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[Intervention Review]

Late (≥ 7 days) inhalation corticosteroids to reduce bronchopulmonary dysplasia in preterm infants

Wes Onland[1], Martin Offringa[2], Anton van Kaam[1]

[1]Department of Neonatology, Emma Children's Hospital AMC, University of Amsterdam, Amsterdam, Netherlands. [2]Child Health Evaluative Sciences, Hospital for Sick Children, Toronto, Canada

Contact address: Wes Onland, Department of Neonatology, Emma Children's Hospital AMC, University of Amsterdam, Meibergdreef 9, Amsterdam, 1105 AZ, Netherlands. w.onland@amc.uva.nl.

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ABSTRACT

Background

Bronchopulmonary dysplasia (BPD), defined as oxygen dependence at 36 weeks postmenstrual age (PMA), remains an important complication of prematurity. Pulmonary inflammation plays a central role in the pathogenesis of BPD. Attenuating pulmonary inflammation with postnatal systemic corticosteroids reduces the incidence of BPD in preterm infants but may be associated with an increased risk of adverse neurodevelopmental outcomes. Local administration of corticosteroids via inhalation might be an effective and safe alternative.

Objectives

To determine if administration of inhalation corticosteroids after the first week of life until 36 weeks PMA to preterm infants at high risk of developing BPD is effective and safe in reducing the incidence of death and BPD as separate or combined outcomes.

Search methods

We used the standard search strategy of Cochrane Neonatal to search the Cochrane Central Register of Controlled Trials (CENTRAL 2017, Issue 4), MEDLINE via PubMed (1966 to 19 May 2017), Embase (1980 to 19 May 2017), and CINAHL (1982 to 19 May 2017). We also searched clinical trials databases, conference proceedings, and the reference lists of retrieved articles for randomised controlled trials and quasi-randomised trials**.**

Selection criteria

We included randomised controlled trials comparing inhalation corticosteroids, started ≥ 7 days postnatal age (PNA) but before 36 weeks PMA, to placebo in ventilated and non-ventilated infants at risk of BPD. We excluded trials investigating systemic corticosteroids versus inhalation corticosteroids.

Data collection and analysis

We collected data on participant characteristics, trial methodology, and inhalation regimens. The primary outcome was death or BPD at 36 weeks PMA. Secondary outcomes were the combined outcome death or BPD at 28 days PNA, the seperate outcomes of death and BPD at both 28 days PNA, and at 36 weeks PMA, and short-term respiratory outcomes, such as failure to extubate; total days of mechanical ventilation and oxygen use; and the need for systemic corticosteroids. We contacted the original trialists to verify the validity of extracted data and to provide missing data. We analysed all data using Review Manager 5. When possible, we performed meta-analysis using typical risk ratio (RR) for dichotomous outcomes and weighted mean difference (WMD) for continuous outcomes along with their 95% confidence intervals (CI). We analysed ventilated and non-ventilated participants separately.

We used the GRADE approach to assess the quality of the evidence.

Main results

We included eight trials randomising 232 preterm infants in this review. Inhalation corticosteroids did not reduce the separate or combined outcomes of death or BPD. The meta-analyses of the studies showed a reduced risk in favor of inhalation steroids regarding failure to extubate at seven days (typical RR (TRR) 0.80, 95% CI 0.66 to 0.98; 5 studies, 79 infants) and at the latest reported time point after treatment onset (TRR 0.60, 95% CI 0.45 to 0.80; 6 studies, 90 infants). However, both analyses showed increased statistical heterogeneity (I^2 statistic 73% and 86%, respectively). Furthermore, inhalation steroids did not impact total duration of mechanical ventilation or oxygen dependency. There was a trend toward a reduction in the use of systemic corticosteroids in infants receiving inhalation corticosteroids (TRR 0.51, 95% CI 0.26 to 1.00; 4 studies, 74 infants; very low-quality evidence). There was a paucity of data on short- and long-term adverse effects. Our results should be interpreted with caution because the total number of randomised participants is relatively small, and most trials differed considerably in participant characteristics, inhalation therapy, and outcome definitions.

Authors' conclusions

Based on the results of the currently available evidence, inhalation corticosteroids initiated at ≥ 7 days of life for preterm infants at high risk of developing BPD cannot be recommended at this point in time. More and larger randomised, placebo-controlled trials are needed to establish the efficacy and safety of inhalation corticosteroids.

PLAIN LANGUAGE SUMMARY

Inhalation corticosteroids for bronchopulmonary dysplasia

Review question

Does inhalation of corticosteroids after the first week of life reduce the risk of developing bronchopulmonary dysplasia (BPD) in preterm infants? This review looked at studies comparing preterm infants at risk of developing BPD after the first week of life treated with inhalation corticosteroids to those treated with inhalation placebo.

Background

Preterm infants have an increased risk of developing chronic lung disease or bronchopulmonary dysplasia. Inflammation in the lung seems to play a central role in the development of BPD. Administration of anti-inflammatory drugs known as corticosteroids into the bloodstream (systemically) reduces the risk of BPD but can also cause serious side effects. Administering corticosteroids via inhalation directly into the lungs may reduce these side effects.

Study characteristics

We identified eight studies investigating this therapy in 232 infants. Although we deemed the risk of bias as low, very few studies reported our outcomes of interest.

Key results

The included trials did not show a beneficial effect of inhalation corticosteroids on death or BPD. In addition, the safety of inhalation corticosteroids was assessed in only a small number of trials. Based on these results, inhalation corticosteroids initiated after the first week of life cannot be recommended for preterm infants at risk of BPD. More studies are needed.

Quality of evidence

The quality of the evidence was low to very low for the main outcomes.