

Antihypertensive treatment may have reduced the rate of dementia in older patients with isolated systolic hypertension

Forette F, Seux ML, Staessen JA, et al, for the Syst-Eur Investigators. *Prevention of dementia in randomised double-blind placebo-controlled systolic hypertension in Europe (Syst-Eur) trial*. *Lancet* 1998 Oct 24;352:1347–51.

Question

In older patients with isolated systolic hypertension, can antihypertensive treatment prevent dementia?

Design

Randomised, double blind, placebo controlled trial with up to 5 years of follow up (an optional project in the systolic hypertension in Europe [Syst-Eur] trial).

Setting

106 centres in Europe.

Patients

2470 patients who were ≥ 60 years of age and had a systolic blood pressure (BP) (when seated) of 160–219 mm Hg and a diastolic BP < 95 mm Hg. 2418 patients (98%) were analysed (mean age 70 y, 66% women).

Intervention

After stratification by sex, centre, and previous cardiovascular complications, patients were allocated to antihypertensive treatment ($n = 1238$) or matching placebo ($n = 1180$). The goal of antihypertensive treatment was to reduce systolic BP by ≥ 20 mm Hg or to below 150 mm Hg. Treatment was started with nitrendipine, 10–40 mg/day. If necessary, nitrendipine was combined or replaced with enalapril, 5–20 mg/day; hydrochlorothiazide, 12.5–25 mg/day; or both drugs.

Main outcome measure

Incidence of dementia assessed with the *DSM-III-R*.

Main results

Analysis was by intention to treat. The Syst-Eur trial was stopped early according to preset stopping rules because antihypertensive treatment led to a greater reduction in stroke than did placebo. After a median follow up of 2 years, 11 new cases of dementia occurred in the antihypertensive treatment group (8 Alzheimer's and 3 mixed), and 21 new cases (15 Alzheimer's, 4 mixed, and 2 vascular) occurred in the placebo group ($p = 0.06$)* (table). Time-to-event analysis showed that antihypertensive treatment reduced the dementia rate compared with placebo (3.8 v 7.7 cases/1000 person years, $p = 0.05$).

Conclusion

In older patients with isolated systolic hypertension, antihypertensive treatment may have led to a reduction in dementia.

* p value calculated from data in article.

Antihypertensive treatment v placebo in older patients with systolic hypertension at a median follow up of 2 years†

Outcome	Antihypertensive	Placebo	RRR (95% CI)	NNT (CI)
Dementia	0.8%	1.8%	50.1% (–1.5 to 75.5)	Not significant

†Abbreviations defined in glossary; RRR, NNT, and CI calculated from data in article.

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Abstract and commentary also published in *ACP Journal Club*.

Commentary

Systolic hypertension and dementia are common, especially in old people (≥ 85 years old). The attractive hypothesis that treatment of systolic hypertension reduces the incidence of vascular dementia was a research question of the Syst-Eur trial in 1991.¹ Forette and colleagues attempted to answer a broader question involving all dementias: Alzheimer's disease, vascular, and mixed forms.

With respect to the original question, only 2 cases of vascular dementia occurred, far fewer than originally predicted.¹ The claim that systolic hypertension treatment reduced the incidence of all types of dementia by 50% may constitute a trend, although given that the confidence interval around this estimate included zero, the data are also compatible with no treatment effect. Because these results constitute a post-hoc analy-

sis, the possibility of a false positive result arises. The only other comparable study used different drugs and showed no protection against dementia with control of systolic hypertension.²

Even if the authors' hypothesis is correct, the safety of calcium channel blockers, especially in the elderly, has been recently questioned.³ The generalisability of this efficacy trial is limited because only relatively young patients with few comorbid conditions were included.

What are the clinical implications? Although the exact question initially posed in 1991 was not answered here, the evidence is intriguing and offers hope but, at this stage, nothing more. Good enough reasons (beyond dementia prevention) exist to treat systolic hypertension, at least in people < 85 years old. With respect to

old people with hypertension, especially with comorbid conditions, the jury is still out.

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