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Treating hypertension in acute ischemic stroke

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Editorial Commentary

Treating Hypertension in Acute Ischemic Stroke

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Persistence of the controversy over whether hypertension should be treated in acute ischemic stroke is a testament to the power of tradition and authority in medicine. It also probably reflects the tendency of physicians to be unduly influenced by the most recent adverse events that they remember in their own patients.[1]

Concern about worsening of stroke with excessive lowering of blood pressure has been based to a large extent on inappropriate historical hypotensive therapies that cannot be controlled, such as "sublingual" nifedipine or intramuscular hydralazine.[2] As I pointed out with Del Maestro in 1985,[3] there are some circumstances in which severe hypertension must be treated in acute ischemic stroke. Two examples I have seen are aortic dissection picking off a renal and a carotid origin, with sudden severe renovascular hypertension, hypertensive encephalopathy in the territory of the patent carotid artery, and ischemia in the territory of the occluded internal carotid, and severe hypertension with acute pulmonary edema in the setting of myocardial ischemia, with acute embolic stroke from the myocardial infarction. The question, therefore, is not whether hypertension should be treated in the setting of acute cerebral ischemia but when and how.

Since the publication of the National Institutes of Health trial of recombinant tissue plasminogen activator for acute stroke,[4] treating hypertension in acute stroke has become more common, because tissue plasminogen activator is contraindicated with blood pressures >185 mm Hg systolic or 110 mm Hg diastolic.[5] Guidelines suggest various approaches for the lowering of blood pressure, including intravenous labetalol, nitroglycerine paste, intravenous nicardipine, and, in extreme cases, intravenous nitroprusside.[5,6]

Two articles in this issue of *Hypertension* shed some light on this problem. Geeganage and Bath[7] performed a metaregression analysis of 37 acute ischemic stroke trials involving blood pressure reduction in 9008 patients. They found a U-shaped relationship between blood pressure reduction and outcomes, with the lowest risk of death or dependency at the end of follow-up in patients with blood pressure reductions of ≈14 to 15 mm Hg. Large falls in blood pressure or increases in blood pressure were associated with a higher risk of poor outcomes. Similarly, the authors of the Virtual International Stroke Trial Archive collaboration[8] recently found that high systolic pressures, a small drop in systolic pressure, and large variability in systolic pressure were associated with poor outcomes.

The authors of a Spanish multicenter observational study of blood pressure changes in acute ischemic stroke[9] reported that age determined the effects of blood pressure change on outcome. Systolic blood pressures >180 mm Hg (in the emergency department and after 24 hours) doubled the risk of poor outcomes (modified Rankin score at 3 months), and systolic blood pressures <136 mm Hg increased the risk of poor outcomes by 30%. In patients over age 80 years, a blood pressure reduction >28 mm Hg gave a 21.7-fold increase in the risk of poor outcomes.

High blood pressure during acute stroke aggravates cerebral edema. Because the brain is enclosed by a rigid skull and compartments in the brain are determined by the falx, corpus callosum, and the tentorium of the posterior fossa, cerebral edema results in a progressive reduction in perfusion pressure (systemic blood pressure minus venous and tissue pressure), strangulation of the salvageable penumbra, and progressive infarction. This is why early hemicraniectomy has such dramatic effects in malignant middle cerebral artery syndrome, with a number needed to treat of only 2 to prevent death or severe disability.[10] Thus, it would be expected that, in patients with very high pressures, blood pressure reduction would improve outcomes. On the other hand, excessive blood pressure reduction reduces blood flow in the ischemic penumbra, also leading to worse outcomes.

Reasons why the elderly would fare worse with blood pressure reduction could include pseudohypertension and hypertensive arteriolar hypertrophy from long-standing hypertension. Approximately 4% of elderly patients have a very significant (≈30 mm Hg) difference between their diastolic cuff pressure and intra-arterial pressure.[11–13] Such patients would, therefore, have much lower pressures than measured, when their pressures are treated, and would be expected to have worsening of ischemia in the salvageable penumbra.

Elderly patients are also much more likely to have long-standing hypertension and, therefore, to have hypertensive hypertrophy in their cerebral arterioles. This would render them more intolerant to drops in blood pressure. The Figure is a cartoon illustrating the principle described many years ago by Strandgaard et al.[14] Long-standing hypertension leads to arteriolar hypertrophy, so autoregulation of cerebral blood flow (CBF) is shifted to the right: patients with long-standing hypertension withstand higher pressures and do not tolerate blood pressures as low as those patients without hypertensive arteriolar hypertrophy. In a sense, this is the mirror image of the cerebral hyperperfusion syndrome that is rarely seen after carotid revascularization.[15,16]

The opinions expressed in this editorial are not necessarily those of the editors or of the American Heart Association.

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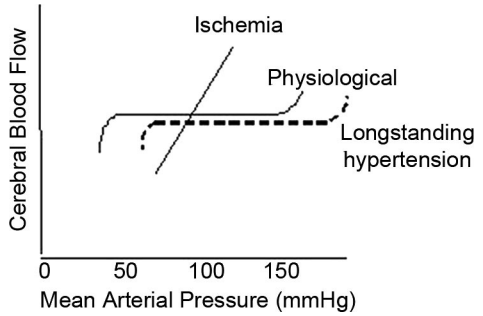

Figure. Loss of CBF regulation during acute ischemic stroke. In physiological conditions, CBF is autoregulated over a wide range of perfusion pressures, from ≈50- to 150-mm Hg mean arterial pressure. This is shifted to the right in long-standing hypertension because of arteriolar hypertrophy. During acute ischemia, CBF becomes pressure passive, resulting in a marked reduction of CBF if pressure drops too low. The threshold at which this becomes a problem will be higher for patients with long-standing hypertension whose CBF autoregulation is shifted to the right.

Blood pressure treatment in acute stroke is, thus, a double-edged sword. Autoregulation is lost in the ischemic region (Figure), so higher pressures aggravate cerebral edema[17,18] and thereby cause progressive ischemia; blood pressure that is too low aggravates ischemia in the salvageable penumbra. Mean arterial pressures at ≈120 mm Hg (representing blood pressures ≈160/100 or 180/90 mm Hg) are probably on the autoregulation plateau for most patients and may represent a reasonable target for blood pressure in acute stroke; this might be shifted up for patients with long-standing hypertension and down a bit for patients with no history of hypertension. Blood pressure should be reduced carefully and only with short-acting intravenous drugs that can be controlled (preferably by infusion rather than bolus injections or by nitrate paste, which can be wiped off if pressures are dropping too low).[2,19] In elderly patients, it may be wise to measure intra-arterial pressure to really know what the pressure is and the effect of treatment. Randomized trial results that tell us when and how to treat hypertension will be most welcome. In the meantime, we need to be thoughtful, careful, and wise.

Disclosures

None.

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