Coadministration of NSAIDs and Antihypertensive Agents

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 if any, visit www.hanstenandhorn.com.

It has been estimated that >50% of the US population over age 65 has hypertension. Only about one third of all hypertensive patients receiving therapy, however, have reached their goal blood pressure (BP). Whereas there are a number of reasons for this poor response to antihypertensive therapy, one that can be easily controlled is the risk of potential drug interactions blunting the effectiveness of antihypertensive drugs. It is the control of BP that reduces the risk of developing a myocardial infarction, heart failure, stroke, and renal disease in hypertensive patients. Current hypertension treatment guidelines recommend starting therapy with a thiazide diuretic and then adding additional drugs as needed to control BP. An analysis of >12 randomized trials of antihypertensive therapy found that a 20% to 40% reduction in cardiovascular disease required only a 5- to 6-mm-Hg decrease in diastolic BP.[1] This magnitude of BP reduction is typically seen with any single antihypertensive drug treatment. It is also represents the usual increase in BP seen when nonsteroidal anti-inflammatory drugs (NSAIDs) interact with antihypertensive drugs.

Hypertensive patients use NSAIDs for a variety of indications. NSAIDs inhibit prostaglandin-mediated vasodilation and promote salt and water retention. Both of these mechanisms may contribute to NSAIDs partially reversing the effects of hypotensive drugs, particularly those agents whose mechanism depends on modulating prostaglandins, renin, or sodium and water balance. The dose and duration of NSAID therapy will partially determine the extent of hypotensive therapy reversal. Higher doses of NSAIDs and chronic therapy extending beyond a week will be more likely to increase BP.

Antihypertensive drugs appear to be affected to variable degrees by NSAIDs. Diuretics, angiotensin-converting enzyme inhibitors (ACEIs), beta-blockers, and angiotensin II receptor blockers (ARBs) are most susceptible to the hypotensive-nullifying effects of NSAIDs. Calcium channel blockers and centrally acting antihypertensives seem to be least affected. For example, one study found that indomethacin reduced the hypotensive effect of enalapril by nearly 50% while having almost no effect on nifedipine.[2] Similarly, NSAIDs will demonstrate differing abilities to offset hypotensive response to therapy. Indomethacin has been the most widely studied and, along with naproxen and piroxicam, appears to produce the greatest effect. Low-dose aspirin (ie, <250 mg/d) and sulindac have the least detrimental effect on BP.[3,4] Elderly patients and those with heart failure may be more sensitive to the effects of NSAIDs on their antihypertensive or diuretic therapy.[5-7]

Based on the evidence for an interaction between NSAIDs and some antihypertensive agents, the pharmacist should be prepared to offer counseling to patients considering coadministration of these classes of drugs. The following points should be considered:

- Although the absolute increase in BP resulting from NSAID coadministration is usually limited to <10 mm Hg, it can result in a 50% reduction in the efficacy of an antihypertensive drug and block the beneficial cardiovascular effects of BP reduction
- Short courses of NSAID therapy (ie, less than a week or 2), even with daily NSAID administration, are unlikely to cause a clinically important increase in a patient's BP
- Short courses of NSAIDs may cause exacerbation of heart failure. Patients should be counseled to report any symptom changes during NSAID administration.
- Low-dose aspirin therapy does not appear to affect the efficacy of antihypertensive drugs or diuretics
- Some NSAIDs, such as sulindac, may produce less blunting of hypotensive efficacy
- Diuretics, ACEIs, ARBs, and beta-blockers are likely to be more affected by NSAIDs than calcium channel blockers or centrally acting agents. Switching to an antihypertensive drug not as susceptible to the blunting effects of NSAIDs should be considered for patients requiring chronic NSAID therapy.
- Consider alternative analgesics, such as acetaminophen, tramadol, or narcotic analgesics, for patients requiring analgesics who are unable to have their antihypertensive regimen altered
- Monitor BP of patients taking NSAIDs for several weeks to determine if they are candidates for drug regimen adjustments. Also, be alert for signs of fluid retention, such as weight gain or peripheral edema.

By following these simple guidelines, pharmacists can ensure that patients will receive the maximum benefit from their antihypertensive drug regimen, even if they require NSAID therapy. PT

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