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Research Paper

# Clinical Profile of Patent Ductus Arteriosus in Preterm Neonates

Medical Science

**KEYWORDS :** Patent ductus arteriosus(PDA), Indomethacin, Ibuprofen

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## ABSTRACT

*Objective and design: Prospective study*

*1. To study the clinical profile of neonates with PDA*

*2. Outcome of medical management in closure of ductus arteriosus.*

*Setting: NICU of a tertiary care centre at Ahmedabad*

*Subjects and intervention: All preterm neonates from October 2012 to September 2013, clinically diagnosed to have PDA were confirmed by 2D ECHO. The clinical profile of these neonates was studied. Those with haemo-dynamically significant PDA were given oral Indomethacin or Ibuprofen according to their clinical condition.*

*Results: In 12 months, 107 preterm neonates had ECHO proven PDA. 80% had hemo-dynamically significant PDA. HMD(37.4%) and septicaemia(33.6%) were most common morbidities associated. Closure rate after medical treatment were 90% in Indomethacin and 88% in Ibuprofen group.*

*Conclusion: High index of suspicion for PDA, early diagnosis and timely intervention can achieve good neonatal outcome. Medical therapy can achieve closure in most of the neonates.*

**Introduction**

A ductus arteriosus (DA) is a bridge or canal connecting the pulmonary artery to the descending aorta during fetal life.[1] This opening is vital during fetal circulation in order for a significant portion of the blood to bypass the pulmonary circulation. The incidence of a persisting patent ductus arteriosus(PDA) can range from 10-60% of neonates inversely related to gestational age and birth weight. Significance of PDA in the medical field lies in fact that infants born prematurely are seen to have a high rate of their PDA not closing after birth resulting in complications. When the PDA does not close, it produces left to right shunting of the blood in the heart. Left to right shunting is associated with pulmonary congestion and decreased blood flow to vital organs and various morbidities and many a times mortality.[2, 3] We conducted this study to find out effects of PDA in our neonates.

**Material and methods:**

A prospective study was conducted from October 2012 to September 2013 at Neonatal Intensive care unit of a tertiary care centre at Ahmedabad. Both intramural and extramural preterm neonates admitted in the NICU within first week of life were included. After informed written consent of parents, preterm neonates who were showing bounding peripheral pulses, hyperdynamic precordium, tachycardia, ejection systolic murmur(continuous or pansystolic murmur) at left infraclavicular region or left parasternal region in first week of life were subjected to 2D echocardiography. Those neonates who were confirmed having congenital heart disease in form of patent ductus arteriosus were included in the study. Preterm Neonates with high suspicion of PDA but Echocardiography were not possible due to any reason were excluded from the study.

All neonates with Echo proven PDA were closely monitored during their NICU stay, and associated morbidities were identified and managed accordingly. Neonates were given oxygen, ventilator support, CPAP support , antibiotics, phototherapy , surfactant according to their co-morbid condition. Size of PDA more than 1.5 mm and absent or retrograde flow in post ductal aorta were considered hemodynamically significant PDA. Neonates having hemodynamically significant PDA, PDA with congestive heart failure or one associated with other non ductus dependent cardiac anamolies,were given medical therapy on basis of associated co-morbid condition. Neonates having renal insufficiency(S. creat > 1.8), thrombocytopenia(<80,000), necrotizing entercolitis, and bleeding(intracranial bleed) were given oral Ibuprofen 10mg/kg, followed at 24 interval by two doses of 5 mg/kg ; and rest of the neonates were given oral Indomethacin 0.2-0.25mg/kg according to day of life 3 doses 12 hours apart. Neonates were followed at 1 month of age and repeat 2D echo done for closure of PDA.[4]

**Results**

Incidence of PDA in preterm was 7.2%. Mean gestational age and birth weight were 32 week and 1.35 kg.

**Table No : 1 Baseline characteristics of Neonates included in the study**

| Parameter | Intra-mural | Extra-mural | Total |
|---|---|---|---|
| Preterm admitted in NICU | 598 | 879 | 1477 |
| PDA (Echo proven) | 42 | 65 | 107 |
| Incidence of PDA | 7% | 7.3% | 7.2% |
| Mean gestational age | 31.9 week | 32 week | 32 week |
| Mean birth weight | 1.33 kg | 1.38kg | 1.35 kg |

80.3% had hemodynamically significant PDA and 25.2% had severe pulmonary hypertension on presentation. Hyaline membrane disease(HMD) was common morbidity associated with PDA(40%), other morbidity were Hyperbilirubinemia(40%), Septicemia(36%), Metabolic complication(15%), Apnoea(9%). 29% Preterm neonates received Surfactant. 17.4% preterm had thrombocytopenia(plt <80,000) and 7.4% preterm had renal insufficiency(S. creat > 1.7).

**Table No 2 : Associated Morbidities**

| Parameter | Intra-mural n=42 | Extramural n=65 | Total n=107 |
|---|---|---|---|
| Hemo-dynamically significant PDA | 33 | 53 | 86 |
| Severe PAH | 11 | 16 | 27 |
| Congestive Heart failure | 7 | 15 | 22 |
| Septicemia | 8 | 28 | 36 |
| HMD | 13 | 27 | 40 |
| Hyper bilirubinemia | 13 | 27 | 40 |
| Altered Renal function tests | 3 | 5 | 8 |
| Thrombocytopenia | 7 | 12 | 19 |
| Apnoea | 3 | 6 | 9 |
| Hypocalcemia | 3 | 5 | 8 |
| Hypoglycemia | 4 | 4 | 8 |

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|---|---|---|---|
| Ventilator support | 5 | 11 | 16 |
| CPAP | 13 | 21 | 35 |
| Surfactant | 9 | 20 | 29 |
| Immunoglobulin therapy | 1 | 2 | 3 |
| Associated other cardiac defect | 4 | 5 | 9 |

86% preterm neonates had received medical therapy; out of which 63% neonates were given oral Indomethacin and 23% were given oral Ibuprofen. Echo proven closure of PDA were 90% and 88.65% in Indomethacin and Ibuprofen group. 9.7% preterm neonates with PDA were expired during their hospital stay.

**Table No: 3 Treatment & outcome**

| Parameter | Intra Mural n=42 | Extra mural n=65 | Total n=107 |
|---|---|---|---|
| Medical therapy within 24 hours ECHO | | | |
| Medical therapy | 33 | 53 | 86 |
| Oral Indomethacin | 25 | 38 | 63 |
| Oral Ibuprofen | 8 | 15 | 23 |
| ECHO proven closure of PDA at 1 month | | | |
| Oral Indomethacin | 20 | 30 | 50 |
| Oral Ibuprofen | 6 | 11 | 17 |
| Mortality | 3 | 8 | 11 |

**Discussion**

Patent ductus arteriosus (PDA) is a major morbidity encountered in preterm neonates, especially in babies less than 28 weeks gestation or 1000g. In our study 1477 preterm neonates were admitted to NICU during last 1 year, of which 107 preterm neonates were having ECHO proven finding of PDA. Out of 598 intramural preterm neonates 42 had PDA with incidence of 7% and 65 from 879 extramural neonates had PDA with incidence of 7.3%. Higher incidence of PDA was found in gestational age < 32 week (20.8%) as compared to >32 week(4.6%). In our study incidence of PDA was lesser than observed incidence of 45% in neonates with birth weight less than 1700 gm and 80% in neonates weighing less than 1200 gm. [1].

Main presenting features of PDA in preterm neonate were tachypnea, tachycardia, bounding peripheral pulses, hyperdynamic precordium, ejection systolic murmur(continuous or pansystolic murmur) at left infraclavicular region or left parasternal region, increase in oxygen demand or increase in need of ventilator support. [1,5,6]

There was higher incidence of HMD(41.5%), Septicaemia(43.7%) and Hyperbilirubinemia(40%) in extramural group as compared to intramural group 31%, 19% and 30.9% respectively. 29 neonates (27.1%) had received pulmonary surfactant due to HMD in both group. Other less common morbidities were Apnoea(8.4%), Hypoglycemia(7.4%) and Hypocalcemia(7.4%). While 5(4.6%) neonates had both renal insufficiency and thrombocytopenia, isolated thrombocytopenia was found in 14(13%) neonates and isolated renal insufficiency was found in only 4(3.7%) neonates.

With improvement of oxygenation in HMD with ventilator, CPAP and surfactant, there is decrease in pulmonary vascular resistance which leads to persistence of ductus and hence delay in closure of ductus. Higher association of HMD in neonate with PDA in our study may be due to above mentioned reason. Septicemia was non specific association due to premature delivery, ventilator care, CPAP care and prolonged hospital stay.[1,4]

86 Preterm neonates having PDA size more than 1.5 mm with equal distribution on both group; 27 neonates(27%) were found having severe pulmonary hypertension at diagnosis. 22(20.5%) preterm neonates were having congestive heart failure at diagnosis due to PDA, requiring decongestive therapy along with medical management for the ductal closure. 63 neonates were given oral Indomethacin from which 7 neonates expired during their hospital stay, 6 neonate had patent ductus at 1 month and 50 neonates achieved closure with medical therapy. Similarly, 23 neonates were given oral Ibuprofen from which 4 neonates expired during their hospital stay, 2 neonates had patent ductus at 1 month and 17 neonates achieved closure with medical therapy. Both the drugs were equally efficacious to achieve closure of ductus and act by similar action via decrease synthesis of prostaglandin. In view of systemic toxicity and limitation of conditions in which Indomethacin use is restricted, oral Ibuprofen can be safe and equally effective alternative therapy for closure of ductus. Similar effectiveness of Ibuprofen over Indomethacin was observed in Sasi and Deorari et al study.[7]. This observation was also supported by Cochrane meta-analysis. [8,9]

Various morbidities associated with persistence or opening of PDA are pulmonary congestion, renal dysfunction, intraventricular hemorrhage (IVH), and gastrointestinal perforation resulting in necrotizing enterocolitis (NEC),leading to poorer outcome hence early diagnosis and timely intervention can achieve good neonatal outcome.[4]

**Conclusion**

Patent ductus arteriosus, is a major morbidity in preterm infants, with incidence inversely related to gestation and birth weight. Bedside functional echocardiography is a valuable tool for early diagnosis, assessment of hemodynamic effects and response to therapy. Ibuprofen with its safety profile, especially reduced risk of NEC and comparable efficacy to Indomethacin is currently widely used drug in treatment of PDA.

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