

Review: angiotension receptor blockers do not differ from ACE inhibitors in chronic heart failure or acute MI

Lee VC, Rhew DC, Dylan M, *et al.* Meta-analysis: angiotensin-receptor blockers in chronic heart failure and high-risk acute myocardial infarction. *Ann Intern Med* 2004;**141**:693–704.

Clinical impact ratings GP/FP/Primary care ★★★★★☆ IM/Ambulatory care ★★★★★☆ Internal medicine ★★★★★☆ Cardiology ★★★★★☆

Q In patients with chronic heart failure (HF) or high risk acute myocardial infarction (MI), what is the efficacy of angiotensin receptor blockers?

METHODS

Data sources: Medline, CINAHL, Database of Abstracts of Reviews of Effects, HealthSTAR, Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews (to 2003); reference lists; and meeting abstracts.

Study selection and assessment: English language randomised controlled trials (RCTs) that compared ARBs with an appropriate control group in patients with chronic HF or high risk acute MI and reported outcomes at ≥ 4 weeks. Study quality was assessed.

Outcomes: all cause mortality and admission to hospital for HF.

MAIN RESULTS

24 RCTs (38 080 patients, 4 wks to 41 mo of follow up) were included. *Chronic HF.* Studies were pooled using a fixed effects model. ARBs reduced hospital admission for HF relative to placebo; for all cause mortality, the benefit for ARBs reached borderline significance (table). ARBs and angiotensin converting enzyme (ACE) inhibitors did not differ for all cause mortality or HF hospital admission (table). ARBs plus ACE inhibitors led to fewer hospital admissions for HF relative to ACE inhibitors alone; the groups did not differ for all cause mortality (table). *Acute MI.* 2 RCTs met the selection criteria. Both studies showed no statistically significant difference between ARBs and ACE inhibitors for all cause mortality or hospital admission for HF. 1 of these RCTs compared ARBs plus ACE inhibitors with ACE inhibitors alone; the groups did not differ for all cause mortality.

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Source of funding: Cedars-Sinai Health System.

CONCLUSION

In patients with chronic heart failure (HF) or high risk acute myocardial infarction, angiotensin receptor blockers do not differ from angiotensin converting enzyme inhibitors for all cause mortality or hospital admission for HF.

Commentary

Many papers have been written about the choice between ARBs and ACE inhibitors for patients with cardiovascular disease, but 2 basic facts dominate decision making: (1) there is no evidence that ARBs are any better as a first line therapy than ACE inhibitors, and (2) ARBs cost much more than generic ACE inhibitors—in the US, \$500–600 more over the course of a year.

So why are we spending so much time and energy on this issue? Why don't all physicians simply prescribe ACE inhibitors first and use ARBs for those patients who develop cough or other side effects?

One reason, of course, is that ARBs are relatively new. Huge sums have been spent bringing ARBs to market, and their manufacturers hope they will be found superior to ACE inhibitors. So they continue to invest in trials that show a wide range of benefits for ARBs. The only problem is that ARBs don't appear any to be better than ACE inhibitors.

ARBs are great drugs; their misfortune is that ACE inhibitors are too. There is good reason why ACE inhibitors were included in the proposed Polypill—the 6 drug combination that 2 English physicians have proposed for all adults over 55 years of age.¹ And there is good reason why ARBs were *not* included in the Polypill proposal. Fewer data support ARBs and ARBs cost more.

The good news from the meta-analysis of Lee *et al* is that evidence is mounting that ARBs are as good as ACE inhibitors. So ARBs increasingly look like a fine alternative for patients who cannot tolerate ACE inhibitors and an effective add-on for some patients with HF already on ACE inhibitors. But ARB manufacturers hoping for evidence that ARBs should be a first choice over an ACE inhibitor are probably close to giving up.

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¹ Wald NJ, Law MR. A strategy to reduce cardiovascular disease by more than 80%. *BMJ* 2003;**326**:1419.

Angiotensin receptor blockers (ARBs) for chronic heart failure (HF) at 4 weeks to 41 months*

Comparisons	Outcomes	Number of RCTs	Weighted event rates	RRR (95% CI)	NNT (CI)
ARBs v placebo	All cause mortality	9	15% v 18%	14% (0 to 27)	40 (21 to ∞)
	HF hospital admission	3	18% v 25%	30% (17 to 40)	14 (10 to 23)
				RRI (CI)	NNH
ARBs v ACE inhibitors	All cause mortality	8	13.4% v 12.8%	5% (–8.8 to 22)	Not significant
				RRR (CI)	NNT (CI)
ARBs + ACE inhibitors v ACE inhibitors alone	HF hospital admission	3	15.0% v 15.6%	4% (–11 to 17)	Not significant
	All cause mortality	7	22.0% v 22.6%	2.3% (–6.1 to 10)	Not significant
	HF hospital admission	4	17% v 21%	19% (11 to 26)	26 (19 to 46)

*ACE = angiotensin converting enzyme. Other abbreviations defined in glossary; weighted event rates, RRR, RRI, NNT, NNH, and CI calculated from fixed effects odds ratios and control rate in article.