Review: Angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers prevent type 2 diabetes

Abuissa H, Jones PG, Marso SP, O'Keefe JH Jr. **Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers for prevention of type 2 diabetes: a meta-analysis of randomized clinical trials.** J Am Coll Cardiol. 2005;46:821-6.

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

QUESTION

In patients with hypertension or other cardiovascular risk factors, do angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs) reduce risk for type 2 diabetes?

METHODS

Data sources: MEDLINE (1990 to 2004), Cochrane Database of Systematic Reviews, *ACP Journal Club*, Database of Abstracts of Reviews of Effects, Cochrane Central Register of Controlled Trials, conference abstracts, and bibliographies of relevant studies.

Study selection and assessment: Randomized controlled trials (RCTs) ≥ 1 year in duration that compared an ACE inhibitor or an ARB with placebo or another antihypertensive medication in patients with a history of hypertension or ≥ 1 cardiovascular risk factor, and reported the incidence of type 2 diabetes.

Outcomes: Incidence of new-onset type 2 diabetes (usually defined as fasting plasma glucose ≥ 126 mg/dL [7.0 mmol/L] on 2 occasions).

MAIN RESULTS

12 RCTs (72 333 patients without diabetes at baseline) met the selection criteria. 7 RCTs used ACE inhibitors and 5 used ARBs. These drugs were compared with placebo, diuretics, β-blockers, or calcium-channel antagonists. The mean duration of follow-up ranged from 1 to 6 years (median 4.5 y). Both ACE inhibitors and ARBs reduced risk for type 2 diabetes (Table).

CONCLUSION

In patients with hypertension or cardiovascular risk factors, angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers prevent the development of type 2 diabetes.

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For correspondence: Dr. H. Abuissa, Mid America Heart Institute, Kansas City, MO, USA. E-mail abuissah@umkc.edu.

Angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs) (intervention) vs placebo or other antihypertensive medications (control) to prevent type 2 diabetes at 1 to 6 years*

Interventions	Number of trials (*n*)	Weighted event rates		RRR (95% CI)	NNT (CI)
		Intervention	Control		
ACE inhibitors	7 (43 746)	4.9%	6.7%	27% (16 to 37)	56 (41 to 93)
ARBs	5 (28 587)	8.1%	10.5%	23% (17 to 29)	42 (33 to 57)
ACE inhibitors or ARBs	12 (72 333)	6.1%	8.1%	25% (18 to 31)	50 (40 to 69)

*Abbreviations defined in Glossary; weighted event rates, RRR, NNT, and CI calculated from data in article using a random-effects model.

COMMENTARY

The review by Abuissa and colleagues adds to the body of evidence, mostly derived from the secondary and post hoc analyses of RCTs, that diabetes incidence may be reduced by renin-angiotensin inhibitors, increased by thiazides and β-blockers, and largely unchanged by calcium-channel blockers (1).

Further evidence is required before renin-angiotensin inhibitors can be definitively considered to prevent diabetes. First, data from ongoing trials examining diabetes incidence as a predefined, primary endpoint are required (1). Second, documentation of a truly preventive (as opposed to a delaying or masking) effect is needed, which should include demonstration of a sustained reduction in diabetes incidence following an adequate, prolonged, drug-free washout period. Third, a blood pressure–independent reduction in diabetes-related macrovascular and microvascular endpoints would prove that the observed reduction in diabetes incidence is clinically relevant. To date, major differences in cardiovascular events among antihypertensive drug classes have not been shown (2), arguing against the clinical relevance of renin-angiotensin–induced reductions in diabetes incidence. One caveat is that such differences may become apparent with longer follow-up.

Blood pressure reduction to target levels, particularly in high-risk hypertensive patients, is paramount, not often attained, and commonly requires multidrug therapy, making the choice of initial therapy somewhat less important. Patients with compelling indications for a particular drug (e.g., β-blockers in heart failure) should not be denied therapy for fear of deleterious metabolic effects. It is reasonable to prescribe renin-angiotensin inhibitors preferentially in patients at high risk for type 2 diabetes, who already require antihypertensive drug treatment and have no compelling indication for a different agent. More definitive data are needed to recommend renin-angiotensin inhibitors solely for diabetes prevention.

Raj Padwal, MD
University of Alberta
Edmonton, Alberta, Canada

References

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