



Do NSAIDs Impair the Cardioprotective Effects of Aspirin?

John R. Horn, PharmD, FCCP, and Philip D. Hansten, PharmD

Drs. Horn and Hansten are both professors of pharmacy at the University of Washington School of Pharmacy. For an electronic version of this article, including references, visit www.hanstenandhorn.com.

Much recent attention, in both the medical literature and the lay press, has focused on whether ibuprofen (eg, Advil, Motrin) can interfere with the cardioprotective effects of low-dose aspirin. The discussion started following publication of the results of a study by Catella-Lawson et al in the *New England Journal of Medicine* in 2001, showing that regular use of ibuprofen inhibited the antiplatelet effect of low-dose aspirin.¹ Numerous articles have followed, but many unanswered questions remain.

Is the Interaction Clinically Important?

Following the Catella-Lawson article, several epidemiologic studies have investigated patient outcomes with low-dose aspirin alone versus low-dose aspirin plus ibuprofen or other nonsteroidal anti-inflammatory drugs (NSAIDs). In general, the epidemiologic studies found a reduced ability of aspirin to protect against cardiovascular disease, but none of the studies can be considered definitive. The most one can say at this point is that ibuprofen may reduce aspirin efficacy, but more study is needed.²⁻⁵

Is the Dose of Ibuprofen Important?

The dose of ibuprofen appears to be important. The original study by Catella-Lawson and colleagues found an inhibition of the aspirin antiplatelet effect with ibuprofen 400 mg

tid, but not when ibuprofen was given once a day and 2 hours after the aspirin. So, at least as far as inhibition of the antiplatelet effect of aspirin is concerned, occasional doses of ibuprofen do not seem to be a problem.

Could the Interaction Be Overcome by Increasing the Aspirin Dose?

It is not known whether increasing the aspirin dose in the presence of ibuprofen would restore the antiplatelet effect of the aspirin.

Also, the current discussion involves the use of low-dose aspirin for the prevention of cardiovascular disease, rather than the use of aspirin as an analgesic. Combining long-term analgesic doses of aspirin with NSAIDs presents other issues, of course, such as a possible increase in gastrointestinal toxicity.

How About NSAIDs Other Than Ibuprofen?

Catella-Lawson and associates found that diclofenac (Cataflam, Voltaren) 75 mg bid did not influence the antiplatelet effects of aspirin. Some of the epidemiologic studies also suggest that ibuprofen may be more likely than other NSAIDs to inhibit the efficacy of low-dose aspirin. Although it is too early to be sure, some NSAIDs may be found not to interact with aspirin.

How About COX-2 Inhibitors?

Cyclooxygenase-2 (COX-2) inhibitors—such as celecoxib (Celebrex), rofecoxib (Vioxx), and valdecoxib (Bextra)—do not affect platelet function and do not appear to impair the antiplatelet effects of aspirin.^{1,6,7} Thus, it does not appear likely that COX-2 inhibitors would interfere with the cardioprotective effects of aspirin.

Other Cardiovascular Effects of NSAIDs

Even if ibuprofen and other NSAIDs eventually prove to have little effect on the cardioprotective effects of aspirin, they need to be used with caution in patients with certain cardiovascular diseases. For example, NSAIDs can increase blood pressure and worsen congestive heart failure, especially in patients receiving angiotensin-converting enzyme inhibitors or angiotensin receptor antagonists.

Recommendations

Although more study is needed to establish whether ibuprofen or other NSAIDs inhibit the cardioprotective effects of aspirin, it would be prudent to take appropriate precautions until more data are available.

- Generally avoid the use of ibuprofen in patients on low-dose aspirin (occasional use of ibuprofen is unlikely to be a problem)
- Warn patients on low-dose aspirin to avoid OTC ibuprofen unless advised to take it by their prescriber
- If appropriate, consider the use of alternatives to ibuprofen, such as acetaminophen (eg, Tylenol), diclofenac, or COX-2 inhibitors
- If it is decided to use ibuprofen, try to avoid administering aspirin less than 2 hours before or 6 hours after ibuprofen

Conclusion

The preponderance of available evidence suggests that regular use of ibuprofen may inhibit the cardioprotective effects of aspirin, but more evidence is needed to establish the clinical importance. Diclofenac and COX-2 inhibitors may be less likely to interact, but little is known about others. 