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VALUE: analysis of results

André J Scheen

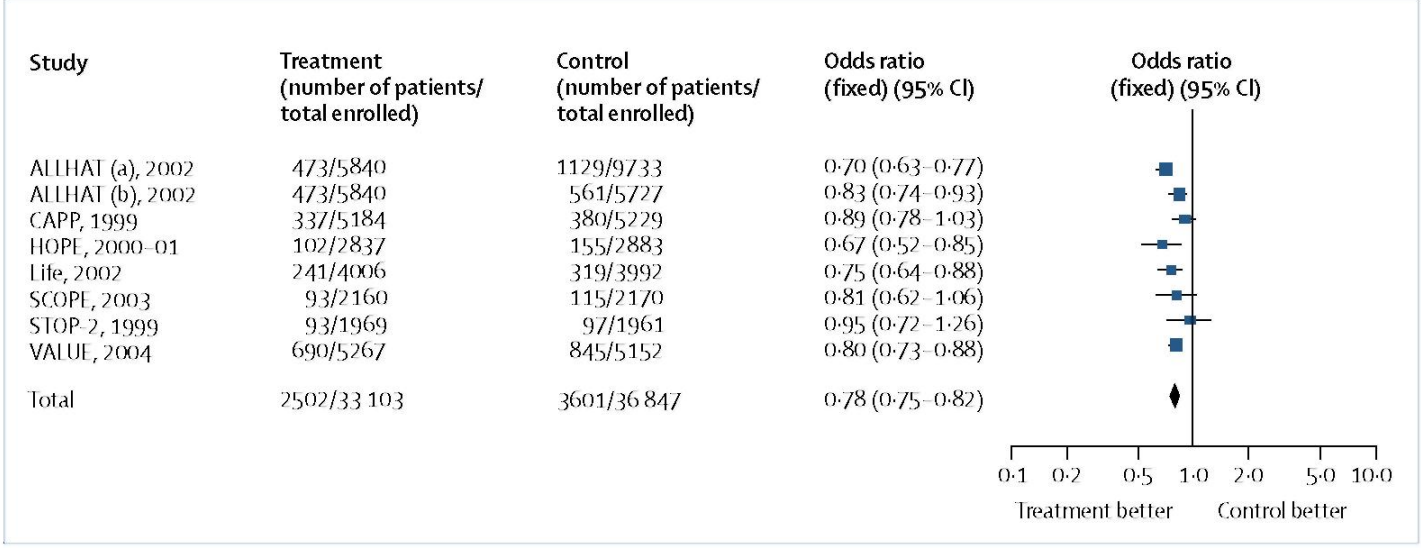
Division of Diabetes, Nutrition and Metabolic Disorders, Department of Medicine, CHU SartTilman, B-4000 Liège, Belgium.
Andre.Scheen@chu.ulg.ac.be

In the VALUE trial,[1] new-onset diabetes arose in significantly fewer hypertensive patients on valsartan, an angiotensin receptor AT1 blocker (ARB), than on amlodipine, a metabolically neutral calcium-channel blocker, after a mean follow-up of 4.2 years. This finding confirms and extends the results of the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)[2] in which the incidence of diabetes was lower in hypertensive patients on lisinopril, an angiotensin converting enzyme (ACE) inhibitor, than on amlodipine. In ALLHAT, the between-group difference was even greater when lisinopril was compared with the diuretic chlorthalidone.

The findings of a systematic review of the published work[3] indicate, in seven large randomised clinical trials done in patients with arterial hypertension with cardiovascular prognosis as primary endpoints, a possible beneficial effect of blockade of the renin-angiotensin system on the frequency on new-onset type 2 diabetes (defined, however, using various criteria and analysed as a secondary endpoint or in post-hoc analysis). Overall, and after a mean follow up ranging from 3.7 to 6.1 years, 2502 new cases of diabetes (8%) were observed in the group of 33 103 patients who received treatment with ACE inhibitors or ARBs by comparison with 3601 of 36 847 (10%) controls (figure). The findings of this analysis showed a mean weighed relative risk reduction of new diabetes of 22% (95% CI 18-25; p<0.0001) after inhibition of the renin-angiotensin system. No significant heterogeneity was observed between trials (p=0.07). The beneficial effect was significant and similar with ACE inhibitors (hazard ratio 0-78; p<0.0001) and with ARBs (0-79; p<0.0001), and observed whatever the comparator considered. The number needed to treat to avoid one new case of diabetes averaged 45 patients over about 5 years. A similar relative risk reduction in the frequency of diabetes after inhibition of the renin-angiotensin system was reported in the CHARM-Overall programme,[4] comparing the effects of candesartan with those of placebo in patients with congestive heart failure (hazard ratio 0.78, 95% CI 0.64-0.96; p=0.020).

Inhibition of the renin-angiotensin system consistently and significantly reduces the incidence of type 2 diabetes mellitus in individuals with arterial hypertension and congestive heart failure. The underlying mechanisms seem complex and include effects of inhibition of the renin-angiotensin system on both insulin action and insulin secretion.[5] Considering the pandemic of the disease, inhibition of the renin-angiotensin system deserves further attention among the strategies aimed at preventing type 2 diabetes mellitus.

Figure: *Meta-ana lysis of seven randomised clinical trials assessing the effect of inhibition of the reninangiotensin system on incidence of new diabetes in patients with arterial hypertension. ALLHAT(a)=comparison of lisinopril vs chlorthalidone. ALLHAT(b)=comparison of lisinopril vs amlodipine.* χ^2 *test for heterogeneity p=0.07. Test for overall effect p<0.0001.*



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