Dexamethasone as adjunctive therapy in bacterial meningitis: a meta-analysis of randomized clinical trials since 1988

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Authors' objectives
To evaluate the effectiveness and safety of dexamethasone in bacterial meningitis in the subcategories of causative organism and timing and nature of antibiotic therapy.

Searching
MEDLINE, Healthline and AIDSLINE were searched (using MeSH: dexamethasone and meningitis) for studies published in any language from 1988 to November 1996. References of articles and conference abstracts were also searched. The authors of retrieved studies were contacted to identify unpublished studies.

Study selection
Study designs of evaluations included in the review
Randomised, concurrently controlled trials of dexamethasone therapy in childhood bacterial meningitis. Nonrandomised studies were eligible for assessment of adverse effects.

Specific interventions included in the review
Dexamethasone as adjunctive therapy in bacterial meningitis. The most commonly evaluated regimen was 0.6 mg/kg per day in 4 doses for 4 days.

Participants included in the review
Children with bacterial meningitis. Reported mean age in studies: 1.2 to 7 years.

Outcomes assessed in the review
Hearing loss and neurological deficits other than hearing loss; adverse effects.

How were decisions on the relevance of primary studies made?
Eligibility was determined from the methods of articles or abstracts reviewed.

Assessment of study quality
The authors do not report the method used to assess validity, or how the validity assessment was performed. It was reported that treatment allocation was not concealed or not stated in 3 studies, and no significant differences on some potential prognostic variables between groups in all studies. The rate of follow-up was also examined.

Data extraction
The data were extracted by using a predetermined protocol and criteria. The procedure was not blinded.

Methods of synthesis
How were the studies combined?
The odds ratio was used to estimate effectiveness, while the risk difference was used for adverse effects. A pooled estimate (and 95% confidence interval) was calculated using a random-effects model.

How were differences between studies investigated?
The chi-squared method was used to test heterogeneity between odds ratios in different strata. A random-effects regression model was used to investigate heterogeneity of outcome between causative organisms.
Results of the review
Eleven randomised controlled trials (848 patients in total) were included.

Severe hearing loss: result of meta-regression suggested the existence of significant heterogeneity by organism (p<0.05 for meningococcal cases vs haemophilus influenzae type b cases vs pneumococcal cases). In Haemophilus influenzae type b meningitis, dexamethasone reduced severe hearing loss (pooled OR 0.31, 95% CI: 0.14, 0.69). In pneumococcal meningitis, the pooled odds ratio for severe hearing loss was 0.52 (95% CI: 0.17, 1.46).

Any hearing loss (6 studies): odds ratio for any hearing loss was 0.44 (95% CI: 0.21, 0.93; p=0.03) in haemophilus influenzae type b meningitis, and 0.80 (95% CI: 0.33, 1.95; p=0.63) in pneumococcal meningitis.

Other neurological deficits: the pooled results of all studies suggested protection against neurological deficits other than hearing loss but was not statistically significant (OR 0.59, 95% CI: 0.34, 1.02).

Pooled odds ratio for mortality was 0.60 (95% CI: 0.36, 1.00). Adverse effects were not significantly increased with dexamethasone except for secondary fever (risk difference 11.2, 95% CI: 1.8, 21.2). The incidence of gastrointestinal tract bleeding increased with longer duration of dexamethasone treatment (0.5% in controls, 0.8% with 2 days of treatment, 3.0% with 4 days of treatment).

Authors' conclusions
The available evidence on adjunctive dexamethasone therapy confirms benefit for Haemophilus influenzae type b meningitis and, if commenced with or before parenteral antibiotics, suggests benefit for pneumococcal meningitis in childhood. Limiting dexamethasone therapy to 2 days may be optimal.

CRD commentary
This review searched several sources for relevant literature and without language restriction. The inclusion criteria has been clearly described and details of included studies presented. The validity of the studies was assessed. The combination of research evidence seems appropriate. Subgroup analyses were conducted to investigate heterogeneity observed between studies. The results of subgroup analyses should be interpreted with caution because the difference between subgroups may be observed by chance. The potential publication bias should also be considered. After the review was completed, authors identified a further trial, in which deaths were more common in the dexamethasone group than in the control group (12/48 vs 5/41; OR 2.05, 96% CI: 0.8, 5.3). The review's conclusions were based on the research evidence presented.

Bibliographic details

PubMedID
9302246

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Adolescent; Adult; Anti-Bacterial Agents /therapeutic use; Anti-Inflammatory Agents /administration & dosage /adverse effects /therapeutic use; Child; Child, Preschool; Dexamethasone /administration & dosage /adverse effects
/therapeutic use; Drug Therapy, Combination; Hearing Loss, Sensorineural /etiology; Humans; Infant; Meningitis, Bacterial /complications /drug therapy; Meningitis, Haemophilus /complications /drug therapy; Meningitis, Pneumococcal /complications /drug therapy; Randomized Controlled Trials as Topic; Regression Analysis

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**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.