**Systemic corticosteroids for community-acquired pneumonia in adults: a systematic review and meta-analysis**

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**Introduction:** Community-acquired pneumonia (CAP) is associated with hospitalization rates of 1–4 per 1000 population, and mortality rates rise to 35% among patients admitted to intensive care. Reduction in pulmonary, as well as systemic, inflammatory response with systemic corticosteroids has theoretical appeal as a means of improving outcome from CAP. An observational study has found steroid administration to be associated with decreased mortality in severe CAP. Since the most recent systematic review 1, 3 additional randomised controlled trials (RCTs) have been published. Our aim was to evaluate evidence from RCTs investigating the effect of systemic corticosteroids as adjunctive treatment for adults with CAP.

**Methodology:** We performed a systematic review of the literature, using searches of the Cochrane Central Register for Controlled Clinical Trials, MEDLINE and EMBASE. Additional searches were performed using reference lists of original studies and reviews; SCOPUS, Open Grey and Mind Cull conference abstract databases; and the metaRegister of Controlled Trials.

Eligibility criteria for a study were:
- Randomized controlled trial
- Included adults with CAP
- Compared systemic corticosteroid administration with placebo
- Reported relevant clinical outcomes

Primary outcome measure was 30-day mortality. Studies were evaluated for risk of bias using the Cochrane Risk of Bias Tool (Cochrane Collaboration 2011). A priori, we intended to evaluate outcomes for patients with and without severe CAP, according to established criteria. Trial authors were contacted for additional information. Data was collated and analysed using Review Manager v5.1 (Nordic Cochrane Centre). A random effects model was used in calculating summary statistics.

**Results:** Searches yielded 722 studies, and an additional 489 conference abstracts. Of these, 7 published and 0 additional unpublished RCTs met inclusion criteria.

**Table 1 Study characteristics**

<table>
<thead>
<tr>
<th>Study</th>
<th>Single/ multi-centre</th>
<th>Number of patients</th>
<th>Severity of pneumonia</th>
<th>Mechanical ventilation at enrolment</th>
<th>Intervention</th>
<th>Primary outcome(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confalonieri 2005</td>
<td>Multi-centre</td>
<td>n=42</td>
<td>100% severe (85% bilateral)</td>
<td>74% Hydrocortisone, 7 days</td>
<td>Prednisolone</td>
<td>ICU, NO, MV, MD166</td>
</tr>
<tr>
<td>Familiar &amp; Gomes 2003</td>
<td>Single-centre</td>
<td>n=16</td>
<td>60% severe (PSI VI, V)</td>
<td>IV an exclusion, 1 day</td>
<td>Prednisolone</td>
<td>Need for IV</td>
</tr>
<tr>
<td>March 2003</td>
<td>Single-centre</td>
<td>n=30</td>
<td>100% severe (85% bilateral)</td>
<td>Single dose hydrocortisone, 7 days</td>
<td>Prednisolone</td>
<td>ICU</td>
</tr>
<tr>
<td>McHardy 1972</td>
<td>Single-centre</td>
<td>n=126</td>
<td>na</td>
<td>na</td>
<td>Clinical features</td>
<td>Mortality</td>
</tr>
<tr>
<td>Meijvis 2011</td>
<td>Dual-centre</td>
<td>n=304</td>
<td>67% severe (PSI IV, V)</td>
<td>na</td>
<td>Hospital length of stay</td>
<td>na</td>
</tr>
<tr>
<td>Amor 2017</td>
<td>Single-centre</td>
<td>n=31</td>
<td>50%, severe (PSI IV, V)</td>
<td>IV an exclusion, 1 day</td>
<td>Prednisolone</td>
<td>Hospital length of stay</td>
</tr>
<tr>
<td>Snijders 2010</td>
<td>Single-centre</td>
<td>n=118</td>
<td>46% severe (PSI IV, V)</td>
<td>na</td>
<td>Clinical features</td>
<td>na</td>
</tr>
</tbody>
</table>

PSI = pneumonia severity index, MV = mechanical ventilation, na = Data not available

Studies varied considerably in terms of methodology, participants, interventions and outcome measures. 3 studies were considered to have elements with high risk of bias: McHardy 1972, Meijvis 2011 and Mikami 2007.

**Effect of interventions:** Reduction in 30-day mortality was found in one study (Confalonieri 2005, n=46) but not confirmed on meta-analysis of data from 3 further studies (n=608, Fig. 1).

**Fig. 1 30-day mortality, corticosteroids vs. control**

Reduction in hospital length of stay (LOS) was reported in 2 studies (Confalonieri 2005, n=46; Meijvis 2011, n=304), but not found to be significant on meta-analysis of data from a total of 4 studies without strong evidence of skew (Fig. 2).

**Fig. 2 Hospital length of stay, corticosteroids vs. control**

Among the sub-group of patients with severe pneumonia (2 studies, n=259) there was a trend to lower 30-day mortality in corticosteroid group (Odds Ratio [OR] 0.26, 95% confidence interval [CI] 0.01, 7.78). Significant reduction in inflammatory markers were reported in 6 studies.

Rates of super-infection were reported in 3 studies (n=563), with trend to higher rates in placebo group (OR 1.23 95% CI 0.32, 4.8). Incidence of hyperglycaemia was significantly greater with corticosteroid treatment (2 studies, n=517, OR 2.69 95% CI 1.67, 4.32).

**Conclusions:** Systemic corticosteroid administration as adjunctive treatment for CAP does not appear to improve relevant clinical outcomes, irrespective of severity, and is associated with a significant increase in the incidence of hyperglycaemia.

**References:**
4. Altman et al. BMJ 1996; 313 1650