Choice of Diuretic Therapy and Reconsideration for Aldosterone Receptors Blockers

To the Editor:

In an interesting editorial, Kaplan1 has focused recently on the choice of thiazide diuretics and concluded that chlorthalidone, alone or in addition to other antihypertensive drugs, may replace hydrochlorothiazide (HCTZ). The author also states that HCTZ and chlorthalidone, even at low doses (12.5 to 25.0 mg), can lower serum potassium and that an addition of small doses of spironolactone or eplerenone could provide maximal antihypertensive efficacy and prevent hypokalemia, particularly in resistant patients.

A very important issue dealing with all diuretics is the volume depletion and activation of the renin-angiotensin-aldosterone system. Diuretics, with the exception of aldosterone receptor blockers, do not directly affect mineralocorticoid receptors. Recent studies of the literature have shown that aldosterone, even in situations of normal sodium intake, can enhance oxidative stress through activation of NADPH oxidase in particular clinical situations. Aldosterone is involved in inflammation atherosclerosis and heart hypertrophy and fibrosis, and the addition of aldosterone receptor blockers prevents the risk of complications in patients with heart diseases treated with other drugs (Randomized Aldactone Evaluation Study and Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study).

Concerning the secondary hyperaldosteronism from diuretics, Brown and colleagues2,3 have compared the effect of HCTZ (25 mg per day) with the effect of spironolactone on the fibrinolytic balance in hypertensive subjects. Although HCTZ and spironolactone increased angiotensin II and aldosterone, only HCTZ increased plasminogen activator inhibitor 1 antigen concentration. Mineralocorticoid receptor antagonism prevents the effect of activation of the renin-angiotensin-aldosterone system on the plasminogen activator inhibitor 1 antigen in normotensive subjects and improves the fibrinolytic balance in hypertensive subjects through a potassium-independent mechanism, the same pro-oxidative effect that is evident when administering triamterene, thus supporting the concept that aldosterone receptor blockers do have a limited use in essential and secondary hypertension, particularly in Europe, as demonstrated by the Guidelines of the European Council of Hypertension (New Consensus Hypertension Guidelines from European Society of Hypertension/European Society of Cardiology 2007: Antihypertensive Treatment), which considers thiazides but not aldosterone receptor blockers for treatment of resistant hypertension, and maybe aldosterone receptor blockers should have a larger prescription, considering that metabolites with minimal (potassium canrenoate and canrenone) or absent (eplerenone) antiandrogenic activity are available in many countries.5

Disclosures

None.

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