

Review: β -blockers are less effective than other antihypertensive drugs for reducing risk for stroke in primary hypertension

Lindholm LH, Carlberg B, Samuelsson O. Should beta blockers remain first choice in the treatment of primary hypertension? A meta-analysis. *Lancet*. 2005;366:1545-53.

Clinical impact ratings: GIM/FP/GP ★★★★★☆ Cardiology ★★★★★☆

QUESTION

In patients with primary hypertension, are β -blockers more effective than placebo or other antihypertensive drugs for reducing stroke, myocardial infarction (MI), and all-cause mortality?

METHODS

Data sources: PubMed and the Cochrane Library.

Study selection and assessment: Randomized controlled trials (RCTs) that compared β -blockers as first-line treatment with placebo, no treatment, or other antihypertensive drugs in patients with primary hypertension, and evaluated all-cause mortality, cardiovascular morbidity, or both. Subgroup analyses were conducted for nonatenolol β -blockers, mixed β -blockers or diuretics, and atenolol.

Outcomes: All-cause mortality, stroke, and MI.

MAIN RESULTS

13 RCTs ($n = 133\,384$) met the selection criteria. β -blockers were compared with placebo or no treatment (7 RCTs, $n = 27\,433$) and other antihypertensive drugs (13 RCTs, $n = 105\,951$). Patients who received β -blockers had a lower incidence of stroke than did patients who received placebo or no treatment, but had a higher incidence of stroke than those who received other antihypertensive drugs (Table). Patients

who received atenolol had a higher incidence of stroke (relative risk [RR] 1.26, 95% CI 1.15 to 1.38) and all-cause mortality (RR 1.08, CI 1.02 to 1.14) than patients who received other antihypertensive drugs, but they did not differ for MI. Patients who received nonatenolol β -blockers or mixed β -blockers or diuretics did not differ from those who received other antihypertensive drugs for any outcome.

CONCLUSIONS

In patients with primary hypertension, β -blockers are better than placebo or no treatment for reducing risk for stroke. Compared with other antihypertensive drugs, β -blockers increase risk for stroke.

Source of funding: County of Vasterbotten, Sweden.

For correspondence: Professor L.H. Lindholm, Umea University Hospital, Umea, Sweden. E-mail Larsh.lindholm@fammed.umu.se. ■

β -blockers vs placebo, no treatment, or other antihypertensive drugs in primary hypertension at mean 4.6 years*

Outcomes	Number of trials (n)	Weighted event rates		RRR (95% CI)	NNT (CI)
		β -blocker	Placebo or no treatment		
All-cause mortality	7 (27 433)	5.4%	5.7%	5.0% (-4 to 14)	Not significant
Stroke	7 (27 433)	2.6%	3.2%	19% (7 to 29)	165 (108 to 447)
MI	7 (27 433)	3.6%	3.9%	7.0% (-5 to 17)	Not significant

Outcomes	Number of trials (n)	β -blocker	Other antihypertensive drugs	RRI (CI)	NNH (CI)
Stroke	12 (105 845)	3.5%	3.0%	16% (4 to 30)	209 (112 to 834)
MI	12 (105 845)	3.9%	3.8%	2.0% (-7 to 12)	Not significant

*MI = myocardial infarction. Other abbreviations defined in Glossary; weighted event rates, RRR, RRI, NNT, NNH, and CI calculated from relative risks in article.

COMMENTARY

Drug trials for hypertension seek blood pressure (BP) reduction to goal levels, acceptable adverse effects profiles, and net benefit for key outcomes, such as MI and stroke.

Correlation remains limited between BP reductions by antihypertensive agents and the ultimate goal of treatment, namely, reduced rates of target organ damage, cardiovascular morbidity, and mortality. Drugs producing similar reductions in BP may produce dissimilar clinical outcomes over the long term.

Despite their traditional place in antihypertensive pharmacology, β -blockers have received mixed reviews about net survival benefit, especially when atenolol has been compared with metoprolol, highlighting the possibility of dissimilar, long-term effects from medications of the same drug class (1). Postulated but as yet unproven causes for dissimilar long-term effects include a deranged lipid profile, exacerbated insulin resistance, and increased platelet aggregation. These alterations may accompany the common dominance of peripheral resistance over cardiac output among older hypertensive patients.

In response to the study by Lindholm and colleagues, clinicians should reconsider important comorbid conditions for individual patients. While those with documented coronary insufficiency or congestive heart failure may exhibit net benefit from using β -blockers as antihypertensive agents, other hypertensive patients may accrue less benefit and can potentially have an increased risk for stroke. The large number of alternative antihypertensive agents allows for some thoughtful substitutions. From this study, alternative drugs include thiazide diuretics, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, and calcium-channel blockers.

Peter Rudd, MD
Stanford University School of Medicine
Stanford, California, USA

Reference

1. Soriano JB, Hoes AW, Meems L, Grobbee DE. Increased survival with β -blockers: importance of ancillary properties. *Prog Cardiovasc Dis*. 1997; 39:445-56.