Aspirin May Offset NSAID-Related Heart Risks

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AMSTERDAM — Concomitant aspirin use may fully reverse the increased atherothrombotic risk associated with cyclooxygenase-2 selective NSAIDs, Dr. Gurkirpal Singh reported at the annual European Congress of Rheumatology.

In addition, aspirin may also reduce—if only partially in some instances—the cardiovascular risk conferred by most traditional nonselective NSAIDs, said Dr. Singh of Stanford (Calif.) University.

Although these findings from a large case-control study provide insight into the mechanism by which NSAIDs increase cardiovascular risk, he stressed that adding a daily aspirin to mitigate that cardiovascular risk is not a practical solution for arthritis patients seeking pain relief. That's because there is some evidence that concomitant use of aspirin and NSAIDs, whether COX-2 selective or not, appears to magnify the risk of NSAID-associated GI bleeding, he said.

Dr. Singh used the California Medicare database to identify all adults with rheumatoid arthritis or osteoarthritis treated with a COX-2 selective or nonselective NSAID from 1999 through the first half of 2004. During nearly 2.4 million patient-years of follow-up, 15,343 arthritis patients experienced an acute MI, 8% of which were fatal. Each MI patient was matched to four controls.

The adjusted relative risk of MI was increased by 31% in patients being treated with rofecoxib and by 12% in patients being treated with celecoxib, compared with the rate in remote users of any NSAID. Both differences were significant.

The MI risk was also increased by 65% in current users of indomethacin, by 52% with meloxicam, and by 47% with sulindac, but was not significantly elevated in current ibuprofen users.

Concurrent use of aspirin completely reversed the increased MI risk associated with rofecoxib, celecoxib, meloxicam, and sulindac. However, the increased risk in current users of indomethacin was only partially and nonsignificantly reduced, such that patients on concomitant aspirin and indomethacin still had a 20% increased risk, he explained.

[But] adding a daily aspirin to mitigate the CV risk isn't practical for arthritis patients seeking pain relief.

DR. SINGH

In a separate presentation, Dr. Steven B. Abramson said Dr. Singh's findings made sense. "My instincts are that there will be some cardioprotection because you're getting 24-hour inhibition of platelets with a single aspirin," added Dr. Abramson, professor of medicine and associate dean for clinical research at New York University.

He noted here is encouraging evidence to suggest that high-dose naproxen alone, among the various selective and nonselective NSAIDs, may be cardioprotective.

It has been shown that 500 mg of naproxen provides good platelet inhibition for close to 12 hours. A recent large meta-analysis of trials comparing COX-2 inhibitors with nonselective NSAIDs, or drugs in either class with placebo, showed that although the COX-2 inhibitors were associated with a 42% relative increase in MIs and other vascular events relative to placebo, a comparable risk was present in patients on high doses of traditional NSAIDs—except for those on naproxen at 500 mg b.i.d. The metaanalysis, led by investigators at the University of Oxford, involved about 145,000 patients in 138 randomized trials, including some unpublished ones on file with manufacturers (BMJ 2006; 332:1302-8).

"It still remains uncertain whether naproxen is cardioprotective, but it probably is at 500 mg twice per day. Over-the-counter naproxen at lower doses is probably not going to be protective based on the available evidence," said Dr. Abramson, who was a member of the FDA's special advisory panel on the COX-2 inhibitors' cardiovascular risk.

He was quick to add, however, that this will have to be shown in prospective clinical trials before the FDA would consider removing the warning of increased cardiovascular risk from naproxen's label, a warning currently applied to all COX-2 selective and traditional NSAIDs. ■

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