TREATING HYPERTENSION IN PATIENTS WITH ELEVATED SERUM CREATININE

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Providers who automatically stop ACE inhibitor therapy when serum creatinine rises may miss an opportunity both to slow the progression of chronic renal disease and to offer cardiovascular protection.

A 70-year-old woman with an aversion to physicians and, subsequently, no known medical history or significant previous medical care sees an internist at the behest of concerned family members. She says that her blood pressure (BP) was measured during a dental appointment long ago and was high.

During her initial visit, her BP, weight, and height are 170/100 mm Hg, 63 kg, and 1.5 m, respectively. Routine laboratory studies are normal except for the following: serum creatinine, 1.7 mg/dL (normal, 0.5 to 1 mg/dL); fasting glucose, 127 mg/dL (normal, 60 to 100 mg/dL); low-density lipoprotein cholesterol, 160 mg/dL (normal, less than 130 mg/dL); and trace proteinuria. The physician prescribes the calcium channel blocker nisoldipine 20 mg to be taken once daily.

At follow-up two weeks later, the patient's BP is 156/90 mm Hg and repeat blood tests confirm diabetes mellitus. The physician adds the angiotensin converting enzyme (ACE) inhibitor lisinopril to her regimen at a dosage of 10 mg daily. Two weeks after that, the patient's BP has dropped to 138/82 mm Hg and her creatinine has risen to 2.1 mg/dL. In response, the physician immediately stops the lisinopril. One month later, the patient's creatinine level has returned to baseline and her BP is 150/92. Reassured that the ACE inhibitor caused the rise in creatinine, the physician accepts the higher BP in favor of lower serum creatinine values and recommends that the patient avoid ACE inhibitors and angiotensin receptor blockers (ARBs) in the future.

CAN YOU IDENTIFY THE ERRORS?

It's possible to reduce BP using calcium channel blockers, but first-line therapy for hypertension is a thiazide diuretic, as was recently demonstrated by a large, randomized, controlled trial.[1] Although, compared to placebo, calcium channel blockers reduce the risk of

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stroke, major cardiovascular events, and death from cardiovascular causes, they don't reduce the risk of coronary artery disease, heart failure, or death from any cause as do thiazides.[2] If you were to use a calcium channel blocker to treat hypertension in this patient, then it should be a nondihydropyridine agent, such as diltiazem or verapamil, because this group has been associated consistently with a beneficial effect on kidney function.[3] Although 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins) should not be withheld from people with high cholesterol and chronic renal insufficiency, there is evidence that they are underused in this setting.[4,5]

The more important error in this case, however, was immediately stopping the ACE inhibitor after an initial, nonprogressive rise in serum creatinine. In this context, the elevation was likely an indirect indication that long-standing, detrimentally high, intraglomerular pressure had been reduced.[3] Instead of stopping the ACE inhibitor and missing the opportunity to use an agent that can both slow the progression of chronic renal disease and offer cardiovascular protection, the provider should have continued the drug and rechecked the lab values in one week to confirm that the creatinine concentration had stabilized over the course of therapy.[3] Generally, ACE inhibitors can be used with creatinine levels up to 2.1 or 2.2 mg/dL without difficulty.

Many physicians' initial response to deteriorating renal function is to decrease the dose of antihypertensive medication.[3] As BP rises, serum creatinine returns to baseline—an event the physician welcomes. Unfortunately, such an approach impedes the preservation of renal function over the long term and should be discouraged.[3] Patients with hypertension whose serum creatinine rises moderately with ACE inhibitor therapy are often those who would benefit most from tight BP control.

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GETTING TO THE ROOT OF THE PROBLEM

If serum creatinine rises 20% to 30% and then stabilizes, there's no reason to stop ACE inhibitor therapy—especially if good BP reduction has been achieved.[3] If the initial increase in serum creatinine is greater than 30% or if repeat measurements show a progressive rise in this value, then stop ACE inhibitor therapy and look for contributing causes of renal dysfunction. These would include bilateral, high-grade renal artery stenosis or—if the patient has only one kidney—unilateral renal artery stenosis; severe polycystic kidney disease with extrinsic compression of the renal arteries; intravascular volume depletion; heart failure; concurrent use of nonsteroidal anti-inflammatory drugs (NSAIDs); or sepsis.[3]

In patients with hypertension and chronic renal insufficiency, it's not uncommon for the serum creatinine level to rise as BP is lowered—especially now that the guidelines governing BP control have become more stringent.[2,6] This phenomenon usually occurs in chronic renal failure (particularly in that due to long-standing hypertension) and rarely is seen in normal renal function. It results from a shift in the autoregulatory relationship between the intraglomerular pressure and mean arterial pressure.[3]

In chronic renal failure, intraglomerular hemodynamics are more sensitive to changes in mean arterial pressure and more dependent on efferent artery tone. Additionally, the preglomerular circulation loses its ability to respond appropriately to a reduction in mean arterial pressure. This causes intraglomerular pressure and, subsequently, the glomerular filtration rate, to drop dramatically at a BP that normally wouldn't affect renal function.

In many patients, however, this initial decline in renal function will resolve after long-term BP control.[2,3] In the case of intravascular volume depletion or decreased effective arterial volume (as occurs in heart failure), maintenance of optimal renal hemodynamics is more dependent on efferent arteriolar tone, upon which ACE inhibitors exert much of their effect.

GOOD NEWS IN TREATMENT

Fortunately, thiazide diuretics, the clear first-line therapy for hypertension, are among the least ex-

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pensive antihypertensive agents and have few adverse effects. Furthermore, there are several ways to minimize adverse effects of ACE inhibitor therapy, so that it may remain part of the antihypertensive regimen.[3]

First, hypertensive patients who have chronic renal failure need to have their serum potassium level checked one to two weeks after starting an ACE inhibitor or an ARB. Those who develop hyperkalemia should follow a low potassium diet with specific precautions against salt substitutes. You can add thiazide or loop diuretics to the ACE inhibitor regimen, but remember that thiazide diuretics lose much of their effectiveness in moderate to severe renal failure when the glomerular filtration rate declines below 30 to 50 mL/min.[7] Be sure to discontinue such medications as NSAIDs, which can cause hyperkalemia by interfering with renal potassium excretion. Finally, if the renal failure is more severe with concurrent metabolic acidosis, sodium bicarbonate treatment or other forms of bicarbonate replacement, such as citrate, might be warranted. If these measures fail to bring the serum potassium concentration below 5.6 mmol/dL, discontinue the ACE inhibitor or ARB and initiate treatment with another antihypertensive that doesn't affect potassium clearance. Finally, patients with diabetes are at particularly high risk for nephropathy. Antihypertensive drug therapy, especially with ACE inhibitors, is indicated in such patients even if BP is only at the high end of normal.[2]

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