Original Article

Effect of Late (>7 Days) Low-dose Dexamethasone on Ventilated Preterm Neonates to Prevent Bronchopulmonary Dysplasia: A Quasi-experimental Study

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Abstract

Objective: To evaluate whether late (>7 days) low-dose dexamethasone, given according to the DART protocol, improves respiratory parameters and facilitates extubation in ventilator-dependent preterm neonates, while also assessing short-term complications and BPD status at 36 weeks' postmenstrual age.

Methods: This quasi-experimental study was conducted in the Department of Neonatology at the Pakistan Institute of Medical Sciences, Islamabad. Preterm neonates requiring mechanical and/or non-invasive ventilation received late (>7 days) low-dose dexamethasone using the Dexamethasone-Aided Respiratory Therapy (DART) protocol. The FiO_2 and mean airway pressure (MAP) were recorded before and during treatment. Dexamethasone was administered for up to 10 days and discontinued if pulmonary haemorrhage, intraventricular haemorrhage, or death occurred. The outcomes included changes in FiO_2 and MAP, extubation within 10 days, BPD at 36 weeks' postmenstrual age, and adverse events.

Results: Ninety-three infants were enrolled (mean gestational age 29.6±2.1 weeks; mean birth weight 1160±250 g). FiO_2 decreased from 0.56±0.11 to 0.33±0.08 (mean difference −0.229; 95% CI −0.251 to −0.208; $p<0.001$) and MAP from 12.3±2.5 to 8.9±2.0 cmH_2O (mean difference −3.40; 95% CI −3.91 to −2.90; $p<0.001$). Successful extubation occurred in 75.3% of the patients (70/93). BPD was diagnosed in 26.9% of patients at 36 weeks' postmenstrual age. Transient hyperglycaemia (11.8%) and hypertension (6.5%) were medically managed, and no gastrointestinal perforation or steroid-related mortality occurred.

Conclusion: Late low-dose dexamethasone administration via the DART protocol was associated with reduced ventilatory requirements and high extubation rates, with manageable short-term adverse effects. Controlled studies are needed to confirm its role in BPD prevention and refine patient selection in local NICU practices.

Keywords: Bronchopulmonary Dysplasia, Dexamethasone, DART, Anti-Inflammatory Agent, Infant, Premature.

Introduction

Preterm birth is a major global problem. Each year, about 15 million infants are born preterm, and very preterm neonates face the highest risk of complications that can persist beyond the neonatal period.[1] Bronchopulmonary dysplasia (BPD) – often defined by the need for supplemental oxygen and/or respiratory support at 36 weeks' postmenstrual age (PMA)—remains one of the most common morbidities of prematurity and is linked to adverse long-term outcomes, including neurodevelopmental impairment.[2]

BPD arises through multiple interacting pathways; however, ongoing pulmonary inflammation is a key contributor. Mechanical ventilation, infection, and repeated oxidative stress can intensify inflammatory activity, interfere with alveolar and microvascular maturation, and ultimately result in simplified alveoli with disordered vascular growth.[3] For this reason, systemic anti-inflammatory therapy—especially corticosteroids—has been explored to support ventilator weaning and possibly limit ongoing lung injury. Dexamethasone, a potent glucocorticoid, may aid extubation by improving lung mechanics while reducing airway oedema and inflammation.[4] Concerns

emerged, however, when early high-dose regimens were associated with adverse outcomes, including neurodevelopmental impairment and cerebral palsy, prompting a shift away from routine prophylaxis toward more selective use. [5]

To limit these risks, clinicians have moved toward shorter courses and lower cumulative doses intended to preserve respiratory benefits while reducing harm. The Dexamethasone-Aided Respiratory Therapy (DART) regimen described by Doyle et al. uses a low total dexamethasone exposure (0.89 mg/kg) and is initiated after the first postnatal week.[6] Evidence from randomised and observational studies suggests that late, low-dose dexamethasone can improve extubation success and reduce ventilator dependence, with a more favourable safety profile than earlier high-dose approaches when used in carefully selected high-risk infants. [7,8] Meta-analyses similarly support late postnatal steroids for infants who remain difficult to wean from mechanical ventilation and are at high risk of BPD.[9]

This question is particularly relevant in low- and middle-income settings such as Pakistan, where prematurity-related respiratory illness is common, and care may be limited by resources, uneven access to advanced ventilation, and inconsistent antenatal corticosteroid use.[10] Reported BPD rates among ventilated preterm neonates vary across tertiary centres and may remain higher than those seen in high-income settings.[11] Despite this, local evidence on standardised low-dose dexamethasone regimens – particularly DART – is sparse. Practice may range from complete avoidance of postnatal steroids to heterogeneous, non-standardised dosing determined by clinician preference, contributing to variability in outcomes and limiting the development of consistent protocols.

Therefore, generating context-specific evidence is important. Differences in baseline risk, infection burden, antenatal care, and NICU infrastructure may influence both response and safety, making direct extrapolation from other populations uncertain. We therefore evaluated late (>7 days) low-dose dexamethasone (DART protocol) in ventilator-dependent preterm infants admitted to the NICU at PIMS, Islamabad, assessing changes in respiratory support, extubation success, steroid-related complications, and BPD at 36 weeks' PMA.

Materials And Methods

This single-arm, quasi-experimental interventional study was conducted in the Neonatal Intensive Care Unit (NICU) of the Children's Hospital, Pakistan Institute of Medical Sciences (PIMS), Islamabad. The unit provides tertiary-level care and receives critically ill preterm infants from the region. Data collection was completed over three months.

This manuscript was prepared in accordance with the Transparent Reporting of Evaluations with Nonrandomised Designs (TREND) statement to improve transparency in reporting the design, intervention, participant eligibility, outcomes, and analytical approach of this nonrandomised interventional study.[12]

Ethical approval was obtained before enrolment (reference number: F.1-1/2015/ERB/SZABMU/1434). Parents or legal guardians provided written informed consent after receiving information regarding the study's purpose, procedures, potential risks, and expected benefits. Participant confidentiality was maintained during data collection, handling, and analysis.

Preterm neonates were consecutively enrolled according to the predefined eligibility criteria. Infants were eligible if they: (i) had gestational age 28–36 weeks, (ii) had birth weight <2000 g, (iii) were >7 days of postnatal age but <36 weeks' postmenstrual age at enrolment, and (iv) required ongoing invasive and/or non-invasive ventilation with FiO_2 ≥0.30, with no meaningful reduction in respiratory support during the preceding 72 hours.

Infants with haemodynamically significant patent ductus arteriosus, air-leak syndromes, congenital malformations, genetic or metabolic disorders, or prior exposure to postnatal steroids were excluded. Additional exclusion criteria included necrotising enterocolitis, focal intestinal perforation, and severe intraventricular haemorrhage on cranial ultrasonography.

The required sample (n=93) was estimated using OpenEpi for a single-proportion calculation, assuming a 40% BPD incidence among ventilated preterm infants receiving low-dose dexamethasone, with 95% confidence and a 10% margin of error. The estimate was reviewed by a biostatistician at the Shaheed Zulfiqar Ali Bhutto Medical University (SZABMU).

All enrolled infants received systemic dexamethasone via the parenteral route according to the standardised Dexamethasone-Aided Respiratory Therapy (DART) protocol for up to 10 days. The regimen consisted of 0.075 mg/kg every 12 hours on days 1–3, 0.05 mg/kg every 12 hours on days 4–6, 0.025 mg/kg every 12 hours on days 7–8, and 0.025 mg/kg once daily on days 9–10 (cumulative dose 0.89 mg/kg). Therapy was stopped if pulmonary haemorrhage occurred, if intraventricular haemorrhage was newly detected or worsened, or if the infant deteriorated clinically and died.

Data were captured using a structured proforma. At dexamethasone initiation, baseline demographic and clinical details were recorded, including gestational age, birth weight, sex, mode of delivery, antenatal corticosteroid exposure, surfactant administration, cranial ultrasound findings, and initial respiratory status. Respiratory variables included

FiO_2, mean airway pressure (MAP), ventilator mode/settings, oxygen saturation, and PaO_2/FiO_2 ratio; arterial blood gas results were entered when available. Infants were reviewed daily during therapy, and serial measurements of FiO_2, MAP, ventilator mode, oxygen saturation trends, and available arterial blood gas parameters were recorded. A positive clinical response was defined as reduced ventilatory support requirements (lower FiO_2 and MAP) along with improvement in oxygenation indices.

Primary outcomes included change in FiO_2 and MAP before and after therapy, successful extubation within 10 days of initiating dexamethasone, total duration of mechanical/non-invasive ventilation and oxygen therapy, day of successful extubation after starting therapy, and complications during therapy (pulmonary haemorrhage, intraventricular haemorrhage, and death). Secondary outcomes included BPD status at 36 weeks' postmenstrual age, categorised as no BPD, mild, moderate, or severe, according to the National Institutes of Health criteria.

Analyses were performed using SPSS version 25 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation or median (interquartile range), as appropriate. Categorical variables are reported as counts and percentages. Pre- and post-treatment respiratory parameters were compared using paired t-tests, and mean differences with 95% confidence intervals (CI) were calculated. Categorical outcomes were assessed using the chi-square or Fisher's exact tests, where appropriate. A two-sided p-value <0.05 was considered to be statistically significant. Reporting completeness was cross-checked against the TREND checklist before the final submission.

Results

Participants and Baseline Characteristics

A total of 93 ventilated preterm neonates who met the inclusion criteria were enrolled in the study. Eighty-eight infants completed the full 10-day DART regimen; five infants (5.4%) died during the treatment period due to complications of prematurity and sepsis, and these deaths were considered unrelated to steroid administration. The baseline characteristics are summarised in Table 1. The mean gestational age was 29.6 ± 2.1 weeks, and the mean birth weight was 1,160 ± 250 g. There was a slight male predominance (52/93 [55.9%]). Antenatal corticosteroid exposure was documented in 61/93 (65.6%) patients, and surfactant therapy was administered in 74/93 (79.6%) patients. A 5-minute Apgar score of <7 was recorded in 38/93 (40.9%) patients. Culture-proven sepsis occurred in 19/93 (20.4%) patients. Grade III/IV intraventricular haemorrhage was present in 3/93 (3.2%) patients. Before dexamethasone initiation, the mean FiO_2 requirement was 0.56 ± 0.11, and the mean MAP was 12.3 ± 2.5 cmH_2O.

Table 1: Baseline Demographic and Clinical Profile of Enrolled Infants (n = 93)

Characteristics	Value
Gestational age, weeks	29.6 ± 2.1
Birth weight, grams	1,160 ± 250
Male sex	52 (55.9%)
Female sex	41 (44.1%)
Antenatal steroid exposure	61 (65.6%)
Surfactant therapy received	74 (79.6%)
Apgar score at 5 min <7	38 (40.9%)
Initial FiO_2 requirement	0.56 ± 0.11
Initial mean airway pressure (cmH_2O)	12.3 ± 2.5
Sepsis (culture-proven)	19 (20.4%)
Intraventricular hemorrhage (Grade III/IV)	3 (3.2%)

Changes in Respiratory Parameters after Dexamethasone

Significant improvements were observed in oxygenation and ventilatory requirements after therapy (Table 2). The mean FiO_2 decreased from 0.56 ± 0.11 before treatment to 0.33 ± 0.08 by day 10 (mean difference −0.229; 95% CI −0.251 to −0.208; $p<0.001$). Mean MAP decreased from 12.3 ± 2.5 to 8.9 ± 2.0 cmH_2O (mean difference −3.40; 95% CI −3.91 to −2.90; $p<0.001$). Oxygenation indices improved, with the PaO_2/FiO_2 ratio increasing from 150 ± 38 to 240 ± 50 (mean difference +90.0; 95% CI 79.5 to 100.5; $p<0.001$). The mean oxygen saturation increased from 87.4 ± 4.5% to 93.8 ± 3.1% (mean difference +6.40; 95% CI 5.57 to 7.24; $p<0.001$).

Table 2: Changes in Respiratory Parameters Before and After Dexamethasone Therapy

Parameter	Before DART	After DART (Day 10)	Mean Difference	95% CI	*p*-value
FiO_2	0.56 ± 0.11	0.33 ± 0.08	-0.23	−0.251 to −0.208	<0.001*
MAP (cmH_2O)	12.3 ± 2.5	8.9 ± 2.0	-3.4	−3.91 to −2.90	<0.001*
PaO_2/FiO_2 ratio	150 ± 38	240 ± 50	+90	79.5 to 100.5	<0.001*
Oxygen saturation (%)	87.4 ± 4.5	93.8 ± 3.1	+6.4	5.57 to 7.24	<0.001*

Clinical Outcomes and Adverse Events

Within 10 days of dexamethasone initiation, 70/93 infants (75.3%) were successfully extubated. The mean duration until successful extubation was 8.2 ± 2.6 days after starting the therapy. The mean duration of mechanical/non-invasive ventilation was 11.3 ± 4.8 days, and the mean total duration of oxygen therapy was 18.6 ± 6.2 days (Table 3).

Adverse events during therapy were infrequent in this study. Pulmonary haemorrhage occurred in 2/93 (2.1%) patients, and intraventricular haemorrhage (any grade) was documented in 3/93 (3.2%) patients. Transient hyperglycaemia occurred in 11/93 (11.8%) patients and hypertension in 6/93 (6.5%) patients; both were managed medically. No gastrointestinal perforations or steroid-related mortalities were observed.

BPD Outcomes at 36-week Postmenstrual Age

By 36-week postmenstrual age, 68/93 (73.1%) infants had no BPD. BPD occurred in 25/93 (26.9%) infants, classified as mild in 14 (15.1%), moderate in 7 (7.5%), and severe in 4 (4.3%) cases (Table 3).

Table 3: Clinical Outcomes Following DART Therapy and BPD Status at 36-weeks PMA

Primary Clinical Outcomes following DART Therapy	
Outcome	**Mean ± SD / n (%)**
Total duration of oxygen therapy (days)	18.6 ± 6.2
Total duration of mechanical ventilation (days)	11.3 ± 4.8
Day of successful extubation	8.2 ± 2.6
Pulmonary hemorrhage	2 (2.1%)
Intraventricular hemorrhage (any grade)	3 (3.2%)
Death during therapy	5 (5.4%)
Secondary Outcome: BPD Severity at 36 Weeks PMA	
Outcome	**n (%)**
No BPD	68 (73.1%)
Mild BPD	14 (15.1%)
Moderate BPD	7 (7.5%)
Severe BPD	4 (4.3%)
Total with BPD	25 (26.9%)

Discussion

In this quasi-experimental cohort of ventilator-dependent preterm neonates, late (>7 days) low-dose dexamethasone administered using the Dexamethasone-Aided Respiratory Therapy (DART) approach was associated with significant short-term improvement in respiratory support requirements, reflected by lower inspired oxygen fraction (FiO_2) and reduced mean airway pressure (MAP), and a high proportion of infants achieving successful extubation within 10 days. These findings are consistent with the broader evidence that late systemic postnatal corticosteroids can facilitate weaning from mechanical ventilation and reduce ventilator exposure in carefully selected high-risk infants.[13]

Systematic syntheses comparing postnatal steroid strategies indicate that timing and cumulative dose meaningfully influence benefit–risk balance, with low-dose dexamethasone regimens generally positioned to support extubation

while limiting toxicity relative to historical higher-dose practices.[14] Contemporary guidance emphasises selective use in infants with high predicted BPD risk who cannot be weaned from ventilation.[15] Reviews aimed at clinicians similarly highlight that the most consistent short-term benefit is improved extubation success and reduced intensity of respiratory support, which aligns with the physiological rationale of reducing inflammation and airway oedema in evolving lung injury.[16]

Although the present study did not include a concurrent control group, the observed pattern of rapid reduction in ventilator settings during treatment is comparable to reports evaluating DART or DART-adjacent approaches in high-risk populations, where extubation is commonly used as a pragmatic near-term endpoint.[17] Evidence syntheses of randomised trials reinforce that systemic corticosteroids can improve respiratory outcomes, while underscoring ongoing uncertainty about long-term neurodevelopmental effects and the need for risk-stratified decision-making.[18] Data on timing also suggest that delayed initiation may be associated with different respiratory trajectories, emphasising the importance of defining an optimal therapeutic window within a structured protocol.[19]

Adverse effects in our cohort were limited to transient hyperglycaemia and hypertension, both of which were medically managed, with no gastrointestinal perforation or steroid-related mortality. Real-world population data show substantial variation in postnatal steroid use and patient selection, supporting standardised protocols and consistent monitoring for metabolic and cardiovascular complications.[20] Neurodevelopmental considerations remain central; recent cohort work examining late postnatal steroid exposure and developmental outcomes highlights the need for longer-term follow-up alongside respiratory endpoints.[21] At the same time, emerging imaging and neurodevelopmental analyses continue to refine understanding of potential harms and modifiers of risk.[22]

Interpretation of BPD incidence should acknowledge definitional variability and evolving grading frameworks at 36 weeks' postmenstrual age, which can affect comparability across settings.[23] Recent systematic evaluations also indicate that no single BPD definition consistently predicts long-term outcomes, underscoring the importance of transparent reporting and follow-up beyond discharge.[24] Newer protocolized approaches, including severity score–guided initiation, aim to better target therapy to those most likely to benefit.[25] In this context, recent meta-regression suggests that the benefits of systemic corticosteroids may be concentrated among infants at higher baseline BPD risk, supporting individualised treatment decisions.[26]

Conclusions

Late (>7 days) low-dose dexamethasone using the DART protocol was associated with improved ventilatory requirements and a high extubation rate in preterm infants requiring ongoing ventilatory support, with short-term adverse effects that were manageable. Because this single-arm quasi-experimental study lacked a concurrent control group, controlled studies with longer follow-up are needed to confirm the effectiveness and better define the benefit–risk balance.

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