



Systemic Corticosteroids for Bronchiolitis in Children Aged Less than Two Years: A Systematic Review

Elahe Heidari (MD)¹, Maryam Emadzadeh (MD)², Ezzat Khodashenas (MD)¹, Faride Najm Sarvari* (MD)³, Hamid Ahanchian (MD)¹, Amin Heidari (PharmD)⁴, Mahdi Mottaghi (MD)³

¹Department of Pediatrics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

²Clinical Research Unit, Mashhad University of Medical Sciences, Mashhad, Iran.

³General physician, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

⁴Faculty of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran.

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ABSTRACT

Introduction: Bronchiolitis is the main cause of lower respiratory tract infection during the first year of life. This systematic review aimed to assess the effectiveness of systemic corticosteroids in the treatment of bronchiolitis in children aged less than two years during their first hospitalization.

Methods: This systematic review was conducted via searching in databases such as PubMed, Scopus, Web of Science, and Cochrane Library until August 2019. Randomized clinical trials regarding the effects of systemic corticosteroids on children with bronchiolitis aged less than two years were evaluated in the retrieved studies. The quality of the studies was assessed based on the Jadad scale.

Result: Three studies were included in this systematic review. In two studies, dexamethasone versus placebo were used, and in one study, prednisolone was applied. In one study, use of dexamethasone versus placebo resulted in the faster resolution of respiratory distress, shorter duration of respiratory distress syndrome, reduced oxygen therapy time, and reduced length of hospital stay. In another study, children receiving treatment with dexamethasone had no significant difference in the clinical score, respiratory rate, and pulmonary function compared to the control group. In another study, use of prednisolone within two weeks led to the partial improvement of rhinitis, wheezing, breathing problems, nocturnal respiratory symptoms, and coughing. However, no significant difference was observed between the prednisolone treatment and control groups after 12 months.

Conclusion: Despite the improvements in respiratory symptoms, evidence is scarce regarding the effectiveness of systemic corticosteroids in the treatment of bronchiolitis in children aged less than two years. Therefore, well-designed randomized clinical trials on large sample sizes are required in this regard.

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Introduction

Bronchiolitis is a viral infection defined as the inflammation of bronchioles. If not treated, it may lead to the increased production of mucus and airway obstruction. Bronchiolitis is prevalent among infants and young children (1). Approximately

20% of children develop bronchiolitis within the first year of life (2). In general, the disease is characterized by rhinorrhea, expiratory wheezing, and respiratory distress, which are most commonly associated with the respiratory syncytial virus (RSV) (3). Currently, no RSV vaccine is available at

*Corresponding author: Farideh Najm Sarvari.

General physician, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

E-mail: farideh_najm@yahoo.com

Tel: +989394624241

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the public disposal(4). RSV infection is associated with a high rate of mortality in children in case there is no access to safe, efficient, and relatively economical prevention methods (3, 5). RSV-IVIG and palivizumab have been approved for the prevention of RSV infection in high-risk children (6, 7). Despite their effectiveness, these approaches are extremely costly.

Today, supportive care is considered to be a major approach to bronchiolitis management, including the monitoring of the respiratory system, fever reduction, fluid therapy, upper airway suction, and oxygen therapy (8). Furthermore, pharmacological treatments are routinely used, while their effectiveness remains controversial (9).

Systemic corticosteroids are one of the pharmacological approaches used for the treatment of bronchiolitis (10), which could affect the clinical symptoms of bronchiolitis (11). Several studies have evaluated the efficacy of systemic corticosteroids in the treatment of children with bronchiolitis proposing inconsistent results (12-14).

This systematic review aimed to assess the effectiveness of systemic corticosteroids in the treatment of bronchiolitis in hospitalized children aged less than two years.

Methods

Study Design

This was a systematic review based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

Search Strategy

The review was conducted via searching in databases such as PubMed, Scopus, Web of Science, and Cochrane Library until August 2019 to find the randomized clinical trials investigating the effects of systemic corticosteroids on the children aged less than two years with bronchiolitis during their first hospitalization. Mean respiratory rate, mean oxygen saturation, mean length of hospital stay, rate of improvement, and other outcomes were extracted from the retrieved articles and recorded. In addition, the e-publications ahead of printing were searched in PubMed, and the quality of RCTs was evaluated based on the Jaded scale (15).

Various keywords were used in the literature search, including bronchiolitis or "respiratory syncytial virus" or RSV and "corticosteroid" or "anti-inflammatory agent". It is notable that the keywords were searched individually and in the combined form.

Inclusion and Exclusion Criteria

The inclusion criteria of the study were the randomized controlled trials comparing systemic

corticosteroids with placebo or other compounds in the children with bronchiolitis aged less than two years during the first hospitalization. Only the full texts of English articles were selected.

Summaries of conference papers, review articles, editors' notes, letters, case reports, and animal studies were excluded. In addition, several published reports from one study were excluded, and only those containing comprehensive information were selected, which were identified by assessing similarity, center similarity, study time-frame, and statistical similarity results by the authors.

Selection of the Related Studies

Two independent authors selected the related studies in two stages. At the first stage (screening), the researchers intervened the articles meeting the inclusion and exclusion criteria by reading the abstracts and/or titles of the integrated search results, as well as those that seemed to be related and required further exploration in full text. At the second stage, the full text of the screened articles was carefully reviewed, and the articles meeting the inclusion criteria were systematically reviewed. It is also notable that the references of the articles were properly reviewed for further relevant articles.

Data Extraction

For each selected article, a table was designed to record the extracted, including the name of the first author, year of publication, country, number of the patients in each group, age of the patients, and type of comparison between the study groups. Furthermore, data on the mean respiratory rate, mean oxygen saturation, mean length of hospital stay, rate of improvement, and other outcomes reported in each study were recorded.

Quality Assessment of the Studies

The quality of the selected studies was assessed based on the Jadad scale and three criteria of randomization, blindness, and reporting of the deleted/missing items. The total score of the scale is calculated within the range of 3-5. The quality of the articles was reviewed by two independent researchers (E. H. and F. N.). Any disagreement in the article reviews was resolved by discussion or a third party (M. E.) to judge the final opinion.

Results

Literature Search and Study Selection

The literature search resulted in 2,574 relevant articles, some of which were eliminated due to duplication. In addition, we removed books, book sections, review articles, and animal studies, and some studies were excluded due to their quasi-experimental design.

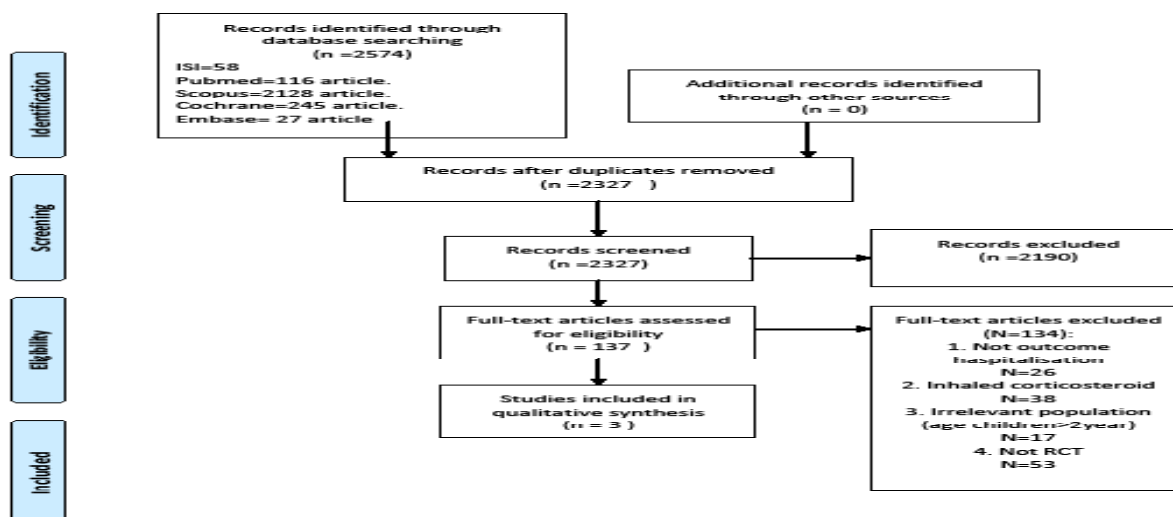


Figure 1. Applied search and the corresponding search flowchart

Table 1. Quality assessment of included studies into systematic review according Jadad Score

Author	Randomization			Blinding			Report of dropping out	Total score
	Mention randomization	Appropriate Method	Inappropriate Method	Mention blinding	Appropriate method	Inappropriate method		
Teeratakulpisarn, 2007 Thailand	*	*	-	*	*	-	*	5
Boeck, 1977 Belgium	*	?	-	*	*	-	*	4
Jartti, 2014 Japan	*	*	-	*	*	-	*	5

Table 2. Characteristics of included studies, RCT; randomized clinical trial

Name	country	Age	Sample size (intervention group)	Sample size (control group)	Study design	Comparison
Teeratakulpisarn, 2007	Thailand	Under 2 years old	89	85	RCT	Dexamethasone versus placebo
Boeck, 1977	Belgium	Under 2 years old	14	15	RCT	dexamethasone versus placebo
Jartti, 2014	Japan	3-23 month	34	40	RCT	Prednisolone versus placebo

Finally, three articles were selected for the systematic review (12-14), all of which were randomized controlled trials. Figure 1 shows the diagram of the study selection process. Table 1 shows the details of the quality assessment of the selected studies based on the Jadad scale. Table 2 shows the details of the selected studies.

Effects of Systemic Corticosteroids

Effects of systemic corticosteroids were investigated in three articles. In a study conducted on 179 patients, Teeratakulpisarn compared single-dose parenteral dexamethasone with placebo and reported the faster resolution of respiratory distress (risk ratio: 1.56; 95% CI: 1.14-2.13; $P=0.005$), 11.8 hours shorter mean duration of respiratory distress syndrome (95% CI: 3.9-19.7; $P=0.004$), reduction of 14.9 hours in the mean time required for oxygen therapy (95% CI: 5.3-24.4; $P=0.003$), and 13.4 hours shorter mean length of hospital stay (95% CI: 2.6-24.2; $P=0.02$) (12).

In another study by Jartti, 74 infants with the mean age of 13 months were evaluated, and the short-term outcomes (within two weeks) indicated that rhinitis, wheezing, intense breathing problems, nocturnal respiratory symptoms, and cough significantly decreased in the prednisolone group compared to the placebo group ($P<0.05$). On the other hand, no significant difference was observed in the long-term (within 12 months) outcomes between the study groups ($P>0.30$). In the mentioned study, prednisolone versus placebo could reduce the risk of recurrence within two and 12 months in 25 infants with more than 7,000 rhinovirus copies/ml (most sensitive group) (14). In another study, Boeck investigated the effects of dexamethasone and placebo on 29 infants with bronchiolitis and no history of related diseases (mean age: 194 days). According to the findings, the clinical score, respiratory rate, and pulmonary function test on the third day were almost similar between the intervention and control groups ($P>0.05$) (13).

Discussion

In the present study, we systematically reviewed randomized clinical trials evaluating the effectiveness of systemic corticosteroids in the treatment of bronchiolitis in hospitalized children aged less than two years. Several studies have been focused on the efficacy of corticosteroids in bronchiolitis treatment, while only three studies met the inclusion criteria. Owing to the heterogeneous results, meta-analysis was not possible.

Evidence is scarce regarding the efficacy of various pharmacological treatments in bronchiolitis, and this issue is further emphasized in children due to ethical matters (16). According to the cur-

rent review, although systemic corticosteroids lead to some improvements in the clinical symptoms of bronchiolitis, their effects are not conclusive and may be insignificant to physicians.

The small number of the reviewed studies and minimally reported effects of corticosteroids made it difficult to determine the efficacy of the treatment. In the reviewed studies, significant differences were reported between the intervention and placebo groups by Teeratakulpisarn et al., which involved a larger sample size compared to the other studies (179 patients) (12). In the studies by Boeck and Jartti, 29 and 62 patients were investigated, respectively (13, 14), which seems to be a small sample size for a randomized clinical trial. As a result, the authors reported no significant differences between the study groups, which could be due to the small sample size. On the other hand, the efficacy of the drug treatments could potentially depend on disease severity, and the discrepancy in the findings of the reviewed studies could be attributed to the differences in the severity of bronchiolitis in the patients, which was not discussed in the selected articles.

Corticosteroids are used in the treatment of bronchiolitis owing to their anti-inflammatory properties, as well as the similarities between bronchiolitis and asthma. Theoretically, it is expected that corticosteroids be effective in the treatment of lower respiratory tract viral infections. However, the findings of the current review and the published documents provided inadequate evidence to support the efficacy of corticosteroids in the outcomes of bronchiolitis, especially in the long run (9).

In present review, some questions could not be properly addressed regarding the efficacy of systemic corticosteroids in the treatment of bronchiolitis, and a well-designed randomized clinical trial on a large sample size may be required in this regard.

Conclusion

According to the results, despite some improvements in respiratory symptoms, evidence is scarce regarding the efficacy of systemic corticosteroids in the treatment of bronchiolitis in children aged less than two years. Therefore, it is recommended that well-designed randomized clinical trials be conducted on large sample sizes in order to achieve accurate results.

Limitations of the Study

One of the limitations of the present study was that despite the attempt for a comprehensive search, some articles were missed as we only included the articles published in English language. In addition, the proposed findings were not con-

clusive due to the highly heterogeneous data and small number of the reviewed articles.

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Conflict of Interest

The authors declare no conflict of interest.

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