains high.¹ Pulmonary blood flow may be increased by an aortopulmonary anastomosis but this procedure is technically difficult in the neonatal period.² In patients whose pulmonary circulation is dependent on the patency of the ductus arteriosus, treatment with oral prostaglandin may be used to maintain an adequate pulmonary blood flow. This enables surgical intervention to be postponed.³ If the pulmonary arteries grow during this period a palliative aortopulmonary anastomosis will become technically less difficult. It can then be expected to be associated with fewer late complications—such as kinking of a main pulmonary artery. There is little information available on the rate of growth of the main pulmonary arteries in either the normal infant or in infants being treated with oral prostaglandins. The present study was carried out in order to assess growth of the pulmonary arteries as assessed by measurements of the right main pulmonary artery (RMPA) in a series of patients treated with oral prostaglandin E₂ and in a control series of normal infant hearts.

Patients and methods

Necropsy specimens of 13 normal hearts were

studied. Specimens were excluded from this study if the cause of death was recorded as congenital diaphragmatic hernia or if there was a record of multiple congenital anomalies. Causes of death most often recorded were acute respiratory disease, septicaemia, and sudden infant death syndrome. In these specimens the RMPA was measured internally by the use of calibrated probes.

The case records of 28 patients who had been treated with oral prostaglandin E₂ were reviewed. There were 11 patients with ductus-dependent pulmonary circulations in whom it was possible to obtain sequential measurements of the RMPA during treatment. These patients were usually stabilised on prostaglandin E₂, 125 µg four hourly. In the neonatal period, the diameter of the RMPA was measured just proximal to its first division on anteroposterior projections of the cineangiograms. Correction was made for magnification. Subsequent assessment was made by one of us (D I H) at the time of surgical intervention (usually palliative aortopulmonary anastomosis, Table). The haemoglobin concentration was noted at the time of the neonatal cardiac catheterisation and again at operation.

Results

In normal necropsy specimens there was a linear

Table Clinical summary

Case	Diagnosis	Right main pulmonary artery diameter (mm)		Age at operation (months)	Operation	Outcome
		Neonatal catheter	At operation			
1	Severe tetralogy of Fallot	3.7	5	7½	Waterston anastomosis	Late death
2	Tricuspid atresia	5.6	4.5	4	Waterston anastomosis	Death from postoperative sepsis
3	Univentricular heart with pulmonary atresia	5	7	3	Waterston anastomosis	Alive
4	Hypoplastic right heart with critical pulmonary stenosis	5.7	4	2½	Waterston anastomosis	Alive
5	Pulmonary atresia with intact septum	5	8	7	Reconstruction of right ventricular outflow tract	Died on operating table
6	Severe tetralogy of Fallot	4	4	2½	Waterston anastomosis	Alive
7	Pulmonary atresia with ventricular septal defect	4	4	4½	Open infundibulectomy and transannular patching	Alive
8*	Situs inversus and pulmonary atresia with ventricular septal defect	5.6	4	6	Waterston anastomosis	Alive
9	Pulmonary atresia with ventricular septal defect	4.2	6	2	Innominate to pulmonary artery shunt (Goretex)	Died on operating table
10	Pulmonary atresia with ventricular septal defect	5.6	4	4	Reconstruction of right ventricular outflow tract	Alive
11	Univentricular heart (LV type) and pulmonary atresia	4.5	4	2	Reconstruction of right ventricular outflow tract	Alive
					Waterston anastomosis	Alive

* In this case, measurements were taken from the left main pulmonary artery.

relationship between the internal diameter of the RMPA and the infant's weight (Fig. 1). As these diameters were measured on formalin-fixed specimens there may have been some shrinkage at necropsy but this would not have affected the linear nature of the relationship between the diameter of the RMPA and the infant's weight.

The diagnoses in the 11 patients studied are shown

in the Table. The initial measurements of the RMPA were all taken in the early neonatal period. The operative measurements were taken between 2 and 8½ months of age. All the patients studied gained weight satisfactorily preoperatively, but the RMPA development during the same period was unpredictable (Fig. 2). In 4 patients the RMPA grew, in 2 there was no growth, and in the remaining 5 patients

Fig. 1 Correlation between the diameter of the RMPA (necropsy specimens) and body weight in 13 normal infants.

Fig. 2 Relationship of RMPA development and increase in body weight during treatment with oral prostaglandin E_2 in 11 patients.

the RMPA diameter actually decreased. The changes in the haemoglobin concentration from the time of the initial catheter to the time of the operation were studied and compared with the RMPA development during the same period. There was no correlation.

Discussion

During the period of this study the policy in this unit has been to treat patients with ductus-dependent pulmonary circulations with oral prostaglandin E_2 . As the patients themselves continued to grow satisfactorily we had hoped that the pulmonary arteries would do likewise, facilitating later surgical intervention. Unfortunately weight gain was not always associated with pulmonary artery growth. Silove *et al.*³ reported a study in which prolonged oral prostaglandin treatment was given only to patients in whom the pulmonary arteries were considered too small to attempt a shunt operation initially. In their series there was evidence of pulmonary artery growth in 5 patients, all of whom had very small pulmonary arteries at birth (RMPA 3 mm diameter or less).

We were surprised to find that the RMPA diameter had actually decreased in 5 of our patients. We speculate that the calibre of the ductus had gradually decreased in these patients, despite the use of oral prostaglandin therapy. A progressive reduction in pulmonary perfusion would then have followed. This in turn could have resulted in a gradual decrease in the size of the main branch pulmonary arteries.

A decrease in the diameter of the RMPA might be expected to be associated with an increase in tissue hypoxia which in turn would result in an increase in haemoglobin concentration. In this series no correlation was found between pulmonary artery development and changes in haemoglobin concentration during the same periods of time.

If the RMPA at birth is large enough to offer a reasonable prospect of achieving a technically satisfactory shunt, there is little evidence to suggest

that starting oral prostaglandin treatment and postponing surgery improves the long-term outcome. Moreover the institution of prostaglandin therapy often leads to a prolonged time in hospital and to frequent drug administration after discharge. The long-term effects of these highly vaso active agents are as yet poorly defined. In our surgical experience patients thus treated have had a high incidence of tissue friability.

Prostaglandin treatment has contributed greatly to the management of infants with duct-dependent cyanotic congenital heart disease. However, the optimum role of long-term oral prostaglandin E_2 in management has yet to be defined. In patients with main branch pulmonary arteries more than 4–5 mm in diameter there is little to be gained by postponing palliative surgery. It is the small group of inoperable patients with main branch pulmonary arteries of less than 3–4 mm diameter that may benefit from long-term oral prostaglandin therapy. Postponing surgery may result in some patients becoming more difficult surgical prospects, as was the case in the 5 patients in our series in whom the RMPA diminished in size. Thus we would advocate that long-term oral prostaglandin therapy be restricted to those patients in whom the small size of the pulmonary arteries precludes early operation.

References

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