Metabolic neutrality of combined verapamil-trandolapril treatment in contrast to beta-blocker-low-dose chlortalidone treatment in hypertensive type 2 diabetes

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OBJECTIVE: To investigate the metabolic, antihypertensive and albuminuria-modifying effects of a heart rate-modulating calcium antagonist-angiotensin converting enzyme inhibitor combination compared with those of a beta-blocker-low-dose diuretic combination in non-insulin-dependent diabetic hypertensives. DESIGN: A prospective randomized double-blind study. SUBJECTS AND METHODS: Twenty-four diabetics with diastolic blood pressure 90-115 mmHg without azotemia (plasma creatinine level < 150 mumol/l) were evaluated after 4 weeks receiving placebo and 12 weeks receiving treatment either with combined slow-release verapamil (retard formulation) and trandolapril (mean maintenance doses, 180 and 1.6 mg daily) or with atenolol and chlortalidone (71 and 18 mg daily). Insulin sensitivity (by the minimal model method of Bergman), additional metabolic variables, clinic blood pressure, ambulatory blood pressure profile and renal indices were assessed at the end of the placebo and active treatment phases. RESULTS: Compared with placebo, the two therapies produced similar decreases in mean supine clinic blood pressure [10 +/- 3 versus 11 +/- 3% (means +/- SEM)], upright clinic blood pressure (10 +/- 4 versus 11 +/- 4%) and ambulatory daytime blood pressure (9 +/- 2 versus 12 +/- 3%). However, although the verapamil-trandolapril combination was found to be metabolically neutral, the atenolol-chlortalidone combination aggravated insulin resistance [insulin sensitivity index, from (0.8 +/- 0.2) to (0.3 +/- 0.1) x 10(-4)/min per U per ml], increased the serum triglycerides level and decreased the high-density lipoprotein cholesterol and plasma potassium levels. Although both therapies tended to reduce 24 h albuminuria, this was significant for the verapamil-trandolapril treatment only. CONCLUSIONS: Because the effect of any antihypertensive drug, including diuretics and beta-blockers, on cardiovascular morbidity and on mortality in non-insulin-dependent diabetic patients is not known, rational treatment selection can presently be based only on surrogate end-points. Therefore, the triad of metabolic neutrality with antihypertensive and antiproteinuric efficacy supports combined verapamil-trandolapril as a potentially valuable therapy for hypertension accompanying diabetes mellitus.
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