Critical Review Form
Meta-analysis

Parenteral dexamethasone for acute severe migraine headache: meta-analysis of randomised controlled trials for preventing recurrence, *BMJ* 2008; 336: 1359-1361

Objective: To assess "the evidence from controlled trials on the effectiveness and tolerability of parenteral corticosteroids for the relief of acute migraine headache in adults and the prevention of recurrences." (p. 1)

Methods: The authors conducted a well-described electronic search using the Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, LILACS, and CINAHL using search terms "headache" or "migraine" along with several corticosteroid terms removing any limitations for randomized studies to enhance sensitivity. In addition, hand-searches of scientific abstracts for 10-years from major Neurology, Emergency Medicine, and headache journals were assessed. They also searched clinical trial registries, bibliography lists, and contacted pharmaceutical companies. No language restrictions were applied.

Inclusion criteria included randomized controlled trials of parenteral corticosteroids, adults ≥ 18 years, "reasonable criteria" (not defined) to distinguish migraine from other headache types, and ED or Headache Clinic treatment setting for an acute and severe headache. Independently, two investigators screened titles and abstracts for potential study eligibility, while others reviewed the full manuscripts. Pre-tested paper forms were used for data abstraction. The primary outcome was headache recurrence at 24- to 72-hours post ED treatment and assumed patients had complete or substantial migraine relief prior to discharge. Secondary outcomes included immediate reduction in headache pain and treatment-associated adverse events.

The Jadad scale was used to assess quality/internal validity of individual trials. Heterogeneity was assessed using χ^2 and I^2 statistic. After consideration for heterogeneity, pooled results of studies were computed using fixed effects models with subsequent sensitivity analysis conducted for random effects model. Finally, retrospective subgroup analyses of dosage and duration of follow-up were reported.

Guide	Question	Comments
I	***Are the results valid?***	
1.	Did the review explicitly address a sensible question?	Yes – can adjuvant therapy with IV dexamethasone for ED migraine patients reduce headache recurrence within 72-hours?
2.	Was the search for relevant studies details and exhaustive?	Yes. In addition to well-described searches of multiple electronic databases without language restrictions, the authors included hand-searches of bibliographies and relevant scientific abstracts along with original investigator contacts.
3.	Were the primary studies of high methodological quality?	Yes. Five of seven included studies received the highest Jadad rating (5). The remaining two received a Jadad score of 4. Interestingly, one of the "4s" (Fiessler 2006) was rated as a "5" by Singh et al (see PGY-III paper)
4.	Were the assessments of the included studies reproducible?	"No disagreements on inclusion of trials occurred between reviewers" (p. 3) The authors do not report agreement or reliability for the Jadad ratings
II.	***What are the results?***	
1.	What are the overall results of the study?	• 666 potentially relevant studies were identified by the various electronic and hand search strategies with 18 reviewed in full detail excluding 11 for various reasons (not RCT=7, non-migraine =1, non-ED =1, oral steroid = 2). The seven studies included in this meta-analysis represented 738 patients and all used IV dexamethasone (one trial mixed IM and IV). • No significant heterogeneity was identified (I^2 = 3.4%; Cochrane's-Q χ^2 p = 0.40). • Pooled results indicated significant reduction in headache recurrence (RR 0.74; 95%, CI 0.60 – 0.90 with NNT = 9; 95%, CI 6 to 25). • No difference in acute pain relief noted (WMD 0.37) though these four trials exhibited significant heterogeneity (I^2 = 46.2%). • Dexamethasone-treated subjects exhibited less nausea, but more dizziness with no significant differences in restlessness, drowsiness, tingling, or swelling. • No differences noted between IM and IV dosing. • Doses of dexamethasone < 15 mg (3 studies) had non- significant less effect (RR 0.80; 95% CI 0.62 – 1.04) than those using > 15 mg (RR 0.67); 95% CI 0.50 – 0.91)

2.	How precise are the results?	Precise enough to change practice based upon the CIs described above.
3.	Were the results similar from study to study?	"Effect sizes varied slightly among trials; however, heterogeneity was non-significant ($I^2 = 3.4\%$)." (p.3)
III.	***Will the results help me in caring for my patients?***	
1.	How can I best interpret the results to apply them to the care of my patients?	"When added to standard abortive migraine therapy, single dose parenteral dexamethasone is associated with a 26% relative reduction in recurrence headache (NNT = 9) occurring within 72 hours." (p. 6)
2.	Were all patient important outcomes considered?	No assessment of QOL or important subgroups: onset <24 hours prior to ED treatment, previous migraine recurrences, narcotic vs. anti-emetic vs. other abortive therapy.
3.	Are the benefits worth the costs and potential risks?	Yes, if appropriate subsets at high-risk for migraine recurrence can be identified to optimize the risk/benefit ratio.

Limitations

1) **Failure to reference QUOROM or CONSORT guidelines for reporting, although they clearly followed most recommendations.**
2) **Failure to clearly define "reasonable criteria to distinguish migraine from other headache types". Do the authors mean International Headache Society criteria for migraine? Prior research has suggested that EM physicians do not accurately label headaches as migraines by the IHS criteria so clearly defining the target condition is essential.**
3) **No reporting of Jadad study quality assessment reproducibility.**
4) **No tau-squared analysis for heterogeneity.**
5) **No assessment for publication bias (funnel plot, Egger plot, Begg test), although the authors suggest that this may be of lesser concern in Emergency Medicine.**
6) **No analysis of important subsets: treatment < 24 hours, prior history of early migraine recurrence, primary ED abortive therapy).**
7) **No influence analysis performed to test the robustness of findings with each study sequentially removed.**

Bottom Line

A single dose of IV or IM dexamethasone in addition to standard ED migraine abortive care significantly reduces the recurrence of migraine at up to 72 hours (NNT = 9). Doses greater than 15 mg are probably more effective. Future research is needed to identify the subset most likely to benefit (onset < 24h, prior early recurrence following ED management, effectiveness with various abortive regimens (prochlorperazine vs. narcotics vs. other).