New evidence from randomised controlled trials on cardiovascular and gastrointestinal risks of non-steroidal anti-inflammatory drugs reinforces the need to review all patients taking such medication.

New evidence on risks associated with NSAIDs

A n increased risk of heart attack and stroke with some non-selective non-steroidal anti-inflammatory drugs (NSAIDs), such as diclofenac, is well recognised, particularly with long-term use of high doses and in patients who are already at a high risk.

The Medicines and Healthcare products Regulatory Agency (MHRA) has summarised the cardiovascular safety of COX-2 inhibitors and non-selective NSAIDs (tinyurl.com/cox-2-NSAID).

Current advice

The MHRA has advised that systemic diclofenac is now contraindicated in people with established ischaemic heart disease, peripheral arterial disease, cerebrovascular disease or congestive heart failure (tinyurl.com/MHRA-diclofenac). Patients with these conditions should be switched to an alternative treatment at their next routine appointment.

Diclofenac treatment should be initiated only after careful consideration in people with significant risk factors for cardiovascular events, for example hypertension, hyperlipidaemia, diabetes mellitus, or smoking.

The new advice applies to all systemic formulations including those available over the counter in pharmacies; it does not apply to topical formulations.

New evidence

A meta-analysis by the Coxib and traditional NSAID Trialists’ Collaboration (2013) aimed to quantify the cardiovascular and gastrointestinal risks of NSAIDs using data from randomised controlled trials. It included 286 trials of an NSAID compared with placebo and 474 trials of an NSAID compared with another NSAID.

The primary outcomes were major vascular events and upper gastrointestinal complications.

Compared with placebo, major vascular events were significantly increased by more than one third for COX-2 inhibitors and diclofenac 150mg daily. This was mainly due to an increase in major coronary events. The absolute increase in risk was small but serious; compared with placebo, COX-2 inhibitors or diclofenac 150mg daily caused around three additional major vascular events per 1,000 participants per year, one of which was fatal.

ibuprofen 2,400mg daily did not significantly increase the risk of major vascular events compared with placebo; however, it doubled the risk of major coronary events. Naproxen 1,000mg daily did not significantly increase major vascular or coronary events compared with placebo. The proportional cardiovascular and gastrointestinal risks of all NSAIDs appeared independent of baseline characteristics, including vascular risk.

The risk of hospitalisation due to heart failure was approximately doubled by all NSAIDs studied, compared with placebo. In addition, COX-2 inhibitors and diclofenac doubled the risk of upper gastrointestinal complications (mainly bleeds), and ibuprofen and naproxen quadrupled the risk compared with placebo.

BOX 1. COMMENTARY

The new meta-analysis and MHRA alert reinforce previous information about the cardiovascular and gastrointestinal risks of NSAIDs and provide additional support to existing guidance.

The MHRA advises that the decision to prescribe an NSAID should be based on an assessment of a person’s individual risk factors, including any history of cardiovascular and gastrointestinal illness. Naproxen and low-dose ibuprofen (1,200mg per day or less) are considered to have the most favourable thrombotic cardiovascular safety profiles of all non-selective NSAIDs. The lowest effective dose should be used for the shortest duration necessary to control symptoms. However, a cohort study in people who had had a myocardial infarction suggests that even short-term use of NSAIDs (some for as little as one week) is associated with an increased risk of death or recurrent myocardial infarction (Schjerning Olsen, 2011).

The challenge is to ensure that the use of all NSAIDs, of all durations, is reviewed in all settings. In secondary care, this means using alternatives to diclofenac for acute treatment, as well as in long-term treatment, for example for rheumatological conditions. In primary care, patients should be systematically reviewed, starting with those at higher risk of both gastrointestinal and cardiovascular morbidity and mortality (for example older people).

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References


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