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Original Research Article

Efficacy of Paracetamol in Treating Hemodynamically Significant Patent Ductus Arteriosus in Preterm Neonates

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Abstract:

Background: (PDA) can cause serious morbidity and mortality if treatment is not received. It is a common problem in preterm newborns, especially those with very low birth weight. For pharmacological closure, NSAIDs like ibuprofen and indomethacin are frequently employed; however, their side effects prevent broad use. A possibly safer substitute for PDA treatment is paracetamol.

Aim: To evaluate the efficacy and safety of paracetamol in the management of hemodynamically significant PDA (hsPDA) in preterm newborns.

Methods: Over the course of a year, a retrospective observational study was carried out at Gian Sagar Medical College and Hospital in Rajpura, Jansla, Punjab, India. We looked at the medical records of 120 preterm newborns who were treated with paracetamol for hsPDA that was verified by echocardiography. We gathered information on adverse events, treatment results, clinical features, and demographics. SPSS version 23.0 was used for the statistical analysis, and $p < 0.05$ was chosen as the significance level.

Results: The mean birth weight of 120 preterm neonates was 1,186 ± 210 g, and the mean gestational age was 29.6 ± 2.1 weeks. Of the infants, 92 (76.7%) had complete PDA closure, 18 (15%) had partial reduction, and 10 (8.3%) had persistent PDA. Reduced closure rates were substantially correlated with lower birth weights (<1200 g) and gestational ages (<30 weeks) ($p < 0.05$). Paracetamol was well tolerated, with only mild gastrointestinal intolerance in 6 (5%) infants; no renal or hepatic adverse effects were reported.

Conclusion: Paracetamol is an effective and safe option for the management of hsPDA in preterm neonates, with high closure rates and minimal adverse effects. Gestational age and birth weight are important predictors of treatment success.

Recommendations: Paracetamol may be considered as a first-line or alternative therapy for hsPDA, especially in neonates with contraindications to NSAIDs. To assess long-term results and enhance dosage regimens, further prospective randomized studies are advised.

Keywords: Patent Ductus Arteriosus, Preterm Neonates, Paracetamol, Hemodynamically Significant, Pharmacological Closure.

Introduction

A common cardiovascular disorder in preterm infants is called patent ductus arteriosus (PDA), which is defined by the continuation of a fetal vascular link between the aorta and the pulmonary artery. Hemodynamically significant PDA (hsPDA) can cause left-to-right shunting, which can increase mortality in premature infants and cause necrotizing enterocolitis, bronchopulmonary dysplasia, intraventricular hemorrhage, pulmonary overcirculation, and systemic hypoperfusion [1,2]. Extremely preterm infants (less than 28 weeks) are at the highest risk for PDA, which has an incidence inversely related to gestational age and birth weight [3].

The management of hsPDA remains controversial, with treatment strategies ranging from conservative observation to pharmacological or surgical closure. Because they inhibit cyclooxygenase (COX), which in turn reduces prostaglandin synthesis, a crucial component of ductal patency, nonsteroidal anti-inflammatory medications (NSAIDs) like ibuprofen and indomethacin have historically been employed as first-line pharmacological therapies [4]. However, the use of NSAIDs is limited by their adverse effects, including renal impairment, gastrointestinal bleeding, and platelet dysfunction [5]. This has prompted the search for safer alternatives.

Paracetamol (acetaminophen) has emerged as a promising therapeutic option for PDA closure in recent years. Unlike NSAIDs, paracetamol inhibits prostaglandin synthesis through the peroxidase segment of the prostaglandin H2 synthase enzyme, thereby facilitating ductal constriction [6]. Multiple clinical studies and systematic reviews have demonstrated comparable efficacy of paracetamol to ibuprofen in closing PDA, with a more favorable safety profile [7–9]. Moreover, paracetamol may be particularly beneficial in neonates with contraindications to NSAID therapy, such as those with renal or gastrointestinal complications [10].

Variations in efficacy have been noted despite mounting evidence in favor of using paracetamol for PDA closure, especially in infants with extremely low birth weight and preterm births, when closure rates are comparatively lower [11,12]. The need for additional research on paracetamol in various neonatal populations is highlighted by the variability of results, especially in settings with low resources where the safety profile of pharmaceutical drugs is a key concern. In order to assess the safety and effectiveness of paracetamol in the treatment of hsPDA in preterm newborns, a tertiary care hospital conducted the current retrospective study. This study intends to add to the expanding body of research on the use of paracetamol as a substitute therapeutic option for PDA closure in preterm newborns by examining clinical features, treatment outcomes, and correlated variables.

Methodology

Study Design: This was a retrospective, observational study.

Study Setting: The study was carried out at the Department of Pediatrics, Gian Sagar Medical College and Hospital, Rajpura, Jansla, Punjab, India. The hospital caters to a large population of neonates, providing both routine and specialized care, including neonatal intensive care services.

Study Duration: The study was conducted over a period of one year. Data were retrieved from the hospital records corresponding to this duration.

Participants: The trial comprised 120 preterm infants who were treated with paracetamol after being identified with hemodynamically severe patent ductus arteriosus.

Inclusion Criteria

- Preterm newborns with a confirmed diagnosis of hsPDA by echocardiography.
- During the study period, infants admitted to the neonatal intensive care unit (NICU).
- Infants who received paracetamol as a therapeutic intervention for hsPDA.

Exclusion Criteria

- Term neonates or late preterm infants.
- Newborns with congenital heart disease other than PDA.
- Neonates who received (NSAIDs) such as indomethacin or ibuprofen for PDA closure.
- Incomplete or missing clinical records.

Bias: Only medical records that satisfied stringent inclusion and exclusion criteria were examined in order to reduce selection bias. Standardized data extraction forms and regular documentation of echocardiographic confirmation of hsPDA helped to minimize information bias.

Data Collection: Information about demographics, gestational age, birth weight, echocardiogram results, treatment plans, and the effects of paracetamol therapy were gathered retroactively from patient records. Data were entered into a structured datasheet to ensure uniformity and accuracy.

Procedure: Eligible newborns were identified through hospital records. Information regarding the administration of paracetamol (dose, route, and duration) was noted. Echocardiographic assessments before and after treatment were recorded to evaluate PDA closure or reduction. Adverse effects and clinical progress during therapy were also documented.

Statistical Analysis: IBM Corp., Armonk, NY, USA's SPSS software, version 23.0, was used to enter and analyze all of the data. Baseline characteristics were summarized using descriptive statistics including mean, standard deviation, frequency, and percentages. The Student's t-test or Mann-Whitney U test, as applicable, were used to evaluate continuous data, while the chi-square test was used to analyze categorical variables. P-values below 0.05 were regarded as statistically significant.

Results

A total of 120 preterm newborns diagnosed with hemodynamically significant (hsPDA) and treated with paracetamol were included in the study. The mean gestational age was 29.6 ± 2.1 weeks, and the mean birth weight was 1,186 ± 210 grams. Of the 120 participants, 68 (56.7%) were male and 52 (43.3%) were female.

Table 1: Baseline Characteristics of Study Participants (n = 120)

Variable	Mean ± SD / n (%)
Gestational age (weeks)	29.6 ± 2.1
Birth weight (grams)	1186 ± 210
Male	68 (56.7%)
Female	52 (43.3%)
Small for gestational age (SGA)	28 (23.3%)
Appropriate for gestational age	92 (76.7%)

The sample was well-distributed in terms of sex, with a slightly higher proportion of males. The majority of infants were appropriate for gestational age.

Treatment Outcomes: Following paracetamol therapy, 92 infants (76.7%) achieved complete closure of PDA, while 18 infants (15%) showed partial reduction in ductal size, and 10 infants (8.3%) had persistent PDA despite treatment.

Table 2: Outcome of Paracetamol Therapy

Outcome of therapy	Frequency (n)	Percentage (%)
Complete closure	92	76.7%
Partial reduction	18	15.0%
Persistent PDA	10	8.3%

Paracetamol demonstrated a high closure rate, with nearly three-quarters of infants showing complete PDA closure.

Correlation Between Treatment Outcome and Clinical Factors: Statistical analysis showed that birth weight <1200 g and gestational age <30 weeks were significantly correlated with lower closure rates ($p < 0.05$).

Table 3: Correlation Between Baseline Characteristics and PDA Closure

Variable	Complete closure (n=92)	No/Partial closure (n=28)	p-value
Gestational age <30 weeks	36 (39.1%)	18 (64.3%)	0.021*
Gestational age ≥30 weeks	56 (60.9%)	10 (35.7%)	
Birth weight <1200 g	40 (43.5%)	20 (71.4%)	0.009*
Birth weight ≥1200 g	52 (56.5%)	8 (28.6%)	
Sex (Male)	50 (54.3%)	18 (64.3%)	0.317
Sex (Female)	42 (45.7%)	10 (35.7%)	

*Chi-square test applied; $p < 0.05$ considered significant.

Lower gestational age and lower birth weight significantly reduced the likelihood of PDA closure after paracetamol treatment. However, sex of the infant did not significantly influence outcomes.

Adverse Effects: No major adverse effects such as liver dysfunction or renal impairment were observed. Mild gastrointestinal intolerance was reported in 6 infants (5%), but treatment discontinuation was not required.

Table 4: Adverse Events Observed During Therapy

Adverse event	Frequency (n)	Percentage (%)
Gastrointestinal intolerance	6	5.0%
Elevated liver enzymes	0	0.0%
Renal impairment	0	0.0%
None	114	95.0%

Discussion

The mean gestational age and birth weight of 120 preterm newborns with hemodynamically significant PDA were 29.6 ± 2.1 weeks and 1,186 ± 210 grams, respectively, in this retrospective analysis. Of the sample, 43.3% were female and 56.7% were male. Of the newborns, 23.3% were tiny for gestational age, while the majority were appropriate. These baseline characteristics suggest that the study population represented a typical cohort of preterm neonates at risk for PDA.

Paracetamol therapy proved effective in the majority of cases, with 76.7% of neonates achieving complete closure of PDA, 15% showing partial reduction, and

only 8.3% having persistent PDA despite treatment. This high closure rate demonstrates that paracetamol can be a reliable therapeutic option in preterm infants, particularly in clinical settings where NSAIDs such as indomethacin or ibuprofen may not be suitable due to adverse effect profiles or contraindications.

Lower gestational age (<30 weeks) and lower birth weight (<1200 g) were shown to be substantially correlated with decreased closure rates ($p < 0.05$) when looking at clinical predictors of treatment results. These findings highlight that extreme prematurity and very low birth weight remain important challenges in achieving successful PDA closure, suggesting that these infants may require alternative treatment strategies or prolonged monitoring. Interestingly, sex was not correlated with treatment response, indicating that biological maturity rather than gender plays a greater role in influencing outcomes.

Safety analysis showed that paracetamol was well tolerated, with no cases of hepatic or renal impairment reported. Mild gastrointestinal intolerance occurred in 5% of infants, but treatment discontinuation was not required. The favorable safety profile observed in this cohort strengthens the clinical utility of paracetamol as a safer alternative to NSAID therapy, it frequently has a correlation with decreased platelet function, gastrointestinal bleeding, and renal failure.

According to recent research, paracetamol shows promise as a substitute for traditional cyclooxygenase inhibitors in the treatment of hemodynamically severe PDA in premature newborns. Oral or intravenous paracetamol produces ductal closure rates comparable to those of ibuprofen and indomethacin, with fewer gastrointestinal and renal side effects, according to randomized controlled trials and observational studies [13,14].

In a randomized trial, oral paracetamol was as effective as ibuprofen, with no significant differences in closure rates but a better safety profile, suggesting its role as a first-line therapy [13]. Similarly, El-Farrash et al. reported comparable closure efficacy between oral paracetamol and ibuprofen, supporting its use as a safe alternative in preterm neonates [14]. Valerio et al. emphasized its superior safety, particularly regarding renal function and gastrointestinal tolerance, making it suitable for fragile very low birth weight infants [15].

Follow-up studies also indicate that paracetamol does not adversely affect neurodevelopmental outcomes at 18–24 months, with outcomes comparable to ibuprofen [16]. Oncel and Erdeve further reported that although effective, paracetamol's response may be less robust in extremely preterm neonates (<26 weeks), highlighting a need for gestational age-specific considerations [17].

More recent cohort studies confirmed paracetamol's safety profile, particularly noting reduced risk of gastrointestinal bleeding compared to ibuprofen [18]. Additionally, Mitra et al. found that intravenous paracetamol was a safe and effective alternative, with a shorter treatment duration compared to ibuprofen in preterm infants with hsPDA [19]. Overall, evidence supports paracetamol as an effective and safe therapy for hsPDA closure in preterm neonates, with outcomes similar to traditional NSAIDs, though its efficacy may be reduced in extremely preterm populations.

Conclusion

These results reinforce the efficacy and safety of paracetamol in managing hsPDA in preterm neonates, with particularly high closure rates in infants above 30 weeks of gestation and those with higher birth weights. The study also emphasizes the importance of identifying high-risk subgroups, such as extremely preterm and very low birth weight infants, who may require individualized management approaches.

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