



**Jiten Vora**  
Editor, Cardio Digest

## HYPERTENSION: HERE WE GO AGAIN!

Whilst there is incontrovertible evidence for the association of type 2 diabetes and hypertension resulting in a markedly increased risk of cardiovascular events, death and nephropathy, there is still dispute regarding the choice of class of antihypertensive agent, particularly in relation to type 2 diabetes. We continually hear information about which agent should be used first or second. Large scale studies have assisted in defining hypertension and delineating treatment targets. Such trials have also clearly established the therapeutic benefits of treatment which do not need to be further emphasised here.

Despite the findings of trials such as the UKPDS indicating the need for multiple therapeutic agents, controversy reigns about the superiority or inferiority of different drug classes, further fuelled by the recent publication of the ALLHAT study. Numerous articles have been published as a consequence (some more objective than others). Despite most published trials demonstrating the need for combination therapy in the great majority of patients, even with such combinations the attainment of the proposed targets of a blood pressure of less than 140 mmHg and less than 80 mmHg in type 2 diabetes is difficult. The proposed targets for patients with microalbuminuria and nephropathy are lower (125/75 mmHg) and even more difficult to attain.

Type 2 diabetes trials that compare calcium channel blockers with diuretics or  $\beta$  blockers (INSIGHT, NORDIL, STOP-2) demonstrated that there are no relative advantages for either class of compounds on major cardiovascular events, cardiovascular deaths and total mortality. A minor exception was related to heart failure, which was (not surprisingly) more common in patients receiving calcium antagonists compared with those receiving diuretic therapy as first line treatment (INSIGHT and ALLHAT). The studies comparing ACE inhibitors with calcium antagonists, (such as the ABCD-HT) suggest a minor benefit in favour of ACE inhibitors. However, the large trial comparing losartan with atenolol (LIFE) demonstrated a consistently significant reduction in major cardiovascular events, cardiovascular death and total mortality when patients were treated with losartan compared with atenolol. In patients with microalbuminuria and nephropathy, the angiotensin receptor antagonists demonstrate a significant renoprotective benefit over and above blood pressure control attained with other agents such as amlodipine (except in terms of cardiovascular events or all cause mortality). The ALLHAT trial (the largest trial in hypertension) was supposed to resolve all remaining issues in the treatment of hypertension. However, the design and conduct of the trial make interpretations of results difficult. Indeed despite its enormous size the ALLHAT trial has few practical implications for the management of hypertension except perhaps for the use of diuretic therapy early in the treatment regimen.

Given the overwhelming evidence that a major impact on cardiovascular events results from blood pressure lowering per se, with the proven requirement of combination therapies it is time to move away from the debate of the inferiority or superiority of a particular class of antihypertensive agents and to move on to the attainment of blood pressure treatment targets. Practical regimens will no doubt be developed by individual practitioners and will probably relate to the initial use of diuretics, followed by the use of agents interfering with the renin-angiotensin system with or without  $\beta$  blockade, and then by the use of calcium channel blockers and  $\alpha$  blockade.

Frohlich L, Sowers J (2003) Management of diabetic and hypertensive cardiovascular disease. *Current Hypertension Reports* **5**: 309–15

MacFarlane SI, Faray A, Sowers J (2003) Calcium antagonists in patients with type 2 diabetes and hypertension *Cardiovascular Drug Reviews* **21**(2): 105–18

Ruilope L (2003) Lessons from trials in hypertensive type 2 diabetes patients. *Current Hypertension Reports* **5**: 322–28