

BLOOD PRESSURE TREATMENT IN THE ACUTE STROKE SETTING - CON

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The treatment of hypertension is clearly beneficial over the long term in patients with ischemic and hemorrhagic stroke to prevent recurrent events and has the greatest impact on subsequent recurrence risk of any modifiable stroke risk factor. The management of high blood pressure in the acute phase of hemorrhagic and ischemic stroke is of less clear benefit. Elevated BP is common acutely after stroke and can be related not only to hypertension prior to the event but also to acute stress, increased cardiac output, increased ICP and generalized hypoxia. The lowering of BP in the acute stage of ischemic stroke could be problematic because autoregulation in the brain is lost and cerebral blood flow is directly related to the perfusion pressure. Reducing blood flow could potentially exacerbate ischemic injury within the ischemic penumbra and increase the size of the infarction (1). Conversely, lowering BP may reduce the development of cerebral edema and improve the cardiac status of the patient. Several recent studies have addressed the potential impact of acute BP lowering in hemorrhagic and ischemic stroke.

The INTERACT trial evaluated intensive BP lowering to a target systolic BP (SBP) of <140 mm/Hg versus standard BP management with a target of <180 mm/Hg in intracerebral hemorrhage (ICH) patients with an elevated systolic BP diagnosed within 6 hours of ICH onset (2). The primary outcome measure was the growth of hematoma volume at 24 hours. The intensive intervention group had a significantly lower systolic BP, 146 versus 157 mm/Hg at 1-24 hours and a significantly smaller growth of hematoma volume at 24 hours. However, there was no difference in adverse events or clinical outcome at 90 days in the intensive BP-lowering group. In the ATTACH study from the US, ICH patients presenting within 6 hours of onset and a systolic BP > 200 mm/Hg were given i.v. nicardipine for 18-24 hours with SBP targets of 170-200, 140-170 or 110-140 (3). The drug was well tolerated and there was no difference in 90-day mortality among the 3 groups. These two studies suggest that acute BP lowering therapy is safely tolerated. Larger trials are ongoing to determine if this BP-lowering therapy reduces mortality and/or improves outcome. The current AHA/ASA guidelines for BP management after ICH (4) are as follows:

1. If SBP >200 mm/Hg or mean arterial pressure (MAP) >150 mm/Hg then consider aggressive reduction of BP with a continuous infusion with frequent BP monitoring every 5 minutes
2. If SBP is >180 mm/Hg or MAP is > 130 mm/Hg there is the possibility that of elevated ICP consider monitoring ICP and reducing BP using intermittent or continuous medications while maintaining a cerebral perfusion pressure > 60 mm/Hg
3. If SBP is >180 mm/Hg or MAP > 130 mm/Hg and there is no evidence or suspicion of elevated ICP consider modest BP reduction

These were class C recommendations, meaning they are based upon consensus opinion and not actual clinical trial data. The overall recommendation of acute BP management in ICH concluded that "Until ongoing clinical trials for BP intervention for ICH are completed, physicians must manage BP on the basis of the present incomplete efficacy of evidence".

Treating BP in the acute stage of ischemic stroke also remains controversial. The recently completed trial of the angiotensin-receptor blocker, candesartan, provides the largest dataset to date (5). In this double-blinded, placebo controlled trial that included predominantly ischemic stroke patients enrolled with a baseline BP > 140 mm/Hg, patients were assigned to escalating dose of candesartan or placebo for a seven day treatment period. The two coprimary endpoints were a composite of vascular death, myocardial infarction or stroke and functional outcome at 6 months and data at this time point were available in 1000 candesartan patients and 1004 placebo patients. BP at the 7-day time point was significantly lower in the candesartan group. The vascular endpoints at 6 months occurred slightly more frequently in the candesartan group, 120, than in the placebo group, 112, $p=0.52$. Poorer functional outcome across the range of mRS scores, OR 1.13, 95% CI 0.97-1.32, $p=0.12$. A meta-analysis of this trial and prior acute BP lowering trials was performed and demonstrated that OR for a mRS >2 with treatment was 1.04, CI 0.97-1.12, $p=0.30$. The results of this trial and the accompanying meta-analysis of functional outcome support the recommendations of the last AHA/ASA recommendations for acute ischemic stroke management that were published in 2007 (6). These recommendations are as follows:

1. Patients eligible for treatment with i.v. thrombolysis or acute reperfusion intervention and SBP >185 mm/HG or DBP >110 should have BP lowered.
2. Patients who have other medical indications for aggressive treatment of BP should be treated.

3. For those not receiving thrombolytic therapy, BP may be lowered if it is markedly elevated (SBP >220 mm/Hg or DBP >120 mm/Hg)

The conclusion from the available clinical trial data or lack thereof is that there is little indication to treat most hypertensive hemorrhagic or ischemic stroke patients in the very early phases after their event unless they exhibit the markedly elevated BP ranges suggested by the AHA/ASA guidelines. Long term BP management is appropriate after the occurrence of both stroke subtypes to reduce subsequent risk and should be initiated 24-72 hours after the acute event if there are no contraindications or comorbid conditions such as hypotension (7). For patients with a history of hypertension who were taking antihypertensive medications prior to the most recent event, guidelines recommend restarting medication at 24 hours in stable patients without a contraindication to do so.

References

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