Cardio DIGEST
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Editorial

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Aggressive treatment of hypertension: pros and cons of various drug groups

Numerous studies have suggested treatment with diuretics and/or beta-blockers results in a greater risk for new-onset diabetes, compared with other drug classes (Opie et al, 2004). As many of these trials were of short duration, they were able to report differing effects of antihypertensives on new-onset diabetes, but were not able to address whether this resulted in an increased risk of cardiovascular end-points.

A recent study, of long duration and with sufficient events, allowed for comparison of cardiovascular end-points among people without diabetes, people with new-onset diabetes, and those previously diagnosed with diabetes (Verdecchia et al, 2004). The trial was an analysis of data from the Progetto Ipertensione Monitoraggio Ambulatiore (PIUMA) Observational Registry. Treatment for patients was individualised and included lifestyle changes and pharmacological measures. The period followed was of a median of six years. Thiazide diuretics included hydrochlorothiazide 12.5 mg to 25 mg daily. Within this cohort, 6.5 % had type 2 diabetes at baseline, and an additional 5.8 % developed new-onset diabetes during the course of the study.

Diuretics were utlised in approximately half of those with new-onset diabetes, a significantly higher proportion than 30 % diuretic use in the group of patients not developing diabetes. Angiotensin-converting enzyme (ACE) inhibitors were utilised in 34 %, 50 % and 58 % of patients without diabetes, new-onset diabetes and previously known diabetes respectively. Blood pressures achieved demonstrated a systolic blood pressure of 142 mmHg in those with new-onset diabetes compared with 156 mmHg in those with pre-existing diabetes, thus demonstrating a considerably lower systolic blood pressure in patients with new-onset diabetes. The relative risk of cardiovascular events in patients with new-onset diabetes compared with those patients who did not have diabetes before or during the study, was 2.92 in the new-onset diabetes and 3.57 in those with prior diabetes. The only two factors that are predicted independently for new onset of diabetes were high treatment glucose levels and the use of diuretics, even when prescribed in the low to moderate dose range.

While this study has implications for selection of antihypertensive medication, especially in the presence of inpaired glucose tolerance, it is important to not to form an over-simplified view in which some drug classes tend to cause diabetes (diuretics and beta-blockers) and others prevent it (ACE inhibitors and angiotensin II receptor antagonists). An important finding in the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) study (Dalhof et al, 2004), was that both the beta-blocker and angiotensin II receptor antagonist-based therapies were associated with new-onset diabetes, although the rate was significantly greater in the beta-blocker group. An important question that remains unanswered is whether the blockers of the renin-angiotensin system delay new-onset diabetes rather than prevent it.

While data from such trials may make clinicians who are already reluctant to use diuretics become even more so, it is important to recognise that diuretics, even as low-dose adjuncts to other drugs, are necessary for achieving adequate blood pressure control in many patients, particularly those with diabetes. Ultimately, the most effective strategy for protecting patients with diabetes from cardiovascular events is aggressive treatment of hypertension.

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Dalhof B, Deveraux RB, Kjeldsen SE, et al (2004) Cardiovascular morbidity and mortality in the Losartan Intervention for Endpoint Reduction in Hypertension Study (LIFE): a randomised trial against atenolol. *Lancet* **359**: 995–1003

Opie LH, Schall R (2004) Old antihypertensives and new diabetes. *Journal of Hypertension* **22**: 1453–58

Verdecchia P, Reboldi G, Angeli, et al (2004) Adverse prognostic significance of new diabetes in treated hypertensive subjects. *Hypertension* **43**: 963–69