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Clinical Correlation and Outcome of Duct Dependent Circulation in Neonates

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Abstract

Duct dependant circulations needs high degree of suspicion, early stabilisation with prostaglandin and early diagnosis and treatment. Early PGE1 infusion is an economically viable option in the management of these sick neonates. Majority of them present in the first week of life and do well with prompt and proper approach to the problem. Prostaglandin plays important role as a palliation before undergoing any palliative or definitive surgery. Titration with low effective dose regimen of prostaglandin definitely helps to maintain adequate response without increased complications. Mortality remains high in duct dependent circulation even with use of prostaglandins and interventions.

Keywords: Duct Dependent Circulation; Congenital Heart Disease; Prostaglandins.

Introduction

The incidence of congenital heart disease in general population is approximately 0.8% [1]. The diagnosis is established by 1 week of age in 40-50% of patients with congenital heart disease and by 1 month of age in 50-60% of patients. Most of severe congenital cardiac defects well tolerated in fetus because of parallel nature of fetal circulation.

It is the only after birth when the fetal pathways (ductus arteriosus and foramen ovale) are closed that the full hemodynamic impact of anatomic abnormality become apparent [2]. Congenital lesion that are dependent on the patent ductus arteriosus for circulation can be:

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Anatomical Features with Duct Dependent Systemic Blood Flow

- Hypoplastic left heart syndrome
- Aortic stenosis
- Coarctation of aorta
- Interrupted aortic arch

Anatomical features with Duct Dependent Pulmonary Blood Flow

- Pulmonary stenosis
- Pulmonary Atresia with intact ventricular septum.(Hypoplastic right heart syndrome)
- Tricuspid Artesia
- Tetralogy of fallot

Miscellaneous

- Transposition of great vessels
- Ebstein anomaly

Materials and Methods

The study was conducted in main tertiary care centres in Hyderabad which includes:-

- Krishna Institute of Medical Sciences, Hyderabad
- Lotus Children's Hospital, Hyderabad
- Care Hospital, Hyderabad

* Innova Children's Heart Hospital Hyderabad
- Pragnya Children's Hospital, Hyderabad
- Genesis Hospital, Hyderabad

All centres included in the study have well equipped neonatal cardiac unit for cardiac surgeries and interventional procedures. As the overall incidence of the duct dependent circulation is low, similar centre with well equipped cardiac units were included in the study. The study was conducted during the period of January 2007 to December 2008 (24 months). This study was a prospective and observational study. Study population was composed of 43 babies

Aims and Objectives

Study the outcome of the duct dependent circulation in neonates

Study the efficacy and complications of prostaglandins in duct dependent circulation in neonates

The Inclusion Criteria

Neonates presenting with a duct dependent congenital heart disease.

The Exclusion Criteria

- Congenital heart disease presenting beyond the neonatal period.
- Those with lethal congenital anomalies.

Methods

Ethics approval for the study was obtained from respective hospital. Written information about the study was supplied to each hospital, specifically to a nominated study contact person (for example, neonatologist or pediatric registrar etc.) Respective centre contacted the investigator at the time of the admission of neonate with duct dependent circulation. Pediatric cardiologist and team evaluated the neonate with suspected duct dependent circulation. 2D ECHO was done by Pediatric Cardiologist. Decision regarding starting of prostaglandin was taken by chief pediatric cardiologist so that uniformity was maintained in term of initial starting dose, maintenance dose and cessation of Prostaglandin E_1 infusion. Low dose prostaglandin was started and dose increased to achieve desirable response. Dose was further titrated with clinical response and side effects.

Results

The total no. of neonates recruited in study (n) were 43 (n=43). One neonate with complex congenital heart disease associated with right isomerism was excluded. Out of 43 neonates; 20(48%) were females and 23 (52%) were males. The Sex ratio is M:F = 1.09:1 (Figure 1).

All neonates were categorized according to etiology mainly into three groups:

1. Duct Dependent Pulmonary circulation
2. Duct Dependent Systemic circulation
3. Miscellaneous

Study included 21 neonates with duct dependent pulmonary circulation, 12 with duct dependent systemic circulation and 10 in miscellaneous group.

Anatomical Subset

1. Duct Dependant Pulmonary Circulation (N=21): (Figure 2)

Pulmonary Atresia + Intact Septum	4
Pulmonary Atresia	13
Pulmonary Atresia + Ventricular Septal Defect	6
Single Ventricle + Pulmonary Atresia	1
Complex Atrio Ventricular Septal Defect	2
Critical Pulmonary Stenosis	4

2. Duct Dependant Systemic Circulation (N=12): (Figure 3)

Hypoplastic Left Heart Syndrome	1
Critical Aortic Stenosis	1
Coarctation of aorta	7
Coarctation of aorta + Ventricular Septal Defect	4
Coarctation of aorta + Turners	1
Coarctation of aorta + Taussing Bing	1
Interrupted Aortic Arch	3

3. Duct Dependant Miscellaneous (N=10)

D-Transposition of Great Arteries	:	8
Neonatal Ebsteins	:	2

Neonatal Ebsteins

Group I – (Neonates in which Prostaglandins was used)Prostaglandins was used in 32 neonates**.** Clinical evaluation revealed a reduction in cyanosis in Group 1 patients and this response was seen in less than 15 minutes in all successful cases (31/31). Estimation of arterial saturation by pulse oxymetry revealed increase in Sa02%' (20%) The clinical response was sustained on Prostaglandin E_1 infusion. The patency of ductus arteriosus was also demonstrable on echocardiography with color flow imaging. The mean dose of prostaglandin used was 13±14.3 ng/kg/min and mean duration of prostaglandin therapy was 50.8 ± 47.2 min.

Side Effects: The most serious side effect was apnea, observed in 3 of 28 spontaneously breathing infants. All these babies were intubated and given respiratory assistance. Apnea occurred in the initial one hour of starting PGE_1 infusion in all 3 of these. However, the dose of Prostaglandin E_1 was not increased in any of these after one hour. Hypotension developed in two patients one belonged to Duct Dependent Systemic Circulation group and another to Miscellaneous group. Flushing developed in one case.

Group 2- (Neonates in which Prostaglandins was not used) follow up showed significant amount of death and more number of neonates who left against medical advice due to various reasons. The neonates with specific anatomical subset who remained stable even without prostaglandins use underwent Palliative or definitive procedure.

Table 1: Comparison of before and after Saturations in Prostaglandin group

	Spo2 Before Infusion	Spo2 After Infusion	Dose (Ng/kg/min)	Duration (Hr)
Mean	59.875	79.156	17.5	68.375
Standard Deviation	16.073	13.800	14.085	42.299

All group 1 babies received Prostaglandins in first week of life. These babies exhibited significant improvement in saturations ($P < 0.0001$).

Table 2: Comparison of before and After SBP in Prostaglandin group

Group	No.	Median	25th percentile	75th percentile	Mean	Standard deviation	SEM
SBP Before	32	67.00	60.50	77.00	70.66	14.16	2.50
SBP After	32	78.00	68.00	80.50	74.78	14.11	2.50

Group I neonates showed improvement in blood pressure within first two hours following prostaglandin infusion Table 2 (P=0.011) •SBP- Systolic Blood Pressure

Table 3: Comparison of before and After DBP in Prostaglandin group

Group	No.	Median	25th percentile	75th percentile	Mean	Standard deviation	SEM
DBP Before	32	40.50	32.00	48.00	40.47	10.51	1.86
DBP After	32	40.00	34.50	52.00	44.22	12.10	2.14

Group I neonates showed improvement in blood pressure within first two hours following prostaglandin infusion Table 2 (P=0.022) •DBP- Diastolic blood pressure

Table 4: Comparison of mortality between prostaglandin and non prostaglandin group

Outcome	Group I Prostaglandin	Group II Non-prostaglandin	Total
Died	22 (68.8%)	6(54.5%)	28 (65.1%)
Survived	10 (31.3%)	5 (45.5%)	15 (34.9%)
Total	32 (100%)	11(100%)	43(100%)

Discussion

Duct dependent circulation is a neonatal emergency. Early detection by clinical, pulse oxymetry and Echocardiography is vital to salvage the neonate who presents either with shock or with severe cyanosis. Although it is technically difficult to recruit neonates with duct dependent circulation , we managed to include 43 neonates, with various types of duct dependent circulation from six centres over the period of 2 years.

A majority of neonates presented with cyanosis, shock and metabolic acidosis in case of left sided obstructive lesion and with cyanosis and respiratory distress in case of right sided obstructive lesion in our study. Neonates with transposition of great vessels presented mainly with cyanosis. Cardiac murmur was a constant significant finding noted during the study. Feeding difficulties were also noted in some late presenting cases.

In our study, routine clinical examination helped to detect the majority of newborns with critical Congenital Heart Diseases during the first postpartum days in the neonatal ward. The time of diagnosis was, on an average, the first week for lesions with duct-dependent pulmonary circulation (Tetralogy of Fallot, Pulmonary Atresia), and lesions with admixture (Transposition of Great Arteries), but delayed until second to third week for defects with duct-dependent systemic circulation (Hypoplastic left heart syndrome, Interrupted aortic arch, and particularly critical Coarctation of aorta).

Routine pulse oxymetry played an important role in cases of early as well as late presentation of duct dependent circulation in our study. The mean age of presentation is about 5.20 + 5.50 days which indicates that patent ductus arteriosus is vulnerable to spontaneous closure in first week itself. Neonates with duct dependent systemic circulation presented somewhat later than neonates with duct dependent pulmonary circulation in our study which was not statistically significant. This is probably due to blood Po2 levels were higher in neonates with duct dependent pulmonary circulation than duct dependent systemic circulation, which is one of the reason for constriction of smooth muscles of patent ductus arteriosus.

We did not find any major sex difference in total population**.** This study revealed Pulmonary atresia as the commonest type of duct dependent Circulation. This is probably because of severe cyanosis and hypoxaemia which can be detected by parents and physicians easily and also the response to prostaglandin even in low doses is quite significant in this particular subset. The usage of prostaglandin is liberal in a majority of centre as soon as diagnosis is established. There was less clinical response to prostaglandin in duct dependent systemic circulation where as there was significant improvement of clinical symptoms and saturation in duct dependent pulmonary circulation. The saturation improvement was from 59% to 79% (P <0.0001).

Most of these infants are sick prior to start of Prostaglandin E1 therapy, therefore it may be difficult to decide whether a given complication is due to the drug or due to the clinical course of the baby. In several large series, the incidence of side effects has been reported to vary from 21.5% to 53%. Side effects were seen in 7/43 cases (16.2 %). The most important side effects are hypotension and respiratory depression including apnea. It is observed in several re- ports that the incidence of side effects is related to the dose of Prostaglandin E1 infusion. Study did not specifically address this issue. In another study, the incidence of complications was similar with both low and high dose of Prostaglandin E1 infusion. It is perhaps logical to start with a small dose which can be increased in small increments if there is inadequate response.

We found increase in systolic and diastolic pressure after prostaglandin which was statistically significant (p= 0.011 & 0.022 respectively). In our study, a large no. of group I neonates who received prostaglandin underwent palliative or definitive surgery (24/32). This indicates that palliative and definitive surgeries was done in more hemodynamically stable state after use of prostaglandin.

This study showed difficulties in pre-operative management of neonates with duct dependent systemic circulation in which prostaglandin was used. This is mainly due to the fact that this was a sicker subset. Most of the cases opted against further management mainly due to socio-economical reasons.

In miscellaneous group, in which prostaglandin was used; this study showed that most of neonates underwent Balloon atrial septostomy as a palliative surgery which resulted in marked improvement in oxygenation. They subsequently underwent definitive (arterial switch) surgery.

Group II comprised of neonates who did not receive prostaglandin. Majority of them opted against further management as their natural history of progression was poor. Neonates with good anatomical subset and who remained stable without prostaglandin performed well after surgery.

In our study, mortality of 65% was noted. This may be due to fact that outcome was noted in these neonates with use of prostaglandin and as well as after palliative and definitive intervention. So even though all neonates showed significant clinical improvement in terms of O_2 saturation and blood pressure, did not do well with palliative or definitive surgeries.

Summary

The present study was done to correlate clinical parameters and to study the outcome of duct dependent circulation in neonates. 43 babies were

enrolled for this study. A mortality of 65% observed. The drug Prostaglandin E_1 is a major asset in the medical treatment of infants with ductus dependent congenital heart disease prior to palliative/ corrective procedure.The benefit of the drug is seen even in babies presenting beyond one week of age. However, a careful and cautious approach is necessary while giving the Prostaglandin E_1 infusion as serious side effects may occur. Apnea is a major side effect and babies of Prostaglandin E_1 infusion must be monitored closely. Prostaglandin E_1 infusion may be empirically started prior to further investigations if there is high index of suspicion. Prostaglandin E_1 should be stopped before Patent Ductus Arterious stenting to avoid over dilatation of Patent Ductus Arterious during procedure.

Conclusion

Duct dependant circulations needs high degree of suspicion, early stabilization with prostaglandin and early diagnosis and treatment. Early Prostaglandin E1 infusion is an economically viable option in the management of these sick neonates. Majority of them present in the first week of life and do well with prompt and proper approach to the problem. Prostaglandin plays important role as a palliation before undergoing any palliative or definitive surgery. Titration with low effective dose regimen of prostaglandin definitely helps to maintain adequate response without increased complications. Mortality remains high in duct dependent circulation even with use of prostaglandins and interventions.

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Conflicts of Interest: None

Ethical Standards: Maintained

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