Critical Review Form

Meta-analysis

Blood pressure management in acute stroke: A long-standing debate
European Neurology 2006; 55: 123-135

Objectives: "To present a critical overview of all arguments pro and contra lowering Bp in the setting of stroke on the basis of current observational and randomized evidence, consider the ongoing clinical trials in this area and address the present recommendations regarding the conflicting issue." (p 124).

Methods: Two authors reviewed PUBMED using 9 keys words for observational trials, and PUBMED + Cochrane for interventional trials using 13 key words. Exclusion criteria included articles with insufficient data, outcome measures other than modified Rankin Scale or Barthel's Index, NIHSS, Canadian Stroke Scale, or the Canadian Neurological Score, or duplicate publications. No mention is made of assessing study quality or weighting of the evidence. No meta-analysis was performed.

Guide	Question	Comments
I	***Are the results valid?***	
1.	Did the review explicitly address a sensible question?	Yes. The review addressed the pros and cons of therapeutic manipulation of BP in acute ischemic or hemorrhagic stroke
2.	Was the search for relevant studies detailed and exhaustive?	No, the authors excluded EMBASE and made no attempt to contact investigators or industry sponsors or review reference lists.
3.	Were the primary studies of high methodological quality?	Unknown because the authors made no attempt to grade study quality using scales like Jadad (Control Clin Trials 1996; 17: 1-12) or Chalmers (Control Clin Trials 1981; 2: 31-49).
4.	Were the assessments of the included studies reproducible?	Unknown because no details are provided on inter-rater reliability of article selection or quality assessment. No details are provided on any selection or abstraction discrepancies or consequent resolutions.

II.	*What are the results?*	
1.	What are the overall results of the study?	**Decreasing BP in Ischemic Stroke** **Cons** a) BP normalizes spontaneously within hours or days; b) Maintaining tissue perfusion pressure above a critical level within ischemic penumbra is crucial (based on Dr. Powers work on dysfunctional cerebral autoregulation in the acute phase of ischemic stroke). c) Reducing BP 20 mm Hg in the first hour after AIS followed by the use of BP-lowering medications was the most important negative prognostic factor for early neurological deterioration, infarct volume and 3-month mortality. d) BP elevation may be a compensatory reaction to persistent vessel occlusion. **Pros** a) Elevated BP in AIS is associated with subsequent death/dependency in prior Systematic Reviews; b) Sustained BP elevation is associated with the development of cerebral edema. c) Observational studies suggest increased admission BP is associated with early and late stroke recurrence. • No RCT were identified for clonidine or hydralazine. • Transdermyl nitrates, ACE-inhibitors are best studied with ACCESS (candesartan) showing 52.5% decreased all-cause mortality or vascular events without improvement in the primary outcome at 3-months. • The effects of anti-HTN may go beyond the BP effect (neuro-humoral modulation). • Although labetolol was utilized in the NINDS trial, other B-blockers (atenolol, propranolol) trend towards worse outcomes. **Decreasing BP in Hemorrhagic Stroke** **Cons** a) BP declines to baseline in days spontaneously. b) PET scans suggest zone of hypoperfusion surrounding hematoma without BP medications. **Pros** a) Elevated BP is associated with increased death, disability, or subsequent deterioration. b) Elevated BP is associated with increased risk of cerebral edema, hematoma enlargement, and recurrent hemorrhagic stroke. • Two small observational trials (Rodorf) suggest phenylephrine vasopressor therapy improves post-stroke discharge NIHSS with severe stenosis of ICA or MCA most likely to benefit from vasopressor therapy.

2.	How precise are the results?	No estimates of precision (95% CI) are provided and the results varied significantly by study.
3.	Were the results similar from study to study?	No. Some studies found no effect or even an adverse effect of lowering BP on outcomes while others showed a positive effect. Different agents were used, and the timing of BP manipulation differed by study.
III.	***Will the results help me in caring for my patients?***	
1.	How can I best interpret the results to apply them to the care of my patients?	Based upon this review, BP should not be lowered or raised in acute ischemic stroke or acute hemorrhagic stroke unless they are candidates for thrombolysis (NINDS protocol) or contain other indications to lower the BP (ACS, dissection, HTN encephalopathy, pulmonary edema, etc.)
2.	Were all patient important outcomes considered?	Unfortunately, most studies focus on numbers (BP) rather than functional status or Quality of Life (patient-important outcomes). Different studies looked at different outcomes from physiologic outcomes (cerebral blood flow, MCA velocities) to the clinical outcomes of death or disability.
3.	Are the benefits worth the costs and potential risks?	No, first do-no-harm. In the absence of well-conducted RCT like CHHIPS or ENOS, the effect of managing BP in acute stroke remains uncertain. Dr. Nassief (BJH Neurology) discussed interesting intra-operative CABG data with induced hypotension to facilitate minimal operative bleeding with continuous EEG monitoring suggesting brain activity decreases about 5-minutes after MAP dropped to 50 mm Hg suggesting role for pulse BP therapy in acute stroke (not studied or discussed in any of these papers).

Limitations

1) **Incomplete search strategy.**
2) **No weighting of evidence based upon validated quality scales.**
3) **Rather than a Systematic Review of the available evidence, this is really a well-written editorial with narrative commentary on the state of the literature in 2006.**

Bottom Line

Available evidence and European/American guidelines do not support BP management of stroke if systolic BP < 220 or diastolic BP < 140. If above these thresholds, consider easily titrated short-acting agents like Labetolol or nicardipine with target systolic BP decrease no more than 15%. Drug-induced BP elevation cannot be recommended for management of stroke. The threshold for BP management in hemorrhagic stroke are lower (sBP > 180, dBP > 105). Future RCT like CHHIPS (http://www.ncchta.org/project/1351.asp) and ENOS (http://www.nottingham.ac.uk/stroke-medicine/enos/enostrialdb/) should address the questions posed in this narrative review.