Losartan reduced stroke and new onset diabetes more than atenolol in essential hypertension with signs of left ventricular hypertrophy

Dahlöf B, Devereux RB, Kjeldsen SE, et al. Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. *Lancet* 2002 Mar 23;359:995–1003.

QUESTION: In patients with essential hypertension and signs of left ventricular hypertrophy (LVH), is losartan based treatment more effective than atenolol based treatment?

Design

Randomised (unclear allocation concealment), blinded (patients and monitoring committee), controlled trial with ≥ 4 years of follow up.

Setting

Multicentre trial in Europe and the US.

Patients

9222 patients 55–80 years of age (mean age 67 y, 54% women) with hypertension (sitting blood pressure [BP] of 160–200 mm Hg systolic, 95–115 mm Hg diastolic, or both after 1–2 wks of placebo) and electrocardiographic signs of LVH. Exclusion criteria included secondary hypertension; myocardial infarction (MI) or stroke within the previous 6 months; angina pectoris requiring treatment with β blockers or calcium antagonists; and heart failure or left ventricular ejection fraction $\leq 40\%$. Follow up was 99%.

Intervention

Patients were allocated to losartan based treatment (n=4605) or atenolol based treatment (n=4588). Losartan and atenolol were started at 50 mg/day and combined with low dose hydrochlorothiazide, increased to 100 mg/day, and supplemented with other antihypertensives (except β blockers, angiotensin converting enzyme inhibitors, or angiotensin receptor blockers) to reach a target BP of $< 140/90$ mm Hg.

Main outcome measures

The primary end point was a composite of cardiovascular mortality, MI, and stroke. One of the secondary end points was new onset diabetes.

Main results

Analysis was by intention to treat. The composite end point, fatal or non-fatal stroke, and new onset diabetes occurred less frequently in patients assigned to losartan than in those assigned to atenolol (table). No differences existed between the groups for cardiovascular mortality or MI. BP control, dose titration, and use of other antihypertensives were similar in both groups.

Conclusion

In patients with essential hypertension and signs of left ventricular hypertrophy, losartan reduced strokes and new onset diabetes more than atenolol.

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Losartan based treatment v atenolol based treatment for essential hypertension with signs of left ventricular hypertrophy*

Outcomes	Losartan	Atenolol	RRR (95% CI)	NNT (CI)
Composite end point†	11%	13%	12% (2 to 22)	64 (36 to 418)
Stroke	5%	7%	24% (11 to 36)	61 (42 to 140)
New onset diabetes	6%	8%	24% (12 to 36)	52 (35 to 108)

*Abbreviations defined in glossary; RRR, NNT, and CI calculated from data in article.

†Cardiovascular mortality, stroke, and myocardial infarction.

COMMENTARY

Although effective BP control in patients with hypertension and diabetes has been shown to decrease the frequency of subsequent cardiovascular disease, the added benefits of newer classes of drugs that interfere with the action of angiotensin are unclear.¹ In a large multicentre study, Dahlöf *et al* attempted to differentiate the relative advantages of losartan, a selective angiotensin II type 1 receptor blocker, with those of the more widely prescribed atenolol, a β blocker. The 2 groups were closely matched for key demographic indicators, including severity of hypertension, prevalence of coexisting cardiovascular conditions, Framingham risk scores, and electrocardiographic LVH criteria.

The study found that losartan improved cardiovascular outcomes over a 4 year period. The effect on BP did not differ between the 2 study groups, and so the benefits of the drug arise from an effect over and above control of BP. Fewer patients in the losartan group stopped taking the drug because of serious side effects compared with patients in the atenolol group. This is an important finding because long term compliance with medication treatment is necessary to achieve long term control of hypertension and to improve cardiovascular outcomes.

The results of this study should be viewed in light of several limitations. Although approximately 25% of patients treated for hypertension in this age group had left ventricular diastolic dysfunction with normal ejection fractions, this percentage still reflects only a small subset of patients. Patients with other forms of coronary artery disease, including recent MI or angina pectoris, were excluded. This is an important exclusion criterion because many patients in this age range are often at risk for coronary artery disease. The patients were middle aged or older, mainly Caucasian, and from western countries, and so the results may not be generalisable to other populations. The cost effectiveness of losartan remains unclear, as no economic data were reported in this study.

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1 Neal B, MacMahon S, Chapman N, et al. Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: results of prospectively designed overviews of randomised trials. *Lancet* 2000;356:1955–64.