DOI: 10.4274/anatoljmed.2026.99815
Anatol J Gen Med Res 2026;36(2):212-21

CLINICAL RESEARCH / KLİNİK ARAŞTIRMA

ANATOLIAN JOURNAL of GENERAL MEDICAL RESEARCH

Hemodynamic Effects of an Augmented Low-dose Dexamethasone Protocol in Preterm Infants with Bronchopulmonary Dysplasia

Bronkopulmoner Displazili Preterm Bebeklerde Artırılmış Düşük Doz Deksametazon Protokolünün Hemodinamik Etkileri

Oğuzhan Ay[1], Sezgin Güneş[2], Nurcan Aydoğan[3], Ayşe Şimşek[1,4]

[1]İzmir Democracy University Buca Seyfi Demirsoy Training and Research Hospital, Department of Pediatrics, Division of Pediatric Cardiology, İzmir, Türkiye
[2]University of Health Sciences Türkiye, İzmir City Hospital, Department of Neonatology, İzmir, Türkiye
[3]İzmir Democracy University Buca Seyfi Demirsoy Training and Research Hospital, Department of Pediatrics, İzmir, Türkiye
[4]İzmir Democracy University Faculty of Medicine, Department of Pediatrics, İzmir, Türkiye

Cite as: Ay O, Güneş S, Aydoğan N, Şimşek A. Hemodynamic effects of an augmented low-dose dexamethasone protocol in preterm infants with bronchopulmonary dysplasia. Anatol J Gen Med Res. 2026;36(2):212-21

Abstract

Objective: This study aimed to investigate the cardiovascular impact of an augmented dexamethasone protocol in preterm infants with bronchopulmonary dysplasia (BPD), specifically evaluating changes in hemodynamic parameters before and after treatment.

Methods: A retrospective analysis was conducted on 20 preterm infants (median gestational age: 28 weeks; median birth weight: 1245 g) who received an augmented steroid regimen. Hemodynamic data, including heart rate and arterial blood pressure, were collected from neonatal intensive care unit monitoring and were analyzed using the Wilcoxon signed-rank test. Demographic characteristics were compared with established literature to ensure that the cohort was representative of the high-risk BPD population.

Results: Statistical analysis revealed a significant elevation in systolic blood pressure following steroid administration ($p=0.006$, $Z=1.932$, $r=0.43$). In contrast, no statistically significant differences were observed in heart rate ($p=0.131$), diastolic blood pressure ($p=0.872$), and mean arterial pressure ($p=0.228$). While existing literature often reports a higher risk of BPD and mortality in male infants, this study found no significant gender-based differences in clinical characteristics or in treatment response, suggesting a homogeneous response to the standardized protocol across the cohort.

Conclusion: The findings demonstrate that an augmented dexamethasone protocol is associated with a significant increase in systolic blood pressure, underscoring the dose-dependent nature of corticosteroid-induced cardiovascular adverse effects. Given the increased risk of systemic hypertension, it is critically important to prioritize dose optimization and implement rigorous hemodynamic monitoring during therapy. Prospective trials are essential to refine personalized treatment strategies and to ensure the long-term cardiovascular safety of preterm infants receiving steroid treatment for BPD.

Keywords: Bronchopulmonary dysplasia, preterm infants, dexamethasone, systemic hypertension

Address for Correspondence/Yazışma Adresi: Oğuzhan Ay, MD, İzmir Democracy University Buca Seyfi Demirsoy Training and Research Hospital, Department of Pediatrics, Division of Pediatric Cardiology, İzmir, Türkiye
E-mail: oguzhanay1@gmail.com
ORCID ID: orcid.org/0000-0002-8356-4113

Received/Geliş tarihi: 24.06.2026
Accepted/Kabul tarihi: 25.07.2026
Published date/Yayınlanma tarihi: 31.08.2026

Copyright© 2026 The Author(s). Published by Galenos Publishing House on behalf of University of Health Sciences Türkiye, İzmir Tepecik Education and Research Hospital. This is an open access article under the Creative Commons AttributionNonCommercial 4.0 International (CC BY-NC 4.0) License.

Öz

Amaç: Bu çalışma, bronkopulmoner displazisi (BPD) olan prematüre bebeklerde artırılmış düşük doz deksametazon protokolünün kardiyovasküler etkilerini araştırmayı hedeflemiştir; özellikle tedavi öncesi ve sonrası hemodinamik parametrelerdeki değişiklikleri değerlendirerek.

Yöntem: Artırılmış steroid rejimi alan 20 prematüre bebekte geriye dönük bir analiz gerçekleştirildi (ortalama gebelik süresi: 28 hafta; ortalama doğum ağırlığı: 1245 g). Kalp atış hızı ve arteriyel kan basıncı gibi hemodinamik veriler, yenidoğan yoğun bakım ünitesi izlemiyle toplanarak Wilcoxon imzalı rank testi ile analiz edildi. Kohortun yüksek riskli BPD popülasyonunu temsil ettiğinden emin olmak amacıyla demografik özellikler, mevcut literatürle karşılaştırılmıştır.

Bulgular: İstatistiksel analiz, steroid uygulamasından sonra sistolik kan basıncında anlamlı bir yükselme gösterdi (p=0,006, Z=1,932, r=0,43). Buna karşılık, kalp atış hızında (p=0,131), diyastolik kan basıncında (p=0,872) ve ortalama arteryel basınçta (p=0,228) istatistiksel olarak anlamlı farklar gözlenmedi. Mevcut literatür erkek bebeklerde BPD ve mortalite riskinin daha yüksek olduğunu bildirirken, bu çalışmada klinik özelliklerde veya tedavi yanıtında anlamlı cinsiyet farkları bulunmadı; standardize protokole homojen kohort yanıtı öneriliyor.

Sonuç: Bulgular, artırılmış deksametazon protokolünün sistolik kan basıncında dikkate değer ve anlamlı bir artışla ilişkili olduğunu göstermektedir; bu, kortikosteroid kaynaklı kardiyovasküler yan etkilerin doza bağlı doğasını vurgulamaktadır. Sistemik hipertansiyon riskinin artması nedeniyle, doz optimizasyonuna öncelik verilmesi ve tedavi sırasında titiz hemodinamik izleme yapılması kritik öneme sahiptir. Gelecekteki prospektif çalışmalar, kişiselleştirilmiş tedavi stratejilerini rafine etmek ve BPD için steroid tedavisi gören prematüre bebeklerin uzun vadeli kardiyovasküler güvenliğini sağlamak amacıyla zorunludur.

Anahtar Kelimeler: Bronkopulmoner displazi, prematüre bebekler, deksametazon, sistemik hipertansiyon

Introduction

Prematurity, especially when associated with serious respiratory disorders such as bronchopulmonary dysplasia (BPD), is a significant cause of morbidity and mortality in neonatal intensive care units[1]. In these cases, steroid therapy for developing BPD is an accepted primary treatment aimed at improving respiratory status and facilitating extubation[2,3]. However, ongoing research on corticosteroid dosages and their hemodynamic side effects is critically important for determining optimal treatment strategies[2,4]. In this context, the potential effects of steroid treatment administered at doses higher than those used in the low-dose steroid protocol on the cardiac function in premature infants, particularly regarding long-term outcomes, require in-depth examination. Hemodynamic dysfunction is a common complication, and steroid interactions during this sensitive period may lead to revisions to treatment protocols[1,5]. In extremely preterm newborns, significant respiratory distress due to impaired pulmonary compliance despite surfactant treatment, together with interventions such as mechanical ventilation and hyperoxic gas mixtures, increases susceptibility to chronic pulmonary disorders[6,7]. Although the role of corticosteroids in preventing and treating these chronic disorders is undisputed, the hemodynamic risks associated with optimal dosage and timing of administration have not been fully elucidated[6,8]. Although synthetic glucocorticoids, such as dexamethasone, have been shown to be effective in reducing the risk of BPD in preterm infants, high-dose use is associated with serious cardiac side effects, such as hypertension and hypertrophic cardiomyopathy[2,6]. Therefore, the effects of steroid doses used to treat BPD in premature infants on the cardiac system should be evaluated in detail with respect to both short- and long-term outcomes. In the literature, systemic steroid treatment regimens for BPD are classified as low-dose (cumulative dose under 2 mg/kg), medium-dose (2-4 mg/kg), and high-dose (4-8 mg/kg)[2]. Studies related to dexamethasone: a randomized trial (DART) and augmented low-dose systemic steroid treatment protocols are available in the literature[1,8,9]. This evaluation will contribute to treatment guidelines by retrospectively examining the hemodynamic side effects of the augmented low-dose protocol in preterm infants, which falls within the low-dose systemic steroid treatment regimen, based on echocardiograms, electrocardiograms, and neonatal intensive care follow-up[8]. This study specifically aims to identify adverse hemodynamic effects[10,11]. Evidence indicates that antenatal glucocorticoids accelerate the maturation of the fetal respiratory and cardiovascular systems and are effective in preventing and treating postnatal respiratory distress syndrome[12]. However, the short- and long-term effects of these treatments, especially antenatal maternal corticosteroid use in cases of high-risk preterm birth, on fetal circulation and cardiac function are not fully understood[13]. The benefits of postnatal steroid treatment, such as accelerating weaning from mechanical ventilation and improving respiratory outcomes in preterm infants with BPD, have been demonstrated clinically[6]. Nevertheless, these

benefits must be carefully balanced against possible short- and long-term side effects such as systemic hypertension, hyperglycemia, growth retardation, gastrointestinal bleeding, intestinal perforation, and hypertrophic cardiomyopathy[8,14]. Therefore, the optimal dose and duration of postnatal steroid treatment should be meticulously determined, considering both pulmonary benefits and cardiac risks[8,15].

Specifically, the effects of steroids administered at doses higher than those used in the DART protocol on myocardial growth, functional changes, and vascular remodeling in preterm infants need to be comprehensively examined[6]. In this context, the maturational effects of antenatal glucocorticoid treatment on fetal heart structure and energy metabolism should be compared with the hemodynamic outcomes of postnatal steroid treatment, and the impacts of different dosage regimens on the cardiovascular system should be detailed[16]. Additionally, evaluating the potential effects of such dose differences on hemodynamic parameters such as myocardial hypertrophy, changes in hemodynamic output, and vascular resistance will provide valuable insights for clinical practice. Moreover, the effects of corticosteroid use in preterm infants on long-term cardiovascular outcomes represent a critical research area for assessing the risks of cardiometabolic diseases in adulthood[8,17]. Given cortisol's biological roles and the potential of exogenous hydrocortisone to prevent complications of adrenal insufficiency in preterm infants, the hemodynamic effects of different steroid types should be compared[18]. From this perspective, our study will enhance understanding of the short- and long-term effects of varying steroid dosages on preterm infants' cardiac health, thereby contributing to the optimization of clinical treatment approaches[6].

In this study, the hemodynamic effects of augmented low-dose systemic steroid treatment, compared with the DART protocol, were retrospectively examined in premature infants who developed BPD. The hemodynamic effects of these groups were evaluated using echocardiography, electrocardiography, and follow-up in the neonatal intensive care unit. This study aimed to characterize pre- and post-treatment hemodynamic adverse effects of dexamethasone in preterm infants diagnosed with BPD who had no echocardiographic evidence of hypertrophic cardiomyopathy or ventricular wall thickening. This approach will contribute to treatment optimization by providing clinical evidence for discussions of dosage in the literature.

Materials and Methods

Data Collection and Study Design

20 premature infants diagnosed with BPD and treated with augmented low-dose systemic steroid therapy according to the DART protocol in the Neonatal Intensive Care Unit of İzmir Democracy University Buca Seyfi Demirsoy Training and Research Hospital, within the last five years, were included in the retrospective cohort study. Data were collected by reviewing epicrisis reports, patient files, and electronic records. The collected data encompassed prenatal, perinatal, and postnatal histories; maternal age; gestational age; birth weight; Apgar scores; duration of hospital stay; steroid initiation day and duration; durations of respiratory support; discharge weight; oxygen requirement at 36 weeks; pre- and post-steroid heart rates and systolic and diastolic blood pressures; tricuspid regurgitation and right ventricular systolic pressure; physical examination findings; medical and family history; vital signs; and electrocardiogram and echocardiography reports. Post-steroid comprised measurements obtained within 24 hours of completing the 10-day steroid treatment.

A neonatal intensive care specialist diagnosed BPD according to the Turkish Neonatology Guideline and arranged steroid and other treatments provided in the intensive care unit in accordance with the current guideline[19,20].

Study Steroid Treatment Protocol

The DART protocol is a low-dose dexamethasone regimen developed to facilitate extubation and prevent BPD in ventilator- and oxygen-dependent preterm infants who have developed BPD or are at risk of it[1,2]. This protocol involves intravenous administration over 10 days, consisting of tapering doses targeting a total cumulative dose of 0.89 mg/kg of dexamethasone[2,21]. Our study included 20 preterm infants diagnosed with BPD who received an augmented low-dose steroid treatment that differed from the DART protocol. The median cumulative steroid dose administered to these patients was 1.35 mg/kg. We verified individualized cumulative doses for all participants to ensure adherence to the protocol; we excluded infants receiving non-standard dosages. The institutional low-dose dexamethasone regimen involved intravenous administration of 0.2 mg/kg/day (days 1-3), 0.15 mg/kg/day (days 4-6), and 0.1 mg/kg/day (days 7-9)[1,6].

Exclusion Criteria

Patients not included in the study were excluded according to the following criteria:

• Premature infants treated with a median cumulative steroid dose other than 1.35 mg/kg.

• Patients with missing prenatal, perinatal, postnatal history, physical examination, vital signs, echocardiography data in their files.

• Patients in whom congenital heart disease was detected on echocardiography.

• Patients diagnosed with conditions other than BPD according to the Turkish Neonatology Society guideline.

• Patients with chromosomal anomalies, major congenital malformations, or congenital surfactant deficiency.

• Patients receiving alternative systemic steroid treatments (e.g., hydrocortisone), as well as neonates receiving inotropes with known hemodynamic effects. Patients with high gestational age/birth weight.

• Patients who developed acute kidney injury-defined as a serum creatinine rise ≥0.3 mg/dL within 48 hours or oliguria (<1 ml/kg/h) for ≥24 hours during neonatal intensive care unit follow-up-were excluded from the study[22].

Statistical Analysis

Statistical analyses were performed using the open-source software JASP (version 0.95.4)[23]. Continuous variables were expressed as mean ± standard deviation if normally distributed or as median (minimum-maximum) if not. Categorical variables were presented as numbers (percentages). Normality of continuous data was assessed using the Kolmogorov-Smirnov test. Bivariate associations between continuous variables were evaluated using Pearson's correlation coefficient for normally distributed data and Spearman's rank correlation coefficient for non-normally distributed data. Differences between categorical variables were investigated using the chi-square test (or Fisher's exact test if expected cell counts were <5). Comparisons of quantitative variables between independent groups were performed using Student's independent t-test or for non-normally distributed parameters. Paired pre- and post-steroid comparisons were analyzed using paired t-tests or Wilcoxon signed-rank tests, as appropriate. A p-value <0.05 was considered statistically significant for all tests.

Ethics Committee Approval

Ethical approval for this study was obtained from the İzmir Democracy University Buca Seyfi Demirsoy Training and Research Hospital Non-Interventional Research Ethics Committee (approval no: 2025/530, date: 26.11.2025). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki, and the committee approved a waiver of informed consent for the retrospective analysis of anonymized patient data.

Results

Of the patients included in the study, 4 were born via normal vaginal delivery, while the other 16 were born via cesarean section. The prenatal diagnoses were as follows: gestational diabetes in 2 patients, premature rupture of membranes in 2 patients, maternal hypertension in 2 patients, and chorioamnionitis in 1 patient. Surfactant was administered to 15 patients.

According to the echocardiography reports, the diagnoses documented in the patients' final echocardiograms prior to discharge were as follows: in 1 patient, surgical ligation had been performed for a hemodynamically significant patent ductus arteriosus (PDA) 2 weeks prior to dexamethasone initiation; a hemodynamically insignificant PDA was present in 2 patients; a medium-sized (5-6 mm) secundum atrial septal defect was present in 2 patients; and pulmonary hypertension was not detected in any of the patients who were evaluated with pre- and- post-steroid echocardiography. Echocardiographic evaluation revealed no evidence of hypertrophic cardiomyopathy, interventricular septal thickening, or ventricular wall thickening in any of the patients.

Analysis of the demographic and clinical characteristics of the 20 preterm infants included in our study revealed a median maternal age of 27 years (range: 19-39). The median gestational age was 28 weeks (range: 21-32 weeks), and the median birth weight was 1245 grams (range: 620-1925 grams). The median duration of hospital stay was determined to be 52 days (range: 16-120). The median time to initiation of steroid therapy was 29 days (range: 6-59 days). The median discharge weight was 2800 grams (range: 1805-3130) (Table 1).

Throughout the follow-up period, the mechanical ventilation parameters of enrolled patients were systematically recorded and included in the analysis, whereas incubator and nasal-cannula oxygen support were not included in the quantitative

Table 1. Demographic and clinical characteristics of the preterm infants included in the study			
Variables	**Median**	**Minimum**	**Maximum**
Maternal age (years)	27	19	39
Gestational age (weeks)	28	21	32
Birth weight (g)	1245	620	1925
Length of hospital stay (days)	52	16	120
Postnatal age at steroid initiation (days)	29	6	59
1-minute Apgar score	5	1	8
5-minute Apgar score	7	5	8
Duration of invasive mechanical ventilation (days)	9	3	91
Duration of non-invasive mechanical ventilation (days)	15	0	59
Total duration of invasive and non-invasive respiratory support (days)	45	12	91
Weight at discharge (g)	2800	1805	3130
Oxygen saturation at 36 weeks (%)	97	90	100
Pre-steroid heart rate (bpm)	154	133	168
Post-steroid heart rate (bpm)	142	128	180
Pre-steroid systolic pressure (mmHg)	79	71	96
Pre-streoid diastolic pressure (mmHg)	43	22	52
Pre-steroid mean arterial pressure (mmHg)	56	39	65
Post-steroid systolic pressure (mmHg)	87	70	95
Post steroid diastolic pressure (mmHg)	38	35	55
Post-steroid mean arterial pressure (mmHg)	55	47	67

evaluation. Regarding the duration of respiratory support, the median duration of invasive mechanical ventilation was 9 days (range: 3-91), and that of non-invasive mechanical ventilation was 15 days (range: 0-59). The median total duration of respiratory support was 45 days (range: 12-91 days). At the 36th week, the median oxygenation level was 97% (range: 90-100%) (Table 1).

Upon evaluation of hemodynamic parameters, the median pre-steroid heart rate was 154 (range: 133-168) beats per minute, whereas the median post-steroid heart rate was 142 (range: 128-180) beats per minute. The median pre-steroid systolic and diastolic blood pressures were 79 (range: 71-96) mmHg and 43 (range: 22-52) mmHg, respectively. Following steroid treatment, the medians were 87 (range: 70-95) mmHg for systolic and 38 (range: 35-55) mmHg for diastolic pressure. Pre-steroid mean arterial pressure 56 (range: 39-65) mmHg and post-steroid mean arterial pressure 55 (range: 47-67) mmHg. Median Apgar scores were 5 (range, 1-8) at 1 minute and 7 (range, 5-8) at 5 minutes (Table 1).

Demographic and Clinical Characteristics by Gender

Demographic and clinical characteristics by gender are presented in detail in Table 2. Upon analysis of the demographic data, the median maternal age was 27 years among mothers of female neonates and 28 years among mothers of male neonates (p=0.756). The median gestational age was 28 weeks for female infants and 26 weeks for male infants (p=0.150), while the median birth weight was 1395 g for female infants and 1190 g for male infants (p=0.305). Median Apgar scores at the 1st minute were 5 for females and 4 for males (p=1.0); at the 5th minute, they were 7 for females and 6 for males (p=0.608; Table 2).

The median length of hospital stay was 62 days for female neonates and 46 days for male neonates (p=0.463). Additionally, the median postnatal age at the initiation of steroid therapy was 35 days in females and 25 days in males (p=0.096).

In terms of respiratory support durations, the median duration of invasive mechanical ventilation was 8 days in females and

Table 2. Analysis of demographic variables and clinical outcomes between male and female infants

Variables	Female neonates (n=8) median (Q1-Q3)	Male neonates (n=12) median (Q1-Q3)	p-value
Maternal age (years)	27 (21-31)	28 (22-30)	0.756
Gestational age (weeks)	28 (27-30)	26 (24-28)	0.150
Birth weight (gr)	1395 (1163-1563)	1190 (767-1360)	0.305
1-minute Apgar score	5 (4-6)	4 (3-6)	1.0
5-minute Apgar score	7 (6-8)	6 (6-7)	0.608
Length of hospital stay (days)	62 (46-72)	46 (36-71)	0.463
Postnatal age at steroid initiation (days)	35 (29-44)	25 (15-30)	0.096
Duration of invasive mechanical ventilation (days)	8 (5-11)	14 (7-25)	0.332
Duration of non-invasive mechanical ventilation (days)	12 (5-28)	17 (0-41)	0.814
Total duration of respiratory support (days)	30 (22-43)	63 (24-69)	0.111
Weight at discharge (g)	2860 (2680-2953)	2770 (2504-2903)	0.694
Oxygen saturation at 36 weeks (%)	98 (97-99)	97 (96-98)	0.546
Pre-steroid heart rate (bpm)	158 (151-165)	153 (138-155)	0.069
Post-steroid heart rate (bpm)	154 (140-161)	139 (133-149)	0.960
Pre-steroid systolic blood pressure (mmHg)	79 (72-85)	79 (73-85)	1.0
Pre-steroid diastolic blood pressure (mmHg)	43 (41-47)	42 (41-48)	0.938
Pre-steroid mean arterial pressure (mmHg)	57 (54-58)	55 (51-58)	0.508
Post-steroid systolic blood pressure (mmHg)	85 (71-89)	88 (83-92)	0.437
Post-steroid diastolic blood pressure (mmHg)	38 (37-55)	38 (36-46)	0.504
Post-steroid mean arterial pressure (mmHg)	55 (48-64)	55 (53-57)	0.908

14 days in males (p=0.332); the median duration of non-invasive mechanical ventilation was 12 days in females and 17 days in males (p=0.814); and the median total duration of respiratory support was 30 days in females and 63 days in males (p=0.111). The median weight at discharge was 2860 g in females and 2770 g in males (p=0.694). Oxygen saturation at 36 weeks was 98% in females and 97% in males (p=0.546).

Upon examination of hemodynamic parameters, the median pre-steroid heart rates were 158 bpm in female neonates and 153 bpm in male neonates (p=0.069); the median post-steroid heart rates were 154 bpm in female neonates and 139 bpm in male neonates (p=0.960). The median pre-steroid systolic blood pressure was 79 mmHg in both females and males (p=1.0); the median pre-steroid diastolic blood pressure was 43 mmHg and 42 mmHg, respectively (p=0.938). Post-steroid systolic blood pressures were 85 mmHg in females and 88 mmHg in males (p=0.437), and diastolic blood pressures were 38 mmHg in both groups (p=0.504). Pre-steroid mean arterial pressure was 57 and 55 mmHg (p=0.508); post-steroid mean arterial pressure was 55 and 55 mmHg (p=0.908). No statistically significant differences were observed between genders across all parameters analyzed (Table 2).

Hemodynamic Findings Before and After Steroid Treatment

The impact of steroid therapy on hemodynamic parameters was evaluated using the Wilcoxon signed-rank test, a paired-samples test. No statistically significant difference was observed between pre- and post-steroid heart rates (p=0.131, Z=-1.529, r=0.34). In contrast, a significant change was noted when comparing pre- and post-steroid systolic blood pressure (p=0.006, Z=1.932, r=0.43), indicating an increase in systolic blood pressure following steroid administration. However, no statistically significant difference was detected between pre- and post-steroid diastolic blood pressure (p=0.872, Z=-1.181, r=0.04). Furthermore, mean arterial pressure values were analyzed to determine the differences between pre- and post-administration measurements (p=0.228, Z=0.765, r=0.20) (Table 3, Figures 1-4).

Table 3. Comparative analysis of hemodynamic parameters before and after steroid treatment

Pre-post steroid data	W	z	r	p-value
Pre-post steroid heart rate	133.00	-1.529	0.34	0.131
Pre-post steroid systolic pressure	47.00	1.932	0.43	0.006
Pre-post streoid diastolic pressure	99.50	-0.181	0.04	0.872
Pre-post steroid mean arterial pressure	76.00	-0.765	0.20	0.228

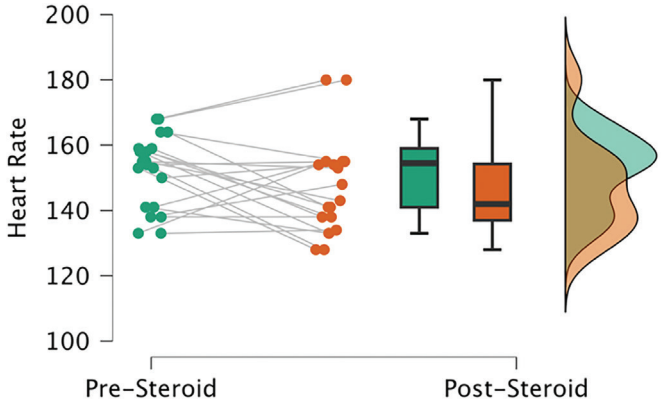

Figure 1. Distribution of heart rate before and after augmented dexamethasone treatment

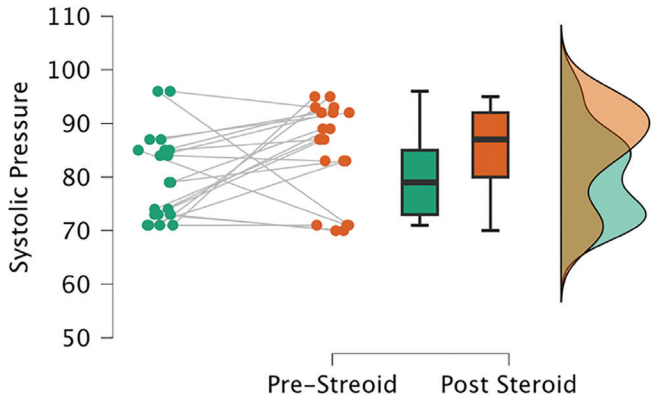

Figure 2. Distribution of systolic pressure before and after augmented dexamethasone treatment

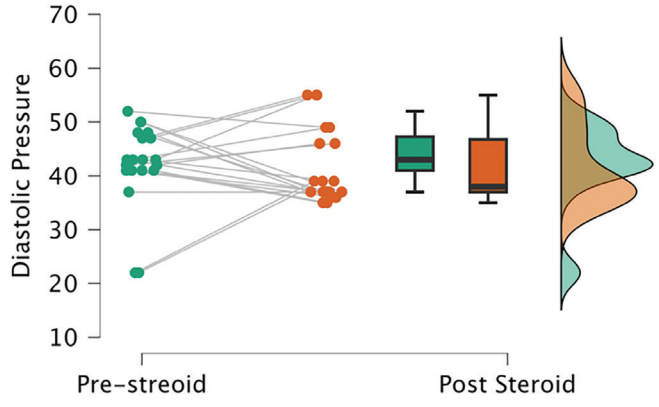

Figure 3. Distribution of diastolic pressure before and after augmented dexamethasone treatment

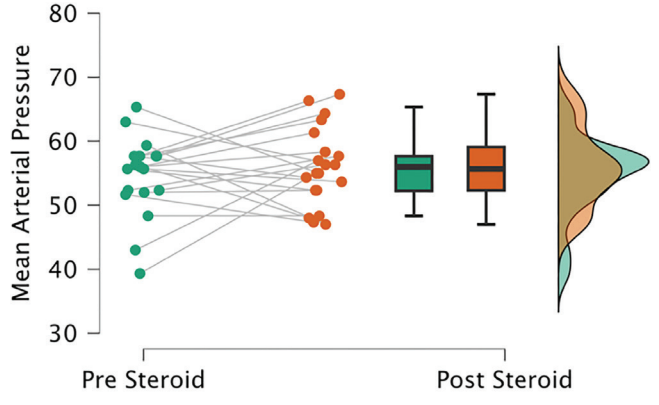

Figure 4. Distribution of mean arterial pressure before and after augmented dexamethasone treatment

Discussion

Demographic data in our study are consistent with those reported in the existing literature for preterm infants who develop BPD[2,11]. Within the general cohort, the median maternal age was 27 years. The median gestational age was 27 weeks for female infants and 28 weeks for male infants (overall median: 28 weeks). The median birth weight was 1395 g for females and 1190 g for males (overall median: 1245 g), while the median length of hospital stay was 62 days for females and 46 days for males (overall median: 52 days). These values parallel the demographic profiles typically reported in populations at risk for BPD; for example, gestational age <28 weeks and birth weight <1500 g are standard cohort criteria in systemic steroid studies[2,24].

As the differences between genders were not statistically significant, the cohort's homogeneity is consistent with that of similar retrospective and randomized controlled trial cohorts in the literature[25]. However, findings in the literature suggest that male preterm infants face higher risks of BPD and pulmonary hypertension and have higher mortality than female preterm infants[26,27]. Conversely, some studies indicate that female infants tend to have lower birth weights and are weaned from supplemental oxygen later than male infants[28]. In this context, the absence of significant differences between genders in BPD development or steroid treatment response in our study may reflect the unique clinical characteristics of this population (e.g., similar distributions of gestational age and birth weight) or the potential effects of a standardized treatment approach[29].

Furthermore, the literature reports that male preterm infants require corticosteroid therapy more frequently (23.6% in males vs. 20.1% in females) and receive more repeat courses (mean 1.67 in males vs. 1.59 in females)[29]. This discrepancy may be associated with hormonal differences or with the more severe disease progression often observed in males; therefore, the role of sex in BPD pathogenesis warrants further investigation to facilitate personalized treatments[29]. In this regard, a deeper understanding of the role of sex in BPD pathogenesis and treatment response is critical for developing personalized therapeutic strategies. Further research into the sex-specific effects of steroid dosages and timing could contribute to treatment optimization by elucidating the underlying biological mechanisms. Additionally, the significant change in systolic blood pressure observed in our study warrants detailed investigation of the cardiovascular regulatory mechanisms associated with steroid therapy in preterm infants.

Our study investigated the hemodynamic effects of corticosteroid therapy in preterm infants with BPD, specifically evaluating dose variations by pre- and post-administration measurements. The findings provide significant insights into the safety and efficacy of corticosteroid use in this population, particularly when compared with widely accepted low-dose strategies[30]. The slightly higher steroid dose used in our study resulted in a significant increase in systolic blood pressure[7,24]. This observation aligns with meta-analyses reporting an elevated risk of systemic hypertension in regimens in which the dexamethasone dose exceeds 0.25 mg/kg and supports the conclusion that the cardiovascular adverse effects of corticosteroids are dose-dependent[7,11,25]. Consequently, given that the risk of hypertension increases in regimens where the dexamethasone dose exceeds 0.25 mg/kg/day, it is critical to prioritize dose optimization, evaluate alternatives such as hydrocortisone that may carry lower cardiovascular risks, and elucidate long-term hemodynamic effects through prospective randomized controlled trials[2,7,11,24]. Advancing our understanding in these areas is essential for improving BPD outcomes and refining current therapeutic strategies[9,31].

In preterm infants with BPD, systemic steroid use does not reduce mortality; however, dexamethasone decreases the risk of BPD but may increase the risk of hypertension and hyperglycemia[2,11]. Such effects on hemodynamic parameters are particularly significant in studies comparing different dosage regimens, where high-dose protocols have been reported to shorten the duration of mechanical ventilation while potentially increasing adverse effects, such as hypertension and hyperglycemia[24]. In this context, the significant change in systolic blood pressure caused by our augmented low-dose steroid protocol highlights the delicate balance between dose optimization and minimizing hemodynamic side effects in BPD management. Indeed, studies evaluating changes in blood pressure and heart rate relative to corticosteroid dosages have demonstrated the direct impact of these pharmacological agents on the cardiovascular system[2,7,24]. This situation emphasizes that the benefit-risk balance of steroid use must be carefully evaluated, particularly in the management of BPD in preterm infants. Although the use of steroids in the treatment of BPD offers undeniable therapeutic benefits, individualizing dosage adjustments is critical to minimize potential adverse effects on hemodynamic function[32].

Study Limitations

This study is subject to several limitations. The small sample size and retrospective design primarily constrain the generalizability of the findings, owing to inherent challenges in conducting prospective studies among preterm infants. Additionally, the lack of long-term cardiovascular outcome assessments precludes definitive conclusions regarding the protocol's overall safety profile. Accordingly, prospective randomized controlled trials with larger cohorts and longer follow-up are essential to comprehensively evaluate the effects of augmented steroid dosages on clinical outcomes.

Conclusion

This study retrospectively evaluated the adverse hemodynamic effects of an augmented low-dose dexamethasone protocol in preterm infants who developed BPD, using echocardiography, electrocardiography, and neonatal intensive care unit follow-up data. Our findings, consistent with existing literature, demonstrate that increases in steroid dosages can lead to significant effects on blood pressure and may have long-term consequences for hemodynamic function. This retrospective analysis underscores the need for a more comprehensive investigation into the relationship between steroid dosage and hemodynamic adverse effects and further supports the evidence that dexamethasone elevates the risk of systemic hypertension. On the other hand, the observation that hydrocortisone does not consistently reduce BPD risk even at high doses, nor does it show a marked increase in cardiovascular adverse effects, suggests that the hemodynamic profiles of different corticosteroids may diverge.

Ethics

Ethics Committee Approval: Ethical approval for this study was obtained from the İzmir Democracy University Buca Seyfi Demirsoy Training and Research Hospital Non-Interventional Research Ethics Committee (approval no: 2025/530, date: 26.11.2025).

Informed Consent: The committee approved a waiver of informed consent for the retrospective analysis of anonymized patient data.

Footnotes

Authorship Contributions

Surgical and Medical Practices: O.Y., S.G., Concept: O.Y., S.G., A.Ş., Design: S.G., Data Collection or Processing: N.A., Analysis or Interpretation: O.Y., Literature Search: O.Y., S.G., Writing: O.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Al-Taweel HM, Abdelhady ISI, Irfan N, et al. Comparing low-dose (DART) and enhanced low-dose dexamethasone regimens in preterm infants with bronchopulmonary dysplasia. Front Pediatr. 2023;11:1261316.
2. Raghuveer TS, Zackula RE, Lakhotia R, Binder SA. Systemic steroids and bronchopulmonary dysplasia: a systematic review and meta-analysis. J Perinatol. 2026;46:144-54.
3. Rosano K, Bery S, Marasch J, Farrell R, Mastrandrea LD, Ryan RM. Predicting iatrogenic adrenal insufficiency in neonates exposed to prolonged steroid courses: do cortisol levels help? J Perinatol. 2024;44:1658-62.
4. Sehgal A, Steenhorst JJ, Mclennan DI, Merkus D, Ivy D, McNamara PJ. The left heart, systemic circulation, and bronchopulmonary dysplasia: relevance to pathophysiology and therapeutics. J Pediatr. 2020;225:13-22.e2.
5. Huysman MW, Hokken-Koelega AC, De Ridder MA, Sauer PJ. Adrenal function in sick very preterm infants. Pediatr Res. 2000;48:629-33.
6. Vrselja A, Pillow JJ, Black MJ. Effect of preterm birth on cardiac and cardiomyocyte growth and the consequences of antenatal and postnatal glucocorticoid treatment. J Clin Med. 2021;10:3896.
7. Boscarino G, Cardilli V, Conti MG, et al. Outcomes of postnatal systemic corticosteroids administration in ventilated preterm newborns: a systematic review of randomized controlled trials. Front Pediatr. 2024;12:1344337.
8. Olaloko O, Mohammed R, Ojha U. Evaluating the use of corticosteroids in preventing and treating bronchopulmonary dysplasia in preterm neonates. Int J Gen Med. 2018;11:265-74.
9. Gilfillan MA, Kiladejo A, Bhandari V. Current and emerging therapies for prevention and treatment of bronchopulmonary dysplasia in preterm infants. Paediatr Drugs. 2025;27:539-62.
10. Esterman E, Goyen TA, Jani P, et al. Systemic postnatal corticosteroid use for the prevention of bronchopulmonary dysplasia and its relationship to early neurodevelopment in extremely preterm infants. World J Pediatr. 2023;19:586-94.
11. Szabó H, Baraldi E, Colin AA. Corticosteroids in the prevention and treatment of infants with bronchopulmonary dysplasia: part I. systemic corticosteroids. Pediatr Pulmonol. 2022;57:600-8.
12. Karlsson R, Kallio J, Toppari J, Scheinin M, Kero P. Antenatal and early postnatal dexamethasone treatment decreases cortisol secretion in preterm infants. Horm Res. 2000;53:170-6.
13. Henry A, Shand A, Welsh A. The short term fetal cardiovascular effects of corticosteroids used in obstetrics. Australas J Ultrasound Med. 2013;16:135-41.
14. Lardón M, Uberos J, Narbona E. Does corticosteroid treatment during the pre and postnatal periods affect the neurodevelopmental outcome of premature newborns? Biomedica. 2017;37:104-11.
15. Zhao C, He L, Li L, et al. Prenatal glucocorticoids exposure and adverse cardiovascular effects in offspring. Front Endocrinol (Lausanne). 2024;15:1430334.
16. Sakurai K, Takeba Y, Osada Y, et al. Antenatal glucocorticoid administration promotes cardiac structure and energy metabolism maturation in preterm fetuses. Int J Mol Sci. 2022;23:10186.
17. Ninan K, Liyanage SK, Murphy KE, Asztalos EV, McDonald SD. Evaluation of long-term outcomes associated with preterm exposure to antenatal corticosteroids: a systematic review and meta-analysis. JAMA Pediatr. 2022;176:e220483.
18. Jensen EA, Rysavy MA, Kusuda S; Tiny Baby Collaborative Steering Committee. Use of hydrocortisone in extremely preterm infants: emphasis on those born least mature. J Perinatol. 2025.
19. Northway WH Jr, Rosan RC, Porter DY. Pulmonary disease following respirator therapy of hyaline-membrane disease. Bronchopulmonary dysplasia. N Engl J Med. 1967;276:357-68.

20. Arsan S, Korkmaz A, Oğuz S. Turkish Neonatal Society guideline on prevention and management of bronchopulmonary dysplasia. Turk Pediatri Ars. 2018;53:S138-50.
21. Doyle LW, Davis PG, Morley CJ, McPhee A, Carlin JB; DART Study Investigators. Low-dose dexamethasone facilitates extubation among chronically ventilator-dependent infants: a multicenter, international, randomized, controlled trial. Pediatrics. 2006;117:75-83.
22. Bateman DA, Thomas W, Parravicini E, Polesana E, Locatelli C, Lorenz JM. Serum creatinine concentration in very-low-birth-weight infants from birth to 34-36 wk postmenstrual age. Pediatr Res. 2015;77:696-702.
23. JASP. A fresh way to do statistics. [JASP (version 0.95.4) (Computer Software)]. (2025). Available from: https://jasp-stats.org/
24. Onland W, van de Loo M, Offringa M, van Kaam A. Systemic corticosteroid regimens for prevention of bronchopulmonary dysplasia in preterm infants. Cochrane Database Syst Rev. 2023;3:CD010941.
25. Kiss JK, Gajda A, Mari J, Bereczki C. Blood pressure in preterm infants with bronchopulmonary dysplasia in the first three months of life. Pediatr Nephrol. 2024;39:2475-81.
26. Altit G, Bhombal S, Hopper RK, Tacy TA, Feinstein J. Death or resolution: the "natural history" of pulmonary hypertension in bronchopulmonary dysplasia. J Perinatol. 2019;39:415-25.
27. Çakır U, Tayman C. Effect of sex and mode of delivery on systemic inflammatory indices in preterm infants. Cukurova Med J. 2023;48:1347-56.
28. Collaco JM, Aherrera AD, McGrath-Morrow SA. The influence of gender on respiratory outcomes in children with bronchopulmonary dysplasia during the first 3 years of life. Pediatr Pulmonol. 2017;52:217-24.
29. Lee R, Kostina E, Dassios T, Greenough A. Influence of sex on the requirement for and outcomes following late postnatal corticosteroid treatment. Eur J Pediatr. 2023;182:1417-23.
30. Mataloun MMGB, Gibelli MAC, Kato AV, Vaz FAC, Leone CR. Use of corticosteroids and the outcome of infants with bronchopulmonary dysplasia. Revista do Hospital das Clínicas. 1999;54:175-80.
31. Sung TJ. Bronchopulmonary dysplasia: how can we improve its outcomes? Korean J Pediatr. 2019;62:367-73.
32. Kiss JK, Gajda A, Mari J, Nemeth J, Bereczki C. Oscillometric arterial blood pressure in haemodynamically stable neonates in the first 2 weeks of life. Pediatr Nephrol. 2023;38:3369-78.