Corticosteroid administration and outcome of adolescents and adults with acute bacterial meningitis: a meta-analysis

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CRD summary
This review suggested that adjunctive corticosteroids were beneficial for treating adults and adolescents with bacterial meningitis in settings similar to high-income countries with a low prevalence of HIV infection. This was a well-conducted review and the author’s cautious conclusions reflected evidence obtained from a small number of studies.

Authors’ objectives
To evaluate the effects of adjunctive corticosteroids in adolescents and adults with acute bacterial meningitis.

Searching
MEDLINE, EMBASE, Web of Science and Scopus were searched for studies published after 1980. Search dates ranged from 1966 to February 2008. Search terms were reported and included the use of a randomised controlled trials filter.

Study selection
Randomised controlled trials (RCTs) that compared adjunctive corticosteroids with placebo in patients aged 14 years or over with clinically suspected or proven bacterial meningitis were eligible for inclusion. Patients had to be treated with antibacterial agents and studies had to assess short-term (within two months of diagnosis) all-cause mortality. The review assessed additional outcomes that included hearing loss and neurologic sequelae.

In the included studies, acute bacterial meningitis was diagnosed by clinical and cerebrospinal fluid criteria. All studies started dexamethasone (doses ranged from 32mg/day to 40mg/day or 0.8mg/kg/day) before or within three hours of the start of antibiotic therapy. Included studies were set in Europe, Malawi and Vietnam. Studies differed with respect to rates of human immunodeficiency virus (HIV) infection (90% in Malawi, 0.3% in Vietnam and not reported in European studies), antibiotics used (amoxicillin in European studies and ceftriaxone in the others) and type of bacterial meningitis. Where reported, patients ranged in age from over 14 to 79 years.

Two reviewers independently selected studies.

Assessment of study quality
Two reviewers independently assessed study validity using criteria proposed by Juni et al. that examined potential for selection, performance, outcome ascertainment and attrition biases. Disagreements were resolved by consensus. Studies with inadequate allocation concealment were apparently excluded.

Data extraction
Numbers of events were extracted for each study and used to calculate relative risks (RR) with 95% confidence intervals (CI).

Two reviewers independently extracted outcome data.

Methods of synthesis
Pooled relative risks with 95% CIs were calculated using the DerSimonian and Laird random-effects method. The number needed to treat (NNT), with 95% CI, was calculated. Heterogeneity was assessed using the $I^2$ statistic. Prespecified subgroup analyses were use to examine treatment subgroup interactions and compare high-income versus low-income countries and low versus high prevalence of HIV. Countries that scored less than 0.7 on the United Nations Human Development Index were classified as low-income countries.
Results of the review
Four RCTs (n=1,261) were included in the review. Studies were judged to be of high quality. All studies reported adequate allocation concealment, randomisation and outcome assessment and intention-to-treat analysis. Losses to follow-up ranged from 0 to 2.3%.

Short-term mortality rates ranged from 10% to 54%. There was no significant difference between corticosteroids and placebo in short-term mortality (25.9% versus 27.9%, RR 0.81, 95% CI 0.54 to 1.20, I²=54%). Corticosteroids were associated with a significant reduction in risk of hearing loss (RR 0.73, 95% CI 0.55 to 0.97, I²=0%) and a non-significant reduction in risk of neurologic sequelae other than hearing loss (23.5% versus 30.8%, RR 0.67, 95% CI 0.45 to 1.01, I²=56%).

A significant interaction was found between the effects of corticosteroids and income status of the country and between effects and prevalence of HIV infection. In high-income countries, corticosteroids were associated with a significant reduction in short-term mortality (RR 0.5, 95% CI 0.27 to 0.92, I²=0%, NNT to prevent one death=12.5) and a significantly lower risk of neurologic sequelae other than hearing loss (RR 0.58, 95% CI 0.36 to 0.94, I²=0%, NNT=11.0). In studies assumed to have a low-incidence of HIV (European studies), corticosteroids were associated with significantly lower short-term mortality compared to placebo (RR 0.66, 95% CI 0.44 to 0.99, I²=0%).

Authors’ conclusions
Findings suggested that adjunctive corticosteroids were beneficial in settings similar to high-income countries with a low prevalence of HIV infection.

CRD commentary
The review question was clear and supported by appropriate inclusion criteria. Several relevant sources were searched, but it was unclear whether any language restrictions were applied and exclusion of unpublished studies made the review at risk of publication bias. Methods were used to minimise reviewer error and bias during study selection, data extraction and validity assessment. Study validity was assessed and results were reported; studies were considered to be of high quality. Studies were pooled using meta-analyses and various predefined subgroup analyses were used to examine potential sources of heterogeneity. There were considerable clinical differences between the small number of included studies and this was reflected in the statistical heterogeneity. Subgroup analyses were conducted and efficacy benefits were found only for high-income countries with an assumed low prevalence of HIV. This was a well-conducted review and the author's cautious conclusions reflected the evidence presented from a small number of studies.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that further studies were required to determine reasons why corticosteroids did not improve survival rates in HIV-infected patients with bacterial meningitis.

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