Review: Angiotensin II receptor antagonists prevent headache in patients with mild-to-moderate hypertension

Etminan M, Levine MA, Tomlinson G, Rochon PA. **Efficacy of angiotensin II receptor antagonists in preventing headache: a systematic overview and meta-analysis.** Am J Med. 2002;112:642-6.

QUESTION

Do angiotensin II receptor antagonists prevent headaches?

DATA SOURCES

Studies were identified by searching MEDLINE, EMBASE/Excerpta Medica, the Cochrane Library, and International Pharmaceutical Abstracts using combinations of the terms candesartan, eprosartan, losartan, irbesartan, tasosartan, telmisartan, and valsartan and the terms headache, headache disorders, cluster headaches, tension headaches, and migraine; scanning reference lists of retrieved studies; and contacting pharmaceutical manufacturers.

STUDY SELECTION

Randomized controlled trials ≥ 1 week in duration were selected if they compared angiotensin II receptor antagonists with placebo in patients who were taking no other antihypertensive agents and if headache was measured as a primary outcome or adverse event.

DATA EXTRACTION

Data were extracted on number of participants, study duration, and the specific drug assessed.

MAIN RESULTS

27 studies (n = 12 110) that involved the use of angiotensin II receptor antagonists for treatment of mild-to-moderate hypertension (sitting diastolic blood pressure of 95 to 115 mm Hg) were included in the analysis. Patients were treated with candesartan (n = 1508), eprosartan (n = 695), irbesartan (n = 2843), losartan (n = 1429), tasosartan (n = 2090), telmisartan (n = 522), or valsartan (n = 3023). Meta-analysis using a random-effects model showed that patients who received angiotensin II receptor antagonists had a lower risk for headache than did patients who received placebo (Table). Analysis using meta-regression showed an odds ratio of 0.81 (95% CI 0.68 to 0.93) for headache per unit dose of losartan (defined as 50 mg).

CONCLUSION

Angiotensin II receptor antagonists prevent headache in patients with mild-to-moderate hypertension.

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Angiotensin II receptor antagonists vs placebo for preventing headache*

Outcome	Weighted event rates		RRR (95% CI)	NNT (CI)
	Angiotensin II receptor antagonists	Placebo		
Headache	11%	15%	31% (24 to 38)	21 (18 to 27)

*Abbreviations defined in Glossary. RRR (CI) calculated from data in article; NNT (CI) calculated from relative risk reported in article and weighted event rates provided by author. Length of follow-up ranged from 4 to 52 weeks.

COMMENTARY

The meta-analysis by Etminan and colleagues addresses an interesting question. Do angiotensin II receptor antagonists, similar to β-blockers, calcium channel blockers, and angiotensin-converting enzyme inhibitors (1, 2), reduce the frequency of headaches in patients with hypertension? The pooled results show a reduction in headache frequency with angiotensin II receptor antagonists. The findings should be interpreted with caution, however, because headache was not the primary outcome in any of the individual studies; the angiotensin II receptor antagonists chosen were not standardized; doses were not equivalent; and the definitions and types of headaches were not specified. Did the patients in these studies have tension headaches, migraine headaches, nasosinus headaches, or cluster headaches? Meta-analysis of secondary study endpoints should be considered hypothesis-generating, and the authors rightly call for a clinical trial to confirm the findings of this meta-analysis. The mechanism of action of all these agents on headache remains unclear, as a cause–effect relation between blood pressure and headache has not been clearly shown. A recent 11-year prospective study of 22 685 adults found a reduced risk for non-migraine headache in patients with hypertension and no relation between hypertension and migraine headache (3).

What will I do in my practice? For patients with migraine headaches, I will continue to favor β-blockers followed by calcium channel blockers and perhaps angiotensin-converting enzyme inhibitors for prophylaxis, especially when comorbid hypertension exists. I will use angiotensin II receptor antagonists as needed for hypertension control and hope that the hypothesis of this study is proven correct.

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Reference

1. **Schrader H, Stovner LJ, Helde G, Sand T, Bovim G.** Prophylactic treatment of migraine with angiotensin converting enzyme inhibitor (lisinopril): randomised, placebo controlled, crossover study. BMJ. 2001;322:19-22.
2. **Welch KM.** Drug therapy of migraine. N Engl J Med. 1993;329:1476-83.
3. **Hagen K, Stovner LJ, Vatten L, et al.** Blood pressure and risk of headache: a prospective study of 22 685 adults in Norway. J Neurol Neurosurg Psychiatry. 2002;72:463-6.