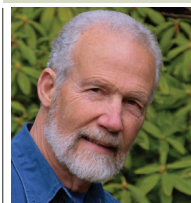# Antiplatelet Effects of Aspirin: Which NSAIDs Interact?

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TABLE: INHIBITION OF ASPIRIN EFFICACY			
Probably	**Possibly**	**Probably Not**	**Unknown**
Ibuprofen	Celecoxib[a] Indomethacin Naproxen[a]	Acetaminophen Diclofenac Meloxicam Sulindac	All other NSAIDs[a]

[a]Conflicting data; more information needed

Low-dose aspirin is widely used as prevention for myocardial infarction and other cardiovascular diseases, but there is evidence that concurrent use of NSAIDs may inhibit the antiplatelet effect of aspirin.[1] There appear to be differences, however, in the relative likelihood of the various NSAIDs to interact with aspirin.

Mechanism

Aspirin acts by acetylating platelet COX-1, thus irreversibly inhibiting platelet function. Ibuprofen appears to block the access of aspirin to the active site on the platelet, although other mechanisms may also be involved.[1,2] Other NSAIDs may or may not interact similarly, as described below.

> It would be prudent to err on the side of caution in dealing with these interactions.

Platelet Studies

In healthy subjects on aspirin 81 mg/day for 6 days, ibuprofen 400 mg given 2 hours before each aspirin dose blocked the antiplatelet effect of aspirin, as did multiple daily ibuprofen given 2, 7, and 12 hours after the aspirin. But a single daily dose of ibuprofen given 2 hours after each dose of aspirin did not interact.[2] Aspirin has a very short half-life (~15-20 minutes) so it makes sense that giving ibuprofen 2 hours after the aspirin would avoid the interaction.

Other studies in healthy subjects also found ibuprofen to inhibit the antiplatelet effects of aspirin.[3,4] Naproxen and indomethacin may also inhibit the antiplatelet effects of aspirin, but acetaminophen, diclofenac, meloxicam, and sulindac may not.[2-7] One study found celecoxib to have no effect on the antiplatelet effect of aspirin,[4] while another suggested an interaction.[8]

Patient Studies

In 18 patients on ibuprofen or naproxen who were also receiving aspirin to prevent stroke, platelet function was found to be similar to patients not taking aspirin. When the NSAID was stopped or given in a dosing schedule to avoid the aspirin, repeat testing in 2 to 4 weeks found the expected antiplatelet effect of aspirin.[9] Most large outcome trials of patients taking aspirin for cardioprotection suggest that concurrent ibuprofen use reduces aspirin efficacy.[10-13] These outcome trials also found that diclofenac, naproxen, and a COX-2 inhibitor (lumiracoxib) may not interact.[10,13] Not all studies have found reduced aspirin efficacy with NSAIDs,[14,15] but the bulk of the evidence suggests that an interaction does exist.

Recommendations

Given the substantial evidence of interaction, and the potential severity of reduced aspirin efficacy (eg, myocardial infarction, stroke), it would be prudent to err on the side of caution in dealing with these interactions. Thus, one should assume that ibuprofen can reduce aspirin efficacy, and either avoid ibuprofen altogether or give it 2 hours after the aspirin. It may not be possible to avoid the interaction if ibuprofen is taken more than once daily. Naproxen and celecoxib are probably less likely than ibuprofen to interact with aspirin, but there is some evidence of interaction. So pending additional information, it would be prudent to avoid them as well. Drugs least likely to interact with aspirin appear to be acetaminophen and diclofenac, but the evidence suggests that meloxicam and sulindac may also avoid the aspirin interaction (see Table). The effect of NSAIDs on the efficacy of other antiplatelet drugs (eg, clopidogrel, prasugrel) is not established, but combining NSAIDs with such antiplatelet drugs may increase the risk of gastrointestinal bleeding. ■

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