

EFFECTIVENESS

Matters

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Drug Treatment of Essential Hypertension in Older People

- Hypertension is very common, occurring in over 50% of older people, and is a major risk factor for stroke and ischaemic heart disease.
- Drug treatment of hypertension in older people saves lives and prevents unnecessary morbidity.
- Treating isolated systolic hypertension also saves lives.
- There is strong evidence to support the use of diuretics as first line agents.
- Antihypertensive treatments are most cost-effective when targeted at older patients.
- There is evidence of under detection and under treatment of hypertension.
- Factors influencing patient adherence are not well understood and require further research.

Effectiveness Matters is based upon the findings of recent high quality systematic reviews. In this issue we explore the evidence for the drug treatment of hypertension in older people with the aim of preventing cardiovascular disease.

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A Clinical Imperative

Cardiovascular diseases remain the major cause of death for older people in the UK.

Hypertension is widely considered to be one of the most important risk factors for these diseases and is strongly associated with death from stroke, congestive heart failure and coronary heart disease. Using a conservative definition of essential hypertension (≥ 160 mm Hg systolic or 95mm Hg diastolic), it is estimated that in the UK more than half of the 10 million people over the age of 65 are hypertensive.¹ The high prevalence of the disease and rapidly growing number of older people suggest that hypertension is an enormous public health problem and yet detection and treatment remain relatively low.

Effectiveness of Antihypertensive Therapy in Older People

Antihypertensive drug treatments are effective at reducing mortality and morbidity in older people. A recent systematic review by the Cochrane Collaboration analysed data from 15 studies containing more than 21,000 patients over 60 years of age.² The analysis showed that antihypertensive drug therapy was associated with significant reductions in, mortality due to stroke, coronary heart disease (CHD), all cardiovascular causes and overall mortality (Table 1). These results are comparable with other reviews that have shown similar reductions in overall mortality.³⁻⁷

Significant reductions in morbidity from stroke or CHD can also be achieved through antihypertensive drug treatment. Combining mortality and morbidity data shows even larger effects.^{2,4} To prevent one stroke in the over 60s would mean treating only 50 patients for five years, compared with 168 under the age of 60.³

The under treatment of isolated systolic hypertension (ISH) in older people is a particular concern. Systematic reviews of antihypertensive drug treatment ISH have shown that reductions in stroke events and

mortality from cardiovascular disease are similar to those in table 1.^{2,5}

There is very little evidence on which to base treatment decisions for patients in their 80s and above. When published, the result of the Hypertension in the Very Elderly Trial (HYVET)8 will hopefully help to inform treatment decisions for this patient group. Until then the best evidence is presented in a meta-analysis of seven studies that provided data on 1670 patients over the age of 80 (Table 2).⁹ The analysis showed that there were significant reductions in morbidity from stroke, heart failure and cardiovascular events, although there was no significant reduction in mortality rates.

For first line therapy, systematic reviews suggest there is strong evidence to support the use of thiazide diuretics and some evidence for the use of beta-blockers.¹⁰ For the newer antihypertensive drugs, these reviews do not yet provide sufficient evidence to make conclusions about their effects on morbidity and mortality.

The decision to treat a patient with hypertension should take into account their individual risk of cardiovascular events as well as patient preferences. Published guidelines are available to help make an informed decision.^{11,12} In older people, age is likely to be the dominant risk factor and in most cases drug treatment should be considered. There is no evidence from systematic reviews to determine the optimal level to which blood pressure should be reduced, but based on epidemiological evidence it is clear that any reduction is likely to be beneficial.¹³

Cost-Effectiveness

Swedish studies have shown that cost-effectiveness improves either as the age of the patient increases or the initial blood pressure increases.^{14,15} A USA study found that generic diuretics and beta-blockers were the most cost-effective drug classes, however, the difference was smaller in patients over 60.¹⁶ Although the costs of drugs and follow-up care in the NHS may differ to Sweden or the USA, it is likely that

Table 1. Reduction in mortality and morbidity of older patients.

	Percentage of cases prevented [†] (95% Confidence Interval)			
	Cardiovascular Events*	Stroke	Coronary Heart Disease	All-cause Mortality
Mortality ²	30% (19 to 39)	40% (21 to 54)	26% (14 to 36)	16% (6 to 25)
Morbidity ⁴	NC	35% (24 to 45)	15% (1 to 27)	NA
Combined M/M ²	33% (25 to 41)	37% (28 to 45)	20% (10 to 30)	NA

[†] Treated for approximately 5 years, reduction compared to controls. Patients were largely ambulatory outpatients, although not exclusively, and treated for 2 to 7 years. Mean blood pressure at study entry across all studies was 177/90mmHg (includes patients with isolated systolic hypertension in some studies). The mean reduction in blood pressure at the end of study was 13.3mmHg Systolic, and 7.7mmHg Diastolic.

* Cardiovascular = both strokes and CHD events including sudden death. NA = Not Applicable, NC = not calculated.

the lower cost antihypertensive drugs are also cost-effective for the older patient cared for in the NHS. The actual cost-effectiveness in the UK will depend not only on drug cost, but also on the relative effectiveness of the newer drugs and additional treatment costs (adverse effects, secondary drugs etc.).

Adverse Effects

All the main classes of antihypertensive drugs are associated with adverse events. In general the symptoms are mild (e.g. dizziness, headache, or rash) and in the majority of older patients severe side effects (arrhythmias or renal dysfunction) can be avoided by careful monitoring. In a direct comparison between the older antihypertensive drugs (beta-blockers and diuretics) and the newer angiotensin converting enzyme (ACE) inhibitors and calcium channel blockers, there was no evidence that the newer drugs were associated with fewer side effects.¹⁷ A similar evaluation restricted to older people has not been undertaken.

A correlation has been shown between calcium channel blockers and increased death rates in older people. The analysis was based on early trials of a drug that had a short half-life and caused rapid reductions in blood pressure.¹⁸ There is no evidence from systematic reviews that slow release formulations or new variants with a longer half-life are similarly associated with an increased mortality rate in this patient group. Two studies of long-acting calcium channel antagonists have shown evidence of efficacy and safety.^{19, 20}

Quality of Life

In a meta-analysis of patients from all age groups there was no indication that antihypertensive drugs had a negative impact on their quality of life, and there was some evidence of beneficial effects.²¹ The impact of drug therapy on the quality of life for older people has not been systematically reviewed and has generally been poorly assessed in the literature. Analysis of interview questionnaires and reports of drop-out and sideeffect rates, tend to suggest that there are no significant negative effects on quality of life.^{22,23} A more

Implications

- Through the wider use of antihypertensive therapies more older people would be able to maintain a healthy and active lifestyle
- There is good evidence that treating hypertension in older patients is effective
- Diuretics and/or beta-blockers should be first-line agents
- Systems to ensure that older people with hypertension are diagnosed, treated and followed up need to be developed
- A system of audit should be cultivated to assure adequate treatment
- High quality research on patient adherence with antihypertensive medications is needed

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detailed assessment of quality of life has been presented in a randomised controlled trial which assessed cognitive impairment, activities of daily living, depressive symptoms and mood changes in older patients. The majority of patients in the active arm were treated with a beta-blocker, diuretic or the two in combination. The results showed that there was no significant difference in quality of life between antihypertensive drug treatment and the placebo.²⁴

Table 2. Reduction in the morbidity of patients aged 80+ years.

	Percentage of cases prevented [†] (95% Confidence Interval)		
	Cardiovascular Events*	Stroke	Heart Failure
Morbidity	22% (2 to 60)	34% (10 to 52)	39% (10 to 60)

[†] Treated for approximately 3.5 years, reduction compared to controls.

Patients were largely ambulatory outpatients, although not exclusively. Mean blood pressure at study entry across all studies was 180/84mmHg (includes patients with isolated systolic hypertension in some studies). Age ranged from 80 - 99 years. 95% confidence intervals estimated from graph.

*Cardiovascular events = both strokes and CHD events.

Barriers to Wider Coverage

Despite initiatives to improve detection and treatment, surveys suggest that half of the population with hypertension is undetected, while half of those detected are not treated, and in half of those treated their hypertension is uncontrolled (the rule of halves).²⁵

Adherence is considered to be poor in patients with hypertension, although few trials have examined this issue with respect to older people.²⁶ Although it is a widely held belief that a reduction in the frequency of dosing should result in increased adherence there are too few good quality studies available to demonstrate that this is the case.²⁶

Surveys of GPs suggest a reluctance to consider treatment at levels quoted in guidelines.²⁷ Reasons for this are in part historical; high blood pressure in the past has been considered a part of the ageing process, while genuine concern remains regarding co-existing illness and polypharmacy. In addition there are very real fears about the resource implications of treating more than half of the population over 65.²⁸

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