EDITORIAL

Blood Pressure and Acute Ischemic Stroke

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Blood pressure (BP) is very commonly elevated during acute ischemic stroke and remains elevated for several days, before generally spontaneously returning to baseline values. In some specific cases, infarction involving the lateral medulla (Wallenburg syndrome), leads to hypertension and it can be shown that this region of brain is important in blood pressure control.[1,2] Similarly infarction of the insula may result in varying degrees of autonomic dysfunction, including acute hypertension. Acute hypertension may also been seen as a terminal event among patients with massive edema and rostral-caudal herniation, either due to malignant middle cerebral artery or cerebellar infarction; however, this occurs usually in the 24-96-hour timeframe after stroke onset. Thus, there is some pathobiological evidence that ischemic stroke causes neurogenic hypertension.

In contrast, it is also clear that long-term hypertension is a fundamental cause of stroke. Population studies suggest that the attributable risk of all stroke (including hemorrhagic forms) is about 35%.[3] Long-term reduction in blood pressure has been well shown in both primary and secondary prevention strategies to mitigate stroke occurrence.[4] Malignant hypertension may be associated with brain and retinal dysfunction. Recent evidence suggests that hypertension variability is an important predictor of stroke[5] and there has always been a temporal association between acute hypertension, stimulated by illicit drug use (eg. Cocaine) or other cause and intracerebral hemorrhage.[6] However, it is generally more common that acute stroke causes the hypertension rather than the other way around.

Acute hypertension is eminently treatable. In other conditions of the cardiovascular system such as acute myocardial infarction or aortic dissection, treatment limits the ongoing process and improves outcome. Preliminary evidence in the setting of acute intracerebral hemorrhage suggests that treatment of acute hypertension limits hemorrhage expansion.[7,8] Similarly, it is common practice to treat elevated blood pressure in the setting of aneurysmal sub-arachnoid hemorrhage to prevent the risk of early re-bleeding until the aneurysm can be secured by surgical clipping or endovascular coiling. However, in acute ischemic stroke, very little reliable guidance is available to justify acute treatment. In truth we have very little idea how important it is as a predictor of outcome and whether or not it should be treated. If it is to be treated, we do not know to what target or with what drugs.

In this issue of the Journal, Zhang and colleagues followed 2675 ischemic stroke patients from Shandong Province in eastern China[9]. Extreme elevations of blood pressure within the first 72 hours of admission were strongly associated with neurological disability or death. This effect was not driven by stroke severity. Importantly, mid-range BP elevation, up to a systolic BP 180 mmHg, was not statistically relevant in predicting poor outcome. Only extremes of systolic BP > 220 mmHg predicted poor outcome.

The results support findings from the International Stroke Trial-1, which demonstrated that there was a U-shaped relationship between acute blood pressure and outcome. Very high or very low BP in the first 48 hours was associated with a worse outcome at six months.[10] Thus, this report is confirmatory and suggests that Asian ethnicity, compared to a predominant Caucasian population in IST-1, is not a major issue in predicting the outcome of acute hypertension. Knowing that very high or very low BP is associated with poor outcome does not, however, help us much therapeutically.

In the setting of thrombolysis, guidelines suggest treatment of elevated BP > 185/110, but this is not an evidence-based threshold. The ideal threshold may be higher or lower than that. The Acute Candesartan Cilexetil Therapy in Stroke Survivors study trial examined lowering of BP with candesartan, beginning within 24 hours of stroke onset, only among patients without substantial stenosis of their carotid arteries and continuing treatment for one year.[11] The study was designed as a pilot study, but an unexpected positive result in favour of the treatment group emerged, even though the study was underpowered at the planning stage. Blood pressure lowering using an angiotensin receptor blocker appeared to be useful and this result is being investigated further in a larger trial. In contrast, induced hypertension has been shown to improve neurological function in some acute ischemic stroke patients with intracranial occlusions.[12-14] It seems likely, path-ophysiologically, that BP lowering may be harmful when there is a known intra- or extra-cranial arterial occlusion, but could be helpful when the arteries are open or have been recently reperfused.

Geeganage et al attempted to summarize diverse treatment data on acute hypertension treatment using meta-analysis and concluded that there was a U-shaped response curve. A modest degree of BP lowering improved average outcomes; but more extreme BP lowering or no treatment resulted in worse outcomes.[15]

There is a great need for trials that examine acute medical therapy for acute ischemic stroke. The treatment of hypertension and the treatment of hyperglycemia are two obvious therapeutic targets. There are good pathophysiological reasons to think that treatment trials of antihypertensive therapy in acute ischemic stroke should be stratified by whether or not an intra- or extra-cranial arterial occlusion is present or not. We await expectantly the results of the Intensive blood pressure reduction in acute cerebral haemorrhage trial which will inform us about the medical management of intracerebral hemorrhage; a similar trial is desperately needed in acute ischemic stroke.

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