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NEWS BRIEFS from the Aspirin Foundation

Aspirin tolerability - new evidence

After more than 100 years of research into aspirin, it would be reasonable to assume that there's nothing new to learn. Aspirin is, after all, a household name. It is the gold standard against which other anti-inflammatory agents, analgesics and anti-thrombotic agents are measured. But, as the current wave of observational studies on cancer risk has shown, we are still far from understanding the potential of this deceptively simple medicine.

One issue that continues to provoke controversy is the gastric side effects of aspirin - but are these concerns well-founded? A meeting of eminent medical scientists and clinicians in Bensberg, Germany, in June 2004 considered the evidence - old and new - of the gastric tolerability of aspirin. The meeting addressed some common misconceptions about aspirin and showed how more recent key research findings have challenged some widely-held beliefs.

There's nothing more to learn about the gastric safety of aspirin?

What we take as accepted fact may be wrong. We now have a better understanding of the gastroprotective role of the COX enzyme and we know that risk factors such as concurrent medication and alcohol use are important contributors to the gastric effects associated with aspirin as an OTC analgesic¹. Furthermore, aspirin has been shown to be a free radical

scavenger that may actually protect endothelial cells from oxidative stress^{2,3}.

Is aspirin the worst OTC analgesic for side effects?

Put simply - no. A review in 2002 by the US Food and Drug Administration concluded that there was no basis for choosing one OTC NSAID (including aspirin, ibuprofen, naproxen and ketoprofen) over another on grounds of safety⁴. A large epidemiological study confirmed that OTC analgesics have similar safety records⁵ and single-dose studies in typical OTC indications (migraine, tension-type headache) have identified very few, if any, serious adverse events⁶⁻⁸.

Gastric injury with regular low-dose aspirin

The annual incidence of significant gastric bleeding in patients taking low-dose aspirin is 1 - 2 per 1000 compared with a background rate of 1 per 1000. It is not known whether this small difference is causally linked with aspirin because most affected patients have risk factors such as advanced age, alcohol use, smoking and *H pylori* infection⁹⁻¹¹.

Different formulations don't affect the risk of gastric irritation?

It has long been held that gastric irritation associated with aspirin is a systemic effect and therefore unaffected by different formulations. However, clinical trials and endoscopic findings show that enteric-coating, buffering, modifying solubility¹² and the inclusion of vitamin C reduce irritation of the stomach lining¹³

and improve the patient-reported experience of taking aspirin¹⁴.

A single aspirin tablet can harm the stomach?

Many single-dose studies have shown that OTC doses of aspirin are well tolerated in a range of indications. Experience in placebo-controlled trials involving thousands of patients and widespread OTC use over many years has shown that the risk of severe side effects has been minimal^{6-8, 15, 16}.

Side effects reported in clinical trials are always due to the study drug?

Distinguishing side effects from disease symptoms can be difficult and providing information about side effects to patients may increase reporting - even among those taking a placebo^{17, 18}.

Aspirin is an outdated treatment for arthritis?

Evidence from large patient databases show that aspirin is well tolerated in the treatment of pain and inflammation associated with rheumatoid arthritis and osteoarthritis¹. It may even be better tolerated than some NSAIDs^{1, 19}.

COX-2 selective NSAIDs are safer than aspirin?

It's widely perceived that COX-2 selectivity is associated with a superior gastric safety record compared with aspirin and non-COX selective NSAIDs. However, the increase in prescriptions for COX-2 selective agents has exposed more people to risk and corresponded with an increase in cases of gastric haemorrhage, particularly among older people²⁰. COX-2 selectivity alone does not guarantee that a drug will not damage the stomach lining and, because COX-2 selective NSAIDs have not been shown to offer greater efficacy, there is a need

for caution regarding long-term use and high-dose treatment^{21, 22}.

SUMMARY

Like any drug, aspirin carries a risk of side effects but there is no evidence that the frequency and intensity of gastric side effects is greater than with other OTC analgesics. Aspirin has a favourable benefit-risk ratio for all its licensed indications and its gastric safety is well established when used as an analgesic, in low doses to prevent myocardial infarction and stroke, and in the treatment of rheumatoid arthritis and osteoarthritis.

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