Short-Term Outcome of PDA Ligation in the Preterm Infants at King Chulalongkorn Memorial Hospital, Thailand

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Background: *Failure of the ductus arteriosus to close after medical treatment is usually associated with many severe cardio-respiratory morbidities. Therefore, surgical ligation of symptomatic PDA is indicated in preterm newborn infants who do not respond or have contraindication of medical treatment.*
Objective: *To report the short-term outcomes of PDA ligation in preterm infants at a tertiary care hospital in Thailand.*
Material and Method: *Medical records of 42 preterm infants who underwent surgical ligation of PDA at King Chulalongkorn Memorial Hospital were reviewed. All of the infants had symptomatic PDA that failed to respond to medical treatment or had a contraindication to indomethacin or ibuprofen. Surgical ligation of PDA was performed under general anesthesia. Morbidity and mortality occurring during hospitalization were reported.*
Results: *There were 42 preterm infants in the present study. All of them had large PDA with intractable congestive heart failure. Mean $\pm$ SD of birth weight and gestational age were 1,206 $\pm$ 567 grams and 28.7 $\pm$ 3.6 weeks respectively. Mean $\pm$ SD of the infants' weight and age at the time of surgery were 1,089 $\pm$ 549 grams and 17.5 $\pm$ 12 days respectively. Data on the size of PDA was available on 21 preterm infants. Their ductus diameter (Mean $\pm$ SD) was 3.1 $\pm$ 1.1 mm. All infants were successfully extubated after PDA ligation. Twelve events of complications occurred in 11 infants (26.7%). All of the complications were of mild degree and resolved within a few days except one infant with left phrenic nerve injury that needed surgical plication of the diaphragm. Two infants died at 37 and 160 days after surgery and the latter infant developed IVH grade IV on the 15th day postoperatively. These complications were probably not related to PDA ligation.*
Conclusion: *PDA ligation was performed successfully on 42 preterm infants who had medical failure or had contraindication to medical treatment. Cardio-respiratory illnesses improved significantly after ligation. Two infant mortalities were not related to the procedure. Overall complication of surgery was 26.7% and resolved without sequelae.*

Keywords: *Patent ductus arteriosus, Infant, Very low birth weight Ligation*

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Prematurity and respiratory distress syndrome (RDS) are two important predisposing factors of patent ductus arteriosus (PDA). Failure of the ductus arteriosus (DA) to close in preterm infants is not the result of an abnormality of the ductus arteriosus itself but rather due to abnormal stimuli such as acidosis, prolonged hypoxia and continuing high circulatory prostaglandin levels[1]. Clinical presentation of PDA usually occurs in ventilated infants recovering from RDS. Some of the infants may develop intra-ventricular hemorrhage (IVH), heart failure, pulmonary hemorrhage and increasing O_2 and ventilator support with the presence of PDA. Closing the PDA will ameliorate

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these complications. Although the majority of infants with PDA responded well to medical management that included fluid restriction and indomethacin or ibuprofen administration. The response rate was 75-91%[2-5]. Cotton et al[6] evaluated the effects of medical and surgical treatment on the respiratory course in small preterm neonates who were ventilator dependent. They found that infants treated surgically had a shorter duration of mechanical ventilation and were able to achieve a sustained appropriate caloric intake earlier. Hence, ductal closure should be attempted by surgery if medical treatment is ineffective or contraindicated. Surgical ligature of a PDA in preterm infants has been shown to achieve a high success with low complication rate[7]. However, this procedure is seldom performed in Thailand. It is available in only a few tertiary care centers. The purpose of the present study is to assess short-term outcomes of surgical ligature of PDA in the preterm infants at King Chulalongkorn Memorial Hospital (KCMH), one of the tertiary care hospitals in Thailand.

Material and Method

The authors reviewed the medical records of 45 preterm infants who underwent surgical ligation of PDA between April 1996 and December 2008 at King Chulalongkorn Memorial Hospital. Clinical data were collected including demographic information, post-operative cardio-respiratory condition, duration of mechanical ventilation, diagnosis of intra-ventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), and mortality during hospitalization. IVH was screened by bedside cranial ultrasonography on every preterm infant with birth weight < 1,500 gram during the first 2 weeks of life and thereafter if it was suspected clinically. Bell's stage 2 of NEC was included[8]. BPD was defined as requirement of supplemental oxygen at 36 weeks post conception age (with characteristic chest radiographic abnormalities). Fundoscopy was performed on the preterm infants every 1-2 weeks by ophthalmologists until the retina was mature. Infants diagnosed with PDA were initially treated with fluid restriction and indomethacin or ibuprofen administration if there was no contraindication. A second course of medical treatment was indicated when the ductus arteriosus failed to close or reopened. Infants with symptomatic PDA who failed to respond to intravenous indomethacin or oral ibuprofen or had a contraindication to medication were enrolled for PDA ligation. Diagnosis of PDA was confirmed preoperatively with echocardiography performed by a pediatric cardiologist. All of the infants were transported from neonatal intensive care unit (NICU) to the distant operating room. Surgical ligation of PDA was performed under general anesthesia. The surgical approach to the PDA was left lateral thoracotomy through the fourth intercostal space. The vagus and phrenic nerves are identified, and the posterior pleura is opened over the descending aorta. Careful dissection is made above and below the PDA. When the instrument passes freely behind the PDA, two heavy braided ligatures (silk 2-0) are passed around it. The ligatures are then tied in sequence to ligate the PDA. Wounds are closed with running sutures. Small intercostal drainage tube is placed in the left pleural space only in infants who have air leakage from the lung during the procedure. Transportation back to the NICU is conducted in the same manner as the pre-operative transport. Surgical complications, post-operative hemodynamic changes, successful extubation rate, and survival rate of the infants before discharge were reported as number of events.

Results

Forty-two preterm infants were included in the present study. Male: female ratio was 27:15. Mean $\pm$ SD of BW and GA were 1,206 $\pm$ 567 grams and 28.7 $\pm$ 3.6 weeks respectively. There was only one small for gestational age infant. Mean $\pm$ standard deviation (SD) of body weight and age at surgery were 1,089 $\pm$ 549 grams and 17.5 $\pm$ 12 weeks respectively. Associated congenital anomalies were found in four infants, one each with esophageal atresia and tracheo-esophageal fistula, gastroschisis, omphalocele, and congenital cardiomyopathy. Thirty-six infants (85.7%) had idiopathic respiratory distress syndrome. Three infants born before the year 2000, when intravenous indomethacin was not available in Thailand, were treated with oral ibuprofen. Other infants were treated with intravenous indomethacin. All but one infant were unable to be weaned off the ventilators before PDA ligation. Indication for surgery was the presence of a large PDA with intractable congestive heart failure. Data of PDA size at the time of surgery were available in 21 infants. The Mean $\pm$ SD of PDA diameter was 3.1 $\pm$ 1.1 mm (Table 1). Although six infants (13.3%) developed BPD, none of them needed O_2 supplementation at discharge. IVH grade 1-3 was found in six infants (13.3%) before PDA ligation, all hemorrhage resolved spontaneously later.

All infants were successfully extubated and survived after PDA ligation. However, two infants died at 37 and 160 days postoperatively. The cause of death was sepsis, unrelated with PDA ligation. There were 12 events of surgical complications in 11 infants (26.7%), (Table 2). These complications had been corrected appropriately. Wound infection and pulmonary hypertension resolved within a few days. Intra-operative bleeding was immediately corrected with blood transfusion.

One infant developed hemodynamic decompensation at 3 hours after PDA ligation but responded well to intravenous dopamine and dobutamine. Pneumothorax due to accidental tear of left lung in three preterm infants resolved within a few days after intercostal drainage. One infant had left phrenic nerve paralysis and was treated with surgical plication of left diaphragm 14 days after PDA ligation. IVH grade IV was found in one preterm 26 weeks gestation infant on the 15th day after PDA ligation. It resolved spontaneously without developing post-hemorrhagic hydrocephalus. ROP was diagnosed in five infants, two with stage 2 and one each with stage 1, 3, and 4. The infant with stage 4 ROP died 160 days after PDA ligation. ROP stage 3 in another infant regressed after laser photocoagulation. The rest of them regressed completely.

Table 1. Data of infants underwent surgical ligation of PDA

Characters	Preterm (n = 42)
BW, grams, mean ± SD	1,206.0 ± 567.0
GA, weeks, mean ± SD	28.7 ± 3.6
Weight at surgery, grams, mean ± SD	1,089.0 ± 549.0
Age at surgery, days, mean ± SD	17.5 ± 12.0
Size of PDA, mm, mean ± SD	3.1 ± 1.1
Number of infants with RDS (%)	36 (85.7)
Number of infants with other anomalies (%)	4 (9.5)
Number of infants with ventilator dependent (%)	41 (97.6)

BW = body weight, GA = gestational age

Table 2. Complications after PDA ligation

Types	No. of events
Minimal wound infection	3
Transient pulmonary hypertension	2
Intra-operative bleeding	1
Hemodynamic decompensation	1
Pneumothorax	3
Lt. phrenic nerve paralysis	1
IVH grade IV	1

Discussion

The present study showed a satisfactory result of PDA ligation in preterm infants, even in the very extremely low birth weight ones. The smallest infant was 645 grams with gestational age of 25 weeks. All infants recovered uneventfully except two infants who died from sepsis which, the authors believed, was not related to the surgical procedure itself. Naik-Mathuria et al[9] demonstrated that preoperative symptoms related to respiratory insufficiency, hypotension, apnea, and pulmonary edema in the infants improved after PDA ligation. Clinical symptoms of the presented infants also did improve postoperatively. Although there were 12 events (26.7%) of complications occurring in the present study, the rate was less than those reported in other studies[10-13]. Ten infants with complications were in very low birth weight category, their body weights ranged between 540-1,005 grams. Therefore, the size of the infants may be a factor attributable to surgical complications. Harting et al[10] reported a high incidence (28%) of hemodynamic decompensation (hemodynamic instability requiring inotropic support) in preterm infants after PDA ligation, which was found in only one (2.2%) of the patients. The hemodynamic instability resolved within 24 hours after intravenous inotropic infusion. Noori et al[14] performed echocardiogram before and after PDA ligation in 23 very preterm infants. They demonstrated that left ventricular (LV) output decreased and systemic vascular resistance increased after surgery. The LV myocardial performance index (MPI), a measure of global myocardial performance, deteriorated acutely after ligation but improved in 23.5 hours later. These changes were due primarily to a decrease in LV preload.

Transient postoperative pulmonary hypertension was documented in two patients. The right to left shunting of blood responded well to hyperventilation. Minimal pneumothorax in three patients caused by accidental pleural tear during operation was also resolved within a few days after ipsilateral intercostal drainage.

Phrenic nerve paralysis as a sequelae after PDA ligation has never been reported. However, there were several reports of recurrent laryngeal nerve injury in English literature[11-13]. Infants with recurrent

laryngeal nerve injury were diagnosed by identification of vocal cord paralysis under flexible laryngoscopy, and the presence of stridor and feeding difficulty. None of the presented infants experienced these symptoms. However, the authors did not perform laryngoscopy on the infants; some of them might have developed such nerve injury and might have been underdiagnosed. Furthermore, the majority of infants with recurrent laryngeal nerve injury tend to be asymptomatic despite vocal cord paralysis and compensation appeared to occur rapidly. The patients generally had no long-term problems with the airway or feeding[12]. This complication, however, should be aware of in every infant after surgical ligation.

BPD and IVH was diagnosed in six infants (13.3%). The authors believe these complications were rather related to the underlying prematurity. IVH grade I-III in five infants were noted preoperatively and resolved spontaneously without sequelae. The infant with IVH grade IV was the smallest one in this cohort. She developed IVH on the 15th day after PDA ligation. This complication could be unrelated to the surgery. The authors think the important factors affecting the adverse outcome in very low birth weight infants are not related to PDA ligation but the preoperative conditions related to the underlying prematurity.

The presented study showed that surgical ligation of PDA can be performed safely with good result on every preterm infant in our hospital. The size of the infants should not discourage them from surgery.

Conclusion

PDA ligation was performed successfully on 42 preterm infants who did not respond to medication nor had contraindication to medical treatment. Cardiorespiratory illnesses improved significantly after surgery. There were only two deaths (mortality rate of 4.4%), which were not related to the procedure. The overall postoperative complication rate was 26.7% and resolved without sequelae. The authors propose that surgical ligation of PDA should be performed in a tertiary care hospital for every preterm infant with significant PDA who has medical failure, regardless of their body weight.

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ผลการผ่าตัดปิด พี ดี เอ ในทารกแรกเกิดก่อนกำหนดในระยะสั้นที่โรงพยาบาลจุฬาลงกรณ์

วิชัย เบญจชลมาศ, จุล นำชัยศิริ, พรเทพ เลิศทรัพย์เจริญ, สันติ ปุณณะหิตานนท์, พิมลรัตน์ ไทยธรรมยานนท์

***ภูมิหลัง**: หลอดเลือดดัคตัสอาเทอริโอซัสหรือพีดีเอ (PDA) ของทารกแรกเกิดก่อนกำหนด ที่ไม่ปิดภายหลังการรักษาด้วยยามักทำให้เกิดภาวะแทรกซ้อนทางระบบหัวใจและทางเดินหายใจอย่างรุนแรง ดังนั้นจึงเป็นข้อบ่งชี้ให้ทำการผ่าตัดปิดหลอดเลือดที่ก่อให้เกิดอาการนี้*

***วัตถุประสงค์**: เพื่อรายงานผลการผ่าตัดปิดหลอดเลือดพีดีเอในทารกเกิดก่อนกำหนดในโรงพยาบาลระดับตติยภูมิแห่งหนึ่งในประเทศไทย*

***วัสดุและวิธีการ**: ทำการศึกษาเวชระเบียนทารกแรกเกิดก่อนกำหนดทั้งหมดที่ได้รับการผ่าตัดปิดหลอดเลือดพีดีเอในโรงพยาบาลจุฬาลงกรณ์ทารกทุกคนมีอาการป่วย อันเป็นผลจากหลอดเลือดนี้ และไม่ตอบสนองต่อการรักษาด้วยยา หรือ มีข้อห้ามใช้ยา indomethacin หรือ ibuprofen ที่ใช้ปิดหลอดเลือดพีดีเอการทำผ่าตัดปิดหลอดเลือดนี้กระทำภายใต้การดมยาสลบทารก และรายงานภาวะแทรกซ้อนและอัตราการเสียชีวิตขณะอยู่ในโรงพยาบาล*

***ผลการศึกษา**: มีทารกเกิดก่อนกำหนดที่ได้รับการผ่าตัดปิดหลอดเลือดพีดีเอ 42 ราย ทุกคนมีหลอดเลือดพีดีเอใหญ่ที่ก่อให้เกิดอาการหัวใจล้มเหลว ทารกมีน้ำหนักแรกเกิดและอายุครรภ์เฉลี่ย ± ค่าเบี่ยงเบนมาตรฐานเท่ากับ 1,206 ± 567 กรัม และ 28.7 ± 3.6 สัปดาห์ ตามลำดับ น้ำหนักและอายุวันทำผ่าตัดเฉลี่ย ± ค่าเบี่ยงเบนมาตรฐาน เท่ากับ 1,089 ± 549 กรัม และ 17.5 ± 12 วัน ตามลำดับ ขนาดเส้นผ่าศูนย์กลางหลอดเลือดพีดีเอ ขณะผ่าตัด ที่วัดไว้จำนวน 21 ราย โดยเฉลี่ย ± ค่าเบี่ยงเบนมาตรฐานเท่ากับ 3.1 ± 1.1 มม. ทารกทุกคนมีอาการดีขึ้นหลังผ่าตัด สามารถถอดเครื่องช่วยหายใจได้ พบภาวะแทรกซ้อน 12 อย่างเกิดขึ้นกับทารก 11 ราย (ร้อยละ 26.7) ภาวะแทรกซ้อนทั้งหมดอาการไม่รุนแรงและหายเร็ว ยกเว้นทารกรายที่เกิดการบาดเจ็บที่เส้นประสาทเลี้ยงกะบังลมต้องแก้ไขด้วยการทำผ่าตัดยึดกะบังลม (Plication of diaphragm) ทารก 1 รายเกิดเลือดออกในช่องสมองระดับ 4 (Intraventricular hemorrhage stage IV) เมื่ออายุ 15 วันหลังผ่าตัดและเสียชีวิต ทารกเสียชีวิตทั้งหมด 2 ราย*

***สรุป**: ทำการผ่าตัดปิดหลอดเลือดพีดีเอได้สำเร็จในทารกเกิดก่อนกำหนด 42 รายที่ไม่สามารถรักษาได้ด้วยการให้ยา อาการป่วยทางระบบหัวใจและทางเดินหายใจดีขึ้นชัดเจนภายหลังผ่าตัด มีทารกเสียชีวิต 2 ราย ซึ่งไม่น่าเกิดจากการทำผ่าตัดภาวะแทรกซ้อนในระยะสั้นหลังผ่าตัดเกิดขึ้นร้อยละ 26.7 และทั้งหมดหายเป็นปกติในเวลาต่อมา*