Acute migraine therapy: recent evidence from randomized comparative trials
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CRD summary
The review found that triptan/NSAID combination therapy was more effective than one agent. All triptans were similarly effective, but almotriptan was better tolerated than sumatriptan. Limitations of the review methodology, including a limited validity assessment, meant that the reliability of the results could not be assessed.

Authors’ objectives
To assess the relative effectiveness of various medical treatments for migraine.

Searching
MEDLINE and EMBASE (2002 to November 2007), The Cochrane Library and Odyssey (a proprietary database of Wolters Kluwer Health) were searched for studies published in English. Search terms were listed in the review.

Study selection
Clinical trials of adults patients (18 to 65 years) who had at least one migraine (with or without aura) per month for at least one year were eligible for inclusion. Studies of patients with menstrual migraine were not eligible. Randomised, actively controlled studies of either parallel or cross-over design, of any medical therapy for migraine, which reported a power calculation and had at least 100 patients were eligible. Systematic reviews and/or meta-analyses or RCTs meeting the same patient inclusion criteria were also eligible. To be included, studies had to have reported at least one of the following three endpoints as a primary or co-primary endpoint: proportion of patients pain free within two hours; headache relief within two hours; and/or use of rescue medication. Interventions in the included studies were sumatriptan, sumatriptan/naproxen sodium, indomethacin/caffeine/prochlorperazine (IndoProCaf), ketoprofen, zolmitriptan, eletriptan, caffeine/ergotamine, aspirin, ibuprofen, almotriptan, aspirin/metoclopramide, rofecoxib and naproxen sodium. Dosages were given in the review. The mean age of patients ranged from 33 to 42 years. All trials were sponsored by one or more pharmaceutical companies.

The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity, but the level of blinding was reported.

Data extraction
The authors stated neither how the data were extracted for the review nor how many reviewers performed the data extraction.

Methods of synthesis
The studies were synthesised in a narrative synthesis, combined by intervention.

Results of the review
Thirteen RCTs (9,509 patients) were included in the review: 12 were double-blinded; one was an open-label RCT.

Comparative triptan trials: Two trials, one comparing almotriptan with sumatriptan and one comparing almotriptan with zolmitriptan, found the drugs to be of similar efficacy. Almotriptan 12.5 mg (but not 25 mg) was associated with fewer adverse events than sumatriptan, (9 per cent versus 22 per cent, \(p<0.001\)) and zomatriptan (11 per cent versus 16 per cent, \(p<0.05\)).

IndoProCaf versus sumatriptan: IndoProCaf was associated with a higher pain free at two-hour rate than sumatriptan (49 per cent versus 34 per cent, \(p<0.01\)) in one trial, but there was no significant difference in the same outcome in another trial.
Triptans versus aspirin and non-steroidal anti-inflammatory drugs (NSAIDs): Three trials showed that NSAIDs or aspirin were as effective as triptans; two showed that NSAIDs/aspirin were as effective as each other. Two studies showed that sumatriptan/naproxen sodium combination was more effective than either treatment alone.

Triptan versus caffeine/ergotamine: Eletriptan (40 mg and 80 mg) and almotriptan were significantly more effective at improving pain than caffeine/ergotamine in one trial each (54 per cent and 68 per cent versus 33 per cent, p<0.001 and 21 per cent versus 14 per cent, p<0.05).

**Authors' conclusions**
Triptans and NSAIDs were similarly effective in the treatment of acute migraine. The various triptans were similarly effective, but almotriptan was better tolerated than sumatriptan. Fixed-combination therapy (IndoProCaf) was probably as effective as sumatriptan, but further trials were needed. Multi-targeted therapy was more effective than a triptan or NSAID alone.

**CRD commentary**
The review question was clearly stated and the search strategy appeared appropriate, although the searching of one publisher's database (available since one of the authors works for the publisher), but not other similar databases raised the possibility of bias. Studies were limited to English language papers only, so there was a possibility of language bias.

The inclusion criteria were clearly specified for study design, participants and outcomes, which should have reduced the chance of subjective decisions having been made during the study selection. However, the reviewers included a study which they acknowledged did not meet their inclusion criteria of duration of migraine history. The validity assessment appeared to be restricted to blinding. The narrative synthesis was appropriate. Since the reviewers did not state how the study selection was performed, and the validity assessment was limited, the reliability of the results could not be assessed.

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

Research: Large, well-controlled clinical trials with improved dosing schedules comparing IndoProCaf with sumatriptan were required.

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