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Living FRIendly Summaries of the Body of Evidence Using Epistemonikos (FRISBEE)
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Is dexamethasone as effective as other corticosteroids for acute asthma exacerbation in children?

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Abstract

Dexamethasone has been proposed as an alternative in the treatment of acute asthma exacerbation in children. It allows shortening the duration of treatment, reducing costs and adverse effects. However, it is not clear whether its efficacy is similar to the traditional steroid regimen. To answer this question, we searched in Epistemonikos database, which is maintained by screening multiple information sources. We identified six systematic reviews including 10 randomized trials. We extracted data, conducted a meta-analysis and generated a summary of findings table using the GRADE approach. We concluded dexamethasone has probably fewer adverse effects than others corticosteroids, and might be equally effective in reducing hospitalizations and revisits.

Problem

Systemic corticosteroids, typically oral prednisone, constitute the cornerstone in the treatment of asthmatic exacerbation in children. However, there is concern about their adverse effects in both the short- and long-term. Dexamethasone allows administration for a shorter period of time, which would reduce adverse effects and costs. It is not clear, however, whether its efficacy is similar.

Methods

We used Epistemonikos database, which is maintained by screening multiple information sources, to identify systematic reviews and their included primary studies. With this information, we generated a structured summary using a pre-established format, which includes key messages, a summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

Key messages
- Dexamethasone may be equally effective as other corticosteroids in reducing hospitalizations, and revisit to emergency services or unscheduled medical consultations in children with acute asthma exacerbations, but the certainty of the evidence is low.
- Dexamethasone, in comparison with others corticoids, probably have less adverse effects (vomiting) in children.

About the body of evidence for this question

What is the evidence. See evidence matrix in Epistemonikos later	We found six systematic reviews [1],[2],[3],[4],[5],[6] including 10 primary studies relevant to the question of interest, reported in 13 references [7],[8],[9],[10],[11],[12],[13],[14],[15],[16],[17],[18],[19]. All of them correspond to randomized controlled trials. Two trials [15],[16] were not considered for this summary since they evaluated adult population.
What types of patients were included	Regarding the definition of asthma, the different trials used different inclusion criteria: Three trials [7],[8],[19] required a history of clinical episode of wheezing, two trials [12],[17] history of two or more episodes of wheezing, three trials [11],[13],[14] used as inclusion criteria "history of previous asthma". Regarding to age, eight trials [7],[8],[11],[12],[13],[14],[17],[19] focused on pediatric population; six trials with an age range between 2 to 18 years [7],[8],[12],[14],[17],[19], one trial [11] between 1.5 to 7 years and one [13] between 0.5 to seven years. The inclusion criteria were mild or moderate acute asthma exacerbation in four trials [7],[11],[13],[14], moderate acute asthma exacerbation in one [19], three trials [8],[12],[17] excluded patients with severity factors, either life-threatening exacerbation [8], need of intubation [17], or previous history of severe acute asthma exacerbation/need of intubation [12]. Five trials excluded patients who had received corticosteroids in the last four weeks [8],[11],[12],[14],[17], two trials excluded children who received corticosteroids in the last two weeks [7],[13] and in one trial [19] this information could not be obtained from any systematic review. Six trials [7],[8],[11],[12],[14],[17] excluded patients with some chronic comorbidity, one trial [13] did not exclude for this reason, and this information could not be obtained from any systematic review for one trial [19] Other exclusion criteria were exposure to tuberculosis [8], [11], chickenpox [7],[8],[11],[12] and infection by respiratory syncytial virus [8],[13]. One trial [11] excluded patients who presented two episodes of vomiting during emergency consultation after administration of dexamethasone.
What types of interventions were included	Regarding the intervention group: All of the trials used dexamethasone. It was administered orally in four trials [7],[8],[12],[17], intramuscular in three [11],[13],[14], and nebulized in one [19]. The dose ranged from 0.3 mg/kg/day to 1.7 mg/kg/day. In five trials the treatment lasted one day [7],[8],[11], [13],[14], in two trials [12],[17] it lasted two days, and we were not able to obtain this information for one trial [19]. Regarding the control group: Three trials [7],[8],[11] compared against prednisolone and five trials [12],[13],[14],[17],[19] against prednisone. The comparison was administered orally in all of the trials. The dose varied between 1-2 mg/kg/day. The duration of treatment was 3 to 5 days, except for one trial [14] that lasted two days. We could not obtain this information for another trial [19].
What types of outcomes were measured	The outcomes were pooled by the systematic reviews as follows: • Hospitalization at first consultation. • Relapse, defined as revisit to doctor or emergency service • Admission during relapse • Asthma symptoms measured on PIS scale (Pulmonary Index Score), PSAS (Patient Self-Assessment Score) or PRAM (Paediatric Respiratory Assessment Measure) • Adverse effect: vomiting • Severe adverse effects • Time to complete recovery

Summary of findings

The information about the effects of dexamethasone compared to others corticosteroids is based on eight randomized trials [7],[8],[11],[12],[13],[14],[17],[19] including 1280 patients.
Three trials [7],[8],[17] reported hospitalization at first consultation (1007 patients), eight trials [7],[8],[11],[12],[13],[14],[17],[19] reported relapse (1280 patients) and five trials [7],[8],[11],[12], [17](1112 patients) reported adverse effects (vomiting).
The summary of findings is the following:

- Dexamethasone may be equally effective as other corticosteroids in reducing hospitalizations in children with acute asthma exacerbation, but the certainty of the evidence is low.
- Dexamethasone may be equally effective as other corticosteroids in reducing hospitalizations, and revisit to emergency services or unscheduled medical consultations in children with acute asthma exacerbations, but the certainty of the evidence is low.
- Dexamethasone may be equally effective as other corticosteroids in reducing revisit to emergency service or non-scheduled medical consultation in children with acute asthma exacerbation, but the certainty of the evidence is low.
- Dexamethasone, compared to other corticosteroids, probably has less adverse effects (vomiting) in children with acute asthma exacerbation. The certainty of the evidence is moderate.

Dexamethasone for acute asthma exacerbation in children				
Patients	Children with acute asthma exacerbation			
Intervention	Dexamethasone			
Comparison	Other corticosteroids			
Outcomes	Absolute effect*		Relative effect (95% CI)	Certainty of the evidence (GRADE)
	WITH other corticosteroids	**WITH dexamethasone**		
	Difference: patients per 1000			
Hospitalization at first consultation	118 per 1000	116 per 1000	RR 0.98 (0.70 a 1.38)	⨁⨁◯◯[1,2] Low
	Difference: 2 patients less per 1000 (Margin of error: 35 less to 45 more)			
Relapse	107 per 1000	114 per 1000	RR 1,06 (0.74 a 1.51)	⨁⨁◯◯[1,2] Low
	Difference: 7 patients more per 1000 (Margin of error: 28 less to 55 more)			
Adverse effect: Vomiting	77 per 1000	26 per 1000	RR 0.34 (0.14 a 0.80)	⨁⨁⨁◯[1] Moderate
	Difference: 51 patients less per 1000 (Margin of error: 15 to 66 less)			

Margin of error = 95% confidence interval (CI).
RR: Risk ratio.
GRADE: evidence grades of the GRADE Working Group (see later in this article)

*The risk **WITH other corticosteroids** is based on the risk in the control group of the trials. The risk **WITH dexamethasone** (and its margin of error) is calculated from relative effect (and its margin of error).

[1]We downgraded the certainty of the evidence in one level for risk of bias.
[2]We downgraded the certainty of the evidence for imprecision because the confidence interval is wide.

About the certainty of the evidence (GRADE)*

⨁⨁⨁⨁
High: This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.

⨁⨁⨁◯
Moderate: This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate

⨁⨁◯◯
Low: This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.

⨁◯◯◯
Very low: This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

*This concept is also called 'quality of the evidence' or 'confidence in effect estimates'.
† Substantially different = a large enough difference that it might affect a decision.

Other considerations for decision-making

To whom this evidence does and does not apply

- The evidence presented in this summary only applies to children.
- None of the trials included severe acute asthma exacerbation. However, in absence of direct evidence, it is reasonable to extrapolate these findings to this group.

About the outcomes included in this summary

- We selected for this summary the outcomes hospitalization at first consultation, relapse and adverse effects (vomiting), since they are the critical outcomes for decision-making on this question. This selection is based on the opinion of the authors of this summary, but it generally agrees with the outcomes mentioned by the systematic reviews identified.
- In addition, a search in the database of the COMET Initiative (Core Outcome Measure in Effectiveness Trial Initiative) returned a study [20] interviewing 15 participants, including doctors, physiotherapists and patients (adults, parents and adolescents), which prioritized avoiding hospitalization, relapse, visit to emergency service or doctor, quality of life and number of days of exacerbation, and giving less weight to the adverse effects. However, both quality of life and number of days of exacerbation were only considered by one review [5] which reported the percentage of patients fully recovered at day three.
- It should be noted that most systematic reviews defined relapse as revisit to doctor or emergency service, but we selected the latter because not all revisits correspond to relapses and there is no consensus on the definition of relapse.
- Also, we preferred to use the outcome hospitalization at first consultation instead of hospitalization at relapse, because the second outcome is a subset of the outcome revisit to doctor or emergency service. On the other hand, a reduction in revisits to doctor or emergency service would decrease the number of hospitalizations. However, including admission during relapse does not make any difference in the conclusions of this summary.

Balance between benefits and risks, and certainty of the evidence

- Regarding the risk/benefit balance, it favors dexamethasone because it has similar benefits but less adverse effects. However, it is important to recognize the certainty of the evidence about the benefits is low.

What would patients and their doctors think about this intervention

- Based on the results presented in this summary, most doctors and patients should lean in favor of the use of dexamethasone, mainly because of the reduced risk of vomiting.
- However, some clinicians might prefer the more traditional approach in absense of higher-certainty evidence. On the other hand, a shorter treatment (i.e. 1 or 2 doses of dexamethasone versus 1 to 5 days) could generate insecurity in some parents, even though this is not directly reflected in a higher rate of revisit, as we show in the summary of findings.

Resource considerations

- Administration of dexamethasone requires only 1 or 2 doses, so decreasing adverse effects and reducing costs.

Differences between this summary and other sources

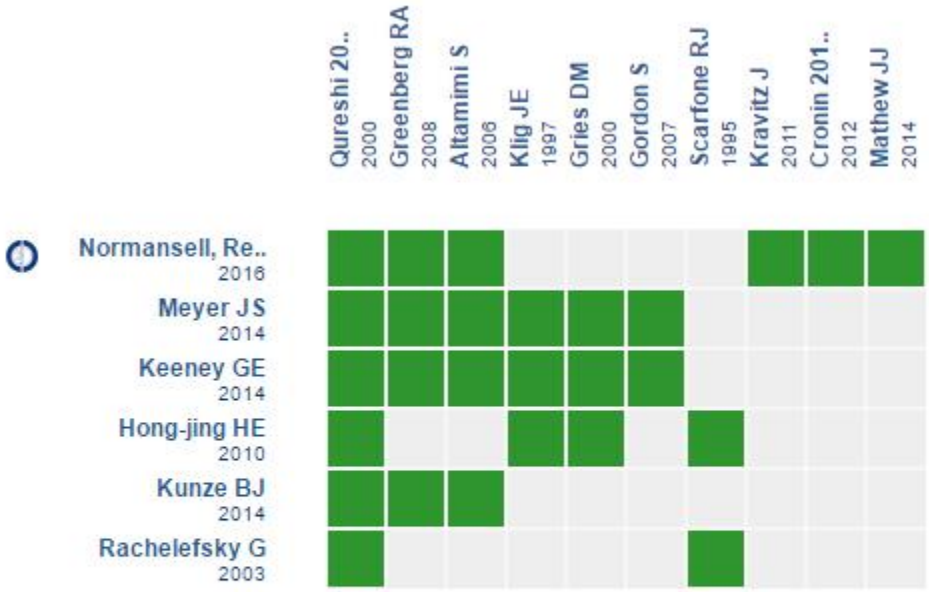
- The conclusions of this summary coincide with those of the systematic reviews identified, with slight differences in the appreciation of the certainty of the evidence.
- This summary partially agrees with the main international guidelines; the GINA 2016 guideline [21] recommends the use of dexamethasone in mild and moderate acute asthma exacerbation, the GEMA guideline [22] does not mention dexamethasone, and the British guideline on the management of asthma [23] states there is still insufficient evidence to support the use of dexamethasone in acute asthma exacerbation.
- It should be emphasized these guidelines incorporate a low proportion of the evidence analyzed in this summary.

Could this evidence change in the future?

- The probability that future research will change the conclusions of this summary is high for the benefits and low for the adverse effects due to the certainty of the existing evidence.
- We identified four ongoing randomized trials answering the question of this summary [24],[25],[26],[27] in the International Clinical Trials Registry Platform of the World Health Organization (WHO), which could improve the certainty of the existing evidence.

How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.



Starting from any systematic review, Epistemonikos builds a matrix based on existing connections in the database.
The author of the matrix can select relevant information for a specific health question (typically in PICO format) in order to display the information set for the question.
The *rows* represent systematic reviews that share at least one primary study, and *columns* display the studies.
The boxes in green correspond to studies included in the respective reviews.

Follow the link to access the **interactive version:** Dexamethasone versus others corticoids for acute asthma exacerbation

Notes

The upper portion of the matrix of evidence will display a warning of "new evidence" if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier. After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated notifications any time new evidence potentially relevant for the question appears.

The details about the methods used to produce these summaries are described here http://dx.doi.org/10.5867/medwave.2014.06.5997.

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database (www.epistemonikos.org).

These summaries follow a rigorous process of internal peer review.

Conflicts of interest
The authors do not have relevant interests to declare.

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