

A non-prescription analgesic alleviated migraine headache pain and symptoms

Lipton RB, Stewart WF, Ryan RE, et al. *Efficacy and safety of acetaminophen, aspirin, and caffeine in alleviating migraine headache pain. Three double-blind, randomized, placebo-controlled trials. Arch Neurol* 1998 Feb;55:210-7.

Question

In patients with a history of migraine headache, can a non-prescription combination product (Excedrin Extra-Strength that contains acetaminophen [paracetamol], aspirin, and caffeine) reduce migraine headache pain and symptoms?

Design

3 randomised, double blind, placebo controlled trials with data combined for presentation.

Setting

20 clinical centres in the US.

Patients

1357 patients (mean age 36.7 y, 79% women) with a history of confirmed migraine headaches (International Headache Society criteria). Inclusion criteria were age ≥ 18 years, good health, migraine headache frequency from 1 headache every 2 months to 6 each month, moderate headache pain without treatment, and vomiting $< 20\%$ of the episodes. 92% of patients used their assigned medication.

Intervention

677 patients were allocated to active medication (2 tablets of unbranded Excedrin Extra-Strength tablets, Bristol-Myers Squibb, that contained acetaminophen, 250 mg; aspirin, 250 mg; and caffeine, 65 mg in each tablet) to treat pain from 1 acute self recorded migraine headache. 680 patients were allocated to placebo. Rescue medication could be taken after 2 hours.

Main outcome measures

Self reported pain intensity differences from baseline, proportion of patients with pain reduced to mild or none at 2 and 6 hours, symptoms, and functional ability. Secondary outcomes were the same measures at 1, 3, and 4 hours, and need for rescue medications.

Main results

Pooled analysis showed more patients in the active drug group had reduced pain ($p < 0.001$) and no pain ($p < 0.001$) than in the placebo group at 2 and 6 hours (table). More patients in the placebo group had used rescue medicine by 6 hours. All the symptoms that were assessed (pain, nausea, photophobia, phonophobia, and functional disability) were less frequent at 2 and 6 hours for patients in the active drug group ($p \leq 0.01$ for all comparisons). No serious adverse effects occurred in either group.

Conclusion

A non-prescription combination product that included acetaminophen, aspirin, and caffeine alleviated migraine headache pain and symptoms.

Acetaminophen, aspirin, and caffeine (active drugs) v placebo for migraine headache

| Outcomes | Active drugs | Placebo | RBI (95% CI) | NNT (CI) |
|------------------------|--------------|---------|----------------------|----------------|
| Reduced pain at 2 h | 59% | 33% | 81% (59 to 106) | 4 (3 to 5) |
| Reduced pain at 6 h | 79% | 52% | 52% (40 to 66) | 4 (3 to 5) |
| No pain at 2 h | 21% | 7% | 192% (111 to 304) | 8 (6 to 10) |
| No pain at 6 h | 51% | 24% | 117% (84 to 155) | 4 (3 to 5) |
| No rescue drugs by 6 h | 88% | 73% | 20% (14 to 27) | 7 (5 to 10) |

*Abbreviations defined in glossary; RBI, NNT, and CI calculated from data in article.

Source of funding: Bristol-Myers Squibb Co, New York, NY.

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A modified version of this abstract appears in ACP Journal Club 1998 Sept-Oct and Evidence-Based Medicine 1988 Sept-Oct.

Commentary

Most patients with migraine use non-prescription medications that have not undergone adequate clinical investigation. Lipton *et al* used high quality, high power, clinical trials to investigate a 20 year old popular remedy and produced important results for patients with migraine and for clinicians. The design methodology, using a placebo control, is appropriate to determine the efficacy of this intervention. The trials confirmed for the first time that a single dose non-prescription drug combination was effective in the treatment of single episode uncomplicated migraine headache and associated symptoms. This efficacy was reflected in the relatively few patients who required the use of a rescue medication by 6 hours: 12% of the patients taking the drug combination

compared with 27% taking the placebo.

This study excluded the 25-35% of patients with migraine who were usually severely incapacitated during their attack and the indeterminate number of people who develop rebound headache that is often attributed to the overenthusiastic use of non-prescription drugs that contain caffeine.^{1 2} No indication of the efficacy of this treatment was shown for another large group of patients with migraine—women with hormonal imbalances. Caution is also needed for patients who are sensitive to any of the individual drugs contained in this preparation (acetaminophen, aspirin, and caffeine) and in similar non-prescription drug combination products.

It is tempting to suggest that in the absence of similar combination products

1 tablet of aspirin, 1 of acetaminophen, and a cup of strong coffee may be just as effective. In practice, many patients with uncomplicated single episode migraine who use a single dose strategy for self medication should benefit from this effective and safe combination product.

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1 Mannix LK, Frame JR, Solomon GD. Alcohol, smoking, and caffeine use among headache patients. *Headache* 1997;37:572-6.

2 Moore KL, Noble SL. Drug treatment of migraine: part I. Acute therapy and drug-rebound headache. *Am Fam Physician* 1997;56:2039-48.