PIC Question of the Week: 1/16/06

Q: Are there any general recommendations for the drug therapy of low-renin hypertension?

A: In the renin-angiotensin-aldosterone system (RAAS), renin (secreted by the kidney) converts angiotensinogen to angiotensin I. Angiotensin I is converted to angiotensin II by the action of angiotensin converting enzyme (ACE; also known as kininase II). Angiotensin II stimulates adrenocortical secretion of aldosterone and has direct vasopressor activity. The RAAS contributes to the maintenance of plasma volume and blood pressure. Renin levels may vary in patients with *essential* hypertension. They are generally low in cases of *secondary* hypertension due to diabetic nephropathy, primary aldosteronism, benign or malignant adrenocortical tumors that secret excess deoxycorticosterone, and familial forms of salt-sensitive hypertension. Due to variations in plasma renin activity, patients can be classified as having low-, normal-high-, or high-renin essential hypertension. Patients with low-renin essential hypertension (LREH) are characterized by having increased sensitivity to dietary salt, changes in plasma volume, and reduced response to ACE inhibitors, angiotensin receptor blockers (ARBs), and beta-blockers. They usually respond to calcium channel blockers, aldosterone inhibition, or diuretics. Those of African-American and Asian decent, diabetics, and the elderly are common groups who have the clinical features of salt-sensitivity, low-renin levels, and adequate response to diuretics. These patients may not optimally respond to monotherapy with ACEs, ARBs, and beta-blockers; however, the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) concluded that African-Americans can obtain successful blood pressure control if these agents are combined with a diuretic. Diuretics are usually effective for the treatment of LREH, but may produce metabolic complications such as hypokalemia, hyperglycemia, hyperuricemia, etc. Combining an ACE inhibitor with a diuretic should have a synergistic effect, particularly in LREH where increased aldosterone production has been observed. Aldosterone antagonists such as eplerenone (Inspra®) may be effective alternatives in patients with low-renin hypertension that is unresponsive to ACE inhibitors, ARBs, or diuretics.

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