

Amlodipine plus perindopril was better than atenolol plus bendroflumethiazide for reducing complications in hypertension

Dahlöf 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.

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

QUESTION

In patients 40 to 79 years of age with hypertension and ≥ 3 other cardiovascular (CV) risk factors, is amlodipine plus perindopril more effective than atenolol plus bendroflumethiazide for reducing CV outcomes?

METHODS

Design: Randomized controlled trial (Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm [ASCOT-BPLA]).

Allocation: Concealed.*

Blinding: Blinded (outcome assessors).*

Follow-up period: Median 5.5 years.

Setting: 686 family practices in the Nordic countries and 32 regional centers in the United Kingdom and Ireland.

Patients: 19 257 patients 40 to 79 years of age (mean age 63 y, 77% men) who had hypertension and ≥ 3 other CV risk factors. Exclusion criteria included previous myocardial infarction (MI), currently treated angina, and a cerebrovascular event within the previous 3 months.

Intervention: Amlodipine, 5 to 10 mg, adding perindopril, 4 to 8 mg as required ($n = 9639$), or atenolol, 50 to 100 mg, adding bendroflumethiazide, 1.25 to 2.5 mg, and potassium as required ($n = 9618$).

Outcomes: Composite endpoint of nonfatal MI (including silent MI) and fatal coronary heart disease. Secondary outcomes included all-cause mortality, total stroke, all coronary events, total cardiovascular events and procedures, and cardiovascular mortality.

Patient follow-up: 100% (intention-to-treat analysis).

MAIN RESULTS

The groups did not differ for the composite endpoint (Table). The rates of all-cause mortality, total stroke, all coronary events, total CV events and procedures, and CV mortality were lower in the amlodipine group than in the atenolol group (Table).

CONCLUSIONS

In patients with hypertension, amlodipine plus perindopril did not differ from atenolol plus bendroflumethiazide for reducing the rate of nonfatal myocardial infarction and fatal coronary events. However, amlodipine plus perindopril was better at reducing the rates of all-cause mortality, total stroke, all coronary events, total CV events and procedures, and CV mortality.

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*See Glossary.

Amlodipine plus perindopril vs atenolol plus bendroflumethiazide for hypertension at median 5.5 years†

Outcomes	Amlodipine	Atenolol	RRR (95% CI)	NNT (CI)
Composite endpoint	4.5%	4.9%	9.7% (-2.6 to 20.5)	Not significant
All-cause mortality	7.7%	8.5%	10.2% (1.2 to 18.4)	116 (61 to 1010)
Fatal and nonfatal stroke	3.4%	4.4%	22.7% (10.9 to 32.9)	101 (65 to 223)
All coronary events	7.8%	8.9%	11.8% (3.1 to 19.7)	96 (55 to 377)
Total cardiovascular events and procedures	14.1%	16.7%	15.2% (9.3 to 20.6)	40 (29 to 67)
Cardiovascular mortality	2.7%	3.6%	23.3% (10.1 to 34.5)	121 (76 to 299)

†Composite endpoint = nonfatal myocardial infarction (including silent infarction) or fatal coronary heart disease. Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

The ASCOT-BPLA trial by Dahlöf and colleagues compared a calcium blocker (and if required, an angiotensin-converting enzyme inhibitor) with a β -blocker (and if required, a diuretic) in high-risk patients with hypertension. They found no difference in the primary composite outcome. However, benefits favoring amlodipine plus perindopril were reported across several clinically important secondary outcomes.

Some cautions are noteworthy. Foremost is the choice of a β -blocker as a comparator for first-line therapy. Ever since the MRC trial showed that atenolol was not better than placebo (1), many have had reservations about β -blockers (2). Second, the dose of bendroflumethiazide (1.25 to 2.5 mg/d) was lower than the 10 mg/d used in previous trials that showed a benefit. This, in part, may account for the difference in blood pressure (BP) of 2.7/1.9 mm Hg between the groups in ASCOT-BPLA, favoring the amlodipine group. However, the accompanying multivariable analyses (3) suggested a drug-specific effect beyond just a difference in BP.

For clinicians, results from ASCOT-BPLA should not affect consideration of thiazide diuretics as a highly appropriate first-line option for many, if not most, low- and high-risk patients with hypertension. This observation is supported by large trials, such as ALLHAT (4), that

found no evidence of superiority of calcium blockers in primary outcomes and evidence of superiority of thiazide diuretics for some clinically important secondary outcomes. Furthermore, many hypertensive patients with various forms of heart disease (e.g., a previous MI or tachyarrhythmias) will benefit from use of β -blockers.

Overall, ASCOT-BPLA results support existing data suggesting that β -blockers should not be considered first-line therapy for hypertension without other compelling indications. However, it does not diminish the position of thiazide diuretics as a highly appropriate first-line therapy for many patients with hypertension.

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References

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