Should exercise be considered as an alternative to drug treatment in patients with low risk mild hypertension?

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Word count: 796 words

Editorial

High blood pressure affects 1 in 5 adults globally¹ and is a major risk factor for cardiovascular disease. Clinical guidelines have traditionally recommended that patients with a sustained clinic blood pressure of $\geq 140/90$ mmHg be considered for lifestyle or pharmacological intervention, depending on their underlying risk of cardiovascular disease.² However, recent guidelines from the American College of Cardiology/American Heart Association (ACC/AHA)³ recommended doctors begin antihypertensive treatment at lower thresholds, based on results from the SPRINT trial.⁴ This study showed that aggressive treatment to systolic levels below 120 mmHg can reduce the risk of cardiovascular disease compared to standard targets.⁴ These recommendations are controversial because they apply the results from a trial which enrolled high risk individuals, to much larger populations of low risk patients where there is as yet no evidence to support prescription of antihypertensive treatment. Indeed, for patients with low cardiovascular disease risk and 'mild' hypertension (*i.e.* sustained blood pressure between 140/90-159/99 mmHg), there is no evidence for pharmacotherapy from trials or meta-analyses.⁵ Studies in such a low-risk group would require unfeasibly large sample sizes to detect small treatment effects--due to the low prevalence of outcome events in this population.

How low is too low to treat hypertension with medication?

We recently studied whether antihypertensive treatment is safe and effective in people with low risk mild hypertension.⁶ Using data from the electronic health records of 38,286 eligible patients, we found no evidence of an association between exposure to antihypertensive treatment and mortality or cardiovascular disease during a median follow-up period of 5.8 years. There was however, evidence that treatment may be associated with an increased risk of adverse events such as hypotension (HR, 1.69; 95% CI, 1.30-2.20), syncope (HR, 1.28; 95% CI, 1.10-1.50), electrolyte abnormalities (HR, 1.72; 95% CI, 1.12-2.65) and acute kidney injury (HR, 1.37; 95% CI, 1.00-1.88). Although these data are observational, and potential for bias from unmeasured confounding cannot be ruled out, they do highlight uncertainty around the appropriateness of treatment in low risk mild hypertensives. Such uncertainty led to the UK's National Institute for Health and Care Excellence (NICE) **choosing to not recommend targets as low as those encouraged by the ACC/AHA** in its forthcoming update of clinical guidelines.

Is exercise the superior first line therapy?

So if pharmacological treatment in patients with low risk mild hypertension is not appropriate, what is the alternative? In this issue of the *British Journal of Sports Medicine*, Associate Professor Huseyin Naci *et al.*,⁷ present a network meta-analysis of trials examining the blood pressure lowering effect of exercise compared to similar trials examining the efficacy of antihypertensive treatment. In patients with a baseline blood pressure of $\geq 140/90$ mmHg, antihypertensive treatment and exercise had a comparable effect on blood pressure at follow-up.⁷ Whilst the review did not seek to compare the effect of exercise and treatment on 'hard outcomes' such as cardiovascular disease, a previous review by the same authors reported that exercise can have comparable effects to antihypertensive treatment on mortality, secondary prevention of coronary heart disease, rehabilitation after stroke, and treatment of heart failure.⁸

Despite the effectiveness of exercise at reducing blood pressure, there is debate as to which populations should be targeted with such interventions. Naci *et al.*,⁷ included studies which examined patients without previous cardiovascular disease or diabetes (*i.e.* patients with a low risk of cardiovascular disease), with a mean age between 50-55 years and a mean baseline systolic blood pressure of 132-160 mmHg. Our observational study⁶ examined similar low risk patients, aged 55 years, with a mean systolic blood pressure

of 146 mmHg at baseline. Since we observed an increased risk of adverse events in this population, data from the Naci *et al.*,⁷ review make a strong case that such patients should be targeted for a strategy where physical activity is the primary treatment—not antihypertensive medication. However, to many people, taking a pill will always be perceived as being easier than going for a 40-minute run twice per week. Thus, the decision to take medications or increase physical activity will always lie with the patient. Data from our observational study⁶ and that of Naci *et al.*,⁷ are important to ensure these decisions are well informed. Better understanding of the potential harms of therapy in all populations might encourage better uptake of physical activity as a therapy for hypertension.

Mild hypertension often affects low risk individuals--those who may not suffer cardiovascular disease for many years. Whilst the benefits of lowering blood pressure are unquestionable, the method with which this is achieved can be debated. Low risk mild hypertensive patients are typically aged in their 50s and not afflicted by multiple conditions. For them, physical activity could be the ideal way of reducing blood pressure, obtaining additional health benefits (metabolic, cognitive) whilst avoiding adverse events associated with antihypertensive treatment.

Funding: JS receives funding from the Wellcome Trust/Royal Society via a Sir Henry Dale Fellowship (ref: 211182/Z/18/Z). He also receives funding from the NIHR School for Primary Care Research and the NIHR Collaboration for Leadership in Applied Health Research and Care Oxford at Oxford Health NHS Foundation Trust.

Competing interests: None declared.

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