

McCorry DC, Gray RN. Oral sumatriptan for acute migraine. Cochrane Database of Systematic Reviews 2003 Issue 3. Art # CD002915.

Design: Meta-analysis of randomized trials

PICOS:

- **Patient population:** Adults (18 or over) with migraine with or without aura, meeting the diagnostic criteria of the International Headache Society
- **Interventions:** Oral sumatriptan in at least one treatment arm of included studies, in doses of 100mg, 50 mg, or 25 mg
- **Comparison intervention:** placebo, other drug treatments, no treatment, or behavioral/physical therapies
- **Outcomes:** Complete resolution of headache pain, reduction in pain intensity, functional disability, or headache recurrence
  - o Primary timeframe for headache response was 2 hours from the time of taking sumatriptan; if 2 hour data were not reported, the time closest to 2 hours was recorded
- **Study types:** Randomized, double-blind trials for an acute attack of migraine; if trials reported data on multiple attacks, the data for the first attack was used

Study selection:

- Databases were MEDLINE and CENTRAL (Cochrane Central Register of Controlled Trials) from 1966 through 2001
- Assessment of quality was based on randomization, allocation concealment, description as double-blind, adequacy of the reporting of the method of double-blinding, and a description of withdrawals and dropouts
- Two authors rated the article quality, with disagreements resolved through discussion
- When crossover trials were included, they were analyzed as if they were parallel group trials, using data from the first observation period
- The quality of the studies was generally good; with a maximum score of 5, 6 trials had a score of 5, 11 had a score of 4, and 8 had a score of 3

Results:

- 32 publications describing 25 separate trials were included, 20 parallel-group and 5 crossover trials
- 15 trials compared sumatriptan with placebo, 4 with NSAIDs, 7 with other triptans, and 2 with other drug therapies for migraine
- Most trials reported headache relief, rather than complete pain relief, as the principal outcome
- Numerous comparisons were made, involving different doses of sumatriptan, placebo was the most common comparison, and 100 mg was the most common dose of sumatriptan used for comparison
- 14 trials compared 100 mg sumatriptan with placebo

- 8 trials (2221 participants) had complete headache relief at 2 hours as the primary outcome; all 8 reported sumatriptan more effective than placebo, with homogeneous effect sizes; the summary odds ratio for complete relief was 4.2, and the number needed to treat was 5.1
- 11 studies (2940 participants) used headache relief at 2 hours as the primary outcome; all showed a significant benefit of sumatriptan over placebo; even though there was more heterogeneity for this comparison than for the 8 trials testing complete pain relief, the value of the  $I^2$  statistic (>50% generally considered important heterogeneity) was 47%
- 5 studies compared 50 mg sumatriptan with placebo; these were also homogeneous in reporting that sumatriptan was better than placebo
- 3 trials compared 25 mg sumatriptan with placebo; similar to the trials with higher doses, these studies also reported sumatriptan better than placebo
- Studies comparing different doses of sumatriptan (100 mg vs 50 mg, 100 mg vs 25 mg, 50 mg vs 25 mg) yielded responses for headache relief and for pain-free response which did not differ in a statistically significant manner
- Sumatriptan was compared with other triptan drugs (rizatriptan, naratriptan, zolmitriptan, almotriptan, eletriptan) in several dose combinations; most comparisons did not show statistically significant differences between triptans
  - Rizatriptan 10 mg and eletriptan 80 mg provided better pain-free response at 2 hours compared with 100 mg sumatriptan; both of these comparisons were in single RCTs only
- Sumatriptan 100 mg was compared with two preparations of salicylate drugs with divergent results
- Sumatriptan was superior to a combination of 900 mg aspirin plus 10 mg metoclopramide, but was statistically equivalent to a combination of 1620 mg of lysine acetylsalicylate plus 10 mg metoclopramide for headache relief
- Sumatriptan was compared with other NSAIDs (diclofenac and tolfenamic acid); headache relief did not differ in either comparison
- Sumatriptan 100 mg was superior to ergotamine tartrate 2 mg plus caffeine 200 mg in a single RCT; 35% of sumatriptan patients were pain-free at 2 hours, compared with only 13% of ergotamine patients; in addition, substantial pain relief was reported at 2 hours by 66% of sumatriptan patients but only 48% of ergotamine patients
- A single RCT compared sumatriptan 25 mg with a combination of 65 mg isometheptene mucate plus 100 mg dichloralphenazone plus 325 mg acetaminophen; headache relief at 2 hours did not differ between groups

Authors' conclusions:

- Sumatriptan is clearly superior to placebo for migraine relief
- The 100 mg dose of sumatriptan is the most often studied dose; although doses of 25 mg and 50 mg are also effective, there is too little data to provide precise estimates of their efficacy and adverse effect profile compared with 100 mg

- Two studies failed to show any difference in headache recurrence when a second dose of sumatriptan is given 2 to 4 hours following the initial dose; any difference in recurrence rate is likely to be small
- Comparisons between sumatriptan and other triptans do not provide clear evidence to support clinically important differences between them
- Sumatriptan is superior to ergotamine plus caffeine

Comments:

- Although a very large number of comparisons were made, the meta-analysis shows strong evidence of superiority of sumatriptan to placebo
- The single parallel-group RCT of sumatriptan vs. ergotamine was large enough and precise enough to provide good evidence of the superiority of sumatriptan over ergotamine for headache relief
- There is too little data on other comparisons to provide evidence of the superiority of any triptan to any other triptan
- The quality of the included trials appears to be sufficient to support more than one evidence statement regarding sumatriptan

Assessment: Adequate to provide strong evidence that sumatriptan is superior to placebo for migraine relief, good evidence that sumatriptan is superior to ergotamine plus caffeine, and insufficient evidence to conclude that any member of the triptan class of drugs is superior to any other member of that class