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

Vichai Benjacholmas MD*, Jule Namchaisiri MD*, Pornthep Lertsarpcharoen MD**, Santi Punnahitananda MD**, Pimolrat Thaithumyanon MD**

* Department of Surgery, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
** Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

** 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 ± SD of birth weight and gestational age were 1,206 ± 567 grams and 28.7 ± 3.6 weeks respectively. Mean ± SD of the infants’ weight and age at the time of surgery were 1,089 ± 549 grams and 17.5 ± 12 days respectively. Data on the size of PDA was available on 21 preterm infants. Their ductus diameter (Mean ± SD) was 3.1 ± 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

**J Med Assoc Thai 2009; 92 (7): 909-13**

**Full text. e-Journal:** http://www.mat.or.th/journal
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 (2). 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 ligation 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 (3). 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 ± SD of BW and GA were 1,206 ± 567 grams and 28.7 ± 3.6 weeks respectively. There was only one small for gestational age infant. Mean ± standard deviation (SD) of body weight and age at surgery were 1,089 ± 549 grams and 17.5 ± 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 ± SD of PDA diameter was 3.1 ± 1.1 mm (Table 1). Although six infants (13.3%) developed BPD, none of them needed O2 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.

**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

**Table 1.** Data of infants underwent surgical ligation of PDA

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

BW = body weight, GA = gestational age

**Table 2.** Complications after PDA ligation

<table>
<thead>
<tr>
<th>Types</th>
<th>No. of events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal wound infection</td>
<td>3</td>
</tr>
<tr>
<td>Transient pulmonary hypertension</td>
<td>2</td>
</tr>
<tr>
<td>Intra-operative bleeding</td>
<td>1</td>
</tr>
<tr>
<td>Hemodynamic decompensation</td>
<td>1</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>3</td>
</tr>
<tr>
<td>Lt. phrenic nerve paralysis</td>
<td>1</td>
</tr>
<tr>
<td>IVH grade IV</td>
<td>1</td>
</tr>
</tbody>
</table>
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 under-diagnosed. 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. Cardio-respiratory 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.

References

ผลการผ่าตัดปิดพีดีเอในทารกแรกเกิดก่อนกำหนดในระยะสั้นที่โรงพยาบาลจุฬาลงกรณ์

วิชัย เบญจชุมมาศ, จุล นาระชีริ, พรเทพ เลิศทรัพย์จันทร์, สันติ ปุณณะทิตานท์, พิมลรัตน์ ไทยธรรมยานนท์

ภูมิหลัง: หลอดเลือดดัคตัสอาเทอริโอซัสหรือพีดีเอ (PDA) ของการเกิดก่อนกำหนดก่อนหลอดเลือดที่ไม่เปิดภายหลังการรักษาด้วยยาทำให้เกิดภาวะพรลทารกที่มีระบบหัวใจและทางเดินหายใจอย่างรุนแรง ดังนั้นจึงเป็นข้อบ่งชี้ให้ทำการผ่าตัดปิดหลอดเลือดที่ก่อให้เกิดอาการนี้

วัตถุประสงค์: เพื่อมารายการผลการผ่าตัดหลอดเลือดพีดีเอในทารกแรกเกิดก่อนกำหนดในโรงพยาบาลระดับตติยภูมิแห่งหนึ่งในประเทศไทย

วัสดุและวิธีการ: ทำการศึกษาคัดเลือกทารกแรกเกิดก่อนกำหนดทั้งหมดที่ได้รับการผ่าตัดปิดหลอดเลือดพีดีเอในโรงพยาบาลจุฬาลงกรณ์ทารกทุกคนเมื่ออาการโดย ซึ่งเป็นผลจากหลอดเลือดพีดีเอ และไม่ตอบสนองต่อการรักษาด้วยยา หรือมีข้อห้ามใช้ indomethacin หรือ ibuprofen ที่ใช้ปิดหลอดเลือดพีดีเอจากการทำผ่าตัดปิดหลอดเลือดพีดีเอ กระทำภายใต้การดมยาสลบทารก และรายงานภาวะแทรกซ้อนและอัตราการเสียชีวิตของทารกในโรงพยาบาล

ผลการศึกษา: มีทารกแรกเกิดก่อนกำหนดที่ได้รับการผ่าตัดปิดหลอดเลือดพีดีเอ 42 ราย ทุกคนมีหลอดเลือดพีดีเอใหญ่ที่ก่อให้เกิดอาการรุนแรงและหลาย ทำให้หายจากหลอดเลือดพีดีเอ ประมาณ 1,206 ± 567 กรัม และ 28.7 ± 3.6 สบวมที่ ตัวเด็ก น้ำหนักและอายุการผ่าตัดเฉลี่ย 3.1 ± 1.1 มม. การทำผ่าตัดปิดหลอดเลือดพีดีเอสภาวะระบบหัวใจและทางเดินหายใจมีการติดเชื้อทางเดินหายใจ 11 ราย (26.7) และภาวะแทรกซ้อนที่เกิดขึ้นอาจเกิดจากการทำผ่าตัดปิดหลอดเลือดพีดีเอ Plication of diaphragm) 1 รายเกิดจากภาวะแทรกซ้อนที่เกิดขึ้นหลังการผ่าตัด 4 (Intraventricular hemorrhage stage IV) เมื่ออายุ 15 วันหลังผ่าตัดและเสียชีวิต ทำให้เสียชีวิตทั้งหมด 2 ราย

สรุป: ทำการผ่าตัดปิดหลอดเลือดพีดีเอสำเร็จในการเกิดก่อนกำหนด 42 รายที่ไม่สามารถรักษาได้ด้วยการยาอาการรบกวนระบบหัวใจและทางเดินหายใจพีดีเอในระยะสั้นหลอดเลือดพีดีเอ 26.7 และทั้งหมดหายเป็นปกติในเวลาต่อมา