

# Newsletter



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## GI safety of ibuprofen confirmed - again

A study for the World Health Organisation has confirmed that ibuprofen is associated with the lowest risk of gastrointestinal (GI) complications among NSAIDs (Richy F et al. *Ann Rheum Dis* 2004;63:759-66).

Investigators conducted a meta-analysis of controlled trials reporting the adverse effects of NSAIDs conducted between 1985 and 2003. The 32 randomised trials and 13 cohort studies included a total of 5,325 patients taking an NSAID and 3,453 controls. In the three studies involving ibuprofen, the median dose was 1200 mg/day. GI complications were defined as any ulcer, bleeding, perforation, hospitalisation or related death.

Overall, the relative risk of GI complications with NSAID use was 1.54 (CI<sub>95%</sub> 1.4 - 1.7) in randomised trials over 28 days, or 2.2 (CI<sub>95%</sub> 1.7 - 2.9) in cohort studies over one year. Of seven NSAIDs assessed, the risk was greatest with indomethacin (RR 2.25, CI<sub>95%</sub> 1.10 - 5.07) and lowest with ibuprofen (RR 1.19, CI<sub>95%</sub> 0.93 - 1.54); relative risks were also significantly increased for naproxen (1.83), diclofenac (1.73) and piroxicam (1.66). Complications associated with indomethacin tended to occur after 7 days compared with 2 - 3 months with other NSAIDs. The authors confirm current advice that NSAIDs should be prescribed cautiously for patients who need long term management.

## OTC analgesic consumption by coxib users

Patients at increased risk of gastrointestinal complications are often prescribed a COX-2 selective NSAID and advised to avoid non-selective agents. However, people with arthritis often self-medicate with an OTC analgesic to treat breakthrough pain and, because non-COX selective NSAIDs are freely available without prescription, they may unwittingly be exposing themselves to risk.

Outside the realms of clinical trials, little is known about the scale of this potential problem. Now a US study has revealed the extent to which patients taking a COX-2 selective NSAID also use OTC NSAIDs - and the figure for OTC ibuprofen is reassuringly low (Cox E et al. *Arch Intern Med* 2004;164:1243-6).

The telephone survey of 324 adults taking rofecoxib or celecoxib showed that three-quarters had taken an OTC analgesic on at least one day during the previous month. Forty-eight percent of respondents took aspirin, virtually all for cardioprotection; paracetamol use was reported by 43 percent, and ibuprofen and naproxen use by 7 and 3 percent respectively.

However, a substantial group of respondents reported more frequent use of analgesics. In the previous month, a quarter had taken two or more OTC drugs and just over half had used an OTC analgesic on at

least 15 days. Aspirin was still the most widely used drug by far (45 percent), with frequent ibuprofen use reported by 2 percent of respondents.

These findings indicate a low level of self-medication with NSAIDs among people prescribed a COX-2 selective agent. Instead, the risk from the widespread use of low-dose aspirin is probably more important.

### **Observational study finds no evidence of ibuprofen - aspirin interaction**

Epidemiologists have found no evidence that ibuprofen reduces the cardioprotective effects of aspirin in a large case-control study of coronary deaths (*Circulation* 2004;109:3000-6).

They identified 4,975 cases of acute myocardial infarction and coronary death in the UK between 1997 and 2000. Compared with 20,000 controls matched for age, sex and calendar year, the adjusted odds ratio for death among NSAID users was 1.07 (CI<sub>95%</sub> 0.95 - 1.20). This was unaffected by the duration of treatment or the dose of NSAID, and the odds were similar for cases with or without a history of coronary disease.

There were no significant differences in risk associated with the different NSAIDs. The odds ratio for any NSAID plus aspirin compared with aspirin alone was 1.10 (CI<sub>95%</sub> 0.89 - 1.37), with a similar result specifically for ibuprofen plus aspirin. The authors conclude that their study does not support the existence of a clinically meaningful interaction between ibuprofen and aspirin.

### **Ibuprofen longer-acting for fever in children**

A new meta-analysis has shown that ibuprofen reduces fever in children more effectively than paracetamol for up to 6 hours (Perrott DA et al. *Arch Pediatr Adolesc Med* 2004;158:521-6).

Australian investigators analysed 17 randomised blinded comparisons of ibuprofen and paracetamol in children with fever or moderate to severe pain. Considering only the effects of the first dose, they found that ibuprofen 5 - 10 mg/kg reduced temperature by more than paracetamol 10 - 15 mg/kg after 2, 4 and 6 hours (effect sizes 0.19, 0.31 and 0.33 respectively) and that the highest doses of ibuprofen (10 mg/kg) were more effective still (effect sizes 0.34, 0.81, 0.66 respectively). The analgesic efficacy of ibuprofen and paracetamol were similar and there was no evidence of a difference in major or minor adverse events.

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