

Incidence, Options of Medical Intervention and Post-Intervention Follow-up of Patients with Patent Ductus Arteriosus: An Experience in Combined Military Hospital, Dhaka

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Abstract

Introduction: Patent Ductus Arteriosus (PDA) is the fifth most common congenital cardiac defect. A large number of neonates with PDA get admitted to hospital each year. If it remains undetected in the neonatal period, patient may develop several consequences in later life which are very difficult to manage.

Objectives: To determine the incidence of PDA in newborn and its outcome following different modalities of medical intervention.

Methods: This cross-sectional observational follow-up study carried out in Combined Military Hospital (CMH), Dhaka from January 2016 to December 2017. Total 50 cases of isolated PDA were included in this study.

Results: Out of 50 cases, 80% were preterm and 20% were term. Most of the PDA (35) were of moderate size. Total 11 patients had spontaneous closure and 21 patients had closure after Indomethacin therapy. Among 8 patients who did not respond to Indomethacin, 1 died during the therapy and 7 patients underwent successful trans-catheter coil occlusion where 1 patient required second coil implantation. Remaining 10 patients were selected for trans-catheter device closure and complete closure was observed in 100% of these cases within 3 months of device deployment.

Conclusion: Early diagnosis, appropriate pharmacological and medical interventional management can cure nearly all the cases of PDA, avoiding surgery which is also a gold standard safe and effective alternative treatment of PDA.

Key words: Patent Ductus Arteriosus (PDA), Combined Military Hospital (CMH), Indomethacin, Coil occlusion.

Introduction

PDA is a common congenital heart defect which is defined as failure of the ductus arteriosus (DA) to close within 72 hours after birth¹ which may result in significant infant morbidity and mortality rates that approach 30%².

Potential complications of large PDA after birth include heart failure, renal dysfunction, necrotizing enterocolitis (NEC), intraventricular hemorrhage (IVH), altered postnatal nutrition and growth^{3,4}. In addition, PDA is a risk factor for the development of chronic lung disease⁵. The occurrence of PDA is inversely related to gestational age and weight, with an even greater incidence in preterm infants. The incidence of PDA in term infants has been estimated to be 57 per 1,00,000 live births⁶, whereas every third preterm infant with a birth weight (BW) of <1500 g (very low birth weight [VLBW]) can be expected to have a persistent PDA⁷.

Clinical presentation depends on the size of the PDA. Infants with a small PDA are often asymptomatic. Those with a larger PDA may have symptoms of heart failure, growth retardation and prone to develop lower respiratory tract infections.

Three management strategies are currently available for PDA: 1. Fluid restriction, diuretics, high flow oxygen, 2. Medical intervention including pharmacologic, trans-catheter closure (device and coil) and 3. Surgical ligation. Pharmacologic closure can be achieved by intravenous Indomethacin, oral Ibuprofen or Paracetamol. The aim of this study was to determine the incidence and outcome of PDA in newborn after different modalities of medical interventions available in CMH, Dhaka.

Materials and Methods

Patients visiting to paediatric outdoor and admitted paediatric patients in CMH, Dhaka were screened for PDA. Total 50 infants and older children less than 2 years with isolated PDA confirmed by echocardiography were included in this study. It was a hospital based cross sectional observational study carried out in an advanced paediatric cardiac unit of CMH Dhaka over a period of 2 years (from January 2016 to December 2017). Patients beyond 2 years of age, having any syndrome and PDA associated with any other congenital heart defects were excluded from this study. Among study population, 11 patients were included in observation group for spontaneous

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closure of PDA with only high flow oxygen, fluid restriction and diuretic support. Remaining 39 patients were included in medical therapy group for anti-failure and pharmacologic intervention by Indomethacin, Ibuprofen and Paracetamol. Patients with PDA that were not closed after observation and medical therapy were selected for trans-catheter closure by coil or device depending on PDA size and patient's condition. All patients were discharged home on following day after procedure and followed-up at 1, 3, 6 and 12 months of procedure and then yearly afterwards as outdoor basis.

Results

Preterm babies ranging from 29 to 37 weeks were 40(80%) and term babies ranging from 37-40 weeks were 10(20%) (Figure-1). According to peak pressure gradient, 12(24%) patients had small PDA, 35(70%) patients had moderate PDA and 03(6%) patients had severe PDA (Table-I). Initially, 50 patients were divided into two groups (medical therapy group and observation group). In medical therapy group, 39 patients were included (10 received only anti-failure and 29 received both anti-failure and different pharmacologic intervention) and 11 preterm patients were included in observation group for spontaneous closure of PDA (Figure-2).

On follow-up, all preterm patients of observation group (11) had their PDA closed spontaneously within 3 months (100% closure). Out of 39 patients of medical therapy group, 29 patients received both anti-failure therapy and different modalities of pharmacologic intervention (15 Indomethacin, 7 Ibuprofen and 7 Paracetamol). Among them, 21(42%) patients had their PDA closed (12 closed after Indomethacin, 5 closed after Ibuprofen and 4 closed after Paracetamol therapy) and 8(16%) patients had their persistent PDA including 1 who died after Indomethacin while was on early anti-failure therapy. Remaining 10 patients of medical therapy group received only anti-failure and no patient had their PDA closed on follow-up. So, after medical therapy, 17 patients had their PDA open and 1 patient died (Table-II).

Total 17 patients were selected for transcatheter intervention. Among them, 7 patients underwent coil occlusion and all cases (100%) had their PDA closed including one who developed residual shunt after first coil deployment and required second coil implantation. Remaining 10 patients underwent transcatheter device closure and all the cases (100%) closed successfully (Table-III).

During follow-up, out of 40 preterm babies, 1 developed heart failure, 1 developed impaired renal function, 5 developed bleeding manifestation and 1 died after Indomethacin while on early anti-failure therapy. Out of 10 term babies, 3 developed heart failure and 1 developed intravascular hemolysis (Table-IV). Finally, among the 40 preterm neonates, 21 had PDA closure after anti-failure therapy and pharmacologic intervention, eleven had spontaneous closure with only fluid restriction, oxygen supplementation and diuretics, 4 had closure after coil occlusion, 3 had device closure and 1 died. Among term babies, 3 had closure after coil occlusion and 7 had successful device closure (Figure-3).

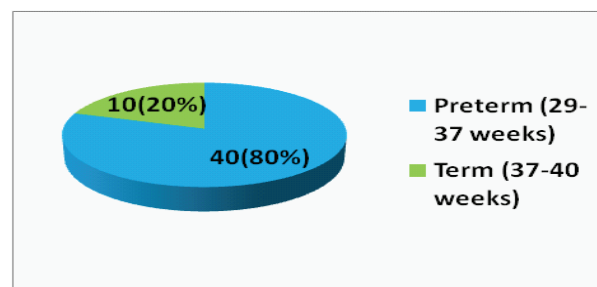


Figure-1: Distribution of patients according to gestational age (n=50)

*Above figure shows preterm babies ranging from 29-37 weeks were 80% (40) and term babies ranging from 37-40 weeks were 20% (10).

Table-I: Classification of PDA according to peak pressure gradient

Type	Peak pressure gradient (mm of Hg)	Frequency (n)	Percentage (%)
Small	>60	12	24
Moderate	40-60	35	70
Severe	<40	03	6

*Above table shows most of the patients (70%) had moderate size PDA.

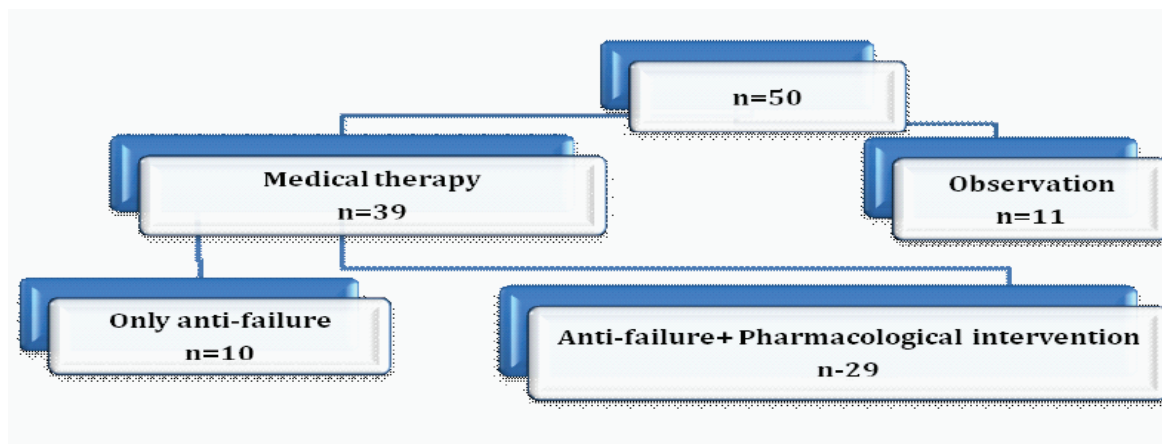


Figure-2: Distribution of neonates in different treatment groups (n=50)

Figure-2 shows that out of 50 patients, initially 11 patients were included in observation group and 39 patients were selected for medical therapy group for different modalities of medical therapy.

Table-II: Outcome of PDA after observation and medical therapy (n=50)

Treatment Modality		Number of patients (n)	PDA closure (n)		Percentage of closure (%)
			Closed	Not-Closed	
Observation group		11	11	00	100
Medical therapy group	Anti-failure therapy & pharmacologic intervention	29	21	08 ^a	42
	Indomethacin	15	12	03	
	Ibuprofen	07	05	02	
	Paracetamol	07	04	03	
	Only anti-failure therapy	10	00	10	00
Total		50	32	18 ^b	

Above table shows that 11 cases were included in observation group and all cases (100%) had PDA closure. Among 39 patients of medical therapy group, 29 patients received both anti-failure therapy with different pharmacologic intervention and 21(42%) patients had their PDA closed. Remaining 10 patients got only anti-failure therapy and no patient had PDA closure on follow-up. ^aOne patient died after Indomethacin while was on anti-failure therapy. ^bTotal 17 patients had PDA open and 1 died.

Table-III: Outcome of PDA after trans-catheter intervention (n=17)

Name of intervention	Number of patients (n)	PDA closure (n)		Percentage of closure (%)
		Closed	Not closed	
1. Coil occlusion	07	07 ^a	00	100
2. Device closure	10	10	00	100

Above table shows, among 17 patients who had PDA open after medical therapy, 7 patients underwent coil occlusion and 10 patients underwent device closure. All cases had successful closure. ^aOne patient developed residual shunt which was later occluded after second coil implantation.

Table-IV: Complications during follow-up of PDA cases (n=50)

Age group	Total patients	Heart failure	Impaired renal function	Intravascular hemolysis	Bleeding manifestation	Death
Pre-term	40	01	01	--	05	01
Term	10	03	--	01	--	--
Total	50	04	01	01	05	01

Above table shows, out of 40 preterm babies, 1 developed heart failure, 1 developed impaired renal function, 05 developed bleeding manifestation and 1 died after getting Indomethacin while was on anti-failure therapy. Out of 10 term babies, 03 developed heart failure and 1 developed intravascular hemolysis.

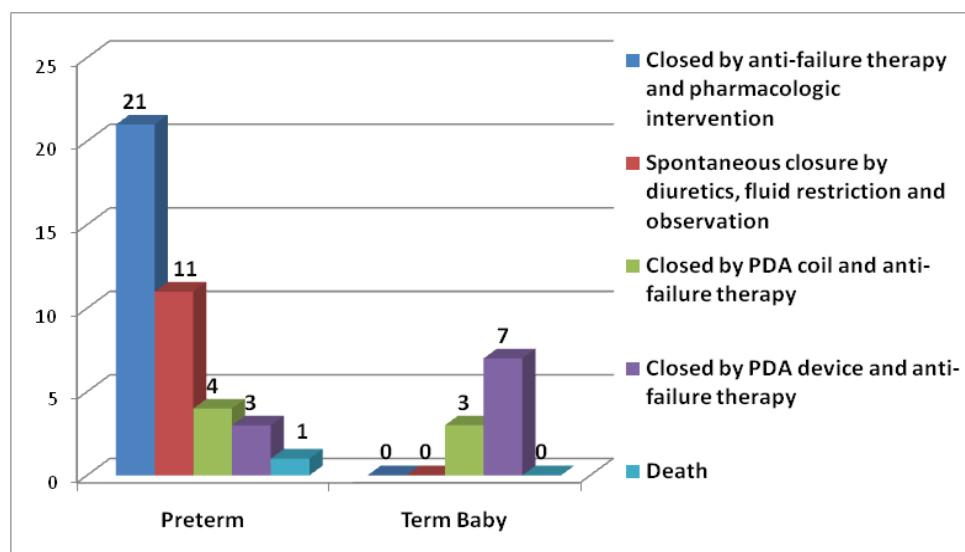


Figure-3: Outcome after 2 years of treatment (n=50)

Discussion

In this study, 80% patients were preterm. In several studies, the incidence of PDA among preterm infants varied from 20% to 60%³, depending on the diagnostic criteria used and the population studied. In this study, 11(22%) preterm with small PDA were observed for spontaneous closure with conservative therapy and within 3 months, all cases (100%) showed spontaneous closure of PDA which consisted with Herman's study⁸. A total of 39(78%) patients received pharmacologic manipulation. Among them, 10(20%) patients received only anti-failure therapy but none had their PDA close on follow-up. Remaining 29(58%) patients received different modalities of medical therapy and most of the patients (21 out of 29) had their PDA closed. Pharmacologic manipulation is given mainly to pre-term newborn, and almost 90% closure can be achieved if given within 7 days of age⁹. Indomethacin is currently the drug of choice for closure of the PDA in premature infants. There are several studies that have shown equal effectiveness with Ibuprofen but minimum chance of toxicity whereas Paracetamol use is emerging as another less toxic option^{10,11}. Indomethacin closes the PDA in most cases at the expense of some worrying side effects like reduced cerebral blood flow¹², oliguria, hyponatremia, gastrointestinal complications and bleeding disorder. We used Indomethacin following the dose schedule¹³ and very few patients developed minor complications which were managed promptly. This finding consisted with Begum NNF study⁹. In almost 100% cases, we successfully completed the course of Indomethacin therapy which matches with other study¹⁴, including one who died after completion of Indomethacin while was on early anti-failure therapy. In this study, when medical treatment failed, we selected those cases for trans-catheter intervention as was opted in Philip's study¹⁵.

All (7) the cases, who failed to close after different modalities of pharmacologic intervention, underwent PDA coil occlusion and 100% PDA were closed including one who developed residual shunt and closed later after second coil implantation which consisted with Savitri's study¹⁶. Remaining 10(20%) patients, who received only anti-failure therapy, were selected for device closure depending on PDA size, patient's condition, age and weight. In this study, closure was observed in 100% cases within 3 months of device deployment that consisted with other studies^{16,17}. Before discharge, patients were checked for vascular access and other procedural complications. Echocardiographic monitoring of device position, residual flows and turbulence in aorta and left pulmonary artery (LPA) were done at pre-discharge at 1, 3, 6, 12 months of procedure and then yearly thereafter as outdoor basis.

Despite one death, very few patients developed complications like heart failure, impaired renal function, intravascular hemolysis and bleeding manifestations which were managed promptly. Heart failure was more common in term and all patients with bleeding manifestation were also term infants. Heart failure was due to large size of PDA and delayed presentation. Some of the complications developed due to Indomethacin and Ibuprofen are as observed in several other studies^{10,11}. Thus this study confirms the safety of using pharmacologic intervention and trans-catheter PDA closure both early and during a long term follow-up. In the present study, implantation of PDA device was attempted in 10 cases and successfully occluded all. Similar results were reported by other authors^{17,18}. Reopening after successful device implantation was not reported to date and there was high complete cure rates found at follow-up evaluation as observed in other studies^{17,19,20}.

Conclusion

If any patient with PDA doesn't respond or found unsuitable to medical or trans-catheter intervention, can be closed surgically which is also the gold standard alternative treatment of PDA. Trans-catheter intervention is safe, effective and less invasive if it is done in center with expert hand where this type of intervention is done routinely.

Limitation of the study

The limitation of this study is that it was done in a selected group of population amongst the children of Armed Forces personnel who were in well reach of health service. Patient who was diagnosed as large PDA in the neonatal period required surgical ligation but the center did not have the facility for surgery in small neonate. So this study would not be a representative of the total PDA cases as well as the total outcome of the treated PDA group.

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