

Eastern Virginia Medical School Journal Club: Systematic Review/Meta-analysis
 Adele Tse, MD
 July 2011

<p>Citation: Kamel H, Navi BB et al. Hypertonic saline versus mannitol for the treatment of elevated intracranial pressure: A meta-analysis of randomized clinical trials. <i>Crit Care Med.</i> 2011;39 (3):601-2</p>	
<p>SCREENING</p>	
<p>1. Why was the study done (what was the research question)?</p> <p><i>(P – I – C – O the study)</i></p>	<p>P=Patients with ICP elevations I= Is the use of hypertonic saline C=Compared to Mannitol O= More effective at lowering of ICP</p>
<p>VALIDITY</p>	
<p>2. Is it a systematic review of high-quality studies which are relevant to your question?</p> <p><i>(Did it identify the population, interventions, and outcomes studied?)</i></p>	<p>RCT with some method of quantitative ICP measurement and with pts with evidence of elevated ICP. Looked at studies that compared effects on ICP of equiosmolar doses of hypertonic saline and mannitol (at least 3%Na). -unblinded and blinded trials apparently attempted to select RCT's -QUORUM statement appears however unclear that they were in compliance with checklist. -looked at age, sex, # episodes of elevated ICP treated, total osms of tx dose, mean bseline of ICP, lowest ICP or max mean change within 60 mins of intervention. -outcomes studied: % of cases with control of ICP as defined by each study. Looked at adverse effects: arf, pulm edema, hypotension, coagulopathy, extravasation -included tx for new recurrent ICP in same pt but excluded repeated tx for same episode of elevated ICP</p>
<p>3. Does it describe a comprehensive search for all relevant studies?</p> <p><i>(Did they search all relevant databases? use an appropriate search strategy? seek personal contact with experts? include unpublished and non-English studies?)</i></p>	<p>Yes. Included terms of elevated icp, tbi, hemorrhage, stroke. Limited to RCT. One investigator reviewed the titles and abstracts of all studies and excluded irrelevant ones. 2 investigators reviewed selected articles using structured form to determine eligibility and extract data. Disagreements resolved by consensus or third investigator. If clarifications or further info needed, the study authors were contacted.</p>
<p>4. Were the criteria for study inclusion pre-determined and clearly stated?</p>	<p>Yes. RCT, unblended and blinded; studies with quantitative measurements of ICP and trials with fixed doses of NS or mannitol.</p>
<p>5. Did the authors adequately assess the quality of the included studies?</p>	<p>Yes. All trials had small power. 5 trials with 112 patients with a total of 184 episodes of elevated ICP. No pediatric trials. Did not have enough data to do subgroup analysis nor was there a-priori sub-group identification.</p>
<p>CLINICAL IMPORTANCE</p>	
<p>6. What were the results of the review?</p> <p><i>(Are the results of all included studies clearly displayed? Are the results similar from study to study? Is there a clinical bottom line? If the study results combined, was it appropriate to do so?)</i></p>	<p>Yes with RR and forest plots. RR of ICP control was 1.16 and of difference in mean ICP reduction was 2. Studies favoring hypertonic saline -outcome based on each study's clinical definition of icp control and they were all quite heterogeneous</p>
<p>-Mannitol in controlling icp in 78% of episodes (CI .67-.86)</p>	

<p>7. How precise are the results? <i>(What is the confidence interval? p-value?)</i></p>	<p>Hypertonic effected in 93% (CI .85-.97) both stat significant. -pooled RR of ICP control using hypertonic vs mannitor 1.16 (CI 1-1.33, p= 0.046) CI crosses 1 but P p value<0.05. none of the individual studies has stat significant RR though -mean difference in icp reduction using hypertonic vs mannitor was 2. (CI -1.16 to 5.7, p=0.276) not stat significant. But 2 of the studies had stat. significant reduction; both of these studies had a power of 9 each. - no difference based on type of hypertonic saline, dose per treatment, baseline mean icp. (no stats discussed)</p>
<p>8. Did the interpretation of the review's results accurately reflect the results themselves? Are the results generalizable to my patient population?</p>	<p>They found hypertonic saline trended towards being more effective but this was not statistically significant. The results are not powered and there are insufficient evidence to be conclusive.</p>

Clinical Bottom Line: Evidence is non-definitive regarding any advantages to treating ICP with hypertonic saline over Mannitol. Application of use of QUORUM recommendations for quality of studies was unclear. Dosages of HS used to treat patients was varied and results cannot be applied.