Cochrane Corner

What's new in using blood pressure medication

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There have been a number of recent randomised controlled trials and systematic reviews of treatment of hypertension as a means of primary prevention against cardiovascular disease. They are the:

ALLHAT TRIAL: Chlorthalidone better than ACE and calcium channel blocker

The publication of the ALLHAT trial in December 2002 is important as it is the largest drug vs drug comparison of antihypertensive medications.[1] Its findings favour the use of the low dose diuretic over amlodipine and lisinopril. Chlorthalidone was only better than amlodipine for the outcome of congestive heart failure (numbers needed to treat {NNT}=40) but when compared with lisinopril was significantly better for stroke (NNT=143), combined cardiovascular disease (NNT=42), heart failure (NNT=100) and angina (NNT=100). It will be recalled that the doxasosin arm of this trial was stopped early when it was found that chlorthalidone was significantly better than doxasosin for the outcome of congestive heart failure. The one proviso in interpreting these results is that 40% of the participants were Afro-American and it is known that diuretics have better effects in lowering blood pressure than ACE inhibitors in this group. Interestingly this was achieved with a slight elevation (3%) in the fasting glucose for chlorthalidone, no change for amlodipine and a 3% reduction for lisinopril. This suggests that while there are small metabolic changes with low dose diuretics they do not translate into cardiovascular endpoints. Chlorthalidone is fully funded in New Zealand. There is no head to head comparison of bendrofluazide vs chlorthalidone so it is not clear if one is better than the other.

HOPE TRIAL: Ramipril better than placebo for patients at high risk of cardiovascular disease

The HOPE trial found a cardiovascular disease (CVD) benefit of about 3.74% over four years in patients taking ramipril versus placebo (NNT=104 per year).[2] This was achieved with a much lower blood pressure reduction (a few mm Hg) than would be expected for such a reduction in CVD. Half of the patients had hypertension and one other cardiovascular risk factor. Many of them had vascular disease or diabetes. It is not clear if this is a benefit of ramipril or a class effect of ACE. Thus it is not clear what to do in New Zealand as ramipril is not funded. The possibilities include waiting for more studies or else starting a different ACE.

LIFE TRIAL: Losartan better than atenolol in high risk patients with LV hypertrophy

This trial compared losartan (an angiotensin II blocker) with atenolol in high risk patients with left ventricular hypertrophy.[3] The losartan produced a 1.78% reduction in cardiovascular events when compared with atenolol over four years (NNT=224 per year). This is the first comparison of these two drugs so it would be helpful to have confirmation of this finding in other studies. A curious small print finding was a reduction in the uric acid in the losartan group which may be of use in those patients prone to gout. A possible treatment strategy could be to start a diuretic and a beta-blocker for patients with LV hypertrophy and, if the blood pressure is not well controlled, make an application for candesartan. This would be generalising from one angiotensin II blocker to another and assuming that any benefit from losartan could be transferred to candesartan.

Blood pressure lowering in the elderly

A Cochrane review of pharmacotherapy for hypertension meta-analysed 15 RCTs of mainly beta-blocker and diuretic therapy in subjects aged over 60 years and found that diuretics and beta-blockers were effective for diastolic and isolated systolic hypertension (ISH) and that long acting dihydropyridine calcium channel blockers (felodipine is an example) were also effective in isolated systolic hypertension.[4] Treatment was effective in patients aged 60–80 years. The Systolic Hypertension in the Elderly study found a benefit in patients up to the age of 85 years. For ISH the initial treatment should be either a diuretic or a long acting dihydropyridine calcium channel blocker.

Systematic review of betablockade after myocardial infarction

A recent systematic review of beta blockade after myocardial infarction found a significant benefit for metoprolol, propranolol and timolol but insufficient evidence for atenolol (NNT=84 per year).[5] Although many patients are on atenolol they should perhaps be on one of the more effective agents.

Antihypertensives for hypertension and Post MI

	Long term success	Evidence	Advantages	Disadvantages
ALLHAT	4.5 years on average. Chlorthalidone better than lisinopril and amlodipine NNT = 42 to 143	RCT[1]	Low dose diuretics are cheap and effective	Slight increase in fasting glucose but compensated by blood pressure lowering and CVD protection
HOPE	At 4 years NNT = 104. Ramipril better than placebo	RCT[2]	Reduction in CVD may be independent of blood pressure lowering	Ramipril not funded in New Zealand
Life	Losartan better than atenolol in high risk patients with LV hypertrophy NNT = 104	RCT[3]	First study to show an angiotensin 2 blocker better than older medication	Losartan is expensive and requires a special authority. Also this is the only study to show this.
Blood pressure lowering in the elderly	Beta-blockers and diuretics good for high blood pressure in the elderly. Long acting dihydropyridine also good for isolated systolic hypertension	Cochrane review[4]	All three classes of medication are funded and relatively cheap	Not clear what to do with those over 85 years
Post MI prevention of sudden death	NNT 84 per year for metoprolol, propanolol and timolol	Systematic review[5]	All three medications are funded and cheap	May need to change patients from atenolol

NNT = numbers needed to treat for one year
RCT = randomised controlled trial
CVD = cardiovascular disease
LV = left ventricular

References

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2. The heart outcomes prevention evaluation (HOPE) study investigators. Effects of an angiotensin-converting-enzyme inhibitor ramipril on cardiovascular events in high risk patients. N Engl J Med 2000; 342:145–53.
3. Dahlof B, Devereux RB, Kjeldsen SE, et al. Cardiovascular morbidity and mortality in the losartan intervention for endpoint reduction in hypertension study (Life) a randomised trail against atenolol. Lancet 2002; 359:995–1003.
4. Mulrow C, Lau J, Cornell J, Brand M. Pharmacotherapy for hypertension in the elderly (Cochrane review). In: The Cochrane Library. Issue 4 2002, Oxford: Update software.
5. Freemantle N, Cleland JG, Young J, Mason J, Harrison J. B blockade after myocardial infarction: systematic review and meta regression analysis. BMJ 1999; 318:1730–7.

Members of the Royal New Zealand College of General Practitioners can have access to the full reviews by contacting Cherylyn Pearson at the College in Wellington. For the access codes to the Cochrane library contact cpearson@rnzcgp.org.nz at the College. Access to clinical evidence can be obtained at http://www.clinicalevidence.org/