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Controversies in Hypertension

The benefits of treating high blood pressure (BP) are supported by an enormous evidence base. However, the results of recent hypertension trials have also raised some controversies, such as whether the concepts of arbitrary BP thresholds and single risk factor intervention are outdated, and whether new antihypertensive drugs offer benefits for cardiovascular prevention beyond "BP lowering".

Blood pressure is a continuous risk factor

While there is admittedly need for arbitrary divisions to guide diagnosis and treatment, this ignores the fact that BP has a continuous positive relationship to cardiovascular mortality across all BP values, with no evidence of a threshold down to 115/75 mmHg. In fact, there is a doubling in cardiovascular mortality for every 20/10 mmHg increase in systolic/diastolic BP. This means that even a BP in the "high-normal" range is significant because someone with a usual BP of 135/85 mmHg compared to 115/75 mmHg still has a two-fold higher risk of BP-related mortality. From a population perspective, changes in diet and lifestyle that reduce BP by just a few mmHg in the whole population would give more overall benefit than much larger individual reductions in the minority with severe hypertension. In this regard, it is notable that the DASH diet (http://dashdiet.org/), which combines dietary sodium restriction with a high-fruit and high-vegetable intake, can lower systolic BP by around 7 mmHg.

Targeting CVD risk rather than hypertension

Antihypertensive therapy should be aimed at reducing the risk of stroke or heart attack, and not just blood pressure. It is therefore impossible to target treatment appropriately without assessing the patient's total cardiovascular risk. Individuals with multiple risk factors or a history of vascular disease will be at higher absolute risk of cardiovascular events at all levels of BP than individuals with isolated hypertension, and will consequently derive greater benefit from antihypertensive therapy. At the same time, non-hypertensive individuals will become candidates for BP reduction if their absolute cardiovascular risk is high. Likewise, most persons with treated hypertension are at sufficient absolute cardiovascular risk to benefit from additional statin therapy even in the absence of dyslipidaemia, as was established in the lipid-lowering arm of the ASCOT study.

Lessons from recent hypertension trials

Intervention studies have shown that seemingly small BP changes can result in substantial cardiovascular benefits. A systolic BP differential of -4 mmHg is associated with a 23% reduction in relative risk of stroke, 15% reduction in heart attack, and 14% reduction in total mortality. Earlier placebo-controlled trials have provided definitive evidence of treatment benefit with various drug classes, including thiazide diuretics, ß-blockers, calcium channel blockers (CCBs), angiotensin converting enzyme inhibitors (ACEIs), and angiotensin II receptor blockers (ARBs). Focus has now shifted to "head to head" trials that compare new and old antihypertensive drugs, and test whether treatment based on different drug classes would offer advantages "beyond BP lowering". These recent large-scale trials have clarified the debate and emphasised that it is the magnitude of the BP reduction, and not the drug class, which is the major driver of clinical benefit. However, in comparison with other antihypertensive drugs, ß-blockers (primarily atenolol) appear inferior particularly for stroke prevention, hence they are no longer considered a first-line agent in uncomplicated hypertension. Clinical data also suggest that CCBs might offer more selective benefit for stroke prevention, and ACEIs/ARBs in heart failure prevention. However, the hypothesis that newer antihypertensive drugs have cardiovascular benefits beyond their BP effects is largely unproven.

Antihypertensive drug combinations

In any case, most patients need a combination of drugs from different pharmacologic classes to achieve BP targets. Based on the available evidence, the most effective combination is an ACEI (or ARB) with a CCB. However, the combination of diuretic +/- ACEI is well suited to treatment of systolic hypertension in the elderly. This was tested in the recent HYVET trial of hypertensive patients aged 80 years or more, in whom this treatment regimen was highly effective in reducing incident stroke, heart failure, and total mortality. The recent ONTARGET trial is also important in that it showed a lack of benefit and potential harm from an ACEI plus ARB combination compared to an ACEI alone for cardiovascular prevention in high risk patients; hence, this combination should be avoided in routine clinical practice.

The J-curve controversy

The debate over the J-curve, the concept that there is a "normal" BP below which there is a paradoxical increase in mortality, has re-emerged because people are now advocating treating to much lower BP goals. The Heart Foundation currently recommends a BP target of <130/80 mmHg for persons with high risk conditions including diabetes, coronary heart disease, stroke/TIA, and chronic kidney disease. However, many argue that there is still no compelling clinical trial evidence that maintaining a systolic BP<130 mmHg is beneficial, and point to some observational data that suggest that 'tight' BP control may increase mortality. However, it must be emphasised that even "J-curve" proponents agree that doctors should not be deterred from pursuing aggressive control of hypertension when, currently, BP targets are achieved in only about one-third of patients.

About the Author

Joseph Hung holds current appointments as Winthrop Professor of Cardiology, UWA, and Consultant Cardiologist at Sir Charles Gairdner Hospital. He did his advanced training in Cardiology at the Royal Prince Alfred Hospital, NSW, and then fellowships abroad at Stanford University Medical Centre (USA) and Montreal Heart Institute (Canada). He combines clinical and research interests in novel risk factors in the prevention, diagnosis, investigation, and treatment of ischaemic heart disease, arrhythmias, valvular heart disease, and heart failure. He consults privately at Wembley and Joondalup.