Is It Time to Redefine the Role of β Blockers in Treating 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.

Study Overview

Objective. To determine if β blockers differ in efficacy from other drugs used to treat primary hypertension.

Design. Meta-analysis of randomized controlled trials.

Setting and participants. The Cochrane Library and PubMed were used to find randomized controlled trials involving patients with primary hypertension who were treated with a β blocker as first-line therapy. 13 studies comparing a β blocker with another drug and 7 studies comparing a β blocker with placebo or no treatment were included in the analysis.

Main outcome measures. All-cause mortality, stroke, and myocardial infarction (MI).

Main results. There was a trend toward increased all-cause mortality for patients assigned β blockers compared with other antihypertensive drugs (relative risk [RR], 1.03 [95% confidence interval {CI}, 0.99–1.08]). Stroke risk was higher for patients assigned β blockers compared with other antihypertensive drugs (RR, 1.16 [95% CI, 1.04–1.30]); risk of MI was similar. In trials that compared atenolol with another antihypertensive drug, the RR of stroke with atenolol was 1.26 (95% CI, 1.15–1.38), and all-cause mortality was increased (RR, 1.08 [95% CI, 1.02–1.14]). Trials comparing nonatenolol β blockers to other antihypertensive drugs had relatively few patients and did not show significant differences between these treatments. Compared with placebo or no treatment, risk reduction with β blockers was less than expected based on historical comparison to placebo-controlled trials of other antihypertensive drugs.

Conclusion. β blockers may be less effective than other first-line antihypertensive medications in preventing stroke.

Commentary

β Blockers have been a mainstay in the antihypertensive armamentarium for decades and are recommended as a first-line treatment option in national guidelines [1]. β Blockers also have proven benefits for patients with left ventricular systolic dysfunction, prior MI, or angina pectoris. This meta-analysis by Lindholm et al, however, suggests that β blockers are not the best initial choice for the primary prevention of stroke, and perhaps death, among patients with hypertension.

There are several plausible, albeit speculative, explanations for Lindholm et al's findings. First, blood pressure may not have been controlled to the same extent in the β-blocker groups. This meta-analysis did not adjust for differences in achieved blood pressure. While some trials included in this meta-analysis reported similar blood pressure control, others (eg, the Anglo-Scandinavian Cardiac Outcomes Trial–Blood Pressure Lowering Arm [2]) did not achieve the same blood pressure reduction in the β-blocker group as the comparison group. The pathophysiology of hypertension varies with age and disease duration, with elevated cardiac output observed in younger patients with hypertension [3]. Therefore, β blockers may not be as effective at lowering blood pressure in middle-aged and older patients with more longstanding hypertension, characteristics of many study participants involved in the major hypertension trials. β Blockers could potentially be a good choice for younger, lower-risk patients early in the course of their hypertension, but there is scant trial evidence addressing this population.

Second, worse stroke and mortality outcomes could be due to the mild adverse effects of β blockers on glucose and lipid metabolism. These effects may be magnified when β blockers are combined with thiazide-type diuretics compared with other drugs that do not have these adverse effects (eg, angiotensin-converting enzyme inhibitors, calcium channel blockers, angiotensin II receptor blockers). Third, intermittent nonadherence to β blockers could lead to a withdrawal phenomenon that could be harmful for some patients [4]. However, this phenomenon has not been well described in actual practice.

Applications for Clinical Practice

In middle-aged and older patients with hypertension, especially those with cardiovascular disease risk factors or left ventricular hypertrophy, a β blocker may not be the best initial choice of antihypertensive drug. Controlling blood pressure,

however, frequently requires combining multiple medications or making drug substitutions when 1 medication is not tolerated or is ineffective. For any individual, finding a regimen that is well-tolerated, affordable, and achieves blood pressure control remains the main goal. This meta-analysis should not dissuade physicians from using β blockers in patients with indications for which their benefits have been proven, such as heart failure with left ventricular systolic dysfunction or prior MI. There is little direct evidence to inform the initial drug choice for younger, low-risk patients with primary hypertension.

–Review by Stephen D. Persell, MD, MPH

References

1. Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report [published erratum appears in JAMA 2003;290:197]. JAMA 2003;289:2560–72.
2. Dahlof B, Sever PS, Poulter NR, et al. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre randomised controlled trial. Lancet 2005;366:895–906.
3. Lund-Johansen P. Central haemodynamics in essential hypertension at rest and during exercise: a 20-year follow-up study. J Hypertens Suppl 1989;7:S52–55.
4. Miller RR, Olson HG, Amsterdam EA, Mason DT. Propranolol-withdrawal rebound phenomenon. Exacerbation of coronary events after abrupt cessation of antianginal therapy. N Engl J Med 1975;293:416–8.

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