· Original Article in English ·

Do intra-operative fluids influence the need for post-operative cardiotropic support after a PDA ligation?

Brigitte LEMYRE[1], *Ling LIU*[2], *Gregory Paul MOORE*[1], *Sarah Linda LAWRENCE*, *Nicholas J. BARROWMAN*[1]

(1. *Department of Pediatrics*, *University of Ottawa*, *Ottawa*, *Canada*;
2. *Department of Neonatology*, *Children's Hospital of Guiyang*, *Guizhou*, *China*)

Abstract: **Objective** To investigate the effect of intra-operative intravenous fluids on post-operative hemodynamic stability. **Methods** We performed a retrospective cohort study of 98 preterm infants who underwent a patent ductus arteriosus (PDA) ligation in one NICU between 2001 and 2007. The primary outcome was the need for cardiotropic support within 24 hrs of ligation. **Results** Twenty-seven infants (28%) required post-operative cardiotropic support. The amount of intra-operative fluids varied between 0 and 50.4 mL/kg (median: 10.2 mL/kg). No intra-operative fluid was recorded in 26 patients. Fluids were not associated with the need for post-operative cardiotropic support ($P = 0.10$). Using a multivariate logistic regression model, age at ligation, weight at ligation and pre-operative FiO_2 were significant predictors of post-operative cardiotropic support. **Conclusions** Intra-operative fluids do not appear to be associated with the need for post-operative cardiotropic support. A prospective cohort study may help identify modifiable risk factors and improve outcomes in this population. [**Chin J Contemp Pediatr**, **2011**, **13** (**1**):**1 – 7**]

Key words: Hemodynamics; Patent ductus arteriosus ligation; Premature infant

[CLC number]R541.1 [Document code]A [Article ID]1008 – 8830(2011)01 – 0001 – 07

A patent ductus arteriosus (PDA) can be a significant problem in premature infants, and its management is currently being debated[1-3]. Left to right shunting through the PDA can result in increased pulmonary blood flow and systemic hypoperfusion and has been associated with intraventricular haemorrhage, necrotizing enterocolitis (NEC) and chronic lung disease[4-6]. Indomethacin, usually considered first line medical therapy has a high rate of failure, especially in those under 27 weeks of gestation[7]. When medical treatment fails or is contraindicated, surgical ligation is considered[8-9].

Surgical ligation of the PDA abolishes the left-to-right ductal shunting; however, it is associated with complications including air leaks, wound infections, intra-operative bleeding, left vocal cord palsy and cerebral hemorrhage[10-11]. A post-ligation cardiac syndrome has also been described, which involves decreased left ventricular output and myocardial performance after PDA ligation[12-15]. Risk factors for this dysfunction include pre-operative cardiotropic support, low Apgar score at 1 minute, low cortisol level pre-operatively, size of the PDA, lower gestational age and younger age at surgery[13-16]. Infants who suffer from this condition may be at increased risk of dying prior to discharge[15].

Giving intravenous (IV) fluid to very immature infants during their surgery may be necessary to ensure tolerance of the anaesthetic agents which decrease cardiac output. However, there appears to be great institutional and individual variability in the amount of fluid routinely given to infants undergoing a PDA ligation. It was our impression that infants who receive more IV fluids during the operation undergo a more difficult post-operative course, with hemodynamic instability requiring cardiotropic support and/or ventilation/oxygenation problems which may require high frequency ventilation (HFV) in the immediate post-operative period. There is a lack of evidence with regards to optimal fluid loading intra-operatively in infants undergoing a PDA

[Received]March 6, 2010; [Revised]October 12, 2010
[Biography]Brigitte LEMYRE, M.D., Associate professor of Pediatrics, University of Ottawa Hospital. Email: blemyre@toh.on.ca.

ligation.

The objective of this study was to investigate the effect of IV fluids received intra-operatively on post-operative hemodynamic stability. We hypothesized that those receiving more fluid would be more likely to need cardiotropic support post-operatively.

Patients and methods

Study objective

The primary aim was to investigate the independent association between intra-operative fluids (crystalloids and colloids) during the ligation and postoperative need for cardiotropic support. The secondary aim was to explore whether intra-operative fluids were associated with other post-operative variables such as mortality and need for high frequency ventilation (HFV).

Design

We performed a retrospective cohort study at an outborn tertiary care neonatal intensive care unit (NICU).

Study population

Premature infants born under 32 weeks gestation and admitted to the NICU at the Children's Hospital of Eastern Ontario (CHEO), Ottawa, Canada between January 1, 2001 and December 31, 2007 who underwent a ligation for a clinically significant PDA were included. Infants with complex cardiac malformations, in which a PDA was only a part of their cardiac problems, were excluded.

A clinically significant PDA was defined by a moderate or large PDA on two-dimensional (2D) echo in a patient dependent on a ventilator (or rarely CPAP dependent) or with evidence of poor peripheral circulation (high lactate, metabolic acidosis or poor urine output) attributable to the PDA. The determination of a moderate or large PDA was made by a paediatric cardiologist, based on the size of the PDA relative to the size of the baby's aorta and the baby's weight. Hemodynamic significance was established based on the presence of a left to right shunt and dilatation of the left atrium or ventricle. The usual medical therapy at our referring centres was 1-2 courses of indomethacin (one course being 3 doses of 0.1-0.2 mg/kg given at 12 h intervals). Infants who failed indomethacin or who had contraindications to indomethacin were candidates for surgical ligation.

Infants referred were admitted to CHEO at least 24 hours prior to surgery. Their ventilation was optimized with permissive hypercapnia as a target (PCO2 50-65 mmHg with pH $\geqslant$7.25) and parenteral nutrition was administered the day of surgery and for the next 24-48 hours. Fentanyl was the analgesic of choice during surgery, usually at doses of 15 micrograms/kg along with a muscle relaxant. Post-operatively, all neonates received either morphine or fentanyl by continuous infusion, which was tapered over 24-48 hours, based on an objective assessment of pain using the Premature Infant Pain Profile (PIPP).

The goal for blood pressure post-operatively was to achieve a mean blood pressure (MBP) equal or greater than the corrected gestational age with evidence of adequate peripheral perfusion (capillary refill time $\leqslant$3 seconds). One or two 10 mL/kg normal saline boluses were usually provided before commencing cardiotropic agents. Our practice was then to start a dopamine infusion at a rate of 5 to 10 micrograms/kg minutely to a maximum of 15 micrograms/kg minutely and then adding either epinephrine or dobutamine. Hydrocortisone was considered after the failure of 1 to 2 cardiotropic agents and the dosage range was 2-6 mg/kg per day.

HFV was used as rescue, for infants who continued to have respiratory acidosis or high settings on conventional ventilation (rate >60/min or peak inspiratory pressure >24 cmH_2O).

Data collection

Baseline neonatal characteristics related to the delivery, resuscitation and pre-ligation respiratory and hemodynamic condition were recorded. Physiologic markers of cardio-respiratory stability were extracted from medical records. Fluids above maintenance included crystalloids (normal saline and Ringer's lactate) or colloids (albumin or packed red blood cells) and dose and duration of cardiotropic support agents (dopamine, dobutamine, and epinephrine) and hydrocortisone were recorded. The fluid volume required to give IV anaesthetic medications was not included.

Outcome measures

The primary outcome was the need for cardiotropic support within 24 hours of ligation. For patients on cardiotropic support pre-operatively, this was defined as

needing a higher dose of cardiotropic support (≥2.5 micrograms/kg minutely more than pre-operatively) within the first 24 hours post-operatively. Secondary outcomes were need for HFV and mortality within 30 days of surgery.

Sample size

Approximately 18-25 infants per year meet eligibility criteria and undergo a PDA ligation at CHEO, thus approximately 130 infants from 2001-2007. The same surgeon has performed all PDA ligations since 2001. Previous publications suggest that 20%-30% of those infants have a need for post-operative cardiotropic support[12, 16]. We abstracted data from all eligible patients in the time period chosen, to ensure a sufficient convenience sample.

Statistical analysis

Patient characteristics at baseline were summarized using mean and standard deviation (SD), median and range, and frequency and percentage as appropriate. Similarly, characteristics of infants who did and did not receive post-operative cardiotropic support were compared descriptively.

The volume of IV fluids received intra-operatively was compared between infants who needed post-operative cardiotropic support and those who did not using Wilcoxon's rank sum test. Other potential predictors were compared using either Wilcoxon's rank sum test of Fisher's exact test, as appropriate. Logistic regression models were used to adjust for other potential predictors of the need for post-operative cardiotropic support. Initially a model was fit with just the mean volume of IV fluid received intra-operatively as an independent variable. Subsequently other candidate predictors (age at ligation, birth weight and gestational age) were included in the model, based on previous studies[13-16]. Likelihood ratio tests were used to test whether predictors were statistically significant. All tests were two-sided, with *P*-values less than 0.05 judged to be statistically significant. This study was approved by the CHEO Research Ethics Committee.

Results

Between January 2001 and December 2007, 103 patients meeting inclusion criteria were admitted to CHEO for a PDA ligation. Five patients with complex cardiac malformations were excluded. Thus, 98 patients were included in the study.

The baseline characteristics of included infants are described in Table 1. Dopamine was the cardiotropic agent used in 11 of the 12 infants who received pre-operative cardiotropic support.

Table 1 Baseline characteristics of included patients (n=98)

Characteristic	Range	Median(IQR)	Mean(SD)	n(%)
Gestational age(weeks)	23-31	26 (25-27)	26.1 (1.8)	
Birth weight(g)	491-1950	835.5 (709.5-1017)	910 (307)	
Apgar score at 1 min	0-9	5 (2-6)		
Apgar score at 5 min	1-9	7 (5-8)		
FiO_2 24 h before ligation(%)	21-100	40 (30-47)	42.4 (19.1)	
Prior indomethacin				79(81)
Pre-operative ventilatory support				95(97)
Pre-operative cardiotropic support				12(12)

Overall, 27 infants (28%) required post-operative cardiotropic support. Twenty six received dopamine with 6 infants receiving more than 1 cardiotropic agent and 3 who received hydrocortisone. The amount of fluid received during surgery, above maintenance, varied between 0 and 50.4 mL/kg, with a median of 10.2 mL/kg (interquartile range 0-18.7 mL/kg), with the vast majority of infants receiving normal saline. According to their medical record, 26 infants did not receive any fluid above their maintenance IV rate during the surgery.

Demographic, pre-operative characteristics and intra-operative factors of infants who did and those who did not require post-operative cardiotropic support are included in Table 2. Infants requiring post-operative cardiotropic support were smaller at birth, younger (in days of life), weighed less at surgery, were receiving more oxygen pre-operatively, were more likely to be on pre-operative cardiotropic support and received more

fentanyl intra-operatively. The amount of fluids received intra-operatively was not significantly associated with the need for post-operative cardiotropic support. Re-running the analysis excluding the 26 infants who received no fluid intra-operatively did not change the results ($P=0.19$).

To investigate which factors were associated with the need for post-operative cardiotropic support, we used a multiple logistic regression model. The priori model included intraoperative fluids and age at ligation as explanatory variables. Based on findings in Table 2, pre-operative FiO_2, pre-operative cardiotropic support, fentanyl dose and weight at surgery were added. In the fitted model, age at ligation, weight at surgery and pre-operative FiO_2 were found to be statistically significant. Intra-operative fluid was not statistically significant (Table 3). The strongest predictor was age in days at surgery, where no infant older than 25 days of life required post-operative cardiotropic support.

Table 2 Subgroup characteristics and intra-operative factors [median(IQR)]

Characteristic	Need for cardiotropic support ($n=27$)	No need for cardiotropic support ($n=71$)	P value
Gestational age (weeks)	25(25-26)	26(25-27)	0.09
Birth weight (g)	771 (659-860)	890 (750-1064)	0.02
Apgar score at 1 min**	4 (1-8)	5 (0-9)+	0.27
Apgar score at 5 min**	7 (3-9)*	7.5 (1-9)+	0.60
Age at PDA ligation(days)	14 (10-19)	25 (19-28)	<0.001
Pre-operative FiO_2(%)	40 (36-55)	35 (30-44)	0.03
Weight at PDA ligation (g)	800 (759-977)	1067 (901-1280)	<0.001
Cardiotropic support within 24 hrs of surgery△	8 (29.6)	4 (5.6)	0.003
Indomethacin prior to ligation△	21(77.8)	58 (81.7)	0.78
Large PDA at surgery△	13(48.1)	40 (56.3)	0.50
Total fluid intake within 24 hrs of surgery (mL/kg)	154(141-167)	148(140-161)	0.38
Mean airway pressure within 24 hrs of surgery (cmH_2O)	11(9.85-11.75)	9.85(8.95-12.00)	0.10
Intra-operative factors			
Intra-operative fluids (mL/kg)	15.2 (4.7-23.6)	8.9 (0-16.74)#	0.10
Intra-operative fentanyl (mcg/kg)	17.4 (12.5-26.1)*	10.9 (6.2-17.8)+	0.04

* based on 26 observations; + based on 70 observations; # based on 69 observations; ** median (range); △ n(%)

Table 3 Odds ratio of candidate risk factors

Characteristic	Unadjusted odds ratio (95% *CI*)	Adjusted odds ratio (95% *CI*)	Unit	P value*
Intra-operative fluids	1.33 (0.90-1.95)	1.74 (0.96-3.16)	10 ml/kg	0.07
Age at PDA ligation	0.83 (0.77-0.91)	0.75 (0.66-0.86)	1 day	<0.0001
Pre-operative FiO2	1.34 (1.06-1.69)	2.29 (1.39-3.77)	0.10	0.001
Pre-operative cardiotropic support	6.84 (1.86-25.22)	1.30 (0.22-7.65)	–	0.77
Weight at PDA ligation	0.79 (0.66-0.95)	0.76 (0.60-0.98)	100 g	0.03
Intra-operative fentanyl	1.04 (0.99-1.08)	1.06 (0.99-1.13)	mcg/kg	0.09

* P value for adjusted odds ratio

Only two patients died within 30 days of surgery; therefore we were unable to examine any association between mortality and intra-operative fluid intake. Six patients required HFV post-operatively. The median amount of fluid above maintenance for these patients was 4 mL/kg (IQR 0-18.4mL/kg) versus 10.5 mL/kg (0.7-18.4mL/kg) for those who did not require HFV ($n=92$), which was not statistically significant (Wilcoxon rank sum $P=0.55$).

Discussion

Timing and ideal candidates for ligation are currently unclear largely due to debates regarding the pathophysiology of the PDA and its effects on short and long term outcomes for neonates as well as the limitations in defining what is hemodynamically significant[17-19]. Left-to-right shunt through the PDA likely volume loads the left ventricle (LV) and decreases the afterload.

Doppler studies confirmed that the LV end-diastolic volume, stroke volume, and cardiac output were more than 1.3 fold higher before PDA closure[20]. When the PDA is surgically ligated, there is a sudden increase in the afterload and a decrease in the preload of the left ventricle, with a consequent transient decrease in cardiac output.

Correspondingly, the incidence of post-operative hypotension requiring cardiotropic support was 28% in this population, in keeping with previous reports[14-17]. Whether the post-operative cardiac instability and need for cardiotropic support documented in some infants results from the increased afterload, decreased preload, depressed function of the myocardium from anesthesia, downregulation of vascular receptors or relative adrenal insufficiency is unclear[12-15].

In a single center retrospective study, Teixeira et al[14] found that infants older than 28 days were less likely to develop a post-cardiac ligation syndrome. The incidence of post-operative hemodynamic instability was 15.4%. In a retrospective and prospective observational study, Noori et al[13] showed that the larger the PDA, the greater the reduction in left ventricular output after a ligation, with an incidence of 35% of infants requiring cardiotropic support. In a prospective cohort study, Harting et al[15] found that lower gestational age and corrected gestational age were associated with hemodynamic decompensation post-operatively. This decompensation was noted in 28% of their patients and it was the most significant variable predicting death prior to discharge. In a prospective and retrospective observational study, Moin et al[16] found that lower gestational age and birth weight, as well as higher respiratory support were associated with post-operative hypotension in 32 of their 100 patients.

Contrary to our hypothesis, the amount of intra-operative IV fluids was not associated with post-operative hemodynamic instability. Younger age at ligation was strongly associated with the outcome, as previously described and may be due to a maturational effect[14]. Similarly, every increase of 100 g in weight at surgery was associated with a 23% decrease in the likelihood of needing post-operative cardiotropic support, possibly due to technical aspects related to the surgery and the anesthesia. Pre-operative FiO_2 was also associated with the outcome, as previously described[15-16]. We collected data on the mean FiO_2 within 24 hours of surgery, but did not record oxygenation index or mean airway pressure, which are more robust markers of pulmonary disease. The finding that infants who needed post-operative cardiotropic support were in 10% more oxygen pre-operatively must therefore be taken with caution.

There is a degree of inaccuracy in the charting of IV fluids received during the ligation, particularly the amounts of fluids provided with anesthetic agents, such as saline flushes. These were not recorded in our patients. For infants weighing 500-1 000 g, 5 to 10 mL represents a significant amount of fluid per body weight and it is usual to use such amounts for flushes of anesthetic agents. As such, this leads to an underestimation of intra-operative fluids received and might have limited our ability to find a relationship between fluids and outcome. The amount of fluids received within 24 hours of surgery was comparable between groups. We did not record fluids received over a longer period of time nor did we assess weight gain in our population, thus we cannot accurately assess preoperative fluid overload, which could be of relevance in this particular scenario.

Very premature infants are easy to volume overload and those needing a PDA ligation usually suffer from some degree of pulmonary oedema and frequently have underlying lung disease. Preload in these circumstances could contribute to more stress to a myocardium which has been shown to adapt more poorly to an increased afterload. On the other hand, giving extra fluids intra-operatively once the left heart preload is significantly reduced may minimize early hemodynamic instability and low cardiac output. Balancing fluids in these patients is thus a difficult task, which must be individualized.

A limitation of this study is the retrospective nature of the data collection. The reasons to provide IV fluids intra-operatively and post-operatively and cardiotropic support post-operatively are hard to assess retrospectively. Data on intra-operative cardiovascular physiology was not collected and it is hard to assess whether post-operative hypotension was due to cardiac dysfunction or whether inflammation and leaky capillaries led to the hypotension. The majority of infants who get a

PDA ligation have inflamed lungs, due to over circulation in the pulmonary vasculature and/or damage from mechanical ventilation. They are at risk of right ventricular dysfunction and poor cardiac output even prior to surgery. Point of care echocardiography would have helped answer some of these questions; however this technology is not yet available in our center. Similarly, due to the retrospective nature of the study, data on the PDA itself, besides size (small, moderate or large) was limited.

A prospective cohort study with appropriate recording of fluids and anesthetic agents, intra-operative data on cardiovascular physiology and precise documentation of fluids and inotropes administered with point of care echocardiogram may help identify modifiable risk factors and improve outcomes in this vulnerable population.

Acknowledgments: The authors would like to thank Dr. Kimmo Murto and Dr. Gyaandea Maharajh for their critical review of the manuscript.

[**References**]

[1] Bose CL, Laughon MM. Patent ductus arteriosus: lack of evidence for common treatments[J]. Arch Dis Child Fetal Neonatal Ed, 2007, 92(6): F498-502.
[2] Laughon MM, Simmons MA, Bose CL. Patency of the ductus arteriosus in the premature infant: is it pathologic? Should it be treated? [J]. Curr Opin Pediatr 2004, 16(2):146-151.
[3] Kabra NS, Schmidt B, Roberts R, Doyle LW, Papile L, Fanaroff A. Neurosensory impairment after surgical closure of patent ductus arteriosus in extremely low birth weight infants: results from the trial of indomethacin prophylaxis in preterms[J]. J Pediatr, 2007, 150:229-234.
[4] Jim WT, Chiu NC, Chen MR, Hung HY, Kao HA, Hsu CH, et al. Cerebral hemodynamic change and intraventricular hemorrhage in very low birth weight infants with patent ductus arteriosus[J]. Ultrasound Med Biol, 2005, 31(2):197-202.
[5] Coombs RC, Morgan ME, Durbin GM, Booth IW, McNeish AS. Gut blood flow velocities in the newborn: effects of patent ductus arteriosus and parenteral indomethacin[J]. Arch Dis Child, 1990, 65 (10 Spec No):1067-1071.
[6] Wheatley CM, Dickinson JL, Mackey DA, Craig JE, Sale MM. Retinopathy of prematurity: recent advances in our understanding [J]. Br J Opthalmol, 2002, 86(6):696-700.
[7] Koch J, Hensley G, Roy L, Brown S, Ramaciotti C, Rosenfeld CR. Prevalence of spontaneous closure of the ductus arteriosus in neonates at a birth weight of 1000 grams or less[J]. Pediatrics, 2006, 117(4):1113-1121.
[8] Wyllie J. Treatment of patent ductus arteriosus[J]. Semin Neonatol, 2003, 8(6):425-432.
[9] Pham JT, Carlos MA. Current treatment strategies of symptomatic ductus arteriosus[J]. J Pediatr Health Care, 2002, 16(6):306-312.
[10] Koehne PS, Bein G, Alexi-Meskhishvili V, Weng Y, Buhrer C, Obladen M. Patent ductus arteriosus in very low birthweight infants: complications of pharmacological and surgical treatment [J]. J Perinat Med, 2001, 29(4):327-334.
[11] McNamara PG, Teixeira LS. Enhanced intensive care for the neonatal ductus arteriosus[J]. Acta Paediatr, 2006, 95(4):394-403.
[12] Kimball TR, Ralston MA, Khoury P, Crump RG, Cho FS, Reuter JH. Effect of ligation of patent ductus arteriosus on left ventricular performance and its determinants in premature neonates[J]. J Am Coll Cardiol, 1996, 27(1):193-197.
[13] Noori S, Friedlich P, Seri I, Wong P. Changes in myocardial function and hemodynamics after ligation of the ductus arteriosus in preterm infants[J]. J Pediatr, 2007, 6 (6): 597-602.
[14] Teixeira LS, Shivananda SP, Stephens D, Van Arsdell G, McNamara PJ. Postoperative cardiorespiratory instability following ligation of the preterm ductus arteriosus is related to early need for intervention[J]. J Perinatol, 2008, 28(12):803-808.
[15] Harting MT, Blakely ML, Cox CS, Lantin-Hermoso R, Andrassy RJ, Lally KP. Acute hemodynamic decompensation following patent ductus arteriosus legation in premature infants[J]. J Invest Surg, 2008, 21(3):133-138.
[16] Moin F, Kennedy KA, Moya FR. Risk factors predicting vasopressor use alter patent ductus arteriosus ligation[J]. Am J Perinatol, 2003, 20(6):313-320.
[17] Jaillard S, Larrue B, Raksa T, Magnenant E, Warembourg H, Storme L. Consequences of delayed surgical closure of patent ductus arteriosus in very premature infants[J]. Ann Thorac Surg, 2006, 81 (1): 231-234.
[18] Hsiao CC, Wung JT, Tsao LY, Chang WC. Early or late surgical ligation of medical refractory patent ductus arteriosus in premature infants[J]. J Formos Med Assoc, 2009, 108(1):72-77.
[19] Chorne N, Leonard C, Piecuch R, Clyman RI. Patent ductus arteriosus and its treatment as risk factors for neonatal and neurodevelopmental morbidity[J]. Pediatrics, 2007, 119(6):1165-1174.
[20] Takahashi Y, Harada K, Ishida A, Tamura M, Tanaka T, Takada G. Changes in left ventricular volume and systolic function before and after the closure of ductus arteriosus in full-term infants[J]. Early Hum Dev, 1996, 44(1):77-85.

附中文摘译(刘玲 译):

对于动脉导管未闭(patent ductus arteriosus,PDA),临床上常用的关闭导管的药物是消炎痛,但对于胎龄 < 27 周的早产儿,药物关闭 PDA 的效果较差,如果药物关闭失败或禁忌时,可考虑手术结扎,然而手术也存在相关的并发症,如气漏、伤口感染、术中出血、左侧声带麻痹和颅内出血等,且近年有文献报道结扎导管后,左心功能的负担加重,左心室搏出的血量减少。由于麻醉药物可使心输出量减少,因此手术过程中需要给部分患儿静脉输注生理盐水或胶体液,以增加对手术的耐受性,而每个患儿术中增加的液体量存在较大的个体差异。临床中观察发现术中补液较多的患儿,术后易出现血流动力学的不稳定,需要使用多巴胺、多巴酚丁胺或肾

上腺素等药物或需要高频呼吸机辅助通气。但至今对于导管结扎术中的最佳补液量尚未见文献报道,本研究的主要目的是探讨 PDA 结扎术中补液对术后患儿血液动力学稳定性、死亡率及是否需要高频辅助通气等的影响。研究对象为加拿大渥太华大学附属医院和附属东安大略省儿童医院(CHEO)2001 年 1 月至 2007 年 12 月新生儿重症监护病房胎龄≤32 周,使用药物(消炎痛 0.1 ~ 0.2 mg/kg,口服 1 ~ 2 个疗程,Q12 h)关闭失败或禁忌而接受手术结扎的早产儿(除外导管依赖型复杂性先心病)。这些患儿机械通气参数的设置已达最优化(允许性的高碳酸血症 PCO2 50 ~ 65 mmHg,pH ≥7.25),术中静脉营养持续输注至术后 24 ~ 48 h,术中和术后根据疼痛程度予芬太尼或吗啡镇痛。如果血压低,先予生理盐水扩容,然后用多巴胺持续静滴,速度从每分钟 5 μg/kg 开始,最大增加至每分钟 15 μg/kg,如果血压仍低于正常,可加用多巴酚丁胺或肾上腺素。如应用上述药物后血压仍低,可加用氢化考的松每日 2 ~ 6 mg/kg。如常频呼吸机辅助通气不能维持血气在正常范围,可改用高频呼吸机。观察指标主要为导管结扎术后 24 h 内是否需要使用多巴胺,或患儿术前已经静滴多巴胺,但术后 24 h 内剂量是否较术前增加每分钟2.5 μg/kg;其次是观察患儿术后是否需要改用高频辅助通气以及术后 30 d 内患儿的死亡率。

本研究结果表明 2001 年 1 月至 2007 年 12 月间,共有 103 名患儿接受导管结扎手术,除外 5 例导管依赖型复杂性先心病,研究实际纳入对象 98 名,胎龄为 23 ~ 31 周(平均 26.1 ± 1.8),出生体重 491 ~ 1 950(平均 910 ± 307)g,1 min Apgar 评分 0 ~ 9 分,5 min Apgar 评分 1 ~ 9 分,结扎时日龄 6 ~ 58(平均 22 ± 10)d,术前 79 例患儿(81%)应用消炎痛关闭失败,术前 24 h FiO_2 为 21 ~ 100(平均 42 ± 19)%,术前 95 名患儿(97%)接受了机械通气,12 名(12%)患儿使用了多巴胺。在术前使用多巴胺的 12 名患儿中,术后 11 例仍需要继续使用多巴胺。本研究 98 名接受手术的患儿,27 例(28%)术后使用了多巴胺,其中 6 例还加用了多巴酚丁胺和肾上腺素,3 例使用了氢化考的松。除输注的静脉营养液外,术中临时增加的液量为 0 ~ 50.4(平均 10.2)mL/kg,增加的液体多为生理盐水。98 名患儿中,仅 26 名术中未补液。本研究统计结果发现 PDA 结扎术中输液量与术后多巴胺等药物的应用无相关性($P = 0.10$),但 logistic 多元回归模型分析发现手术时日龄、出生体重和术前 FiO_2 与术后多巴胺的使用有关,尤其是与手术时的日龄关联最大。本研究 2 例患儿术后 30 d 内死亡,但死亡原因无法进一步明确,是否与术中增加的液量有关尚不清楚。6 例患儿术后需要高频通气,但高频通气患儿术中输注液量的多少与未使用高频通气组比较差异无统计学意义($P = 0.55$)。

本研究中因导管结扎致术后低血压而需使用多巴胺等药物的患儿占 28%,与文献报告的一致。据文献报道日龄超过 28 d 的婴儿 PDA 结扎后很少发生血流动力学的改变,术后血流动力学变化的发生率仅为 15.4%。另外 Noori 等学者的一项回顾性和前瞻性纵向研究结果发现:导管直径越大,关闭后左心输出量的降低就越明显,约 35% 需要使用多巴胺等药物。Harting 和 Moin 等的回顾性和前瞻性队列研究也得出:胎龄和出生体重越低,呼吸机参数设置条件越高,术后血流动力学越易失代偿,而一旦失代偿,患儿多在出院前死亡。本研究显示术中输液量与术后血流动力学的变化无关,但手术时日龄与术后血流动力学的不稳定有关,与文献报道一致。此外术前 FiO_2 也与术后多巴胺等药物的使用成正比。但导管结扎过程中最安全的补液量目前尚难确定,必须视个体差异而定。本研究的不足之处是仅为回顾性的统计分析,对患儿术中和术后补液,以及术后使用多巴胺等药物的原因很难进行评价。因为本研究未收集术中患儿心血管生理状况的有关指标,所以很难评估术后低血压是由于心肌收缩力减低还是由于炎症反应致毛细血管的通透性增加或血浆渗出后引起的血压降低。有条件的医院在导管结扎过程中,可用超声心动图监测心功能的变化,然而我院目前尚不具备这一条件。同样,由于本研究为回顾性,而病例资料仅能统计动脉导管的管径,而其他有关资料无法统计。因此,今后如能对这一问题进行前瞻性的研究,并对术中输液量、麻醉药的使用情况、超声心动图监测手术过程中心功能的变化、并准确记录术中增加的液量和多巴胺等药物的使用情况,将有助于找到导管结扎后心功能降低的危险因素,便于今后临床医师采取更为有效的措施,改善患儿的预后。

(本文编辑:邓芳明)