

Review: Atenolol may be ineffective for reducing cardiovascular morbidity or all-cause mortality in primary hypertension

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

QUESTION

In patients with primary hypertension, does atenolol reduce cardiovascular morbidity or all-cause mortality?

METHODS

Data sources: The Cochrane Library, MEDLINE, relevant textbooks, and researchers in hypertension.

Study selection and assessment: Randomized 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 primary hypertension. Studies were also required to have predefined criteria for myocardial infarction, stroke, and cardiovascular death.

Outcomes: Myocardial infarction, stroke, cardiovascular mortality, and all-cause mortality.

MAIN RESULTS

8 RCTs met the selection criteria. 1 of the 8 RCTs had 3 arms corresponding to treatment with atenolol, a thiazide diuretic, or placebo. 2 major comparisons were made. *Atenolol compared with placebo or with untreated controls (4 RCTs, n = 6825):* Mean reduction in blood pressure (BP) attributed to atenolol ranged from 4.0 to 18.0 mm Hg systolic and 2.9 to 11.0 mm Hg diastolic. The groups did not differ for myocardial infarction, stroke, cardiovascular mortality,

or all-cause mortality (Table). *Atenolol compared with other antihypertensive drugs (5 RCTs, n = 17 671):* Comparison antihypertensive drugs included hydrochlorothiazide or bendroflumethiazide (1 RCT), hydrochlorothiazide (1 RCT), captopril (1 RCT), losartan (1 RCT), and lacidipine (1 RCT). 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 myocardial infarction (Table).

CONCLUSIONS

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

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Atenolol vs placebo or no treatment or vs other antihypertensive drugs in primary hypertension at mean 4.6 years*

Comparisons	Number of trials (n)	Outcomes	Weighted event rates	RRR (95% CI)	NNT	
Atenolol vs placebo or no placebo	4 (6392)	Myocardial infarction	7.2% vs 7.2%	1% (-19 to 17)	NS	
		Stroke	7.2% vs 8.2%	15% (-1 to 28)	NS	
		Cardiovascular mortality	8.0% vs 8.0%	1% (-18 to 17)	NS	
				RRI (CI)	NNH (CI)	
			All-cause mortality	13.3% vs 13.3%	1% (-11 to 15)	NS
Atenolol vs other antihypertensive drugs	4 (14 468)	Myocardial infarction	4.5% vs 4.5%	4% (-11 to 20)	NS	
		Stroke	5.2% vs 4.2%	30% (12 to 50)	100 (50 to 100)	
		Cardiovascular mortality	5.4% vs 4.4%	16% (0 to 34)	100 (100 to ∞)	
		5 (17 671)	All-cause mortality	8.1% vs 7.1%	13% (2 to 25)	100 (100 to ∞)

*NS= not significant. Other abbreviations defined in Glossary; weighted event rates, RRR, RRI, NNT, NNH, and CI calculated from data in article using a fixed-effects model.

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 and colleagues 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 for myocardial infarction 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 therapy, with 2 of 4 placebo comparisons involving secondary prevention after transient ischemic 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 randomized to atenolol 50 to 100 mg, then bendroflumethiazide 1.25 to 2.5 mg if needed, or to amlodipine 5 to 10 mg, then perindopril 4 to 8 mg per day if needed. ASCOT was stopped early because, although the groups did not differ for the primary outcome of nonfatal

myocardial infarction 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 new-onset diabetes (HR 0.68, *P* < 0.001).

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

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