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ORIGINAL ARTICLE

Prostaglandin E2 After Septostomy for Simple Transposition

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Abstract In simple transposition of the great arteries (sTGA), balloon atrial septostomy is performed prior to arterial switch to improve mixing of systemic and pulmonary circulations. Following septostomy, some patients are also given prostaglandin E2 (PGE2) until surgical repair. The aims of our study were to identify how often PGE2 is given after septostomy, the indications for starting PGE2, and the effect this has on postoperative outcome. The study was a retrospective review of infants born with sTGA between 2000 and 2005, who underwent arterial switch at Yorkhill Children's Hospital, Glasgow. Over a 5-year period, 26 infants (16 male) with sTGA underwent septostomy. There was a significant rise in mean oxygen saturation following septostomy (mean, 61.4 ± 11.5% before, 81.5 ± 9.4% after; $p < 0.05$). Four of 26 (15%) did not receive PGE2 at all (group 1) and 8 of 26 (30%) received PGE2 before but not after septostomy (group 2). A total of 14 of 26 infants (54%) were given PGE2 following septostomy. This comprised 11 who received PGE2 before and after septostomy (group 3) and 3 who did not receive PGE2 prior to septostomy but did after (group 4). Groups 2 and 3 were compared directly, as they both received PGE2 before septostomy. In group 3, oxygen saturations were lower when PGE2 was started compared with saturations immediately after septostomy (45 ± 23.6% vs. 80 ± 10.3%; $p < 0.05$). Groups 2 and 3 showed no difference in atrial gap after septostomy (9.4 ± 3 vs. 8 ± 1 mm; $p > 0.05$). Fifty percent of infants in group 3 underwent echocardiography prior to restarting PGE2, which revealed a patent arterial duct in all but one patient. Despite PGE2, Group 3 had lower saturations at arterial switch compared with Group 2 (71 ± 14% vs. 82 ± 8%; $p < 0.05$). No difference was observed between group 2 and group 3 with regard to length of cardiopulmonary bypass (group 2, 173 ± 101.4 min, vs. group 3, 157.9 ± 42.1 min; $p > 0.05$). However, the Intensive Care Unit stay was longer for patients who received PGE2 following septostomy (8.5 ± 10.3 vs. 5 ± 0.93 days; $p < 0.05$). Total postoperative stay was also longer for infants who received PGE2 after septostomy (26.8 ± 14.3 vs. 16.8 ± 6.3 days; $p < 0.05$). In conclusion, the use of pulse oximetry has led to an increase in the administration of PGE2 after septostomy. PGE2 administration was associated with a longer ICU stay. The association between administration of PGE2 and longer postoperative stay supports the approach of early surgical repair with minimal preoperative medical intervention.

Keywords Transposition of the great vessels · Prostaglandin E2 · Septostomy · Atrial gap

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Introduction

Simple transposition of the great arteries (sTGA) occurs in approximately 3 neonates per 10,000 live births per year [1]. For survival until definitive surgery, mixing of the

pulmonary and systemic circulations is essential. This may be achieved at the ductal and atrial level. Balloon atrial septostomy was first described in the 1960s [10] and is now widely practiced, although recently concerns have been raised about long-term neurological sequelae [9]. Intravenous prostaglandin E2 (PGE2) to maintain ductal patency was first reported in 1976 [10]. Despite septostomy, a number of infants are given PGE2 to maintain ductal patency prior to arterial switch. The aims of our study were to determine how frequently PGE2 was administered following septostomy, the reasons for starting PGE2, and whether this affected postoperative outcome.

Materials and Methods

The notes on all infants with sTGA born between January 1, 2000, and January, 1, 2005, and who underwent arterial switch at Yorkhill Children's Hospital, Glasgow, were reviewed. Two infants were excluded, as they had naturally wide atrial gaps and did not undergo septostomy. The following parameters were noted for the remaining infants: size of atrial gap after septostomy; ductal patency before and after septostomy; oxygen saturation before septostomy, after septostomy, and prior to arterial switch; dose of PGE2; and when started. Atrial gap size and ductal patency were reviewed on archived echocardiograms. Atrial gap size was measured as the maximum distance between the edges of the atrial gap in any view. Ductal patency was identified using colour flow Doppler. Not all echocardiographic images of ductal patency were archived, therefore written reports and operative notes were also consulted.

Results

Twenty-six infants with sTGA were identified (16 male). All were diagnosed postnatally. The patients were divided into four groups.

Group 1 ($n = 4$): Infants who did not receive PGE2 at any time.
Group 2 ($n = 8$): Infants who received PGE2 before but not after septostomy.
Group 3 ($n = 11$): Infants who received PGE2 before and after septostomy.
Group 4 ($n = 3$): Infants who did not receive PGE2 before but did receive PGE2 after septostomy.

In total, 14 of 26 infants with sTGA were given PGE2 after septostomy (54%). Groups 2 and 3 were directly compared, as both received PGE2 before septostomy.

Before Septostomy

There were no differences between group 2 and group 3 with regard to gestation, age at presentation, maximum dose of PGE2 administered, oxygen saturations at presentation, ductal patency, and assisted ventilation (see Table 1). Infants in group 3 were heavier at birth than those in group 2 (3.9 ± 0.4 vs. 3.3 ± 0.4 kg; $p < 0.05$). One infant in group 3 was acidotic and hypotensive prior to septostomy but responded to fluid resuscitation and PGE2. Overall PGE2 was well tolerated prior to septostomy. One infant (group 3) had a persistent pyrexia that resolved within hours of stopping PGE2.

After Septostomy

A rise in oxygen saturation on pulse oximetry together with appearances on echocardiography indicated a successful septostomy. Mean oxygen saturation after septostomy in group 2 was $82.75 \pm 8.6\%$, compared with $61 \pm 11\%$ before ($p < 0.05$). Mean oxygen saturation after septostomy in group 3 was $80.3 \pm 10.3\%$, compared with $61 \pm 11\%$ before ($p < 0.05$). There was no difference between group 2 and group 3 with respect to atrial gap size, rise in oxygen saturation immediately following septostomy, or ductal patency (see Table 1). In all patients PGE2 was stopped following septostomy.

Group 3

The time between stopping and restarting PGE2 was highly variable (mean, 39.6 ± 62.5 h). In all but one patient, PGE2 was restarted as a result of desaturation on pulse oximeter (mean saturation immediately after septostomy, $80.3 \pm 10.3\%$; mean saturation at the time of restarting PGE2, $44.5 \pm 22.5\%$; $p < 0.05$). The remaining infant had no fall in oxygen saturation but was noted to have a prolonged capillary refill time, and blood gas revealed a metabolic acidosis. No other cause for decompensation was found and PGE2 was restarted, with clinical improvement.

Oxygen was administered to all infants with desaturation but did not increase oxygen saturation in any of them. In every case, the administration of PGE2 resulted in a significant rise in oxygen saturation ($44.5 \pm 22.5\%$ before compared with $70.9 \pm 14.4\%$ after; $p < 0.05$). Only five infants in group 3 underwent echocardiography to assess ductal flow before restarting PGE2. In four, the ducts were found to be widely patent on color Doppler. In the remaining infant repeat echocardiography after administration of PGE2 showed the duct to have reopened. However, at the time of arterial switch, even with PGE2 and a patent duct, group 3 still had significantly lower

Table 1 Comparison between group 2 and group 3

Variable	Group 2 ($n = 8$)	Group 3 ($n = 11$)	p Value
Gestation (weeks)	40.2 ± 1.1	40 ± 0.8	>0.05[a]
Birth weight (kg)	3.3 ± 0.4	3.9 ± 0.4	**<0.05**[a]
Age at presentation (h)	6.87 ± 9.2	9.2 ± 19.8	>0.05[a]
Maximum PGE2 dose pre-BAS (ng/kg/min)	55	41	>0.05[a]
No. of infants acidotic pre-BAS	1 (12.5%)	0	N/A
No. of infants hypotensive pre-BAS	1 (12.5%)	0	N/A
No. of infants intubated and ventilated pre-BAS	6 (75%)	9 (81%)	>0.05[a]
No. of pre-BAS PGE2 adverse reactions	0	1 (9%)	N/A
No. of average saturations pre-BAS	61 ± 11	61 ± 11	>0.05[b]
No. of infants with patent ducts pre-BAS	6 (87.5%)	10 (91%)	>0.05[b]
Atrial gap post-BAS (mm)	9.4 ± 3	8 ± 1	>0.05[b]
Average saturations immediately post-BAS	82 ± 8%	80 ± 10%	>0.05[b]
No. of infants with PGE2 stopped immediately post-BAS	3 (37.5%)	4 (36.3%)	>0.05[b]
PGE2 duration post-BAS (h)	38.2 ± 50.8	32.1 ± 58.4	>0.05[b]
No. of infants with PGE2 restarted	0	11	N/A
Saturations at switch	82 ± 8%	71 ± 14%	**<0.05**[a]
Cardiopulmonary bypass duration (min)	173 ± 101.4	157.9 ± 42.1	>0.05[a]
Postoperative inpatient stay (days)	16.8 ± 6.3	26.8 ± 14.3 (+group 4)	**<0.05**[a]
ICU stay (days)	5 ± 0.93	8.5 ± 10.3 (+group 4)	**<0.05**[a]

PGE2 prostaglandin E2, *BAS* balloon atrial septostomy, *N/A* not applicable

Bold type indicates significant difference

[a] Mann–Whitney *U*-test

[b] ANOVA

saturations than group 2 (70.9 ± 14.4% compared with 82.6 ± 8.45%; $p < 0.05$).

The maximum PGE2 dose used following septostomy in group 3 was lower than that used before septostomy (12 ng/kg/min compared with 55 ng/kg/min; $p < 0.05$). None of these infants developed apnea or other adverse reactions during administration of PGE2 after septostomy. All infants remained on PGE2 as inpatients until switch. In contrast, 50% of group 2 were discharged home preoperatively. It was not possible to review ductal patency prior to switch in group 2, as most infants in this group underwent echocardiography only to verify coronary anatomy preoperatively.

Features of Group 1: No PGE2 Before or After Septostomy

The age at presentation ranged between 14 h and 4 weeks (mean, 2 weeks). Mean oxygen saturation at presentation was 80% before septostomy (range, 80–92%), 83% after septostomy (range, 70–95%), and 75% at the time of arterial switch (range, 55–95%). In all infants, the ducts were noted to be patent on echocardiography from birth, after septostomy, and up to the time of switch, when they were ligated.

Features of Group 4: PGE2 After Septostomy but Not Before

The age at presentation ranged between 5 and 72 h of life (mean, 38.5 h). Mean saturation was 71% at presentation (range, 70–75%), 83% after septostomy (range, 80–85%), and 81% at switch (range, 70–90%). PGE2 was started after septostomy secondary to a fall in saturations in all three patients (mean, 63%; range, 50–75%). Two infants underwent echocardiography immediately before restarting PGE2, and in both the duct was patent.

After Arterial Switch

The total postoperative inpatient stay was significantly longer for the groups that received PGE2 after septostomy than for group 2 (26.8 ± 14.3 vs. 16.8 ± 6.3 days; $p < 0.05$). This was partly due to a prolonged ICU stay for one patient in group 3 who developed a wound infection. However, even excluding this patient, the groups that received PGE2 after septostomy still had a longer postoperative period. Intensive care unit stay was also longer (8.5 ± 10.3 vs. 5 ± 0.93 days; $p < 0.05$). However, there was no significant difference in cardiopulmonary bypass times between the two groups

(173 ± 101.4 vs. 157.9 ± 42.1 min; $p > 0.05$).There was one death in group 3, a patient who died 15 days after surgery, with occluded left and right coronary arteries.

Discussion

At many pediatric cardiac centers it is standard practice to perform a balloon atrial septostomy as palliation for sTGA prior to arterial switch, regardless of ductal patency and presentation of saturation. It is usually safe to perform the procedure at the cotside [8]. Recently, however, concerns have been raised regarding potential long-term neurological sequelae [9]. A previous study showed no correlation between atrial gap size and increase in systemic saturation following septostomy [3]. However, the study did not explore whether atrial gap size affects the commencement of PGE2 after septostomy.

Three previous studies have addressed the administration of PGE2 after septostomy. Two studies were before the era of pulse oximetry. Beitzke et al. [2] reported that 2 of a cohort of 15 patients (14%) required PGE2 after septostomy as a result of a fall in arterial oxygen pressure to <25 mmHg. Similarly, over a four year period, Henry et al. [6] reported that 4 of 43 patients (9%) with sTGA required PGE1 after septostomy to improve oxygenation and relieve acidosis. Our study indicates that the use of pulse oximetry has led to a large increase in the administration of PGE2 following septostomy. An important question is why saturations should fall after septostomy? One possibility is that the atrial gap may contract after septostomy, i.e. it is not actually torn but stretched and increased ductal flow stimulated by PGE2 improves mixing and systemic saturations. Another may be the effect of PGE2 on pulmonary vasculature. Although PGE2 has little effect on pulmonary arteries, prostaglandin receptors are known to exist on pulmonary veins. PGE2 has been shown to relax contracted human and pulmonary venous specimens in vivo [7, 12].

A recent study [5] showed that early cessation of PGE1, less than 2 h after septostomy, was associated with greater rebound hypoxemia than when prostaglandin was stopped more than 2 h following septostomy. The proportion of infants restarting prostaglandin after septostomy was similar to our findings (44% vs. 57% in our study). The authors speculated that PGE1 may have a direct effect on pulmonary vasodilation and pulmonary blood flow. Nevertheless, in our study, administration of oxygen, a potent pulmonary vasodilator, failed to improve oxygen saturations in group 3 prior to restarting PGE2.

An important finding of our study was the association between the administration of PGE2 following septostomy and a prolonged postoperative stay. Surgeons often comment that the administration of intravenous PGE2 seems to result in tissue edema. Theoretically this could make surgery more difficult, although our data did not illustrate longer cardiopulmonary bypass times. In addition, tissue edema may make it harder for a child to wean from the ventilator postoperatively, as well as impair wound healing.

Conclusion

The introduction of pulse oximetry has resulted in a large increase in the number of babies with sTGA receiving PGE2 following septostomy. Not only is PGE2 associated with side effects during administration, but our study suggests that it may be associated with a longer postoperative stay. There has been a move toward earlier arterial switch for babies with sTGA [4]. The concerns about the long-term neurological consequences of septostomy, together with our findings of an association between PGE2 administration and longer postoperative stay, support the approach of early arterial switch with minimal preoperative invasive or medical intervention.

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