Cerebral Hemodynamics, Autoregulation and Blood Pressure Management

Colin P. Derdeyn, MD

Interventional Neuroradiology Service, Cerebrovascular Group, NeuroImaging Laboratory, Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, MO, USA

INTRODUCTION

Chronic hypertension may be the single most important modifiable risk factor for ischemic stroke (19). Anti-hypertensive therapy has been proven to reduce the risk of stroke in prospective, randomized controlled studies (7). Hypertension is common in patients presenting with acute ischemic stroke (4), but its treatment is controversial (9). In contrast to chronic hypertension, there is little clinical trial data to guide decisions regarding anti-hypertensive therapy in acute ischemic stroke. Furthermore, there are potential conflicting mechanisms by which patient outcome could be worsened. Reduction of mean arterial pressure can reduce blood flow to already ischemic regions and result in further ischemic injury. On the other hand, hypertension can increase the risk of cerebral edema or hemorrhage, particularly in patients who have received thrombolytic therapy. In this lecture, we will review the data concerning these two conflicting mechanisms and discuss current guidelines for the treatment of hypertension in patients with acute ischemic stroke.

CEREBRAL HEMODYNAMICS: AUTOREGULATION AND OXYGEN EXTRACTION

Cerebral perfusion pressure (CPP), the driving force for blood through the cerebral circulation is defined as the difference between mean arterial pressure and venous backpressure or intracranial pressure. For patients without venous occlusive disease or increased intracranial pressure, it is reasonable to assume that CPP is equal to mean arterial pressure. Global CPP can be reduced by global hypotension. Regional CPP can be reduced by local arterial stenosis or occlusion, depending on the adequacy of collateral sources of arterial flow.

Two compensatory responses to reduced CPP have been established: autoregulation and increased oxygen extraction (Figure 1). As CPP falls, cerebral blood flow (CBF) is initially maintained by vasodilation of resistance arterioles, a reflex known as autoregulation (14,20). CBF falls slightly through the autoregulatory range, leading to increases in OEF prior to exceeding autoregulatory capacity (8,11,21). It is important to point out that in patients with chronic hypertension the autoregulatory curve is shifted to the left, i.e., autoregulatory failure will occur at higher values of CPP than in normotensive patients (18). The autoregulatory range in normotensive subjects is from 150 to 60 mm Hg.
With further reductions in CPP, the autoregulatory capacity is exhausted and CBF falls as a function of pressure. When CBF falls, increases in oxygen extraction fraction (OEF) will maintain cerebral oxygen metabolism and tissue function up to a point (3,12,13). CPP reductions beyond the point where increases in OEF can compensate will lead to true ischemia, with an insufficient delivery of oxygen to meet metabolic demands. Energy failure will result and permanent injury may ensue depending on the duration and degree of the ischemia.

In Figure 1, point A represents baseline. The distance between points A and B represents the autoregulatory range. The distance between points B and C represent exceeded autoregulatory capacity where cerebral blood flow (CBF) falls passively as a function of pressure. Point C represents the exhaustion of compensatory mechanisms to maintain normal oxygen metabolism and the onset of true ischemia. Cerebral blood flow (CBF) falls slightly, down to 18%, through the autoregulatory range (between A and B) (8,11). Once autoregulatory capacity is exceeded, CBF falls passively as a function of pressure down to 50% of baseline values (between B and C). Oxygen extraction fraction (OEF) increases slightly, up to 18%, with the reductions in CBF through the autoregulatory range (between A and B) (21). After autoregulatory capacity is exceeded and flow falls up to 50% of baseline, OEF may increase up to 100% from baseline (15). The cerebral metabolic rate for oxygen consumption (CMRO2) remains unchanged throughout this range of CPP reduction (between A and C), due to both autoregulatory vasodilation and increased OEF (10,15).

**Figure 1**
Hemodynamic and Metabolic Responses to reduced Perfusion Pressure

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**ACUTE ISCHEMIC STROKE**
In most patients with acute stroke, an artery within the brain becomes acutely occluded, either partially or completely. The degree of blood flow reduction will depend on the degree of occlusion and the adequacy of collateral vessels. Clinical symptoms of ischemic occur with reductions in cerebral blood flow below 20 ml/100g * min. The amount of permanent damage will depend on two factors: the degree and the duration of ischemia. Permanent cell death may occur within minutes in the complete absence of flow. In many patients presenting with acute stroke, some tissue remains viable, but vulnerable if flow is not restored quickly (18). This is the concept of the ischemic core and penumbra. This is also the rationale behind thrombolytic therapy for acute stroke, at present the only proven effective therapy.
Normal autoregulatory vasodilation is impaired in patients with recent or ongoing ischemia. Meyer and coworkers measured CBF in 30 subjects with ischemia or infarction during induced hypotension (17). A 22% drop in mean arterial pressure caused a 12% reduction in hemispheric CBF, when little or no reduction would be expected. The longer the time elapsed from the original ischemic event, the greater the autoregulatory dysfunction. Consequently, this penumbral tissue may be vulnerable to reductions in mean arterial pressure. Some investigators have suggested that the acute elevations in blood pressure commonly observed in patients with stroke are a protective mechanism to maintain flow (16). In addition, blood pressure generally drops to normal levels within days without treatment (6,22). The association between larger drops in pressure and better neurological outcome suggests a relationship between recanalization and blood pressure (6).

While experimental studies have suggested that hypertension increases the risk of brain edema or hemorrhage after ischemic stroke (18), there is little clinical data to prove that this is true in humans. Conversely, there is also little data to show that modest pharmacological reductions in blood pressure in patients with acute stroke adversely affects outcome (5).

CURRENT GUIDELINES

Acute and severe reductions in blood pressure in patients presenting with acute stroke should be avoided. Current treatment guidelines advocate treatment for patients with systolic blood pressures above 185 mm Hg or diastolic pressures above 110 mm Hg, particularly if these patients will receive intravenous tPA (1,2,9). Intravenous labetalol in frequent boluses (10 mg every 10 minutes up to 150 mg) or as a continuous infusion (2 to 8 mg/min after a bolus) is recommended for both patients receiving tPA and for non-thrombolytic patients. Sodium nitroprusside is reserved for severe hypertension (diastolic pressures > 140 mm Hg) or moderate hypertension not responding to labetalol.

REFERENCES


**Top**

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**Top**

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