Timing of patent ductus arteriosus ligation and effects on neonatal clinical outcomes: an international comparison.

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Background

Patent ductus arteriosus (PDA) is common among very preterm infants. If pharmacological closure is ineffective or contraindicated, surgical ligation may be required; however, access to cardiothoracic surgery may influence the ligation timing ligation, with possible clinical effects.

Aim

This study aimed to assess the impact of PDA ligation timing on neonatal clinical outcomes in two tertiary Neonatal Intensive Care Units with different surgical management of PDA: early bedside surgery vs. referral to a pediatric cardiac surgery centre.

Methods

Infants born at Sant'Orsola-Malpighi University Hospital, Bologna, Italy (group 1, bedside ligation) and at Addenbrooke's Hospital, Cambridge, UK (group 2, referred to cardiac surgical centres) who underwent PDA ligation between 2006 and 2016 were included in this retrospective cohort study if fulfilling the following criteria:

- Gestational age (GA) <32 weeks
- Birth weight (BW) <1500 g
- In-born
- Absence of major malformation or congenital heart disease (CHD).

Clinical characteristics, PDA pharmacological and surgical closure, and neonatal clinical outcomes were compared between the 2 groups by Mann-Whitney U-test, Chi-square test and Fisher's exact test (p-value <0.05).

Results

In total, 34 neonates were enrolled in each group. Infants' characteristics and between-group differences are detailed in Table 1. Pharmacological management and the rate of PDA recurrence after pharmacological treatment did not differ between the study groups.

Group 1 underwent PDA ligation significantly earlier than group 2 (median age 12 v 39 days, p <0.001), with no increase in mortality, surgical complications and post-surgical sepsis.

Clinical outcomes and the results of between-group comparison are shown in Table 2. Group 2 had a significantly higher incidence of bronchopulmonary dysplasia at 36 weeks' postmenstrual age (p=0.02), resulting in an increased need for oxygen at discharge (p=0.03).

A significant effect of PDA ligation timing on the need for oxygen at discharge (p=0.02) was confirmed by the multivariate analysis after adjustment for weight and age at PDA ligation, days on MV, use of antenatal and postnatal steroids, delivery mode.

Conclusions

Bedside ligation allowed an earlier surgical PDA closure and was not associated with increased mortality or surgical complication rates. Earlier PDA ligation may reduce the prevalence of oxygen need at discharge, with potential cost-benefit implications, but further studies are needed to evaluate this finding.

Table 1. Clinical characteristics of the study groups and results of between-group comparison.

Clinical characteristics		Group 1 (n=34)	Group 2 (n=34)	P-value
GA (weeks), median (IQR)		25 (23-27)	25 (24-26)	.348
BW (g), median (IQR)		638 (560-782)	701 (637-769)	.244
Apgar score, median (IQR)		8 (5-8)	7 (5-8)	.809
Sex (males), n (%)		20 (59)	21 (62)	.804
Twinhood, n (%)		11 (32)	17 (50)	.139
IUGR, n (%)		6 (18)	7 (20.5)	.758
Delivery mode (C-section), n (%)		20 (59)	10 (29.5)	.015
Antenatal steroids	Complete course, n (%)	15 (44)	24 (70.5)	.009
	Incomplete course, n (%)	9 (26.5)	9 (26.5)	
	Not given, n (%)	10 (29.5)	1 (3)	
PDA size (mm/kg), median (IQR)		4 (3.1-4.8)	4.2 (3.8-4.6)	.284
Pharmacological closure attempted, n (%)		25 (73.5)	25 (73.5)	1

Table 2. Clinical outcomes of the study groups and results of between-group comparison.

Clinical outcomes		Group 1 (n=34)	Group 2 (n=34)	P-value
IVH, n (%)		17 (50)	23 (67.5)	.139
IVH grade	Grade I, n (%)	3 (17.5)	10 (43.5)	0.204
	Grade II, n (%)	5 (29.5)	7 (30.5)	
	Grade III, n (%)	5 (29.5)	2 (9)	
	Grade IV, n (%)	4 (23.5)	4 (17)	
PVL, n (%)		4 (12)	4 (12)	1
NEC, n (%)		9 (26.5)	14 (41)	0.200
SIP, n (%)		3 (9)	2 (6)	0.500
Time to full feeding (days), median (IQR)		47 (34-59)	37 (22-54)	0.140
Sepsis, n (%)		21 (62)	28 (82)	.084
MV duration (days), median (IQR)		29 (20-37)	30 (25-46)	0.335
BPD at 36 weeks PMA, n (%)		21 (60)	31 (91)	0.024
ROP, n (%)		21 (62)	21 (62)	.371
ROP stage	Stage I, n (%)	7 (33.3)	4 (19)	0.410
	Stage II, n (%)	7 (33.3)	11 (52.5)	
	Stage III, n (%)	7 (33.4)	6 (28.5)	
Mortality, n (%)		7 (20.5)	3 (9)	0.305
Length of stay (days), median (IQR)		114 (85-135)	123 (109-135)	0.189
Oxygen need at discharge, n (%)		6 (18)	15 (44)	0.035

Tables abbreviations: BPD=bronchopulmonary dysplasia; IQR=interquartile range; IUGR=intrauterine growth restriction; IVH=intraventricular haemorrhage; NEC=necrotizing enterocolitis; PVL=periventricular leukomalacia; PMA=postmenstrual age; ROP=retinopathy of prematurity; SIP=spontaneous intestinal perforation.