

Systematic Review Snapshot

Clinical Synopsis

TAKE-HOME MESSAGE

Adjunctive dexamethasone in bacterial meningitis may reduce mortality and hearing loss for patients in developing countries. There may be no benefit for individuals in developing nations with a high prevalence of HIV infection.

METHODS

DATA SOURCES

The authors used new and previously identified trials from a Cochrane Database Systematic Review, which included the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2006, issue 2); MEDLINE (1966 to July 2006); EMBASE (1974 to June 2006); and Current Contents (2001 to June 2006) and reference lists of all articles. They also contacted researchers in the field and reviewed literature lists of pharmaceutical companies.

STUDY SELECTION

This meta-analysis included all double-blinded, randomized, placebo-controlled trials since 2001 that evaluated dexamethasone in bacterial meningitis and contained individual patient data. Study subjects included pediatric and adult patients receiving a diagnosis of bacterial meningitis on clinical grounds and cerebral spinal fluid criteria. Computer-generated randomization and adequate treatment concealment were present in all studies.

Is Adjunctive Dexamethasone Beneficial in Patients With Bacterial Meningitis?

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Results

Primary endpoints for meta-analysis subjects.

Outcome	Events/Total (%)		Odds Ratio (95% CI)
	Dexamethasone (n=1,019)	Placebo (n=1,010)	
Death	270/1,019 (26.5)	275/1,010 (27.2)	0.97 (0.79–1.19)
Death or any neurologic sequelae or any hearing loss	541/999 (54.2)	567/988 (57.4)	0.89 (0.74–1.07)
Any hearing loss in survivors	162/672 (24.1)	195/660 (29.5)	0.77 (0.60–0.99)

CI, Confidence interval.
*N=total number of study subjects.

Of the 22 studies identified, 17 were excluded because of a lack of individual patient data or they were not randomized controlled trials. Of the 2,447 patients in the 5 studies, data were available for only 2,029 patients, resulting in 1,019 (50.2%) patients who received dexamethasone and 1,010 (49.8%) patients who received placebo. In patients with an undocumented HIV status, the authors recorded adults from Malawi to have HIV and adults and children from Europe to not have HIV according to epidemiologic risks. The pathologic organism was identified in 80.8% of patients: *Streptococcus*

pneumoniae (46.3% of identified organisms), *Haemophilus influenza* (18%), and *Neisseria meningitidis* (15%). Mortality differed greatly between placebo groups (low of 12% in Vietnam to a high of 53% in Malawian adults).

Commentary

Acute bacterial meningitis is a life-threatening illness with morbid consequences and a mortality rate of 13%.¹ Individuals who survive are at risk for neurologic sequelae and hearing loss. The use of dexamethasone in preventing these outcomes has had mixed results. Initial investigations fo-

DATA EXTRACTION AND SYNTHESIS

The principal investigators in each study provided raw data to study personnel. Fifteen data fields were selected for analysis, to include patient variables, laboratory values (blood and cerebral spinal fluid), and the bacterial pathogen as identified by cerebral spinal fluid microscopy, cerebral spinal fluid or blood culture, polymerase chain reaction, or latex agglutination. The outcomes measured were reported as odds ratios with 95% confidence intervals, and tests for heterogeneity were calculated with Mantel-Haenszel statistics.

cused on *H influenza* type b meningitis, in which a reduction in hearing loss was found in children treated with dexamethasone in addition to parenteral antibiotics.² In 2004, a meta-analysis demonstrated a reduc-

tion in mortality and neurologic sequelae in adults with corticosteroid use.³ This finding was replicated in a Cochrane meta-analysis in 2007, written by the same authors as this 2010 systematic review.⁴ More recent randomized controlled trials have shown variable results, which were included in this 2010 study. Contrary to results of previous meta-analyses, those of this 2010 meta-analysis indicate no significant benefit or harm from the use of adjunctive dexamethasone, possibly because there was a large amount of missing patient data (17%) and the inclusion of 2 prognostically different populations: patients in developing countries with a high prevalence of HIV (dexamethasone was not beneficial) and European patients, for whom the HIV rate is low (dexamethasone showed benefit). Therefore, the applicability of this meta-analysis may vary with the population being considered. These new data should be taken into consideration in deciding whether to use corticosteroids for patients with acute bacterial meningitis.

1. Thigpen MC, Whitney CG, Messonnier NE, et al. Bacterial meningitis in the United States, 1998-2007. *N Engl J Med*. 2011; 364:2016-2025.
2. McIntyre PB, Berkey CS, King SM, et al. Dexamethasone as adjunctive therapy in bacterial meningitis. A meta-analysis of randomized clinical trials since 1988. *JAMA*. 1997;278:925-931.
3. van de Beek D, de Gans J, McIntyre P, et al. Steroids in adults with acute bacterial meningitis: a systematic review. *Lancet Infect Dis*. 2004;4:139-143.
4. van de Beek D, de Gans J, McIntyre P, et al. Corticosteroids for acute bacterial meningitis. *Cochrane Database Syst Rev*. 2007;(1):CD004405.

This is a clinical synopsis, a regular feature of the *Annals' Systematic Review Snapshots* (SRS) series. The source for this systematic review snapshot is: van de Beek D, Farrar JJ, de Gans J, et al. Adjunctive dexamethasone in bacterial meningitis: a meta-analysis of individual patient data. *Lancet Neurol*. 2010;9:254-263.

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