Response to Can Large-Scale Trials or Meta-Analyses Demonstrate Blood Pressure–Independent Effect of Angiotensin Receptor Blockers?

Minami et al.1 put forward an interesting hypothesis on the existence of nonresponders to angiotensin receptor blockers (ARBs). However, this hypothesis does not refute that large trials or their meta-analyses2 can demonstrate blood pressure–independent influence of an antihypertensive drug, if any, but does prove that ARBs are less efficacious than other classes of antihypertensive agents, such as calcium channel blockers, in lowering blood pressure in hypertensive patients. We agree, and there is also evidence that there are more nonresponders to ARBs than to other antihypertensive agents. In theValsartan Antihypertensive Long-Term Use Evaluation Trial, although at the 6-month visit, a larger proportion of patients in the valsartan (80 to 160 mg/d) group proceeded to combination therapy with a diuretic or others than in theamlodipine (5 to 10 mg/d) group (57.3% versus 49.7%; P<0.0001), blood pressure was still significantly higher in the former group by 1.5 mm Hg systolic and 1.3 mm Hg diastolic.3,4 This small but significant blood pressure difference to a large extent may account for the outcome benefit ofamlodipine in comparison withvalsartan. The risk of myocardial infarction and stroke was lower in the amlodipine group than in thevalsartan group by 19% and 15%, respectively. With regard to the blood pressure–lowering efficacy in patients with hypertension, valsartan is not the only loser ARB in comparison withamlodipine. The Japanese Candesartan Antihypertensive Survival Evaluation in Japan Trial demonstrated thatcandesartan was also slightly less efficacious thanamlodipine in lowering blood pressure.5 In this well-designed and well-executed largescale trial, amlodipine was initiated with a dose of 2.5 mg/d, with the possible titration to 5 or 10 mg/d. The corresponding dosages forcandesartan were 4, 8, and 12 mg/d, respectively. Except for the initial 6 months, systolic blood pressure was ≈1 mm Hg lower in the amlodipine group than in thecandesartan group.

In special populations, such as patients with hypertension and diabetic nephropathy, an ARB can also be slightly more efficacious in lowering blood pressure than amlodipine. In theIrbesartan Diabetic Nephropathy Trial, systolic blood pressure reduction was ≈2 mm Hg greater in theirbesartan (300 mg/d) group than in theamlodipine group (10 mg/d).6 Irbesartan, compared withamlodipine, provided more protection against end-stage renal disease (−37%) and doubling of baseline serum creatinine (−23%) but provided less protection against myocardial infarction (+41%; P=0.04) and stroke (+40%; P=0.12). Thus, for the prevention of stroke and myocardial infarction, it would be difficult to expect any benefit from ARBs beyond blood pressure control. Nonetheless, as we wrote in the conclusions of our meta-analysis,2 certain drugs or classes of drugs might confer small blood pressure–independent superior or inferior influence on certain outcome measures or in certain populations. ARBs, as angiotensin-converting enzyme inhibitors, might provide more protection against congestive heart failure and renal dysfunction. However, these benefits might well be attributable to better blood pressure control of ARBs in the arterials because of their vasoactive effect.

Disclosures

None.

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