Neutralization Of The Effects Of Captopril By The Use Of Ibuprofen In An Elderly Woman

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The use of angiotensin converting enzyme (ACE) inhibitors has become more widespread because of their favorable results in lowering blood pressure, as well as their favorable side-effect profile. Many elderly patients have multiple medication changes for chronic diseases, however, and the potential for adverse drug interactions between ACE inhibitors and other medications is always present.

The following case report demonstrates that the hypotensive effect of captopril can be neutralized by concomitant use of ibuprofen, a commonly used nonsteroidal anti-inflammatory agent.

Case Report

A 70-year-old white woman had a history of hypertension that was controlled by methyldopa, 250 mg four times a day, and trichlormethiazide, 2 mg once a day. Her average blood pressure reading while receiving these medications was 130/80 mmHg.

In an attempt to institute monotherapy for the patient's blood pressure, trichlormethiazide was discontinued; no elevation in blood pressure was recorded on close reevaluation. Two weeks later she was referred to a physiatrist for evaluation of osteoarthritis of the hip. She was prescribed ibuprofen therapy, 400 mg four times daily, and had initial pain relief. Her home-monitored blood pressure measurements, however, appeared to rise with the addition of ibuprofen to her treatment regimen.

Two weeks later the patient reported that her home blood pressure reading was 170/110 mmHg. In the office her blood pressure was recorded as 180/125 mmHg despite continued administration of methyldopa. Captopril was prescribed at 12.5 mg three times a day. Three days later her blood pressure while sitting was 90/60 mmHg, with no orthostatic symptoms or changes. The methyldopa dosage was subsequently discontinued. Because her blood pressure measurements continued to be about 160/90 mmHg, her captopril dosage was increased to 25 mg three times a day. During the subsequent 6 weeks the patient's blood pressure measurements ranged from 120/70 to 180/100 mmHg.

Three months after the original visit, the patient's ibuprofen dosage was increased to 800 mg three times a day. Concomitantly her blood pressure measurements became consistently higher than 150/90 mmHg. Her captopril dosage was increased first to 37.5 mg three times a day and then to 50 mg three times a day, with no significant beneficial response in blood pressure control. Hydrochlorothiazide, 12.5 mg daily, was therefore added.

For the next 3 months, during which time the patient took ibuprofen intermittently, her blood pressure values continued to be erratic, but lower, ranging from 120/70 to 156/100 mmHg.

During periods in which the patient was not taking ibuprofen, her blood pressure readings ranged from 122/78 to 137/85 mmHg, contrasting with the blood pressure readings ranging from 160/95 to 165/100 mmHg while she was taking 400 mg of ibuprofen three times a day. Ibuprofen was discontinued, and the patient was prescribed sulindac, 150 mg twice a day. The patient's blood pressure dropped within 2 days to consistent values of about 130/80 mmHg with no further change in her captopril or hydrochlorothiazide dosage. The hydrochlorothiazide was subsequently discontinued, and the patient's blood pressure continues to be well controlled on captopril alone, which she has been taking for a total of 8 weeks. Her pain caused by osteoarthritis has also been well controlled on sulindac. During the time the changes in medication regimens were occurring, the patient was taking no other

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medication, and there had been no other changes in the patient's medication regimen, lifestyle, or health status. Furthermore, the patient's renal function, as measured by serum creatinine (mean = 70 μmol/L [0.8 mg/dL]) and blood urea nitrogen (mean = 8.6 mmol/L [24 mg/dL]), was normal and unchanged during this period.

Discussion

This case report shows that ibuprofen in an elderly patient can interfere with the antihypertensive effects of captopril.

Anti-inflammatory agents are capable of inhibiting antihypertensive effects of certain medications. That different nonsteroidal anti-inflammatory agents interfere with the β-blocker and diuretic classes of antihypertensive medications has been well documented.[1-4] The blunting of the antihypertensive action of ACE inhibitors by indomethacin has also been described.[5,6]

The ability of captopril to reduce blood pressure is believed to be related, in part, to inhibition of the conversion of angiotensin I to angiotensin II[7,8] (Figure 1). In addition, the administration of captopril potentiates the release of bradykinin with its concomitant effects on renal vasodilatation.[9] This effect appears to be mediated by a prostacyclin-like substance that can be inhibited by the administration of indomethacin, ibuprofen, and possibly other nonsteroidal anti-inflammatory agents.[10,11]

With low renin concentrations or in a sodium-restricted state, such as that found in the aged, the potentiation of bradykinin and the prostaglandin system appears to supervene the effects of the renin-angiotensin system as the hypotensive action of captopril.[12-14] Consequently, the effects of ibuprofen on the prostaglandin system can lead to

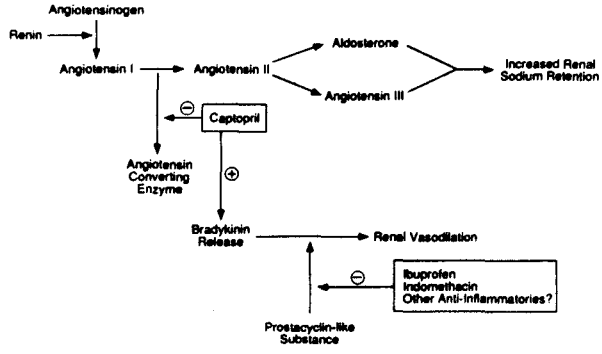

Figure 1. Proposed mechanisms of the antihypertensive effects of captopril.

competitive inhibition of the effects of captopril on this system. This inhibition, in turn, leads to a decrease in the hypotensive effects of captopril when ibuprofen is jointly administered, even in over-the-counter dosages.[15]

The exact pathways by which ibuprofen inhibits the hypotensive effects of captopril in patients with low renin remain unknown, because current effects cannot definitely be ascribed to the changes in tissue hormone production previously described.[16,17] It is possible that lisinopril could be a better alternative in the aged because it has been shown to be resistant to the effects of indomethacin.[18] Until these mechanisms are determined, however, extreme care should be exercised when prescribing captopril and ibuprofen in concert. In addition, if it is necessary to use the two medications together, the patient's blood pressure should be closely monitored.

It is also important to mention that sulindac could be a better alternative if concomitant treatment with an antihypertensive medication is considered. Sulindac has had negligible interactions when used with other antihypertensive agents[19] and certainly should be considered. Sulindac also does not appear to inhibit bradykinin to the extent that other nonsteroidal anti-inflammatory agents do.[20]

Finally, although the 150 mg/d dosage of captopril is sometimes necessary for adequate antihypertensive control,[21] it is a large dosage for an elderly person, even for one who has normal renal function, and, as such, warrants close monitoring of the patient.

Summary

This case report demonstrates that the antihypertensive effects of captopril were neutralized by the concomitant administration of ibuprofen.

If elderly patients on ACE inhibitors show evidence of a "noncompliant" worsening of their hypertension, a thorough review of all the patient's medications, including the use of over-the-counter ibuprofen, should be undertaken.

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