HCTZ Spurs Glucose Intolerance in Hypertension

BY MITCHEL L. ZOLER
Philadelphia Bureau

NEW YORK — An angiotensin receptor blocker was unable to counter the glucose intolerance triggered by a thiazide diuretic in a study of more than 200 patients with both metabolic syndrome and hypertension.

Hydrochlorothiazide (HCTZ) is known to cause glucose intolerance in patients. The new results show that adding an angiotensin receptor blocker (ARB) doesn't eliminate the problem, Dr. George L. Bakris said while presenting a poster at the annual meeting of the American Society of Hypertension.

The implication is that for patients who are hypertensive and who already have impaired glucose tolerance and normal kidney function, antihypertensive regimens should not initially include a thiazide diuretic, said Dr. Bakris, director of the Hypertension/Clinical Research Center at Rush University in Chicago.

For patients with a normal fasting glucose level, this restriction does not apply; they can start on whichever antihypertensive regimen their physician prefers. Additionally, patients with impaired renal function and hypertension need treatment with a diuretic, regardless of what impact the drug might have on their glucose tolerance, Dr. Bakris said in an interview.

The study, conducted by Dr. Bakris and his associates, enrolled 240 patients with hypertension and metabolic syndrome. Their fasting blood glucose level at entry had to be at least 100 mg/dL but no more than 125 mg/dL.

The patients were randomized to treatment with either a combination of the ACE inhibitor trandolapril and the sustained-release formulation of verapamil, a calcium channel blocker, or HCTZ plus the ARB losartan.

The dosages were titrated up as needed to reach a goal systolic pressure of less than 130 mm Hg, and treatment was continued for a year. The maximum daily dosages that the protocol allowed were 4 mg of trandolapril, 240 mg of verapamil, 100 mg of losartan, and 25 mg of HCTZ.

The study's primary end point was the change from baseline to the end of the study in the 2-hour postprandial glucose level using an oral glucose tolerance test. This end point was measured in 90% of the study participants.

For patients with impaired glucose tolerance, initial antihypertensive regimens should not include a thiazide diuretic.

DR. BAKRIS

After a year of treatment, the average 2-hour glucose level was 139 mg/dL in 108 patients treated with trandolapril and verapamil, an average reduction from baseline of 5 mg/dL. In contrast, the average 2-hour glucose level was 168 mg/dL in 107 patients treated with HCTZ and losartan, an average rise of 24 mg/dL, compared with baseline, a statistically significant difference between the two treatment groups.

Patients in the HCTZ plus losartan group had worse glucose tolerance by other, secondary measures as well, including a significantly higher 2-hour postprandial insulin level and an increased level of hemoglobin A_{1c}. By the end of the study, about 25% of patients in the HCTZ plus losartan group had developed new-onset diabetes, compared with about a 10% rate in the trandolapril plus verapamil group, a statistically significant difference.

The HCTZ plus losartan combination was slightly more effective at lowering systolic blood pressure. At the end of the study, about 45% of patients in the trandolapril plus verapamil group were at the goal pressure of less than 130 mm Hg, compared with about 55% of patients in the HCTZ and losartan group, but this difference did not reach statistical significance.

The study was sponsored by Abbott Laboratories, which markets a formulation of combined trandolapril plus verapamil (Tarka).

Dr. Bakris has received research support from, is a speaker for, and is a consultant to Abbott as well as several other drug companies. ■