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REVIEW ARTICLE

Postnatal corticosteroids to prevent bronchopulmonary dysplasia: balancing benefits and risks. A narrative review

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Abstract

This review analyzes the beneficial and adverse effects of corticosteroids used in the prevention and treatment of bronchopulmonary dysplasia, aiming to provide clinicians with evidence-based information.

Keywords: Bronchopulmonary dysplasia. Budesonide. Corticosteroids. Dexamethasone. Hydrocortisone.

Corticosteroides pós-natais para prevenir a displasia broncopulmonar: equilibrando benefícios e riscos. Uma revisão narrativa

Resumo

Esta revisão analisa os efeitos benéficos e adversos dos corticosteróides utilizados na prevenção e tratamento da displasia broncopulmonar do grande prétermo, de forma a poder fornecer ao clínico informações úteis baseadas em evidências.

Palavras-chave: Budesonide. Corticosteroides. Dexametasona. Displasia broncopulmonar. Hidrocortisona.

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Keypoints

What is known

- Postnatal corticosteroids have been used in neonatology to prevent and treat bronchopulmonary dysplasia in preterm infants.
- Clinical trials have examined various corticosteroids, including dexamethasone and hydrocortisone used systemically, and several others used by the inhalation route.
- The use of corticosteroids in preterm infants has shown benefits but also significant risks, such as cerebral palsy.

What is added

- This review summarizes current evidence on the use of postnatal corticosteroids in preterm infants.
- The role of corticosteroids in the prevention and treatment of bronchopulmonary dysplasia is not yet a completely resolved issue.
- Systemic corticosteroids are indicated after the first week of life in ventilator-dependent preterm infants with the aim of enabling extubation.

Introduction

Bronchopulmonary dysplasia (BPD) remains a significant chronic morbidity for preterm infants, posing as a potentially devastating condition with lasting negative impacts on pulmonary function and neurodevelopmental outcomes[1]. Despite advances in obstetric and neonatal care over the last few decades, BPD still affects approximately 50% of preterm infants born before 28 weeks of gestation[2]. The disease, which has a multifactorial etiology and complex pathophysiology, is marked by inflammation in immature lungs and airways[1,3]. Due to their potent anti-inflammatory effects, corticosteroids were introduced around 50 years ago to treat breathing problems in preterm infants[4]. Enthusiasm for the use of corticosteroids to prevent and treat BPD emerged in the 1980s. Since then, more than 80 randomized controlled trials (RCTs) have been conducted, making corticosteroids one of the most researched medications and also one of the most controversial interventions in neonatal medicine[5,6].

Initially, corticosteroids were administered systemically, and the inhalation route was developed later[7]. Clinical trials have examined various corticosteroids, including dexamethasone and hydrocortisone administered systemically, as well as several others administered via the inhalation route[7].

The objective of this review is to summarize the results of the most recent literature on the use of corticosteroids in the prevention and treatment of BPD, with a focus on highlighting the risks versus the benefits. The aim is to provide clinicians with safe and practical information for their decision-making processes.

Methods

A literature search was conducted in the PubMed database for review articles on corticosteroids for preventing and treating bronchopulmonary dysplasia, written in English and published from 2010 onwards. The search included the following keywords: corticosteroids, dexamethasone, hydrocortisone, budesonide, bronchopulmonary dysplasia, surfactant, inhaled, systemic, intratracheal, adverse effects, neurodevelopment and cerebral palsy.

The information from the review articles was analyzed and compiled in this manuscript.

Systemic corticosteroids

The primary corticosteroids administered systemically to prevent or treat BPD are dexamethasone and hydrocortisone[8,9]. Dexamethasone has no affinity for mineralocorticoid receptors; it only exerts glucocorticoid effects. It is approximately 25 times more potent than hydrocortisone and is considered a long-acting agent, with a duration of action exceeding 36 hours[10,11]. The glucocorticoid activity reduces inflammation, suppresses immune function, influences nutrient metabolism and aids in the normal response to stress[12]. Hydrocortisone is the synthetic analog of endogenous cortisol and can exert both mineralocorticoid and glucocorticoid effects, depending on the dose and the patient's state of stress. It exhibits greater glucocorticoid binding in states of high stress and greater mineralocorticoid binding in states of low stress[12-14]. Hydrocortisone is absorbed rapidly through the enteral route and is short-acting, with a duration of action typically ranging from eight to 12 hours[14]. Mineralocorticoid activity enhances sodium absorption and potassium excretion in the nephrons, resulting in passive water retention, increased intravascular volume and elevated blood pressure[12].

Synthetic glucocorticoids with a long biological action and little or no mineralocorticoid activity, such as dexamethasone, can suppress natural cortisol secretion and may leave mineralocorticoid receptors unoccupied for prolonged periods of time. This can lead to neuronal

apoptosis in the developing brain[15,16]. This may explain the neurodevelopmental deficits observed in preterm infants treated with dexamethasone but not with hydrocortisone[9]. A recent systematic review by Jenkinson et al., aimed at determining the cardiopulmonary and cognitive effects during childhood and adolescence of dexamethasone systemically administered to preterm infants during neonatal intensive care, found impaired respiratory and cognitive outcomes[17].

Meta-analyses of RCTs that assessed risks and benefits of systemic corticosteroids to prevent or treat BPD have divided the trials based on the timing of treatment initiation into early (< 7 days after birth) and late (≥ 7 days after birth).

Early (< 7 days after birth) systemic corticosteroids

The administration of systemic corticosteroids during the first six days of life has beneficial effects as it minimizes relative cortisol insufficiency and lung inflammation caused by factors such as ventilation, surfactant deficiency, oxygen toxicity, hypoxemia, chorioamnionitis and early-onset sepsis[7].

The most recent Cochrane systematic review, conducted by Doyle et al., published in 2021, included 32 trials (21 with dexamethasone and 11 with hydrocortisone) with a total of 4,393 participants[9]. In these trials, systemic corticosteroids were compared with a placebo or no intervention. The characteristics of the individual trials varied significantly, particularly in terms of treatment durations and cumulative doses of corticosteroids. The analysis of the results demonstrated that early systemic corticosteroids reduced the rates of BPD at 36 weeks, combined mortality or BPD at 36 weeks, but not mortality alone at 36 weeks (Table 1). Most of the reduction in BPD arises from studies using dexamethasone rather than hydrocortisone. Both dexamethasone and hydrocortisone contribute to a reduction in combined mortality or BPD at 36 weeks. There is also evidence that hydrocortisone reduces mortality at the latest reported age, but dexamethasone does not. Unfortunately, early administration of dexamethasone increases the rate of cerebral palsy and the combined outcome of cerebral palsy or mortality, whereas hydrocortisone does not have the same effect.

One of the studies that yielded interesting results regarding the early use of hydrocortisone is the PREMILOC trial[18]. In this double-blind, placebo-controlled RCT conducted at 21 French tertiary centers, 521 preterm infants ranging from 24 to 27 weeks' gestation were enrolled. Hydrocortisone was administered starting from the first day of life at a dose of 8.5 mg/kg over 10 days. The study found that hydrocortisone reduced the rate of the primary endpoint of BPD or mortality at 36 weeks (hydrocortisone 40%; control 49%, RR 0.82; 95% CI 0.67-0.99; p = 0.04). At the follow-up at 22 months' corrected age, the rates of cerebral palsy were similar in both groups (hydrocortisone 6%; control 5%)[19]. The five-year neurocognitive outcomes of 83 surviving children at one center showed that hydrocortisone treatment was significantly associated with a greater chance of survival at five years of age with a full-scale IQ equal to or greater than 90 compared to the placebo (adjusted odds ratio = 4.26, 95% CI = 1.47-12.36, p = 0.008)[20]. However, the results of the PREMILOC trial require confirmation through additional studies. Therefore, most authors do not yet recommend its routine use.

Other benefits of early systemic corticosteroids include increased rates of successful extubation and lower rates of patent ductus arteriosus and retinopathy of prematurity[9]. However, there are also adverse effects, such as gastrointestinal bleeding, intestinal perforation, hyperglycemia, hypertension, hypertrophic cardiomyopathy and growth failure[9]. These reported benefits and adverse effects are mostly associated with dexamethasone, with the exception of intestinal perforation, which was more common with both hydrocortisone and dexamethasone.

A major limitation of early systemic corticosteroid studies is their lack of sampling power to assess neurodevelopment in childhood. This limitation means they do not allow the risks and benefits to be assessed with certainty[5].

Balancing the risks and benefits of early systemic corticosteroids in the prevention of BPD, it is currently accepted that they should not be used routinely in clinical practice[5]. Due to the encouraging results of the PREMILOC study, more RCTs with early hydrocortisone are needed to assess survival without neurodevelopmental disability. Before the routine use of hydrocortisone can be recommended, further evidence from these trials is needed[5].

Late (≥ 7 days after birth) systemic corticosteroids

The most recent review on late systemic corticosteroids includes 23 trials (21 with dexamethasone and two with hydrocortisone), recruiting a total of 1,817 infants[8]. Most infants were ventilator-dependent at enrolment, and regimens varied significantly in duration and cumulative dose.

Table 1. Summary effects of early (< 7 days after birth) systemic corticosteroids in the various Cochrane reviews

	Dexamethasone	Hydrocortisone	Combined
BPD at 36 weeks	0.72 [0.63, 0.82] **p < 0.001** ns = 17 np = 2,791	0.92 [0.81, 1.06] p = 0.25 ns = 9 np = 1,376	0.80 [0.73, 0.88] **p < 0.001** ns = 26 np = 4,167
Mortality by 36 weeks	1.08 [0.94, 1.23] p = 0.29 ns = 17 np = 2,791	0.85 [0.67, 1.06] p = 0.15 ns = 10 np = 1,385	1.01 [0.90, 1.13] p = 0.92 ns = 27 np = 4,167
Mortality or BPD by 36 weeks	0.88 [0.81, 0.95] **p < 0.001** ns = 17 np = 2,791	0.90 [0.82, 0.99] **p = 0.04** ns = 9 np = 1,376	0.89 [0.83, 0.94] **p < 0.001** ns = 26 np = 4,167
Mortality at latest age report	1.02 [0.90, 1.16] p = 0.73 ns = 20 np = 2,940	0.80 [0.65, 0.99] **p = 0.04** ns = 11 np = 1,433	0.95 [0.85, 1.06] p = 0.38 ns = 31 np = 4,373
Cerebral palsy	1.77 [1.21, 2.58] **p = 0.003** ns = 7 np = 921	1.05 [0.66, 1.66] p = 0.84 ns = 6 np = 1,052	1.43 [1.07, 1.92] **p = 0.02** ns = 13 np = 1,973
Mortality before follow-up	0.99 [0.81, 1.21] p = 0.93 ns = 7 np = 921	0.81 [0.64, 1.02] p = 0.08 ns = 6 np = 1,052	0.90 [0.78, 1.05] p = 0.19 ns = 13 np = 1,973
Mortality or cerebral palsy	1.18 [1.01, 1.37] **p = 0.04** ns = 7 np = 921	0.86 [0.71, 1.05] p = 0.15 ns = 6 np = 1,052	0.03 [0.91, 1.16] p = 0.63 ns = 13 np = 1,973

Data are RR [95% confidence interval].
RR: risk ratio; BPD: bronchopulmonary dysplasia; ns: number of studies; np: number of participants; **bold P:** statistically significant.
Adapted from reference 5.

Late systemic administration of corticosteroids reduced the rates of BPD at 36 weeks, mortality by 36 weeks, combined mortality or BPD by 36 weeks and mortality at the latest reported age (Table 2). All the effects on BPD arise from studies with dexamethasone rather than hydrocortisone. Although the reduction in mortality at the latest reported age seems to arise from studies with hydrocortisone, there is little heterogeneity between the dexamethasone and hydrocortisone subgroups (p = 0.42). There is little evidence that late corticosteroids increase cerebral palsy in later childhood, although there was only one study with hydrocortisone assessing this outcome (Table 2).

In 2022, the results of the hydrocortisone for BPD trial, conducted by the *National Institute of Child Health and Human Development (NICHD) Neonatal Research Network*, were published[21]. In this trial, 800 preterm infants with a gestational age below 30 weeks who had been intubated for at least seven days at 14 to 28 days were randomly assigned to receive either hydrocortisone (4 mg per kilogram of body weight per day tapered over a period of 10 days) or a placebo. Hydrocortisone increased the probability of extubation and reduced the duration of mechanical ventilation. However, hydrocortisone did not affect survival without BPD at 36 weeks nor survival without moderate-to-severe neurodevelopmental impairment or survival without cerebral palsy. The meta-analysis of data from this trial, combined with the other two trials with hydrocortisone included in the 2021 Cochrane review, did not show any differences in the rates of death, BPD or cerebral palsy[7].

In recent studies by Halbmeijer N et al.[22,23], systemic hydrocortisone started in the second week after birth in ventilator-dependent infants born very preterm was not found to be associated with significant differences in brain development or neurodevelopment at two years of corrected age, compared with placebo treatment.

Table 2. Summary effects of late (≥ 7 days after birth) systemic corticosteroids in the various Cochrane reviews

	Dexamethasone	Hydrocortisone	Combined
BPD at 36 weeks	0.76 [0.66, 0.87] **p < 0.001** ns = 12 np = 553	1.10 [0.92, 1.31] p < 0.29 ns = 2 np = 435	0.89 [0.80, 0.99] **p = 0.03** ns = 14 np = 988
Mortality by 36 weeks	0.68 [0.43, 1.08] p = 0.11 ns = 13 np = 594	0.71 [0.49, 1.04] p = 0.08 ns = 2 np = 435	0.69 [0.52, 0.93] **p = 0.02** ns = 15 np = 1,029
Mortality or BPD by 36 weeks	0.75 [0.67, 0.85] **p < 0.001** ns = 12 np = 553	0.98 [0.88, 1.09] p = 0.68 ns = 2 np = 435	0.85 [0.79, 0.92] p < 0.001 ns = 14 np = 988
Mortality at latest age report	0.85 [0.66, 1.11] p = 0.23 ns = 19 np = 993	0.72 [0.52, 1.00] p = 0.05 ns = 2 np = 435	0.80 [0.65, 0.98] **p = 0.03** ns = 21 np = 1,428
Cerebral palsy	1.12 [0.79, 1.60] p = 0.51 ns = 15 np = 855	3.19 [0.35, 29.1] p = 0.30 ns = 1 np = 64	1.16 [0.82, 1.64] p = 0.39 ns = 16 np = 919
Mortality before follow-up	0.82 [0.62, 1.10] p = 0.18 ns = 15 np = 855	0.80 [0.39, 1.63] p = 0.61 ns = 1 np = 64	0.82 [0.63, 1.07] p = 0.14 ns = 16 np = 919
Mortality or cerebral palsy	0.95 [0.77, 1.16] p = 0.58 ns = 15 np = 855	0.98 [0.53, 1.81] p = 0.96 ns = 1 np = 64	0.95 [0.78, 1.15] p = 0.59 ns = 16 np = 919

Data are RR [95% confidence interval].
RR: risk ratio; BPD: bronchopulmonary dysplasia; ns: number of studies; np: number of participants; **bold P:** statistically significant.
Adapted from reference 5.

It can be challenging to choose which corticosteroid to use and at what dose in infants with ongoing lung disease. Two trials examined low-dose late systemic corticosteroids[21,24]. The NICHD Neonatal Research Network Hydrocortisone for BPD Trial used a 24.5 mg/kg cumulative dose of hydrocortisone tapered over 10 days[21]. In this study, hydrocortisone increased the probability of successful extubation by day 10 (44.7% vs. 33.6%, NNT 9). However, it did not reduce the risk of BPD. In the second study, the DART trial[24], dexamethasone at a cumulative dose of 0.89 mg/kg, tapered over 10 days, significantly increased the chance of successful extubation (60.0% vs. 11.7%, NNT 2) without a significant reduction in the risk of BPD. This trial did not show significant neurological harm in survivors at two years' corrected age. However, unfortunately, it was not designed to evaluate neurodevelopmental outcomes. Other trials with late dexamethasone only showed a reduction in BPD when the cumulative dose was 2-4 mg/kg[25].

Other benefits of late systemic corticosteroids include faster extubation[8]. Adverse effects include hyperglycemia, glycosuria, systemic arterial hypertension, cardiomyopathy and severe retinopathy of prematurity[8].

As with trials on the early use of systemic corticosteroids, there are limitations in trials of late systemic corticosteroids. Most studies reporting long-term outcomes were not designed to detect clinically important neurodevelopmental deficits[5].

Based on the results of the trials with late systemic corticosteroids, they should be reserved for infants at high risk of developing BPD to maximize the risk-to-benefit profile. Researchers from the NICHD Neonatal Research Network conducted a propensity score-matched cohort study in 964 extremely preterm infants[26]. The results of this study suggested that corticosteroids were associated with a reduced risk of

death or disability at two years' corrected age in infants at moderate to high pretreatment risk of death or with grade 2 or 3 BPD, but they might pose harm in infants at lower risk[26].

Currently, late systemic corticosteroids are only indicated for ventilator-dependent infants, with the aim of extubating them and reducing the damage caused by prolonged ventilation[27,28].

Inhaled corticosteroids

Four different inhaled corticosteroids (budesonide, beclomethasone, fluticasone and flunisolide) have been studied[5]. Among these, budesonide is the most studied.

Early (≤ 14 days of life) inhaled corticosteroids

Early inhaled corticosteroids reduce the rates of BPD at 36 weeks and the combined outcome of mortality and BPD by 36 weeks (Table 3). Mortality before follow-up and the combined outcome of mortality and cerebral palsy are both higher in the corticosteroids group. The results of the meta-analyses are strongly influenced by the results of the NEUROSIS trial[29]. In this study, inhaled budesonide in preterm infants aged 23-27 weeks' gestational age under respiratory support reduced the primary outcome of death or BPD at 36 weeks. However, there was an increase in mortality by 36 weeks in the budesonide group, which had further increased by two years of age (p = 0.04)[29].

Due to being associated with increased mortality, early inhaled corticosteroids are not recommended[5].

Late (≥ 7 days after birth) inhaled corticosteroids

There is limited data on late inhaled corticosteroids. Only one trial contributed data on BPD at 36 weeks, and only three trials had data on mortality at 36 weeks. Additionally, none of the trials reported on long-term outcomes (Table 3). Based on this evidence, late inhaled corticosteroids are not recommended.

Inhaled versus systemic corticosteroids

The two Cochrane reviews that compare inhaled versus systemic corticosteroids include small numbers of studies and participants, with complex study designs and limited long-term data[30,31]. The lack of evidence of any benefit of inhaled over systemic corticosteroids and the increased mortality with early budesonide prevent their routine use in clinical practice (Table 4)[7].

Table 3. Summary effects of inhaled corticosteroids in the various Cochrane reviews

	≤ 14 days	≥ 7 days
BPD at 36 weeks	0.76 [0.83, 1.48] **p = 0.005** ns = 6 np = 1,285	1.00 [0.59, 1.70] p = 1.00 ns = 1 np = 30
Mortality by 36 weeks	1.09 [0.62, 0.92] p = 0.54 ns = 6 np = 1,285	3.00 [0.35, 25.8] p = 0.32 ns = 3 np = 61
Mortality or BPD by 36 weeks	0.86 [0.75, 0.99] **p = 0.04** ns = 6 np = 1,285	1.10 [0.74, 1.63] p = 0.66 ns = 1 np = 30
Mortality at latest age report	1.36 [1.02, 1.81] **p = 0.04** ns = 3 np = 1,127	3.00 [0.35, 25.8] p = 0.32 ns = 3 np = 53
Cerebral palsy	1.05 [0.67, 1.65] p = 0.83 ns = 3 np = 1,127	Not reported
Mortality before follow-up	1.36 [1.02, 1.81] **p = 0.04** ns = 3 np = 1,127	Not reported
Mortality or cerebral palsy	1.26 [1.00, 1.58] **p = 0.05** ns = 3 np = 1,127	Not reported

Data are RR [95% confidence interval]; RR: risk ratio; BPD: bronchopulmonary dysplasia; ns: number of studies; np: number of participants; **bold P:** statistically significant.
Adapted from reference 5.

Intratracheal corticosteroids administered with a surfactant

The results of a meta-analysis from 2022, including 12 trials and 1,377 ventilated preterm infants, suggested that the early combined utilization of budesonide and surfactant have a superior effect on BPD incidence (risk ratio [RR] = 0.62; 95% CI: 0.54-0.71, p < 0.001], mortality (RR = 0.64; 95% CI: 0.45-0.92, p = 0.016), the composite outcome of BPD and mortality (RR = 0.58; 95% CI: 0.50-0.68, p < 0.001), the additional doses of surfactant (RR = 0.53; 95% CI: 0.44-0.63, p < 0.001), the duration of assisted ventilation (standard mean difference [SMD] = 1.14; 95% CI: 1.58 to 0.70, p < 0.001),

Table 4. Summary effects of inhaled versus systemic corticosteroids in the Cochrane reviews

	≤ 7 days	> 7 days
BPD at 36 weeks	1.45 [0.99, 2.11] p = 0.06 ns = 1 np = 278	1.06 [0.88, 1.29] p = 0.53 ns = 3 np = 431
Mortality by 36 weeks	0.83 [0.56, 1.23] p = 0.36 ns = 2 np = 294	0.94 [0.62, 1.43] p = 0.77 ns = 3 np = 431
Mortality or BPD by 36 weeks	1.09 [0.88, 1.35] p = 0.43 ns = 1 np = 278	1.02 [0.84, 1.23] p = 0.86 ns = 3 np = 431
Mortality at latest age report	No data	No data
Cerebral palsy	1.87 [0.36, 9.72] p = 0.46 ns = 1 np = 91	1.00 [0.34, 2.92] p = 1.00 ns = 1 np = 118
Mortality before follow-up	0.94 [0.47, 1.86] p = 0.85 ns = 1 np = 91	0.83 [0.47, 1.49] p = 0.54 ns = 1 np = 118
Mortality or cerebral palsy	1.07 [0.59, 1.93] p = 0.82 ns = 1 np = 91	0.88 [0.55, 1.39] p = 0.57 ns = 1 np = 118

Data are RR [95% confidence interval]; RR: risk ratio; BPD: bronchopulmonary dysplasia; ns: number of studies; np: number of participants.
Adapted from reference 5.

duration of invasive ventilation (SMD = 1.77; 95% CI: 2.61 to 0.93, p < 0.001) and hospital stays (SMD = 1.11; 95% CI: 1.73 to 0.49, p = 0.001) in preterm infants with respiratory distress syndrome. Moreover, these benefits were not associated with increased adverse outcomes[32].

The intratracheal administration of a corticosteroid combined with surfactant looks promising, and several trials are ongoing.

Summary

The role of corticosteroids in the prevention and treatment of BPD is not yet a completely resolved issue, and further studies are still needed. The systemic route appears to be superior to the inhalation route. Systemic dexamethasone should not be used in the first week of life. Weighing the benefits against the risks, the use of corticosteroids should be considered after the first week of life. However, the benefits of low-dose systemic hydrocortisone used in the first 10 days of life deserve confirmation through further research. When used after the first week of life, corticosteroids should be reserved for high-risk BPD patients, particularly ventilator-dependent infants. Additionally, regardless of the drug used, its dose and duration should be minimized. The use of corticosteroids plus surfactant appears promising, but more research is needed before they can be recommended for routine use. Data on long-term follow-up, including motor and cognitive outcomes, are necessary for a comprehensive understanding of their effects.

Conclusion

Systemic corticosteroids are currently only indicated after the first week of life in ventilator-dependent preterm infants at high risk of developing BPD, with the aim of facilitating extubation. They should be used at the lowest possible dose and duration.

Author contributions

G. Rocha: Literature research, conception and review of the manuscript.

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Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The study does not involve patient personal data nor requires ethical approval. The SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

References

1. Hwang JS, Rehan VK. Recent Advances in Bronchopulmonary Dysplasia: Pathophysiology, Prevention, and Treatment. Lung 2018;196(2):129-138. doi: 10.1007/s00408-018-0084-z.
2. Doyle LW, Ranganathan S, Cheong JLY. Ventilation in Preterm Infants and Lung Function at 8 Years. N Engl J Med. 2017 Oct 19;377(16):1601-1602. doi: 10.1056/NEJMc1711170. PMID: 29045215.

3. Thébaud B, Goss KN, Laughon M, Whitsett JA, Abman SH, Steinhorn RH, et al. Bronchopulmonary dysplasia. Nat Rev Dis Primers 2019;5(1):78. doi: 10.1038/s41572-019-0127-7.
4. Baden M, Bauer CR, Colle E, Klein G, Taeusch HW Jr, Stern L. A controlled trial of hydrocortisone therapy in infants with respiratory distress syndrome. Pediatrics 1972;50(4):526-34.
5. Doyle LW. Postnatal Corticosteroids to Prevent or Treat Bronchopulmonary Dysplasia. Neonatology 2021;118(2):244-251. doi: 10.1159/000515950.
6. Demauro SB, Dysart K, Kirpalani H. Stopping the swinging pendulum of postnatal corticosteroid use. J Pediatr 2014;164(1):9-11. doi: 10.1016/j.jpeds.2013.10.020.
7. Jensen EA, Watterberg KL. Postnatal Corticosteroids To Prevent Bronchopulmonary Dysplasia. Neoreviews 2023;24(11):e691-e703. doi: 10.1542/neo.24-11-e691.
8. Doyle LW, Cheong JL, Hay S, Manley BJ, Halliday HL. Late (≥ 7 days) systemic postnatal corticosteroids for prevention of bronchopulmonary dysplasia in preterm infants. Cochrane Database Syst Rev 2021;11(11):CD001145. doi: 10.1002/14651858.CD001145.pub5.
9. Doyle LW, Cheong JL, Hay S, Manley BJ, Halliday HL. Early (< 7 days) systemic postnatal corticosteroids for prevention of bronchopulmonary dysplasia in preterm infants. Cochrane Database Syst Rev 2021;10(10):CD001146. doi: 10.1002/14651858.CD001146.pub6.
10. Htun ZT, Schulz EV, Desai RK, Marasch JL, McPherson CC, Mastrandrea LD, et al. Postnatal steroid management in preterm infants with evolving bronchopulmonary dysplasia. J Perinatol 2021;41(8):1783-1796. doi: 10.1038/s41372-021-01083-w.
11. Timmermans S, Souffriau J, Libert C. A General Introduction to Glucocorticoid Biology. Front Immunol. 2019 Jul 4;10:1545. doi: 10.3389/fimmu.2019.01545.
12. Williams DM. Clinical Pharmacology of Corticosteroids. Respir Care 2018;63(6):655-670. doi: 10.4187/respcare.06314.
13. de Kloet ER. From receptor balance to rational glucocorticoid therapy. Endocrinology 2014;155(8):2754-69. doi: 10.1210/en.2014-1048.
14. Czock D, Keller F, Rasche FM, Häussler U. Pharmacokinetics and pharmacodynamics of systemically administered glucocorticoids. Clin Pharmacokinet 2005;44(1):61-98. doi: 10.2165/00003088-200544010-00003.
15. Crochemore C, Lu J, Wu Y, Liposits Z, Sousa N, Holsboer F, Almeida OF. Direct targeting of hippocampal neurons for apoptosis by glucocorticoids is reversible by mineralocorticoid receptor activation. Mol Psychiatry 2005;10(8):790-8. doi: 10.1038/sj.mp.4001679.
16. Hassan AH, von Rosenstiel P, Patchev VK, Holsboer F, Almeida OF. Exacerbation of apoptosis in the dentate gyrus of the aged rat by dexamethasone and the protective role of corticosterone. Exp Neurol 1996;140(1):43-52. doi: 10.1006/exnr.1996.0113.
17. Jenkinson AC, Kaltsogianni O, Dassios T, Greenough A. Systematic review of the long-term effects of postnatal corticosteroids. J Perinat Med 2023;51(9):1120-1128. doi: 10.1515/jpm-2023-0297.
18. Baud O, Maury L, Lebail F, Ramful D, El Moussawi F, Nicaise C, et al; PREMILOC trial study group. Effect of early low-dose hydrocortisone on survival without bronchopulmonary dysplasia in extremely preterm infants (PREMILOC): a double-blind, placebo-controlled, multicentre, randomised trial. Lancet. 2016 Apr 30;387(10030):1827-36. doi: 10.1016/S0140-6736(16)00202-6.
19 . Baud O, Trousson C, Biran V, Leroy E, Mohamed D, Alberti C; PREMILOC Trial Group. Association Between Early Low-Dose Hydrocortisone Therapy in Extremely Preterm Neonates and Neurodevelopmental Outcomes at 2 Years of Age. JAMA 2017;317(13):1329-1337. doi: 10.1001/jama.2017.2692.
20. Trousson C, Toumazi A, Bourmaud A, Biran V, Baud O. Neurocognitive outcomes at age 5 years after prophylactic hydrocortisone in infants born extremely preterm. Dev Med Child Neurol 2023;65(7):926-932. doi: 10.1111/dmcn.15470.
21. Watterberg KL, Walsh MC, Li L, Chawla S, D'Angio CT, Goldberg RN, et al; Eunice Kennedy Shriver NICHD Neonatal Research Network. Hydrocortisone to Improve Survival without Bronchopulmonary Dysplasia. N Engl J Med 2022;386(12):1121-1131. doi: 10.1056/NEJMoa2114897.
22. Halbmeijer NM, Onland W, Dudink J, Cools F, Debeer A, van Kaam AH, et al. Effect of Systemic Hydrocortisone on Brain Abnormalities and Regional Brain Volumes in Ventilator-dependent Infants Born Preterm: Substudy of the SToP-BPD Study. J Pediatr 2024;265:113807. doi: 10.1016/j.jpeds.2023.113807.
23. Halbmeijer NM, Onland W, Cools F, Swarte R, van der Heide-Jalving M, Merkus MP, van Kaam AH; STOP-BPD Trial Collaborators. Effect of Systemic Hydrocortisone Initiated 7 to 14 Days After Birth in Ventilated Preterm Infants on Mortality and Neurodevelopment at 2 Years' Corrected Age: Follow-up of a Randomized Clinical Trial. JAMA 2021;326(4):355-357. doi: 10.1001/jama.2021.9380.
24. 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(1):75-83. doi: 10.1542/peds.2004-2843.
25. Ramaswamy VV, Bandyopadhyay T, Nanda D, Bandiya P, Ahmed J, Garg A, et al. Assessment of Postnatal Corticosteroids for the Prevention of Bronchopulmonary Dysplasia in Preterm Neonates: A Systematic Review and Network Meta-analysis. JAMA Pediatr 2021;175(6):e206826. doi: 10.1001/jamapediatrics.2020.6826.
26. Doyle LW, Halliday HL, Ehrenkranz RA, Davis PG, Sinclair JC. An update on the impact of postnatal systemic corticosteroids on mortality and cerebral palsy in preterm infants: effect modification by risk of bronchopulmonary dysplasia. J Pediatr 2014;165(6):1258-60. doi: 10.1016/j.jpeds.2014.07.049.
27. Sweet DG, Carnielli VP, Greisen G, Hallman M, Klebermass-Schrehof K, Ozek E, et al. European Consensus Guidelines on the Management of Respiratory Distress Syndrome: 2022 Update. Neonatology 2023;120(1):3-23. doi: 10.1159/000528914.
28. European Standards of Care for Newborn Health. Medical care & clinical practice. Prevention of Bronchopulmonary dysplasia. https://newborn-health-standards.org
29. Bassler D, Plavka R, Shinwell ES, Hallman M, Jarreau PH, Carnielli V, et al; NEUROSIS Trial Group. Early Inhaled Budesonide for the Prevention of Bronchopulmonary Dysplasia. N Engl J Med 2015;373(16):1497-506. doi: 10.1056/NEJMoa1501917.
30. Shah SS, Ohlsson A, Halliday HL, Shah VS. Inhaled versus systemic corticosteroids for preventing bronchopulmonary dysplasia in ventilated very low birth weight preterm neonates. Cochrane Database Syst Rev 2017;10(10):CD002058. doi: 10.1002/14651858.CD002058.pub3.
31. Shah SS, Ohlsson A, Halliday HL, Shah VS. Inhaled versus systemic corticosteroids for the treatment of bronchopulmonary dysplasia in ventilated very low birth weight preterm infants. Cochrane Database Syst Rev 2017;10(10):CD002057. doi: 10.1002/14651858.CD002057.pub4.
32. Tang W, Chen S, Shi D, Ai T, Zhang L, Huang Y, et al. Effectiveness and safety of early combined utilization of budesonide and surfactant by airway for bronchopulmonary dysplasia prevention in premature infants with RDS: A meta-analysis. Pediatr Pulmonol 2022;57(2):455-469. doi: 10.1002/ppul.25759.