Review: atenolol may be ineffective for reducing cardiovascular morbidity or all cause mortality in hypertension

Carlberg B, Samuelsson O, Lindholm LH. Atenolol in hypertension: is it a wise choice? *Lancet* 2004;**364**:1684–9.

Clinical impact ratings GP/FP/Primary care ★★★★★★☆ IM/Ambulatory care ★★★★★★★ Cardiology ★★★★★☆☆

Q In patients with essential hypertension, does atenolol reduce cardiovascular morbidity or all cause mortality?

METHODS

Data sources: *Cochrane Library*, Medline, relevant textbooks, and researchers in hypertension.

Study selection and assessment: randomised controlled trials (RCTs) that assessed the effect of atenolol (as the sole first line drug in 1 of the treatment groups) on cardiovascular morbidity or mortality in patients with essential hypertension.

Outcomes: myocardial infarction (MI), stroke, cardiovascular mortality, and all cause mortality.

MAIN RESULTS

8 RCTs met the selection criteria. 2 major comparisons were made. *Atenonol compared with placebo or with untreated controls* (4 RCTs, n = 6825). Mean reduction in blood pressure (BP) attributed to atenolol ranged from 4.0–18.0 mm Hg systolic and 2.9–11.0 mm Hg diastolic. The groups did not differ for MI, stroke, cardiovascular mortality, or all cause mortality (table). *Atenolol compared with other antihypertensive drugs* (5 RCTs, n = 17 671). Mean BP change with atenolol compared with alternatives ranged from –1.0 to 1.1 mm Hg systolic and −1.0 to 0.5 mm Hg diastolic. The rates of stroke, and cardiovascular and all cause mortality were greater in the atenolol group than in the other antihypertensive drug group (table). The groups did not differ for rates of MI (table).

CONCLUSIONS

In patients with essential hypertension, atenolol is not better than placebo or no treatment for reducing cardiovascular morbidity or all cause mortality. However, compared to other antihypertensive drugs, it may increase the risk of stroke or death.

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Abstract and commentary also appear in ACP Journal Club.

Commentary

The 1985 MRC trial first suggested that β blockers were relatively ineffective first line treatment for primary prevention of hypertensive outcomes.[1] The meta-analysis by Carlberg *et al* suggests that the performance of atenolol is feeble compared with other antihypertensive drug classes or with placebo. Although BP was lowered with atenolol in all of the included trials, the overall risk of MI and other outcomes was not.

Are all relevant trials included? For the most part, yes—although the large INVEST trial[2] was excluded, its inclusion would not have changed the results. A limitation is that few RCTs have evaluated atenolol as first line, with 2 of 4 placebo comparisons involving secondary prevention after transient ischaemic attacks.

Preliminary results from the large ASCOT open label trial were recently presented to the American College of Cardiology Annual Scientific Session;[3] some 19 000 higher risk patients with hypertension were randomised to atenolol 50–100 mg, then bendrofluazide 1.25–2.5 mg if needed, or to amlodipine 5–10 mg, then perindopril 4–8, mg per day if needed. ASCOT was stopped early because, although the groups did not differ for the primary outcome of non-fatal MI and fatal coronary heart disease, the amlodipine-based arm had lower rates of all cause mortality (hazard ratio [HR] 0.86, p = 0.005) and all coronary events (HR 0.86, p = 0.005). The amlodipine plus perindopril group was also associated with a lower rate of tested new onset diabetes (HR 0.68, p<0.001).

In summary, the meta-analysis by Carlberg *et al* and newer data suggest that atenolol, when used first line for hypertension, is inferior to several other medications.

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1 Medical Research Council Working Party. *Br Med J (Clin Res Ed)* 1985;**291**:97–104.
2 Pepine CJ, Handberg EM, Cooper-DeHoff RM, *et al*. *JAMA* 2003;**290**:2805–16.
3 Anglo-Scandinavian Cardiac Outcomes Trial: Blood Pressure-Lowering Arm: Presented at the American College of Cardiology 2005 Annual Scientific Session (ASCOT - Blood Pressure Arm). www.accardio.org/cs/pops/trialSum.asp?trialID = 1256 (accessed 13 Apr 2005).

Atenolol *v* placebo or no treatment or *v* other antihypertensive drugs in essential hypertension at mean 4.6 years*

Outcomes	Comparisons	Number of trials (number of patients)	Weighted event rates	RRR (95% CI)	NNT
Myocardial infarction	Atenolol *v* placebo or no treatment	4 (6392)	7.2% *v* 7.2%	1% (−19 to 17)	Not significant
Stroke			7.2% *v* 8.2%	15% (−1 to 28)	Not significant
Cardiovascular mortality			8.0% *v* 8.0%	1% (−18 to 17)	Not significant
				RRI (CI)	**NNH (CI)**
All cause mortality	Atenolol *v* other antihypertensive drugs	4 (14 468)	13.3% *v* 13.3%	1% (−11 to 15)	Not significant
Myocardial infarction			4.5% *v* 4.5%	4% (−11 to 20)	Not significant
Stroke			5.2% *v* 4.2%	30% (12 to 50)	100 (50 to 100)
Cardiovascular mortality			5.4% *v* 4.4%	16% (0 to 34)	100 (100 to ∞)
All cause mortality		5 (17 671)	8.1% *v* 7.1%	13% (2 to 25)	100 (100 to ∞)

*Abbreviations defined in glossary; weighted event rates, RRR, RRI, NNT, NNH, and CI calculated from data in article using a fixed effects model.