ORIGINAL ARTICLE

Transporting newborn infants with suspected duct dependent congenital heart disease on low-dose prostaglandin E1 without routine mechanical ventilation

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Aim: To evaluate the safety of transporting newborn infants with suspected duct dependent congenital heart disease (CHD) treated with prostaglandin E1 (PGE1) without routine mechanical ventilation.

Methods: A retrospective population-based audit of newborn infants with suspected CHD transported on PGE1 by the New South Wales newborn and paediatric Transport Service from 1995 through 2005.

Results: Mechanical ventilation was not used prior to treatment with PGE1 in 94 (31%) of the 300 infants. The indications for mechanical ventilation in the remaining 206 infants (69%) included elective mechanical ventilation because of the intention to use PGE1 (n = 125) and severe hypoxaemia, acidosis or cardiorespiratory failure prior to commencing PGE1 (n = 81). 16 (17%) of the 94 infants who were not ventilated initially required mechanical ventilation before transport because of apnoea, which developed within one hour of commencing PGE1. 2 (2.6%) of the 78 infants transported without mechanical ventilation developed apnoea in transit and both were receiving ≥ 15 ng/kg/min of PGE1. Apnoea was more likely to occur in non-ventilated infants when the PGE1 infusion rate was ≥ 15 ng/kg/min compared with < 15 ng/kg/min (14/33 vs 4/61, $\chi^2 = 15.55$, $p < .001$).

Conclusions: Newborn infants with suspected duct dependent CHD treated with low dose PGE1 (< 15 ng/kg/min) may not require mechanical ventilation for safe transport.

Newborn infants with suspected duct dependent congenital heart disease (CHD) are often treated with prostaglandin E1 (PGE1) to promote patency of the ductus arteriosus and physiological stability until the precise nature of the CHD has been defined and definitive treatment instituted.¹ The usual practice has been to mechanically ventilate these infants if they need to be transported to another hospital for the management of their CHD, because PGE1 may cause destabilising apnoea, particularly when it is used in high dosage.^{2–3} However, the efficacy of low-dose PGE1 in maintaining ductal patency in infants with duct dependent CHD and the reduced likelihood of apnoea with low-dose PGE1 suggest that mechanical ventilation may not always be necessary for the safe transfer of these infants,^{4–5} even over long distances,⁶ particularly since mechanical ventilation has its own inherent risks.⁷

The New South Wales neonatal and paediatric Emergency Transport Service (NETS) uses neonatally trained medical and nursing personnel and fixed-wing, rotary-wing and road modes of transport to retrieve critically ill newborn infants across New South Wales (NSW) and the Australian Capital Territory (ACT) and from the South Pacific Island of New Caledonia.⁸ In recent years, NETS in collaboration with neonatologists and/or paediatric cardiologists from Sydney's two children's hospitals has not routinely ventilated newborn infants with suspected duct dependent CHD treated with PGE1.

This study is a retrospective population-based audit of the NETS experience of retrieving newborn infants with suspected CHD treated with PGE1 vis-à-vis the use of mechanical ventilation.

METHODS

Newborn infants (≤ 28 days of age) with suspected duct dependent CHD transported by NETS during the 10-year period from 1995 to 2005 were identified from a prospectively

maintained computer database. The paper records of these neonatal retrievals were then searched to identify infants treated with PGE1. The indications for pre-transport mechanical ventilation included the following: (1) severe hypoxaemia, acidosis or cardiorespiratory failure; (2) apnoea following the introduction of PGE1; (3) elective ventilation because it was the preferred practice of the receiving paediatric cardiologist or neonatologist and/or retrieval medical specialist when there was an intention to treat with PGE1. The maximum dose of PGE1 was grouped as follows: < 15 ng/kg/min, 15–50 ng/kg/min and > 50 ng/kg/min. In addition, information was collected concerning the mode of transport, infants' birth weight and gestation, and the occurrence of apnoea and seizures. Apnoea had to be severe enough to cause a decrease in continuously monitored oxygen saturation for it to be recognised and therefore recorded. Analgesia-sedation was used routinely in the mechanically ventilated infants, but not at all in the non-ventilated infants.

Formal ethics approval was not sought for the study because it was a retrospective audit review and because information that might identify infants was not collected.

Statistical analysis

The data were analysed with χ^2 tests for statistical differences in proportions using SPSS v.11.5 for Windows.

RESULTS

NETS transported 300 newborn infants with suspected duct dependent CHD on a PGE1 infusion during the study period. The infants' median gestation was 40 weeks (range 32–42 week) and the mean birth weight was 3270 g (SD 605 g, range 1400–4835 g). The median interval from receipt of the

Abbreviations: CHD, congenital heart disease; PGE1, prostaglandin E1

request for retrieval to NETS' arrival at the referring hospital was 1 h 37 min (range = 0.2–23 h). The modes of retrieval included road ambulance (n = 166), rotary-wing aircraft (n = 88), and fixed-wing aircraft (n = 46).

The final underlying disease in the 300 infants was as follows: 176 (59%) had cyanotic CHD, 103 (34%) had acyanotic CHD, 18 (6%) had a non-cardiac disorder and in three (1%) the final diagnosis was not recorded in the paper records (table 1).

Mechanical ventilation was not used prior to treatment with PGE1 in 94 (31%) of the 300 infants. The indications for mechanical ventilation in the remaining 206 infants (69%) included elective mechanical ventilation because of the intention to use PGE1 (n = 125) and severe hypoxaemia, acidosis or cardiorespiratory failure prior to commencing PGE1 (n = 81). Sixteen (17%) of the 94 infants who were not ventilated initially required mechanical ventilation before transport because of apnoea, which developed within one hour of commencing PGE1. Thus, 78 infants were treated with PGE1 and transported without mechanical ventilation.

There was no significant relationship between mechanical ventilation and the time interval from request for retrieval to NETS' arrival at the referring hospital or between mechanical ventilation and mode of transport. A PGE1 infusion rate ≥ 15 ng/kg/min was used more frequently in the years 1995–2000 compared with 2001–2005 (126/169 vs 80/131, $\chi^2 = 6.24$, $p < .05$). There was also a reduction in the use of mechanical ventilation in PGE1 treated infants between these two time periods, though it was not significant (132/169 vs 90/131, $\chi^2 = 3.39$, $p = .06$). The 94 infants who were not electively ventilated prior to treatment with PGE1 were not statistically significantly different from the 125 infants who were electively ventilated because of the intention to treat with PGE1 with respect to their gestation, birth weight, mode of transport and underlying disease category.

The PGE1 infusion rate in the 78 infants who were not ventilated in transit was < 15 ng/kg/min in 59 infants and 15–50 ng/kg/min in 19 infants. Two (2.6%) of the 78 infants developed apnoea in transit and in both the PGE1 infusion rate was ≥ 15 ng/kg/min. One of these infants required a brief period of bag and mask ventilation, but neither had to be intubated and mechanically ventilated during transport. In all, 18 (19%) of 94 infants who were not ventilated prior to treatment with PGE1 developed apnoea in association with its use. Apnoea was more likely to occur in non-ventilated infants when the PGE1 infusion rate was ≥ 15 ng/kg/min compared with < 15 ng/kg/min (14/33 vs 4/61, $\chi^2 = 15.55$, $p < .001$).

What is already known on this topic

Low dose prostaglandin E1 compared with high-dose prostaglandin E1 is as effective in promoting patency of the ductus arteriosus in newborn infants with duct dependent congenital heart disease and less likely to cause apnoea.

What this study adds

In contrast to the usually recommended practice, newborn infants with duct dependent congenital heart disease can be safely transported by neonatally trained personnel without mechanical ventilation despite the concomitant use of low-dose prostaglandin E1.

Two (0.7%) of the 300 infants had a seizure in transit. In one infant the seizure was attributed to severe hypoxic-ischaemic encephalopathy and there was no discernible cause in the other.

DISCUSSION

In the past decade, NETS has increasingly used low dose PGE1 in newborn infants with suspected duct dependent CHD and elected not to ventilate them routinely for transport. The NETS practice has been demonstrably safe, since worrisome apnoea has been very uncommon in transit in non-ventilated infants. NETS has not used aminophylline to prevent apnoea during transport in these infants, though the practice has been reported to be efficacious.⁹ Importantly, however, the retrospective nature of the study and the non-systematic use of mechanical ventilation and PGE1 do not allow a recommendation concerning best practice. Nonetheless, the general safety of not using mechanical ventilation to transport infants with duct dependent CHD on PGE1 suggests it may be a reasonable alternative to delivering infants with prenatally diagnosed duct dependent CHD in a co-located obstetric hospital, though the former practice may be disadvantageous in infants with a cardiac anomaly requiring more immediate palliation than treatment with PGE1, such as an urgent balloon atrial septostomy in infants with transposition of the great arteries and a severely restrictive interatrial septum. Nevertheless, the results of the present study suggest that newborn infants with suspected duct dependent CHD can be safely transported

Table 1 Underlying congenital heart disease in infants treated with prostaglandin E1

Category	Diagnosis	Frequency (n = 300)	%
Cyanotic CHD	Transposition of the great arteries	93	31
	RVO obstruction	62	21
	Multiple cardiac anomalies	13	4.3
	Tricuspid valve dysplasia	6	2
	Total anomalous pulmonary venous return	2	0.7
Acyanotic CHD	LVO obstruction	99	33
	Cardiomyopathy	3	1
	Persistent truncus arteriosus	1	0.3
Non-cardiac disease	Non-immune hydrops fetalis	1	0.3
	Persistent pulmonary hypertension of the newborn	10	3.3
	Parenchymal lung disease	4	1.3
	Metabolic acidosis/ HIE	3	1
Disease unrecorded		3	1

Note: CHD, congenital heart disease; HIE, hypoxic-ischaemic encephalopathy; LVO, left ventricular outflow obstruction; RVO, right ventricular outflow obstruction

The LVO anomalies included coarctation of the aorta, aortic atresia or critical aortic stenosis, and hypoplastic left heart syndrome. The RVO anomalies included pulmonary atresia or critical pulmonary stenosis $\pm$ ventricular septal defect, and hypoplastic right heart syndrome.

without mechanical ventilation providing low dose PGE1 (<15 ng/kg/min) is used and the assessment, stabilisation and transport have been conducted by neonatally trained physicians and nurses.

CONCLUSIONS

Newborn infants with suspected duct dependent CHD treated with low dose PGE1 may not require mechanical ventilation for the purpose of safe transport.

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