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Valsartan/Hydrochlorothiazide
A Viewpoint by Henry R. Black

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Angiotensin receptor blockers (ARBs) were added to the therapeutic choices to treat hypertension when losartan was introduced in 1995. Shortly thereafter, valsartan, irbesartan and now candesartan cilexetil and telmisartan became available. These agents block the AT_1 angiotensin receptor subtype, which when activated is responsible for most of the known actions of angiotensin, specifically its pressor and growth-promoting activities. These agents are remarkably well tolerated and all of the current representatives of this new class of antihypertensives have placebo-like tolerability profiles when evaluated in randomised double-blind studies. They have no metabolic effects, with the exception of a lowering of serum uric acid seen with losartan. However, they have not as yet demonstrated the degree of end organ protection and event reduction seen with ACE inhibitors, which block the renin-angiotensin-aldosterone system at a different site in the biochemical cascade.

The major problem some have found with ARBs, especially losartan and valsartan, is that they appear to be relatively weak antihypertensive agents that produce little additional response after a single dose titration (50 to 100mg for losartan and 80 to 160mg for valsartan). The combination of an ARB with a diuretic, however, provides additional reductions in blood pressure with no demonstrable increase in adverse events or biochemical perturbations.

Valsartan/hydrochlorothiazide (HCTZ) is a recently introduced fixed-dose combination now available as valsartan 80mg plus HCTZ 12.5mg or valsartan 160mg plus HCTZ 12.5mg. A large (n = 871) recently published study using a factorial design showed that this combination produced additive blood pressure reduction at all dose combinations and that a dose-response relationship was evident for both agents as monotherapy and for their combination.[1] The reduction in blood pressure for the valsartan 80mg plus HCTZ 12.5mg group, for example, was approximately 15/12mm Hg, while doubling the dose to valsartan 160mg plus HCTZ 25mg reduced blood pressure during the 8 weeks of the trial by 21/16mm Hg. Monotherapy with either agent was not as effective. As might be anticipated, more patients receiving HCTZ 25mg had a 20% drop in serum potassium (11%) than those receiving valsartan 160mg plus HCTZ 25mg (5%).[2] Adverse reactions and other biochemical changes were also insignificant with the combination.

The results of the Hypertension Optimal Treatment Study (HOT), which demonstrated the relative safety of aggressive management of hypertension, combined with the disappointingly low rates of control of hypertension in the US, has put a premium on drugs or regimens that effectively lower blood pressure.[3,4] Adding a small dose of thiazide to an ARB, such as with valsartan/HCTZ, allows the clinician to reduce blood pressure with extremely well tolerated agents and reinforces the concept that the clinician will often need to use >1 drug to reduce blood pressure to goal. Using a fixed-dose combination allows a degree of blood pressure reduction with a single pill therapy, simplifying the regimen for the patient and hopefully improving compliance.[5] ▲

References

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