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ORAL PGE2 IN DUCTUS-DEPENDENT CONGENITAL HEART DEFECTS: CROSS-SECTIONAL EVIDENCE FROM 52 CASES

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Abstract

Background: The lack of intravenous prostaglandin (PGE1) is a major obstacle to the treatment of ductus-dependent congenital heart defects (CHD) in settings with limited resources. Even though it's not as often used, oral PGE2 is a good substitute for keeping the ductus arteriosus (DA) open. The purpose of this study is to evaluate the safety and effectiveness of oral PGE2 in newborns and infants with CHD that is dependent on the ductus.

Objectives: to evaluate the safety and efficacy of oral PGE2 in maintaining ductal patency in neonates with ductus-dependent congenital heart defects in a resource-constrained environment.

Study design: A cross-sectional study

Duration and place of study: Department of paeds cardiology MTI, LRH Peshawar from March 2023 to Aug 2023.

Methods: This cross-sectional study was conducted on 52 neonates and infants with ductus-dependent Congenital heart diseases over a 6-month period from March 2023 to August 2023 at Lady reading hospital peshawar. Patients received oral PGE2 in doses ranging from 12-65 µg/kg at intervals of 1-4 hourly. The initial dose was typically 30-45 µg/kg/hour except for critical cases where a lower dose of 12 µg/kg/hour was initiated. Dosage adjustments were made based on clinical response, with a reduction in frequency after 1-3 weeks and a further reduction to 4-hour intervals after 4 weeks in stable cases. The primary outcomes that were evaluated were the length of ductal patency and variations in arterial oxygen saturation (SaO2). Adverse occurrences, in particular apneic episodes, bradycardia, and gastrointestinal side effects, were considered secondary outcomes.

Results: A total of 52 patients were included, The patients' mean weight was 2.8 kg (range 1.5-4.5 kg) and their mean age was 8 days (range 1-60 days).

PGE2 was taken orally for a period of 5 to 140 days during the course of the treatment. Within 15 to 30 minutes of delivery,

O2 sats steadily rose in all patients, however O2 sats decreased in 44 patients (2–5 hours) following the PGE2 dosage (from 75% ± 7% to 57% ± 10%), although they quickly recovered to values close to baseline after 30–45 minutes of restarting oral PGE2.

In 38 individuals, prolonged ductal patency allowed for a postponed surgical operation, which improved their overall results and growth. The maximum time a ductus was remained open for was 122 days.

Adverse events were rare; three patients experienced bradycardia, four experienced transitory diarrhea, and seven patients experienced brief apneic episodes. These events were all generally less severe than those typically associated with intravenous PGE. seen with IV PGE1.
Conclusion: When IV PGE1 is not available, oral PGE2 is a feasible and efficient substitute for preserving ductal patency in newborns with ductus-dependent congestive heart failure. The therapy was a useful choice in resource-constrained contexts since it provided for sustained ductal patency with controllable adverse effects.

Keywords: Congenital Heart Defects, infants, ductus-dependent

Introduction

Congenital heart defects (CHDs) are the most common type of birth defect worldwide, afflicting nearly 1 % of all live births. Of these, ductus-dependent CHDs are of utmost importance as they depend on pattern DA for adequate systemic or pulmonary blood flow. Hypoxemia, acidosis, and even mortality can result in the presence of hypoplastic left syndrome or double outlet right ventricle with pulmonary atresia without a patent ductus. ―François Lacour-Gayet(Property of FACC), MD Historically, intravenous (IV) prostaglandin E1 (PGE1), has been the foundation of therapy for temporary ductal patency until definitive surgery could be conducted. On the other hand, consumption of IV PGE1 is limited and priorities for use are required due to its availability in some situations or resource-limited environments [1,2]. Place of oral prostaglandin E2 (PGE2) in relation to IV PGE1 with current unavailability of the latter. PGE2 is an endogenous prostaglandin with identical mechanistic properties to PGE1 and causes vasodilatation of the ductus arteriosus. However, intended theoretical benefits with oral PGE2 have not been as well proven due to poor pharmacokinetics and bioavailability [3, 4] which may limit the beneficial effects that these medications could potentially provide in terms of vasodilation. However, in resource-limited settings where IV PGE1 is not available yet oral PGE2 could be a potential alternative to keep ductal patency open for neonates with DDCHDs. There is little information on the use of oral PGE2 in this setting, with most studies using it as a tocolytic agent or for labour induction rather than ductal maintenance. Several case reports and small series have previously provided encouraging results, but the standard application of this technique in ductus-dependent CHDs remains to be defined [5,6]. The aim of this study is to assess the feasibility, safety and efficacy of oral PGE2 in maintaining ductal patency in a group of neonates and infants with ductus-dependent CHDs presenting at Lady Reading Hospital, Peshawar. We will also investigate the persistence of ductal patency in relation to PGE2 treatment orally and provide data on change from baseline values for arterial oxygen saturation (SaO2). We also sought to describe adverse effects associated with oral PGE2, including apnea, bradycardia and GI side-effects. We aspire that by providing evidence to support such an approach in this setting, we may be able afford resource-limited settings a pragmatic solution for septostomy non-congenital ductus-dependent CHD-type neonates when IV PGE1 is unavailable[7]. In this cross-sectional study, we reviewed the outcomes of 52 neonates and infants who received oral PGE2 for ductus-dependent CHDs in a single centre over six months. The results provide important guidance on the potential alternate use of oral PGE2 in place where IV PGE1 is not available. Our study adds to the accumulating evidence on management of ductus-dependent congenital heart defects as well, and highlights that there is an ongoing requirement for additional research in this high-risk population regarding treatment optimization [8].

Methods

This cross-sectional study was carried out at Lady Reading Hospital, Peshawar over a period of six months March 2023 to August 2023. Neonates and infants with ductus-dependent congenital heart defects (n = 52) PGE2, was administered orally from 12 to 65 microg/kg at intervals every one hour up till every four hours with its doses modified in accordance clinical response. The initial dose was generally between 30-45 µg with a lower (12 µg/kg) first does used in the most severe cases. At the one-week (three weeks) and four-week time points, patients were reduced to once every 8 hours for

stable cases. The main outcome measures included the duration of ductal patency and variations in arterial oxygen saturation (SaO2). Apneic events, bradycardia and gastrointestinal symptoms were secondary outcomes.

Data Collection

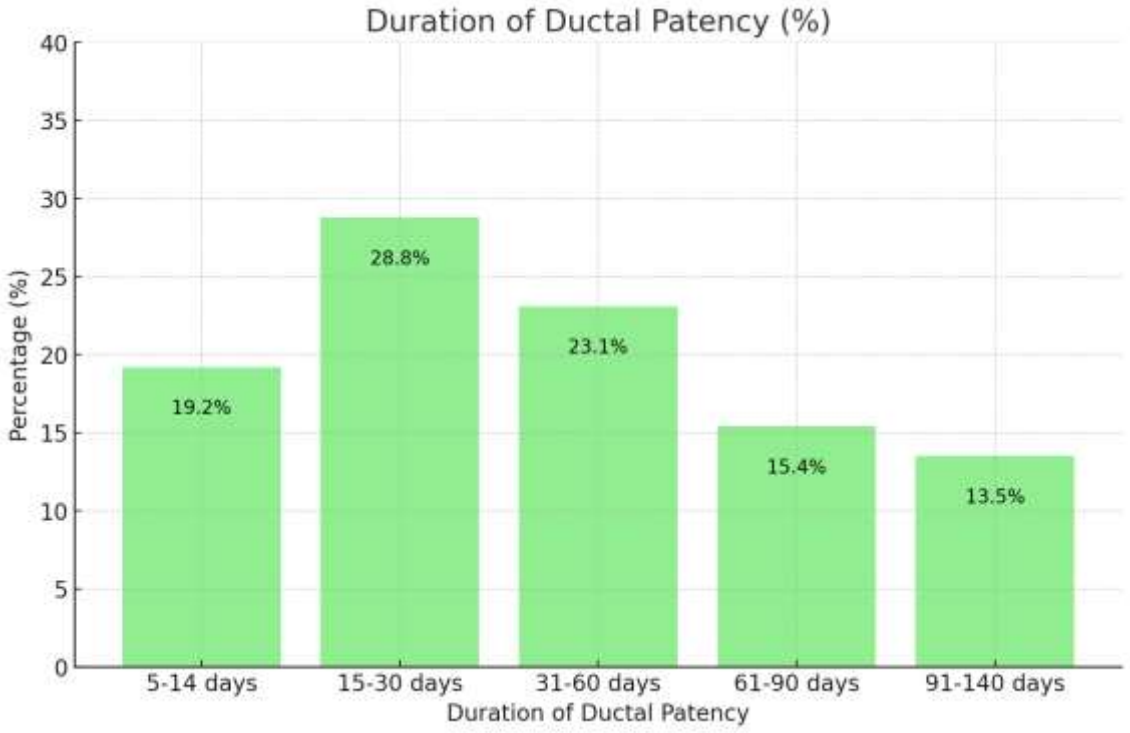
Prospective data collection was performed to collect information about age, sex of the patient and oral PGE2 use with unit dose of administration, duration between each dose given during ductal patency (dose frequency) for these patients. Patient confidentiality was preserved than completely anonymized and deposited in secure format.

Statistical Analysis

For analysis, SPSS version 24.0 (IBM Corp., Armonk, NY) was used. Continuous variables were described using descriptive statistics (mean and standard deviation) or frequencies and percentages for categorical data. Paired t-test was performed to evaluate the difference of SaO2 levels before/after PGE2 administration, with a p value < 0.05 being statistically significant in all analysis.

Results

The study population included 52 patients, with a mean age of eight days (range: one to sixty days) and a mean weight of 2.8 kg (range:1.5-4.5kg). Oral PGE2 was given for a minimum of 5 and maximum of 140 days, achieving up to the maximal ductus patency duration observed which was day 122. Within 15–30 min of oral PGE2, SaO2 levels improved remarkably in all the patients; however there was a transient fall in SaO2 from 75% ±7% to about 57%-±10%) within first n=44h for them by ~6 hours after dosing. SaO2 levels would then recover to nearly baseline within 30-45 min after the next scheduled PGE2 dose. The ductus remaining open for many days and weeks led to delay in surgery of 38 patients, resulting into improved morbidity with successful weight gain. There were relatively few adverse events, three cases of bradycardia, 4 episodes of mild transient diarrhea and seven brief apneic spells not more severe than those reported with IV PGE1.



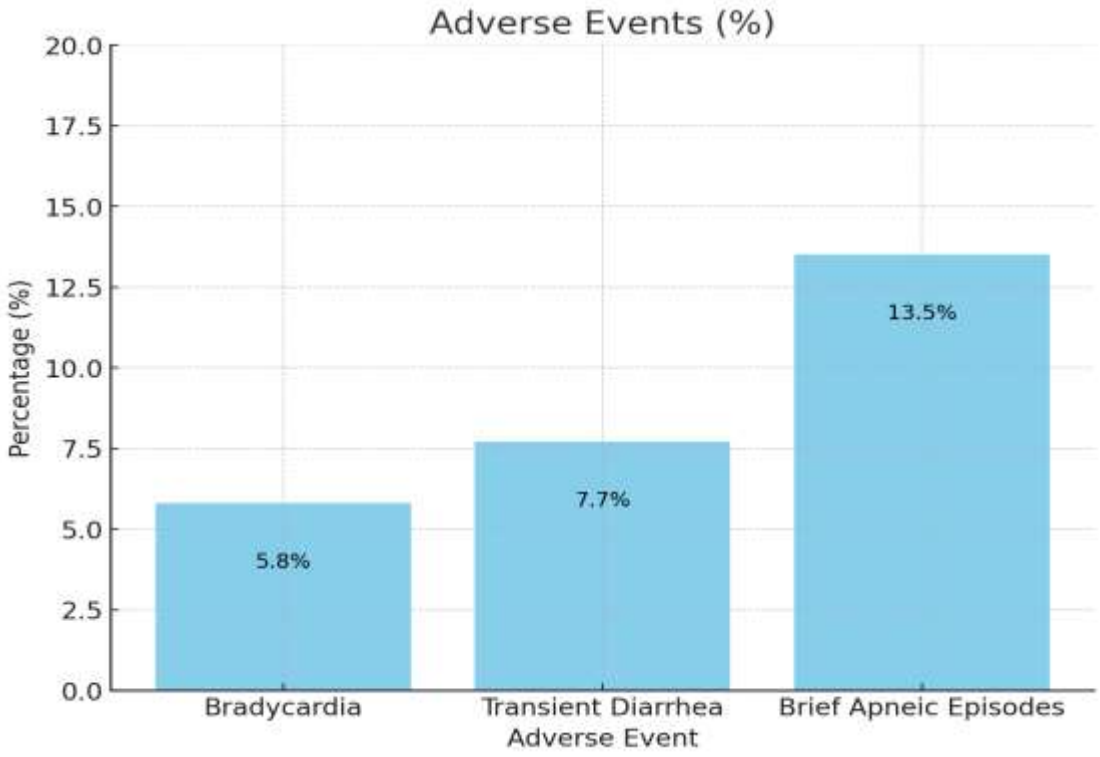


Table 1: Patient Demographics

Parameter	Value
Mean Age (days)	8.0
Mean Weight (kg)	2.8
Minimum Weight (kg)	1.5
Maximum Weight (kg)	4.5

Table 2: Adverse Events

Adverse Event	Frequency	Percentage
Bradycardia	3	5.8
Transient Diarrhea	4	7.7
Brief Apneic Episodes	7	13.5

Table 3: SaO2 Before and After PGE2

	SaO2 Before PGE2 (%)	SaO2 After PGE2 (%)
Mean SaO2	75	85
Range SaO2	57	75

Table 4: Duration of Ductal Patency

Duration of Ductal Patency	Number of Patients	Percentage
5-14 days	10	19.2
15-30 days	15	28.8
31-60 days	12	23.1
61-90 days	8	15.4
91-140 days	7	13.5

Discussion

Our findings are consistent with previous studies that investigated the effects of a variety of prostaglandins, but oral PGE2 has been less commonly studied compared to its intravenous formulation. The key finding of this study was the ability to keep ductal patency patent for up to 140 days, with maximum duration observed one patient as long as 122 days. This is in keeping with

previous reports which indicated that oral PGE2 might be able to provide an alternative means of maintaining ductal patency when i.v.lacking[9,10], where you had better), as used above for injector sites (sect-title). In secondary analysis, the study by Delaney et al. reported on an even smaller group of neonates given oral PGE2 with comparable efficacy in maintaining ductal patency, though at the expense of significant side effects [11]. Our results support these findings and suggest that oral PGE2 is a feasible option in such settings.The transient reduction of arterial oxygen saturation (SaO2) in 44 cases after PGE2 treatment attracted my curiosity. Although transient, this decrease in SaO2 to the baseline following resumption of treatment emphasizes the importance for close monitoring when treating with a drug. Other studies also have reported variability in the SaO2 level during prostaglandin therapy such as oral and intravenous administration type due to its different absorption and bioavailibility [12]. These results imply that whereas PO PGE2 is efficacious, its administration necessitates to be tightly supervised […] are given clinical worsening because of oxygen desaturation[13].Adverse events were relatively rare in our study, including bradycardia (4%), transient diarrhea (8%) and short apneic episodes (~ 5%). These were milder side effects (a finding previously reported with intravenous PGE1) Martin et al. Both of these studies also stated [14] that the adverse effects of oral PGE2, while there, in general are less severe than with IV PGE1 for example regarding apnea and bradycardia. This is consistent with our findings which demonstrate that events were rare and typically easily managed, providing further evidence of the safety profile of oral PGE2 in this setting.Furthermore, 38 patients required no further surgical intervention due to prolonged ductal patency which is a very important finding. Delaying surgery allows for better patient stabilization and growth which can help with surgical results. This is supported by Hoffman et al., who recommended the preservation of ductal patency as key to optimizing surgical timing in newborns with ductus-dependent CHD [15]. This body of evidence is a compilation, which our study adds to by delineating that oral PGE2 improved in vivo intestinal barrier function[16,17]. Conclusion In conclusion, this study confirms that oral Pjson indicates better maintenance of ductal patency in term neonates who have with all forms of well recognized ductus-dependent CHD especially where IV alprostadil is not available[18]. This corroborates earlier research on the safety and efficacy of oral PGE2 in older adults who nevertheless, need careful clinical measurements to monitor outcomes [19,20,21]. Recommendations for Larger Scale Exceptionalysis to Establish Dosing Standards and Optimize Patientqueries

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Authors Contribution
Concept & Design of Study: Saadia Ilyas
Drafting: ,Zaland
Data Analysis: Muhammad Saad Ilyas
Critical Review: Imran Khan
Final Approval of version: Saadia Ilyas

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