

Review: Commonly used antihypertensive therapies and targeted blood pressure–lowering regimens reduce cardiovascular events

Turnbull F. Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively-designed overviews of randomised trials. *Lancet*. 2003;362:1527-35.

QUESTION

In patients at increased risk for cardiovascular (CV) disease, how do blood pressure (BP)–lowering regimens of different drug classes and regimens targeting different BP goals compare in reducing major cardiovascular events (MCEs) and death?

DATA SOURCES

An existing systematic review was updated. Additional studies were identified from a {registry established in 1995*.

STUDY SELECTION AND ASSESSMENT

Studies were selected if they were randomized controlled trials (RCTs) that allocated patients to a BP-lowering drug or placebo, different BP goals, or regimens based on different classes of BP-lowering drugs; had ≥ 1000 patient-years of follow-up; and the main results were not reported before July 1995.

OUTCOMES

A composite endpoint of MCEs (stroke, coronary heart disease, heart failure [HF] causing death or hospital admission, and CV death), death from any CV cause, and total mortality.

MAIN RESULTS

29 RCTs ($n = 162\ 341$, mean age 65 y, 52% men) with mean follow-up of 2 to 8.4 years met the selection criteria. Compared with placebo, regimens containing angiotensin-converting enzyme inhibitors (ACEIs)

reduced the risk for MCEs and total mortality, and calcium antagonists (CAs) reduced the risk for MCEs (Table). Studies targeting lower BP goals also showed greater risk reductions for stroke and MCEs (Table). Compared with control regimens, angiotensin-receptor blocker (ARB)–based regimens reduced the risk for stroke, HF, and MCEs (Table). 4 studies that compared ACEIs with CAs showed a risk reduction for HF with ACEIs (Table), while regimens comparing ACEIs with diuretics or β -blockers did not differ for MCEs or any other outcomes.

Relative risks (RRs) (95% CIs) for angiotensin-converting enzyme inhibitors (ACEIs) or calcium antagonists (CAs) vs placebo, more intensive vs less intensive blood pressure (BP)–lowering regimens, and other BP-lowering regimens vs control at mean 2 to 8.4 years†

Outcomes	ACEIs vs placebo	CAs vs placebo ¹	More vs less	ARBs vs control	ACEIs vs Ds/BBs	CAs vs Ds/BBs	ACEIs vs CAs
Stroke	0.72 (0.64 to 0.81)‡	0.62 (0.47 to 0.82)‡	0.77 (0.63 to 0.95)‡	0.79 (0.69 to 0.90)‡	1.09 (1.00 to 1.18)	0.93 (0.86 to 1.00)	1.12 (1.01 to 1.25)
CHD	0.80 (0.73 to 0.88)‡	0.78 (0.62 to 0.99)‡	0.95 (0.81 to 1.11)	0.96 (0.85 to 1.09)	0.98 (0.91 to 1.05)	1.01 (0.94 to 1.08)	0.96 (0.88 to 1.04)
Heart failure	0.82 (0.69 to 0.98)‡	1.21 (0.93 to 1.58)	0.84 (0.59 to 1.18)	0.84 (0.72 to 0.97)‡	1.07 (0.96 to 1.19)	1.33 (1.21 to 1.47)	0.82 (0.73 to 0.92)‡
MCEs	0.78 (0.73 to 0.83)‡	0.82 (0.71 to 0.95)‡	0.85 (0.76 to 0.95)‡	0.90 (0.83 to 0.96)‡	1.02 (0.98 to 1.07)	1.04 (1.00 to 1.09)	0.97 (0.92 to 1.03)
CV death	0.80 (0.71 to 0.89)‡	0.78 (0.61 to 1.00)	0.93 (0.77 to 1.11)	0.96 (0.85 to 1.08)	1.03 (0.95 to 1.11)	1.05 (0.97 to 1.13)	1.03 (0.94 to 1.13)
Total mortality	0.88 (0.81 to 0.96)‡	0.89 (0.75 to 1.05)	0.96 (0.84 to 1.09)	0.94 (0.86 to 1.02)	1.00 (0.95 to 1.05)	0.99 (0.95 to 1.04)	1.04 (0.98 to 1.10)

†ARBs = angiotensin-receptor blockers; Ds/BBs = diuretics or β -blockers; MCEs = major cardiovascular events (stroke, coronary heart disease, heart failure, and cardiovascular death); CV = cardiovascular. CI defined in Glossary. All significant differences favor the experimental regimens. RRs < 1.0 favor the experimental therapy; RRs > 1.0 favor the alternative therapy.

‡Statistically significant.

CONCLUSIONS

In patients at increased risk for cardiovascular disease, regimens of commonly used antihypertensives and those that target blood-pressure lowering reduce the risks for major cardiovascular events.

Source of funding: National Health and Medical Research Council of Australia.

For correspondence: Dr. F. Turnbull, University of Sydney, Sydney, New South Wales, Australia. E-mail fturnbull@iib.usyd.edu.au.

*Blood Pressure Lowering Treatment Trialists' Collaboration. *J Hypertension*. 1998;16:127-37.

COMMENTARY

The prospective review by the Blood Pressure Lowering Treatment Trialists' Collaboration expands the ongoing debate about antihypertensive treatment choices. 11 of the 29 large trials included were truly "hypertension" trials, while many patients in the other 18 trials had concomitant hypertension and were recruited on the basis of comorbid conditions, resulting in lower mean baseline BP in the latter trials.

This meta-analysis echoes the results of other work in this field (1, 2) and clearly establishes that lowering BP reduces CV risk, larger reductions in BP lead to greater reductions in risk for MCEs, and differences in degree of BP lowering account for many of the differences in CV outcomes seen between drug classes in active-control trials. However, the effect of certain antihypertensive classes on cause-specific CV outcomes or in different patient subgroups (e.g., ACEIs are less protective than thiazide diuretics in black patients) remains uncertain (3).

How should one choose an agent to lower BP? Assuming that a patient does not have diabetes mellitus or HF (for which some drug

classes seem to exert benefits extending beyond their antihypertensive effects), physicians should choose a drug that is affordable and well tolerated, while recognizing that none of the newer agents have been shown to be better than thiazide diuretics in most patients. Often forgotten in debates about choice of initial monotherapy is that most adults with hypertension require more than 1 agent to achieve optimal BP control.

The clinical reality is that although we have a plethora of effective therapies to lower BP, hypertension control is often suboptimal. We must strive to address this care gap.

Finlay A. McAlister, MD, MSc
University of Alberta
Edmonton, Alberta, Canada

References

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