Benefits of drug therapy are unclear for mild hypertension

A Cochrane review concludes that antihypertensive drugs have not been shown to reduce mortality or morbidity in adults with mild hypertension and no previous cardiovascular events. Significantly more people taking antihypertensive treatment discontinued treatment due to adverse effects, compared with placebo. However, the review has some significant limitations.

Overview: Previous meta-analyses have concluded that cardiovascular events and overall mortality are decreased with antihypertensive drug therapy compared with placebo or no treatment. However, these meta-analyses have combined subjects with mild (stage 1) hypertension (blood pressure 140–159/90–99 mmHg) and moderate to severe hypertension (greater than 160/100 mmHg), and also people who have had a previous cardiovascular event (secondary prevention) and those who have not (primary prevention).

When the NICE guideline on hypertension was developed in 2011, the Guideline Development Group discussed whether antihypertensive drug treatment should be offered to all adults with mild hypertension. The uncertainty about whether every adult with mild hypertension should be offered treatment was recognised, particularly in those aged under 40 years. The Guideline Development Group concluded that drug treatment should be offered only to people with mild hypertension who also have higher levels of cardiovascular disease risk.

Current advice: NICE defines mild hypertension as clinic measured systolic blood pressure of 140–159 mmHg and/or diastolic blood pressure between 90–99 mmHg, and ambulatory blood pressure measurement daytime averages of between 135/85 mmHg and 149/94 mmHg.

NICE advises offering antihypertensive drug treatment to people aged under 80 years with stage 1 hypertension who have one or more of the following:

- target organ damage
- established cardiovascular disease
- renal disease
- diabetes
- a 10-year cardiovascular risk equivalent to 20% or greater.

For people aged under 40 years with stage 1 hypertension and no evidence of target organ damage, cardiovascular disease, renal disease or diabetes, NICE recommends considering seeking specialist evaluation of secondary causes of hypertension and a more detailed assessment of potential target organ damage. This is because 10-year cardiovascular risk assessments can underestimate the lifetime risk of cardiovascular events in these people.

The NICE Pathway on hypertension brings together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams.
**New evidence:** This Cochrane review aimed to quantify the effects of antihypertensive drug therapy versus no treatment on mortality and morbidity in adults with mild hypertension and no evidence of cardiovascular disease. It included four randomised controlled trials (RCTs) with 8912 participants (Diao et al. 2012).

The study concluded that, compared with placebo, antihypertensive treatment does not reduce mortality over 4–5 years. There was also no reduction in coronary heart disease, stroke, or total cardiovascular events with antihypertensives.

Withdrawals due to adverse effects were increased by around 9% with drug therapy versus placebo (11.3% vs 2.3%, risk ratio 4.80, 95% confidence interval 4.14 to 5.57). These data were from one RCT that combined figures for adverse effects for all severities of hypertension. However, the authors of the Cochrane review assumed that withdrawals due to adverse effects would be similar in the participants with mild hypertension and those with moderate to severe hypertension.

The conclusions that can be drawn from this study are limited by the small number of events (only 165 of 7080 patients had a cardiovascular event and 167/8912 died). Individual patient data was often not available. Also, the quality of the evidence was found to be poor for the efficacy outcomes, and length of follow-up (5 years or less) may have been insufficient to assess long-term outcomes such as mortality, particularly as patients with mild hypertension would be expected to be at low risk of such events. Importantly, the included studies do not reflect current practice because they were undertaken at a time when drugs such as beta-blockers and methyldopa were used as first-line treatment.

**Commentary:** “This Cochrane review suggests that the absolute benefits of antihypertensive treatment are likely to be small in patients with mild hypertension and no previous cardiovascular events. The study provides no reason to depart from NICE guidance, which recommends only treating patients with mild hypertension who are at high risk of cardiovascular disease. However, it should be noted that recruitment to the studies included in this review took place in the 1970s and 1980s. There was no use of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers or aldosterone antagonists which form the mainstay of contemporary management of hypertension.

“As NICE advises, the benefits and risks of antihypertensive drug treatment should be discussed with patients. In the Cochrane review, the risk of having an adverse effect that led to discontinuation of treatment was found to be nearly 5 times higher with antihypertensive drugs, compared with placebo, based on data from the Medical Research Council trial giving a number needed to harm of 11. Adherence to hypertensive medication is dependent on a large number of factors and the effect of adverse effects on adherence will depend on the use of medicines and doses that are now often different from those used in these RCTs. Many patients take more than one medicine for hypertension, and withdrawal from one drug does not indicate the inability to tolerate all antihypertensives. Nevertheless, given the uncertain benefits of treatment and the risk of adverse effects, it is likely that many patients with mild hypertension will prefer to try lifestyle interventions initially.” – Dr Huw Griffiths, Consultant Cardiologist, Queen Alexandra Hospital, Portsmouth
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