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NEWS BRIEFS from the Aspirin Foundation

ASPIRIN IN THE TREATMENT OF ACUTE MIGRAINE

Standard aspirin tablets have been used successfully for years as a treatment for migraine attacks, but not everyone is able to swallow them without some stomach discomfort. A new form of aspirin, which dissolves in water to make an effervescent drink and is changed chemically ('buffered') to minimise stomach upsets has been recently reviewed for its effects in migraine. The review is summarised here.

(Expert Rev Neurotherapeutics 2006;6:563-73).

How does aspirin relieve migraine attacks?

We don't know exactly how aspirin relieves a migraine attack. It probably involves the blocking of activity of a substance, cyclo-oxygenase (COX) that is involved both in the perception of pain by the brain and in the transmission of the message of pain by nerves to the brain.

Aspirin reduces the release of pain-producing chemicals from nerves involved in 'pain pathways' to the brain. It travels preferentially to, and acts upon, areas of the brain and upper spinal cord involved in making us conscious of pain.

Onset of action

Treatment aims to relieve the migraine, and particularly the headache, as fast as possible. Aspirin comes in many forms, from solid tablets to be swallowed as they are in water, to soluble and 'fizzy' (effervescent) preparations. However, in a migraine attack, the stomach wall may be virtually paralysed (gastric stasis),

slowing the absorption of aspirin tablets that reach it as a solid tablet. That delays their effect.

Healthy volunteers (without a migraine) absorb plain aspirin tablets quite quickly. Their aspirin blood levels reach a peak around 35 minutes after they swallow two 500 mg tablets. It takes two and a half hours before the blood shows peak levels of its active substance (that acts on pain), salicylic acid. How fast and how much of the aspirin is absorbed can be changed by changing the form of the aspirin to be swallowed, to the benefit of migraine sufferers. The new effervescent 'highly-buffered' form we report on here is absorbed much faster than a standard aspirin, reaching peak blood aspirin levels 20 minutes, and peak blood salicylic acid levels 49 minutes, after it is swallowed.

How effective is aspirin in relieving migraine headache?

Many trials have studied the efficacy of different formulations of aspirin in migraines, given on its own or combined with metoclopramide, a drug against nausea and vomiting. In most of the trials, the crucial criterion was to reduce headache from a classification of 'moderate-to-severe' down to one of 'mild or no pain' within 2 hours of a single dose. Other criteria for effectiveness were the proportion of patients who had become pain-free in the two hours, or who had to take extra drugs ('rescue medication') because the treatment had not been effective enough.

In double-blind studies (in which the subjects and the doctors did not know which treatment was being given), 49 to 52 percent of patients responded well to a single

dose of 900 - 1000 mg aspirin in a buffered or mouth-dispersible formulation, compared to 19 to 34 percent given placebo. More patients (14 to 20 percent) were pain-free 2 hours after taking aspirin than after placebo (5 to 6 percent). Fewer of the aspirin takers than those on placebo needed rescue medication during the first 24 hours. Aspirin also improved migraine-associated symptoms such as nausea, photophobia (sensitivity to the light) and phonophobia (sensitivity to noise).

Trials comparing aspirin with other painkillers showed that aspirin 1,000 mg is as effective as paracetamol 1,000 mg alone and as paracetamol 400 mg plus codeine 25 mg.

Doctors use metoclopramide along with painkillers to reduce nausea and to improve the movement of the stomach wall, so as to counter the delay in absorbing the analgesic. Such combined pills are available only on prescription. When water-soluble lysine aspirin (equivalent to 900 mg aspirin) plus metoclopramide 10 mg was compared to placebo, 56 percent of the active drug group responded within 2 hours and 18 per cent reported total headache relief. The corresponding figures for placebo were 28 per cent and 7 per cent.

The combination of aspirin and metoclopramide has also been compared with the triptans in treating three consecutive migraines. Two-hour response rates (the proportion of patients who felt better within two hours) were similar with zolmitriptan 2.5 mg and sumatriptan 100 mg, but sumatriptan was the more effective of the two for the second and third attacks. Lysine aspirin plus metoclopramide was also as effective as an injection of ergotamine 2 mg plus caffeine 200 mg by mouth. However, aspirin plus metoclopramide was no more effective than the effervescent form of aspirin given on its own.

Aspirin can also be given by injection into a vein. Lysinated aspirin given intravenously was shown in trials to be better than placebo and as effective as an injection

of ergotamine 0.5 mg", but it was not as effective as subcutaneous sumatriptan 6 mg.

The new buffered effervescent aspirin led to 55 percent of patients responding within 2 hours, 29 per cent being pain free: this compared with a 37 percent 2-hour response and 17 percent pain free on placebo. This makes it as effective as oral sumatriptan 50 mg and ibuprofen 400 mg. It improves photophobia and phonophobia as effectively as sumatriptan.

Safety and tolerability

Analysis of 16 trials comparing aspirin with placebo and other migraine treatments shows that patients tolerate it much as they do placebo. Eight to 16 percent of patients reported unwanted side effects on aspirin, compared with 3 to 15 percent given placebo. It is generally better tolerated than when combined with metoclopramide (12 – 29 percent) and than triptans (14 – 41 percent). Patients tolerated the effervescent aspirin well. The numbers of digestive upsets reported on it were similar to those reported by patients taking placebo.

Clinical comment

Speaking at an Aspirin Foundation meeting in London in April 2005, Dr Anne MacGregor, Director of Clinical Research at the City of London Migraine Clinic, said that aspirin can be effective even in patients used to taking a triptan for their migraines, and that its effect lasts for at least 6 hours. She believed patients should be encouraged to carry soluble aspirin so that they can take it early in the course of an attack.

ABOUT MIGRAINE

- **Migraine affects around four in every hundred children, the numbers rising steadily from then onwards to the later thirties, when one in four women are affected by it**
- **Migraine is disabling: an attack may force you to go to bed and stay there, for several hours – on average for four and a half hours for men and six hours for women**
- **Migraine interferes with your enjoyment of life, limits daily activities and strains personal and professional relationships**
- **Migraine causes loss of production and increases demand on hard-pressed health care teams**