Critical Review Form
Meta-analysis

Interventions for deliberately altering BP in acute stroke, *Cochrane Database of Systematic Reviews* 2001, Issue 3, Art. No: CD000039. DOI: 10.1002/14651858.CD000039

Objectives: **To assess the effect of lowering or elevating BP on people with acute stroke and the effect of different vasoactive drugs on BP in acute stroke.**

Methods: **The Cochrane Stroke Group developed the search strategy and review methods. Prior to this publication, the Cochrane Stroke registry was last searched in March 2000. Additional search strategies included electronic searches of the Cochrane Database of Systematic Reviews and Clinical Trials, MEDLINE, EMBASE, BIDS ISI, and the ongoing trials section of the journal Stroke. Further information was obtained from researchers in the stroke field and pharmaceutical companies (Bayer, Napp, novateris, Lipha Sante, Hoffmann la Roche, Hoechst, and ucb Pharma). (p 3). Randomized or quasi-randomized trials were included enrolling adults > 18 years with acute ischemic or hemorrhagic stroke with interventions performed *within 2 weeks of the stroke* to decrease or increase the BP. Outcome measures included early (< 1 month) or late (> 1 month) mortality, early neurological deterioration, late disability, stroke recurrence, quality of life, discharge site (to home or institution), and hospital costs.**

Guide	Question	Comments
I	***Are the results valid?***	
1.	Did the review explicitly address a sensible question?	Yes, three sensible questions addressing whether treatment of BP in acute stroke improves cerebral perfusion and/or patient outcomes: (1) Effect of BP lowering in acute stroke. (2) Effect of elevating BP in acute stroke. (3) Effect of various vasoactive drugs on BP in acute stroke
2.	Was the search for relevant studies detailed and exhaustive?	Yes. CDSR and CCTR databases, MEDLINE, EMBASE, BIDS ISI (Science Citation Index), reference lists of review articles, contacted researchers and pharmaceutical companies.
3.	Were the primary studies of high methodological quality?	Methodological filters were applied as per the Cochrane Handbook and treatment effects were weighted with the Peto Odds ratio. 5 studies were included. Lisk 1993; Dyker 1997, only enrolled hypertensive patients. Only 3 studies reported how BP was measured (Lisk, Dyker, Bath). All studies were double-blind, 4 trials were intention-to-treat. 3 trials used CT to identify PICH. Pts were enrolled from 24 hours (Uzuner 1995) to 1 week (Dyker). Only 2 studies used a neurologic assessment scale for outcome (Lisk; Dyker). Outcome ranged from 4 weeks (Uzuner) to 3 months.
4.	Were the assessments of the included studies reproducible?	Yes, the methods of locating, appraising, and extracting relevant data were well described, duplicated, and previously referenced. Reported Kappa scores and discrepancy resolution methods would be interesting for readers to be aware of.
II.	***What are the results?***	

1.	What are the overall results of the study?	• 5 trials involving 218 subjects met inclusion criteria: 3 calcium channel blockers (CCB) 2 ACE inhibitors 1 Clonidine 1 glyceryl trinitrate • Only 2 trials reported randomization methods. • No RCT of elevating BP were identified. • Extensive, disparate delays to enrollment were reporting ranging from 24-hours to 5 days! • Consequently, the authors conclude that the effect of BP lowering on clinical outcome could not be answered. • For one-month mortality, point estimates favor PO CCB, but not IV CCB or nitric oxide (Analysis 01.01 p. 15), but all CI's cross the line of no effect and all sample sizes are < 40 per treatment arm. • Most agents effectively lower systolic BP at one- or three-hours and one- or two-days (Analysis 01.03, 01.04, 01.07, 01.08 pp 16-21). • Heart rate may increase in first 1-3 hours after IV CCB.
2.	How precise are the results?	Wide CI often with significant heterogeneity and small sample sizes.
3.	Were the results similar from study to study?	Most point-estimates favor anti-HTN therapy with CCB or ACE-inhibitor to lower BP within the first 2 days. Only 3 studies permit assessment of patient important outcome (mortality) and 2/3 favor no treatment or elevated BP.
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?	There was not adequate data to determine if lowering or raising BP will affect outcome within the first two weeks following acute hemorrhagic or ischemic stroke. BP control for other reasons (ACS, aortic dissection) may be necessary and should not be dissuaded by this review.
2.	Were all patient important outcomes considered?	No. Only 2 studies used a neurological assessment scale, and no studies reported stroke recurrence rates or quality of life.
3.	Are the benefits worth the costs and potential risks?	No, "first do no harm". Data is equivocal and we should not be treating a number (BP) without better understanding of the treatment's impact on patient-important outcomes.

Limitations

1) **Dated Systematic Review. Why no updates since 2001? Dr. Abdullah Nassief (BJH Neurology) was present at JC and noted the only available RCT since 2001 is ACCESS (Stroke 2003; 34: 1699-1703).**
2) **Potential conflict of interest with SR authors actively involved in several ongoing trials.**
3) **No patient oriented evidence that matters (POEM) were assessed.**
4) **No methods reported for obtaining BP's.**

Bottom Line

Dated SR suggests insufficient evidence exists to guide BP management in the days following AIS or PICH. Future trials should address lowering or raising BP following stroke with specific drugs, doses, time-of-initiation and duration of therapy while assessing POEM's such as functional status, QOL, and stroke recurrence. Several trials are underway including COSSACS (http://www.incirculation.net/whatswhat/11093_71880.aspx) , CHHIPS (http://www.ncchta.org/project/1351.asp) , and ENOS (http://www.nottingham.ac.uk/stroke-medicine/enos/enostrialdb/) to answer many of these questions in coming years.