

Derry S, Moore RA, McQuay HJ. Paracetamol (acetaminophen) with or without an antiemetic for acute migraine headaches in adults. Cochrane Database of Systematic Reviews 2010, Issue 11, Article # CD008040.

Design: Meta-analysis of randomized clinical trials

PICOS:

- Patient population: Adults with migraine with or without aura defined by International Headache Society criteria
- Intervention: Self-administered single dose of acetaminophen taken to treat a migraine headache when pain was of moderate or severe intensity; studies of acetaminophen plus an antiemetic were included, provided that both acetaminophen and the antiemetic were self-administered
- Comparison/control intervention: Placebo by self-administration
- Outcomes: Principal outcomes were measured 2 hours and 24 hours after drug administration; for the 2-hour mark, the major outcome was being pain-free, and the secondary outcome was having pain reduction (headache relief); for the 24-hour mark, the outcomes were sustained pain-free and sustained pain reduction, both of which had to be maintained without use of a second dose of any medication
- Study types: randomized double-blind, placebo-controlled or active-controlled studies with at least 10 participants in each arm, reporting dichotomous (success/failure) data for one of the principal outcomes

Study type and selection:

- Databases searched were MEDLINE, EMBASE, Cochrane CENTRAL, and the Oxford Pain Relief Database through 22 April 2010
- Two authors independently selected studies for inclusion, resolving disagreements through discussion with a third author
- Risk of bias was assessed with a five point scale: being randomized, adequate description of the randomization procedure, being double-blind, adequate description of the double-blinding method, and full accounting for dropouts and withdrawals from the study
- Treatment effects were reported as relative risks (RR) of success, in which RR greater than 1 indicates that acetaminophen is more likely to yield successful treatment of the headache symptoms
 - o Numbers needed to treat (NNT) were calculated as the number of patients who would need treatment with acetaminophen in order to produce one successful therapeutic outcome
- Most studies were parallel group trials; when crossover trials were included, the first-period data were used in the analysis

Results:

- 10 studies, which reported on 12 treatment comparisons, met inclusion criteria for the review; none were considered to present a high risk of bias

- For the comparison of 1000 mg of acetaminophen vs. placebo, 3 studies (717 participants) reported pain-free status at 2 hours, 2 studies (635 participants) reported on headache relief at 1 hour, and 3 studies (717 participants) reported on headache relief at 2 hours
 - o The proportion of patients with pain-free status at 2 hours was 19% for acetaminophen and 10% for placebo (RR of 1.8)
 - o For headache relief at 1 hour, the proportion of patients on acetaminophen was 39% and was 20% for placebo (RR of 2.0)
 - o For headache relief at 2 hours, 56% of acetaminophen patients and 36% of placebo patients had success (RR 1.6)
- For the comparison of 1000 mg acetaminophen vs 2 mg dihydroergotamine, 1 study with 576 participants provided data on pain-free status at 2 hours and on headache relief at 2 hours
 - o Pain-free response at 2 hours was similar for acetaminophen (31%) and for dihydroergotamine (25%)
 - o Headache relief at 2 hours was also similar for acetaminophen (38%) and for dihydroergotamine (28%)
- For the comparison of combinations of acetaminophen with antiemetics (domperidone in one study, metoclopramide in another study), headache relief was also similar at 2 hours for both studies
- Several other comparisons were made; one comparison with a clinically important difference was between acetaminophen plus metoclopramide and sumatriptan on serious adverse events leading to withdrawal from the study
 - o Acetaminophen plus metoclopramide was associated with serious adverse events in 21 of 675 participants (3%); for sumatriptan 100 mg the rate was 41/653 (6%), for a RR of 0.5 in favor of acetaminophen plus metoclopramide

Authors' conclusions:

- Acetaminophen is useful for first-line treatment of migraine headaches which do not cause severe disability
- Acetaminophen plus metoclopramide may be as effective as sumatriptan for the treatment of migraine headaches, and may have fewer adverse effects
- The studies which were included in the analysis may have recruited patients from migraine clinics, and thus may under-represent patients with milder forms of migraine
- However, some of the larger studies also excluded patients with more severe and disabling forms of migraine

Comments:

- The authors examined a set of prespecified outcomes which not all researchers routinely report
- This means that the amount of evidence concerning the effectiveness of acetaminophen may be greater than the meta-analysis was set up to encompass, and that the review gives a conservative estimate of the effectiveness of acetaminophen with and without an antiemetic drug

- Although the authors estimate numbers needed to treat (NNT) in addition to RR when reporting comparative effectiveness of the medications, these should be interpreted with great caution, since differences between studies in the placebo response may make the calculation of NNT unreliable

Assessment: Adequate for good evidence that acetaminophen is an effective first-line treatment for mild to moderate migraine headache, and that the combination of acetaminophen with an antiemetic is comparable to sumatriptan for a single episode of migraine