

Review: β -blockers differ in their efficacy for preventing major cardiovascular events in younger and older patients

Khan N, McAlister FA. Re-examining the efficacy of β -blockers for the treatment of hypertension: a meta-analysis. *CMAJ*. 2006;174:1737-42.

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

QUESTION

When β -blockers are used as first-line treatment of hypertension, does their efficacy for preventing major cardiovascular events differ between younger and older patients?

METHODS

Data sources: PubMed (1950 to January 2006), reference lists of hypertension meta-analyses, and experts in the field.

Study selection and assessment: Randomized controlled trials (RCTs) with blinded assessment of outcome that compared β -blockers with placebo or other antihypertensive drugs as first-line therapy for hypertension. 21 RCTs met the selection criteria: 10 trials ($n = 50\ 612$) involved younger patients (mean age 46 to 56 y), and 11 trials ($n = 95\ 199$) involved older patients (mean age 60 to 76 y).

Outcomes: A composite endpoint of stroke, myocardial infarction (MI), or death; stroke; MI; death; and heart failure.

MAIN RESULTS

In younger patients, β -blockers reduced risk for the composite endpoint more than placebo and did not differ from other antihypertensive drugs (Table). In older patients, β -blockers did not differ from placebo for the composite endpoint and increased risk

more than other antihypertensive drugs (Table). In younger patients, β -blockers did not differ from placebo or other antihypertensive drugs for the individual outcomes of stroke, MI, death, or heart failure. In older patients, β -blockers reduced risk for stroke (relative risk reduction [RRR] 22%, 95% CI 2 to 37) and heart failure (RRR 46%, CI 19 to 63) more than did placebo (groups did not differ for MI or death), but were associated with increased risk for stroke (relative risk increase 18%, CI 7 to 30) compare with other antihypertensive drugs (groups did not differ for MI, death, or heart failure).

CONCLUSIONS

When used as first-line treatment of hypertension, β -blockers are more effective than placebo in younger patients, but not in older patients. β -blockers have similar efficacy to other antihypertensive drugs in younger patients, but are less effective than such drugs in older patients.

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β -blockers as first-line treatment of hypertension in preventing the composite endpoint (stroke, myocardial infarction, or death) in younger (mean age < 60 y) and older (mean age \geq 60 y) patients*

Age group	Number of trials (n)	Weighted event rates		RRR (95% CI)	NNT (CI)
		β -blockers	Placebo		
Younger	3 (19 414)	3.7%	4.3%	14% (1 to 26)	168 (91 to 2342)
Older	5 (8019)	13%	14%	11% (-5 to 25)	Not significant
		β -blockers	Other antihypertensive drugs		
Younger	5 (30 412)	4.9%	5.0%	3% (-7 to 12)	Not significant
				RRI (CI)	NNH (CI)
Older	7 (79 775)	9.9%	9.4%	6% (1 to 10)	179 (107 to 1069)

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

COMMENTARY

Some guidelines now state that β -blockers are not preferred initial antihypertensive therapy for patients without other indications (e.g., angina) for their use (1). Others suggest that β -blockers may still be recommended for first-line treatment of hypertension for patients < 60 years of age, presumably based in part on the systematic review by Khan and colleagues (2). All guidelines recommend thiazides as a first-line choice and calcium-channel blockers as an alternative. Another point of controversy is whether the " β -blocker" in this situation really means atenolol, since it was the drug used in most β -blocker hypertension trials.

How does the review by Khan and McAlister help us? Although the review created an age cutoff of 60 years "because the pathophysiology of hypertension differs in older and younger patients," this notion is contentious. Isolated systolic hypertension is the diagnosis in > 85% of patients > 60 years of age compared with only 25% in those < 50 years, but it is important to note that those 50 to 59 years are a mixed group (3). Furthermore, there is no RCT of hypertension treatment stratified by age to support the notion of differing pathophysiologic mechanisms.

The issue of β -blockers as initial therapy remains unresolved in practice as well. In a review of a Medicaid database from 2001 to 2005, the use of β -blockers as initial therapy remained consistently at 25% in a

population of 5373 patients with newly diagnosed hypertension, seemingly uninfluenced by recent guidelines (4). This finding may indicate that physicians have other reasons for prescribing β -blockers (including perseveration), the newer guideline messages have not yet been communicated well, or physicians simply do not "buy" the message.

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