Major journals

Thiazide-type diuretics in people with hypertension and glucose metabolism disturbances: A first-line therapy?

Marc Evans, Consultant Physician, Llandough Hospital, Cardiff

The combination of type 2 diabetes and hypertension is common and results in a potent risk for cardiovascular disease and end-stage renal disease. Small elevations in blood pressure combined with impairments in glucose homeostasis, such as impaired fasting glucose, also increase risk.

Blood pressure reduction is an effective means of reducing vascular risk in type 2 diabetes, and agents that interfere with the renin–angiotensin system are recommended as first-line therapy in patients with diabetes and protenuria. There is less certainty, however, regarding the optimal choice of first-step antihypertensives in patients with diabetes and little or no renal damage.

The Antihypertensive and Lipid Lowering treatment to prevent Heart Attack Trial (ALLHAT; see right) sought to determine whether treatment with a calcium-channel blocker or an angiotensin-converting enzyme inhibitor decreases clinical complications compared with a thiazide-type diuretic in patients with type 2 diabetes, (n=13 101), impaired fasting glucose (n=1399) or normoglycaemia (n=17 012). This study is the largest and most diverse for comparing first-step antihypertensive drug therapy in patients with type 2 diabetes and impaired fasting glucose.

All study participants were aged 55 years or older, with hypertension and glucose tolerance status defined on the basis of American Diabetes Association criteria. Participants were randomly assigned to double-blind, first-step antihypertensive treatment with chlorthalidone (12.5–25 mg), amlodipine (2.5–10 mg) or lisinopril (10–40 mg). An intention-to-treat analysis of fatal coronary heart disease, non-fatal myocardial infarction, total mortality and other clinical complications was conducted.

Overall, the pattern of efficacy of chlorthalidone compared with amlodipine and lisinopril was similar for the three glycaemic criteria. There were a few statistically significant observations: a higher risk was noted for non-fatal myocardial infarction in the impaired fasting glucose group assigned to amlodipine relative to that for chlorthalidone; stroke was more common in the normoglycaemic participants assigned to lisinopril relative to those on chlorthalidone; and heart failure was more common in participants with either type 2 diabetes or normoglycaemia assigned to amlodipine and lisinopril compared with those on chlorthalidone. These findings must be interpreted with caution, though.

The most conservative interpretation of these data is that there is no evidence of superiority for treatment with lisinopril or amlodipine compared with chlorthalidone in any of the three glycaemic criteria. More detailed analyses of the impact of glucose disorders on clinical outcomes, treatment-related changes in renal function and experience in sub-groups defined by age, ethnic group and sex are awaited.

Nevertheless, accepting the constraints in the interpretation of clinical trials, the data from this study suggest that thiazide-type diuretics should be considered as first-line therapy in patients with hypertension and disturbances in glucose metabolism.

ARCHIVES OF INTERNAL MEDICINE

Complications with diuretics not worse than those with antihypertensives

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓✓

1 There is uncertainty about the optimal first-line antihypertensive to use for people with impaired fasting glucose (IFG) or type 2 diabetes.

2 The authors aimed to establish whether using a calcium-channel blocker or an angiotensin-converting enzyme (ACE) inhibitor led to fewer clinical complications than using a thiazide-type diuretic.

3 An intention-to-treat analysis was carried out in participants from the Antihypertensive and Lipid-Lowering treatment to prevent Heart Attack Trial (ALLHAT), of whom 13 101 had type 2 diabetes, 1399 had IFG and 17 012 had normoglycaemia.

4 For the primary outcome (fatal coronary heart disease or non-fatal myocardial infarction), comparing amlodipine or lisinopril with chlorthalidone, there was no significant risk difference in people with type 2 diabetes or normoglycaemia.

5 There was a significant increase in risk, though, for amlodipine relative to chlorthalidone in people with IFG (relative risk [RR], 1.73; 95% confidence interval [CI], 1.10–2.72; P=0.01).

6 There was also a significant increase in the risk of heart disease in people with type 2 diabetes for amlodipine relative to chlorthalidone (RR, 1.39; 95% CI, 1.22–1.59; P<0.001).

Whelton PK, Barzilay J, Cushman WC et al (2005) Clinical outcomes in antihypertensive treatment of type 2 diabetes, impaired fasting glucose concentration, and normoglycemia: Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *Archives of Internal Medicine* **165**(12): 1401–9

THE NEW ENGLAND JOURNAL OF MEDICINE

Major drug-eluting stents are similarly efficient

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 No published data are available about the relative efficacy of differing drug-eluting stents.

2 This prospective randomised trial aimed to provide efficacy data on paclitaxel- and sirolimus-eluting stents in people with diabetes and coronary heart disease.

3 Of 250 people, 125 each were randomised to receive one or other of these drug-eluting stents. The primary endpoint was in-segment late luminal loss. Secondary endpoints included the need for revascularisation of the initial lesion within 9 months of the first treatment.

4 The sirolimus-eluting stent was found to reduce the extent of late luminal loss, indicating a lower risk of restenosis. No other significant differences were observed between the two stents.

Dibra A, Kastrati A, Mehilli J et al (2005) Paclitaxel-eluting or sirolimus-eluting stents to prevent restenosis in diabetic patients. *The New England Journal of Medicine* **353**(7): 663–70

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

Insulin resistance predicts CHD

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 A large (n=1187), prospective, community-based, observational cohort (≥70 years old) with no congestive heart failure (CHD) or valvular disease at baseline (1990–1995) were followed up until the end of 2002 to determine whether insulin resistance is a predictor of CHD, and whether insulin resistance could provide a link between obesity and CHD.

2 Insulin resistance was found to predict CHD in this cohort, independent of any other risk factors such as diabetes.

3 The presented results also suggest a link between obesity and CHD which, the authors conclude, could result from insulin resistance.

Ingelsson E, Sundstrom J, Arnlov J et al (2005) Insulin resistance and risk of congestive heart failure. *Journal of the American Medical Association* **294**(3): 334–41

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

Lipid ratios and predicting future CV events

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 As current clinical guidelines do not offer any consensus between different lipid ratios and their use in predicting future cardiovascular (CV) events, lipid ratios and their appropriateness to do so was assessed in this prospective cohort study of 15 632 women over 45 years of age.

2 The analysis supports the use of standard (HDL-cholesterol, LDL-cholesterol, and non-HDL-cholesterol) lipid measures and ratios rather than apolipoproteins A-1 and B_{100} in primary CV risk detection.

3 The authors end by stating that their data should not be construed to mean that the aforementioned apolipoproteins should not be used in monitoring patients, such as those taking statins.

Ridker PM, Rifai N, Cook NR et al (2005) Non-HDL cholesterol, apolipoproteins A-1 and B_{100}, standard lipid measures, lipid ratios, and CRP as risk factors for cardiovascular disease in women. *Journal of the American Medical Association* **294**(3): 326–33

ARCHIVES OF INTERNAL MEDICINE

Blood pressure regimens equally effective in diabetes

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓✓

1 The Blood Pressure (BP)-Lowering Treatment Trialist's Collaboration was set up in 1995 to analyse the outcomes of randomised trials of BP-lowering treatment with respect to their effect on major cardiovascular (CV) events.

2 For this paper the Collaboration analysed 27 randomised trials (n=158 709), from which 33 395 people had diabetes, in order to assess the effectiveness of different BP-lowering regimens on major CV events in people with and without diabetes.

3 Regimens based on angiotensin-converting enzyme inhibitors, calcium channel blocker, angiotensin receptor blockers and diuretics/β-blockers all reduced the total number of major CV events to a statistically comparable level.

4 Limited evidence was found to support lower BP goals in diabetes, as they did not produce as significant lowering of major CV events in people with versus without diabetes.

5 The Collaboration concludes that, in treating people with diabetes and high blood pressure, all BP-lowering regimens analysed seem to be equally effective in reducing CV-related short- and medium-term risks of diabetes.

6 This is especially important for those clinicians working in resource-poor areas, where cost of therapy is a crucial consideration.

Turnbull F, Neal B, Algert C et al (2005) Effects of different blood pressure-lowering regimens on major cardiovascular events in individuals with and without diabetes mellitus. Results of prospectively designed overviews of randomized trials. *Archives of Internal Medicine* **165**(12): 1410–9

"The results also suggest a link between obesity and CHD which could result from insulin resistance."