Evidence Update

Summary of a Cochrane systematic review published on 04 December 2015

Corticosteroid therapy during sepsis- is it effective and safe?

A long course of low-dose corticosteroids reduces 28-day mortality without inducing major complications in patients with sepsis

Objective: To examine the effects of corticosteroids on death in patients with sepsis.

33 trials that involved a total of 4268 hospitalized adults and children contributed data for this review.

Steroids in sepsis- what are the issues?

Sepsis, the most severe form of infection, is present when a site of infection is apparent and evidence suggests body-wide, systemic inflammation and organ failures. Septic shock is when severe sepsis is combined with a fall in systemic blood pressure that does not improve even when healthcare staff give intravenous fluids. This could be potentially fatal, with short-term mortality reported to be about 20% to 50%, resulting from hypotension or from progressive multiple organ failure.

Body produces its own corticosteroids, which serve as key defence hormones against infection. Sepsis can interfere with effectiveness of the body’s own corticosteroids. This is the rationale for corticosteroid therapy during sepsis. High dose of bolus corticosteroid therapy has been shown to be ineffective. Clinical trials and other indicators suggest that a low-dose, longer treatment could improve clinical outcomes. This review was performed to find out the truth about the effect of such a dose-duration factor in treatment of sepsis with corticosteroids.

What does this latest research evidence say?

Long course of low-dose corticosteroids, when compared to no-steroids, resulted in:

- ↓ all-cause mortality at 28 days.
- ↓ hospital mortality up to one year.
- ↑ persons recovered from septic shock by day 7.
- ↓ in ICU stay for the survivors.
- No increase in super-infections.
- ↑ incidence of hyperglycaemia & hypernatremia

Low-dose corticosteroid was defined by a total dose per day of 400 mg or less of hydrocortisone (or equivalent). A long course for the intervention was defined by a full-dose treatment duration of three or more days.

What is the quality of this evidence?

All the above findings were based on moderate to high quality evidence.

Can this evidence be applied in my setting?

Beneficial effect of treatment were consistent in terms of 28-day, ICU and hospital mortality. The results of this review could be applied in all healthcare settings.
Corticosteroids for treating sepsis

This table provides more details about the effectiveness of corticosteroid therapy for sepsis. These data are based on the Summary of Findings table from the Cochrane systematic review. The quality of evidence (GRADE) is rated as high, moderate, low or very low. The higher the quality, the more confidence we can have on the interpretation of the results.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No steroids</th>
<th>Corticosteroids (95% CI)</th>
<th>No. of participants</th>
<th>Inference</th>
<th>GRADE Quality of evidence*</th>
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</thead>
<tbody>
<tr>
<td><strong>28-Day all-cause mortality</strong></td>
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<tr>
<td>'long course of low-dose corticosteroids'</td>
<td>321 per 1000</td>
<td>279 per 1000 (250 –311)</td>
<td>2266 (22 studies)</td>
<td>Corticosteroid therapy resulted in lesser number of persons with sepsis dying in 1 month</td>
<td>Moderate</td>
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<td>versus ‘controls’ Follow-up: 14-30 days</td>
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<td><strong>Hospital mortality</strong></td>
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<td>'Corticosteroids’ versus ‘controls’</td>
<td>413 per 1000</td>
<td>351 per 1000 (302-405)</td>
<td>2014 (17 studies)</td>
<td>Corticosteroid therapy resulted in lesser number of persons with sepsis dying in hospital in 1 year</td>
<td>Moderate</td>
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<tr>
<td>Follow-up: 14 to 365 days</td>
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<td><strong>Number of participants with shock reversal at day 7</strong></td>
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<td>'Corticosteroids’ versus ‘controls’</td>
<td>523 per 1000</td>
<td>685 per 1000 (596–790)</td>
<td>1561 (12 studies)</td>
<td>Corticosteroid therapy resulted in more number of persons recovering from septic shock in 1 week</td>
<td>High</td>
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<tr>
<td>Follow-up: 7 to 28 days</td>
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<td><strong>Number of participants with adverse events - superinfections</strong></td>
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<tr>
<td>'Corticosteroids’ versus ‘controls’</td>
<td>161 per 1000</td>
<td>164 per 1000 (140-193)</td>
<td>2567 (19 studies)</td>
<td>Corticosteroid therapy did not increase the number of superinfections when followed up to 3 months</td>
<td>High</td>
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<td>(Follow-up : 14 to 90 days)</td>
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*What does the GRADE quality of evidence mean?

High: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low: Further research is very likely to have an important impact on our estimate of effect, and may change the estimate.

Very low: We are very uncertain about the estimate.

More information

This Evidence Update is only a summary of the key findings of the following Cochrane systematic review. For details, please read the full text: Annane D, Bellissant E, Bollaert PE, Briegel J, Keh D, Kupfer Y. Corticosteroids for treating sepsis. Cochrane Database of Systematic Reviews 2015, Issue 12. Art. No.: CD002243. DOI: 10.1002/14651858.CD002243.pub3

What is a systematic review?
A systematic review seeks to answer a well formulated and specific question by identifying, critically appraising, and summarising the results of all relevant trials, published and unpublished, according to pre-stated and transparent methods.

What is Cochrane?
Cochrane is an international network of more than 28,000 people from over 100 countries. Cochrane is one of the biggest producers of systematic reviews on the effects of healthcare interventions. Cochrane Systematic Reviews are recognized internationally as the benchmark for high quality information. The Cochrane Database of Systematic Reviews is available from www.thecochranelibrary.com

How has the quality of evidence been assessed?
The GRADE system (http://www.gradeworkinggroup.org/intro.htm) considers ‘quality’ to be a judgment of the extent to which we can be confident that the estimates of effect are correct. The quality of evidence is graded after full consideration of the risk of bias of the studies, the directness (or applicability) of the evidence, the consistency and the precision of the results.

This Evidence Update has been prepared for the CME Journal (CMC, Vellore) by Cochrane South Asia, December 2015
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