Critical Review Form
Therapy

Impact of oral dexamethasone versus placebo after ED treatment of migraine with phenothiazines on the rate of recurrent headache: a randomised controlled trial, *Emerg Med J* 2008; 25: 26-29

Objectives: **"To compare the rate of recurrent headache in patients with migraine in the ED randomised to receive either a single dose of oral dexamethasone or placebo at discharge after treatment with intravenous phenothiazines. Secondary aims were to compare the rate of recurrent headache in the subgroup with migraine duration of less than 24 hours and the rate of adverse events between the groups". (p. 26)**

Methods: **This was a double-blinded, randomized, placebo-controlled trial conducted in the ED of three community hospitals in Melbourne, Australia between April 2005 and December 2006. Participates were a convenience sampling of adults over age 17 years after physician-diagnosed migraine headache with the following exclusions: failure to consent, pregnant, study medication allergy, admitted patients, active peptic ulcer disease, DM Type I, corticosteroids for another indication in the preceding 7-days, systemic fungal infections, or previous study enrollment.**

Randomization was performed by a research pharmacist using a random number allocation. All subjects received either 12.5- to 50-mg chlorpromazine or 12.5 mg prochlorperazine IV. At discharge subjects received either 8 mg oral dexamethasone or identical appearing placebo as a single dose. The primary outcome was headache recurrence as reported by telephone follow-up at 48 – 72 hours. Recurrent headache was defined as either "return of headache for those who were discharged from ED pain-free or a worsening of headache (≥ 2 points on a 10-point verbal rating scale) for those who were discharged with residual headache" (p 27). Secondary outcomes included reported adverse effects, post-discharge analgesic use recurrent headache severity, and healthcare provider contact between the ED visit and recommended outpatient follow-up.

Based on a sample size of 66, the study had 80% power to detect a 50% reduction (from 60% to 30%) in headache recurrence with $\alpha = 0.05$. Investigators also conducted a *post hoc* analysis of headache recurrence in the subset treated within 24-hours of symptom onset.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis (answer the questions posed below)?**	
1.	Were patients randomized?	Yes. "Randomization was performed independent of the investigators by a research pharmacist using random number allocation". (p. 27)
2.	Was randomization concealed (blinded)?	Yes. "The patient, clinician and research nurse undertaking follow-up were all blinded to the treatment given. The randomization key was not available to researchers until the study and database had been closed." (p. 27)
3.	Were patients analyzed in the groups to which they were randomized?	Yes. "Intention-to-treat analysis was performed". (p. 27)
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	Yes, although dexamethasone group had lower proportion pain-free at discharge (23% vs. 31% or with pain-scale ≤ 2 (74% vs. 81%) perhaps suggesting more severe or refractory headaches in this group. (Table 1, p. 27)
B.	**Did experimental and control groups retain a similar prognosis after the study started (answer the questions posed below)?**	
1.	Were patients aware of group allocation?	No. "The patent, clinician, and research nurse undertaking follow-up were all blinded to the treatment given'. (p. 27)
2.	Were clinicians aware of group allocation?	No. "The patent, clinician, and research nurse undertaking follow-up were all blinded to the treatment given'. (p. 27)
3.	Were outcome assessors aware of group allocation?	No. "The patent, clinician, and research nurse undertaking follow-up were all blinded to the treatment given'. (p. 27)

4.	Was follow-up complete?	One patient in each arm was lost to follow-up (Fig 1, p.27)
II.	**What are the results (answer the questions posed below)?**	
1.	How large was the treatment effect?	• The cohort consisted of 63 subjects, 76% women with median age 39 years. • Headache recurrence occurred in 33%; (95% CI 22% – 46%). • Headache recurrence occurred in 39% of control group vs. 27% of the dexamethasone group (RR 0.69; 95% CI 0.33 – 1.45, p = 0.47). • Among the subgroup with symptoms < 24h, headache recurrence occurred in 45% of control vs. 15% dexamethasone (ARR 15%; 95% CI 4% – 39%) translating into NNT 3.3 (95% CI 2 to 31; p = 0.08). • Multiple transient side effects were noted in the dexamethasone group (facial flashing, nausea, tingling, blurred vision, and diarrhea).
2.	How precise was the estimate of the treatment effect?	See 95% CI reported above.
III.	**How can I apply the results to patient care (answer the questions posed below)?**	
1.	Were the study patients similar to my patient?	Yes, ED patients with suspected migraine headache.
2.	Were all clinically important outcomes considered?	No - headache recurrence, severity, functional impairment and QOL were not reported.
3.	Are the likely treatment benefits worth the potential harm and costs?	No, not based on the current design and results.

Limitations

1) **Underpowered for treatment effect and proportion lost to follow-up so possible Type II error.**
2) **Potential selection bias since convenience sampling and not using International Headache Association definitions for migraine.**
3) **No assessment for recurrent headache severity, disability, quality of life impact or ED recidivism.**
4) **CONSORT diagram fails to present full spectrum of patients (exclusions, refusals, etc.).**

Bottom Line

Oral dexamethasone after phenothiazines and prior to ED discharge may reduce migraine headache recurrence at 72-hours in selected adults, although future research will need to be appropriately powered to provide a definitive answer.