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Is Acetaminophen a Problem in Hypertensive Patients?

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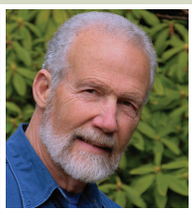

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It has been known for many years that nonsteroidal anti-inflammatory drugs (NSAIDs) can inhibit the effect of antihypertensive medications. We have previously reviewed this effect of NSAIDs,[1] as well as the increased risk for nephrotoxicity when NSAIDs and diuretics are combined in triple therapy with either angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin-receptor blockers (ARBs).[2] The effect of acetaminophen on antihypertensive therapy is less well studied, but acetaminophen has generally been considered less likely than NSAIDs to interact adversely with antihypertensive therapy.

Recent Evidence

In a recently published double-blind crossover study involving mildly hypertensive patients with osteoarthritis, naproxen and acetaminophen were compared in combination with an ACEI (ramipril), an ARB (valsartan), and a direct renin inhibitor (aliskiren).[3]

Naproxen

As expected, naproxen (500 mg daily for 2 weeks) significantly inhibited the antihypertensive effect of ramipril and valsartan. The average increase in blood pressure (BP) was modest, but would probably require adjustment in antihypertensive therapy in some patients. Even small increases in BP can have adverse health effects if the effect is prolonged. Moreover, these patients had mild hypertension, and patients with more severe and refractory hypertension may have more pronounced effects. Interestingly, naproxen did not significantly affect the antihypertensive effect of aliskiren. The reason for this difference is not clear, but the authors offered several possible explanations.

Acetaminophen

The surprise finding in this study was that acetaminophen inhibited the antihypertensive effect of ramipril, valsartan, and aliskiren. The effect on ramipril and valsartan was not quite as large as with naproxen, but the effect was enough to adversely affect at least some patients if acetaminophen is taken long term and the patient is not adequately monitored. Previous study results of acetaminophen use in patients receiving antihypertensives have been conflicting, although the present study is consistent with a recent prospective study showing that acetaminophen produces modest increases in BP in patients with coronary artery disease.[4] Taken together, the evidence suggests that acetaminophen is capable of increasing BP to some degree.

> A recent study suggests that long-term use of acetaminophen could have adverse consequences in hypertensive patients.

Management

So what advice should we give patients with hypertension who are considering taking an NSAID or acetaminophen? Most importantly, as we pointed out in our April 2013 column, triple therapy with NSAIDs, diuretics, and either an ACEI or ARB, appears to increase the risk of nephrotoxicity, and this issue should be discussed with the prescriber. For patients taking only an ACEI or ARB, consider the following recommendations.

Duration

If the NSAID or acetaminophen is to be taken only for a few days to treat an acute problem, the risk appears low unless perhaps the patient has severe or labile hypertension.

Monitoring

If the NSAID or acetaminophen will be taken long term, BP should be monitored, and necessary adjustments made in the antihypertensive therapy.

Type of Antihypertensive

Although the current study found that naproxen did not inhibit aliskiren but acetaminophen did,[3] more research is needed to confirm this finding. NSAIDs may be less likely to interfere with the antihypertensive effect of drugs other than ACEIs and ARBs (such as calcium channel blockers), but it is not known if acetaminophen interacts differently with the various antihypertensive agents.

Closing Thoughts

A new study found that acetaminophen antagonized the antihypertensive effects of an ACEI (ramipril), an ARB (valsartan), and a direct renin inhibitor (aliskiren). Although the effect was modest, this study suggests that long-term use of acetaminophen could have adverse consequences in hypertensive patients if BP is not monitored carefully and appropriate adjustments to antihypertensive therapy are not made. ■

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.