Day case ligation of patent ductus arteriosus in preterm infants: a 10 year review

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Abstract
Since 1978, 136 preterm babies received ligation of a patent ductus arteriosus as day cases. A total of 122 babies whose notes were available for review, with a median gestational age of 27 weeks (range 23–35) and median birth weight of 960 g (range 470–2750), were transported distances of up to 80 miles. The median ages at ligation with and without previous medical management with indomethacin were 23 and 15 days, respectively. One hundred and ten (90%) babies were dependent on ventilatory support, but extubation was achieved at a median time of 10 days after ligation, regardless of postnatal age at the time of ligation. There were no deaths associated with the operation, and no complications resulting from transportation. The hospital mortality was 15 (12·3%), and the most important (and significant) adverse factor was a preoperative fractional inspiratory oxygen content greater than 0·3. The results of this study show that day case ligation of the patent ductus arteriosus is safe, and if it is carried out early will reduce the time before extubation and discharge from the intensive care unit.

The ductus arteriosus persists in 20%–30% of infants who are born weighing less than 2000 g, and causes appreciable morbidity in many.[1-3] The resultant respiratory failure may require prolonged ventilatory support, and is associated with increased mortality. The morbidity can, however, be reduced by early closure of the duct.[4]

Indomethacin is usually the first line of treatment; if this fails ligation of the duct may be considered, but the practical details vary considerably among individual neonatal units. Ducts may be ligated in the incubator in the neonatal unit, or in an operating theatre of the same hospital.[5 6] This, however, requires that a cardiothoracic surgeon has to travel what may be a long distance to and from the neonatal unit, which is not a cost effective use of his time. There has been a single report of neonates undergoing duct ligation as a day case.[7]

It has been our practice to have each baby transported from the referring neonatal unit to this supraregional cardiothoracic centre for duct ligation. The infants were then transported back to their units immediately after the procedure. In this study we report our 10 year experience of day case duct ligation, with reference to the related medical management.

Patients and methods
Between November 1978 and May 1989, 136 preterm infants with isolated patent ductus arteriosus were admitted for ligation, 119 as day cases; 122 patient records were available and have been reviewed. The median gestational age was 27 weeks (range 23–35) and the median birth weight 960 g (range 470–2750, 116 of whom weighed less than 1500 g). Three regional neonatal units referred three quarters of the patients. A number of district general neonatal units collectively referred the remainder. Two of the regional neonatal units are in Leeds, and one is in Sheffield (35 miles away). The district hospitals were scattered throughout Yorkshire and North Trent.

The patent ductus arteriosus was diagnosed and treated in accordance with the medical protocol preferred locally. If these measures failed, ligation was requested. Before ligation the diagnosis was confirmed by a paediatric cardiologist using cross sectional cardiac ultrasonography. Particular care was taken to ensure that it was an isolated problem, and that it was of a size that was likely to be haemodynamically and clinically important.

Ligation of the duct was usually arranged at a day's notice. The responsibilities of the referring medical team were sending one unit of cross matched blood, obtaining parental consent, and providing an experienced nurse and medical escort for the infant. On arrival at this hospital, which was timed to coincide with a space in the routine operating list, the infant was transferred to the operating theatre.

A posterolateral thoracotomy was made through the fourth intercostal space, and the duct ligated with a single 2/0 Persalls suture. The procedure required careful retraction with minimal compression of the lung, to provide good visibility of the operative field while maintaining ventilation of both lungs; we find the Killingbeck paediatric lung retrator indispensible.[8] Chest drainage was not used routinely, but the lungs were fully inflated before the chest cavity was closed.

Demographic statistics and details of medical management before and after operation were recorded, as were the complications, and details of progress after ligation.

The data were not normally distributed, and so non-parametric tests (Mann-Whitney U, Spearman rank correlation, and χ^2 tests) were used for analysis. A probability of <0·05 was accepted as significant.

Results
The various subgroups were comparable (table

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Table 1   Clinical details of infants treated by duct ligation after medical treatment. Figures expressed as median (range) except where otherwise stated

Treatment group	No of infants	Gestation (weeks)	Birth weight (g)	Age at diagnosis (days)	Age at ligation (days) after medical treatment			
					Without indomethacin		With indomethacin	
					No of infants	Median (range)	No of infants	Median (range)
Regional neonatal unit A	30	28 (24–34)	1020 (620–2750)	5	25	16 (5–63)	5	13 (3–17)
Regional neonatal unit B	32	27 (23–33)	1000 (470–2330)	5	16	13·5 (6–25)	16	22·5 (10–42)
Regional neonatal unit C	31	27 (23–35)	940 (550–1550)	6	21	21 (7–44)	10	23 (16–36)
District general hospitals (D)	29	26 (23–34)	920 (680–2340)	7	7	15 (5–39)	22	26 (9–48)
Total	122	27 (23–35)	960 (470–2750)	6	69	15 (5–63)	53	23 (3–48)

1). The median ages at the time of clinical diagnosis of the patient ductus were also similar (roughly 6 days). Of the 122 infants reviewed, 53 had received indomethacin before referral for duct ligation (table 1). Ducts were ligated significantly earlier in patients who did not receive indomethacin (p<0·001).

All hospitals practised some degree of fluid restriction before ligation, but it was possible to withdraw restrictions within five days of operation (table 2). Mechanical ventilation was required by 110 infants (90%) with a median fractional inspired oxygen concentration (F_IO_2) of 0·3 before ligation (table 3). Infants of less than 26 weeks' gestation (43%) or weighing less than 1000 g at birth (51%) were ventilated longer (median 15 and 14 days, respectively) than the older and larger infants (median 8 and 6 days) after ligation (p<0·01). The F_IO_2 given on the day after ligation was temporarily higher,

and was not related to gestational age or birth weight.

After ligation, the median intervals to withdrawal to continuous positive airway pressure (CPAP) and extubation were 7 and 10 days, respectively. Postnatal age at ligation (in those aged 13 days or more) did not influence this (figure). Those in whom the duct was ligated between 9 and 12 days of age, however, had longer median intervals to withdrawal of CPAP (13·5 days, interquartile range (IQR) 7–23), and extubation (20·5 days, IQR 9–25) than those in whom the duct was ligated between 17 and 20 days (6·5, IQR 4–10·5, and 11·5, IQR 5·5–17·5), and those in whom it was ligated when they were more than 25 days of age (7, IQR 2·75–11·75, and 10, IQR 3–15), respectively (p<0·05). Of the three groups in which there were infants older than 17 days, a larger proportion received indomethacin (p<0·05) but there was no difference in the amount of preoperative oxygen supplementation.

No deaths were directly related to the operation, though 15 of the 122 babies (12%) subsequently died of problems associated with prematurity (table 4). Of 63 infants who required preligation F_IO_2 concentrations of over 0·3, 13 died (p<0·05).

Two babies had haemorrhages that required re-exploration, but no damage to major vessels was discovered (table 5), and one of these died five days later of rapidly progressive respiratory failure. One infant had a phrenic nerve palsy of uncertain aetiology; segmental lobar collapse affecting particularly the right upper lobe was a serious problem on day 1. Of the 50 infants who had had cranial ultrasound examinations before

Table 2   Policies of fluid restriction practised in infants with patent ductus arteriosus. Values are expressed as median (interquartile range)

Treatment group	Amount of fluid given (ml/kg/day)	
	Before ligation	After ligation
Regional neonatal unit A	135 (120–150)	150 (150–165)
Regional neonatal unit B	120 (100–130)*	162 (150–175)
Regional neonatal unit C	135 (120–150)	175 (155–175)
District general hospitals (D)	150 (120–150)	150 (150–175)
Those treated with indomethacin	130 (120–150)	160 (150–175)
Those not treated with indomethacin	120 (105–150)	165 (150–175)
Total	130 (120–150)	162 (150–175)

*p<0·05 compared with groups A, C, and D. None of the other differences are significant.

Table 3   Degrees of ventilatory support provided, and intervals between ligation withdrawal of CPAP, and extubation. Values are expressed as median (interquartile range)

Treatment group	Inspiratory oxygen concentration (%)		Intervals (days) from ligation to:	
	Before ligation	After ligation	Withdrawal to CPAP	Extubation
Regional neonatal unit A	35 (30–40)	50 (39–63)	7·5 (4–14)	13·5 (6–23)
Regional neonatal unit B	25 (23–30)*	30 (25–40)**	6 (2–9)***	8·5 (3–13)†
Regional neonatal unit C	30 (25–40)	50 (31–60)	8 (3–14)	10 (4–15)
District general hospitals (D)	50 (30–58)	68 (40–80)	10 (4–18)	14 (5–20)
Those treated with indomethacin	35 (30–60)	43 (30–70)	8 (4–17)	10 (5–20)
Those not treated with indomethacin	30 (25–40)	45 (30–60)	7 (3–14)	11 (4–20)
Total	30 (25–43)	45 (30–65)	7 (4–15)	10 (5–20)

*p=0·001 compared with groups A and D; **p=0·001 compared with groups A, C, and D; ***p=0·05 compared with group D; and †p=0·05 compared with group A.
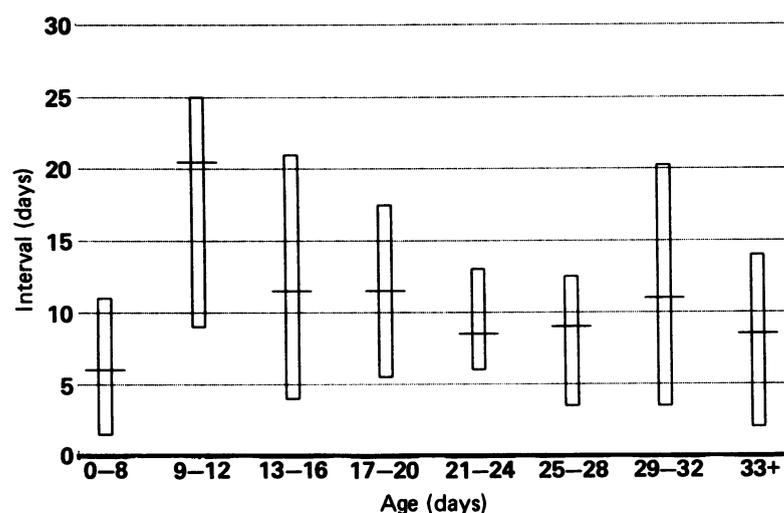
Interval from day of ligation to extubation. The bars indicate the median and interquartile range.

Table 4 Late hospital deaths

Cause	No of infants
Respiratory failure	10
Necrotising enterocolitis	3
Renal failure	1
Septicaemia	1
Total	15/122 (12%)

Table 5 Complications of duct ligation

Complication	No of infants
Haemorrhage	2
Stridor	2
Lobar collapse:	
Right	21
Left	6
Pneumothorax:	
Right	1
Left	6
Total	37/122 (30%)

and after ligation only two showed progression, both from normal to grade 1 intraventricular haemorrhage.

No problems were reported concerning the transportation.

Discussion

This study has shown that day case ligation of the patent ductus arteriosus in preterm infants is safe. There was no mortality associated with the operation or the transport, and morbidity was low. Comparison of the hospital mortality with previous reports (10–40%, most above 20%) indicates that our overall management policy was satisfactory.[1 9 10]

There were no problems reported concerning transportation despite infants weighing as little as 470 (and more recently 430 g) being transfered from hospitals as far as 80 miles away. The smooth transportation of these infants was facilitated by the excellent network of motorways and A roads linking this city with its neighbours.

The results suggest that neonatal unit B, in which fluid restriction was most rigidly practi-

sed, achieved the most favourable ventilatory statistics. Though this is in keeping with previous research, we cannot state categorically that this was the sole reason, as many other variables must be taken into account.[13 14]

Those infants who underwent duct ligation between the ages of 9 and 12 days were the slowest to be weaned from ventilatory support; we are uncertain of the reason for this. Among the older infants more had received indomethacin than among the younger, but there were no differences in demographic or ventilatory measurements.

The observed lobar collapse predisposes to a temporary but manageable deterioration in ventilation after ligation. This, however, is not a problem peculiar to preterm infants, and may be seen in patients of all ages after major thoracic and abdominal operations. More intriguing however, is the tendency to collapse of the right upper lobe. The upper lobe bronchus, which is the most dependent major airway in the supine position, may drain inadequately if ciliary function is upset after the anaesthetic, thereby allowing formation of mucous plugs and subsequent collapse.

Northway and Jacob et al have suggested that delay in achieving duct closure may be detrimental, causing progression to bronchopulmonary dysplasia.[11 12] Duct ligation did, however, control the cardiorespiratory failure with consequent benefits; mechanical ventilation was withdrawn, and the volume of fluid and thus energy was increased to more optimal amounts, so promoting better growth than was encountered preoperatively.

Indomethacin is least successful in closing the ducts of infants with very low birth weights and with severe respiratory distress syndrome requiring assisted ventilation.[15] Rudd et al showed that in a group of babies weighing less than 1500 g at birth the incidence of patent ductus arteriosus was 31%. Of these, 87% initially closed with indomethacin, but 47% reopened.[16] Many of the infants treated by day case ligation of the ductus were comparable with this group (116 (95%) weighed less than 1500 g at birth) and were thus likely to experience reopening of a ductus that had closed after medical treatment, and unlikely to benefit from a protracted trial of this treatment.

Cotton et al reported that extubation was achieved earlier, and after lower expenditure in patients who had undergone early duct ligation rather than awaiting the result of prolonged medical treatment.[17] Other authors have supported this view, reporting that the mortality associated with a haemodynamically important patent ductus had risen significantly since the introduction of indomethacin.[18] They found that results were more satisfactory when early ligation was routine.

Gersony et al, however, reported the results of a multicentre trial that did not confirm these findings.[19] A total of 421 infants were randomised to receive one of three treatment protocols. The first group received indomethacin together with restricted fluids and diuretics as the primary treatment. The second received indomethacin, and the third underwent duct

ligation only after initial fluid restriction had failed to close the duct. The study showed no significant differences between the length of time that ventilatory support was required by each group, or in the incidence of complications such as bronchopulmonary dysplasia, intracranial haemorrhage, and necrotising enterocolitis. The mortality was also similar.

Conclusion

Because our patients are a highly selected group we are not in a position to compare medical and surgical treatment of patent ductus arteriosus. Our results do show conclusively, however, that surgical closure can be done safely even after transportation of the ventilated infant to a cardiothoracic centre with appropriate expertise. Where local circumstances are such that the regional cardiothoracic centre is remote from neonatal intensive care facilities, we believe that the policy of day case ligation of the ductus makes most economic use of the time of the surgeon while keeping responsibility for the ventilation and medical care of the infant in the hands of the referring paediatric team.

We suggest that if a preterm infant who is dependent on the ventilator has an arterial duct of sufficient size to merit medical treatment, then failure of this treatment should lead to immediate consideration of surgical ligation.

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