Effects of Therapeutic Hypothermia and Colloid Resuscitation on Brain Edema after Severe Bleeding and Traumatic Brain Injury in a Rat Model

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Background: Moderate hypothermia is being used in the treatment of traumatic brain injury (TBI) and after cardiac arrest in the past 50 years (1, 2). TBI is not always isolated in most of the traumatic cases severe bleeding accompanies TBI, where major concern becomes fluid resuscitation and brain protection. In this challenging situation choice of fluid in resuscitation is still debatable. Therapeutic hypothermia for protection of brain adds some more questions on the treatment modality. The aim of this study is to find out the effects of therapeutic hypothermia on the protection of brain in concomitant severe bleeding and TBI when different colloids; albumin (20% human albumin) and 6% hydroxyethyl starch used in fluid resuscitation in early phase of an accident.
Our hypothesis is that hypothermia and colloid resuscitation has better effects than the normothermia and colloid resuscitation on brain edema, evaluated histopatologically and brain water content.

Material and Method: Following Animal Ethics Committee Approval; in a normothermia study which constituted of sham group and normothermic groups 30 male Sprague-Dawley rats were used. In this study 18 other rats were formed for moderate hypothermic groups. Six other normal healthy rats (control) were sacrificed for finding out the brain water content of the rats. Brain trauma was performed by lateral fluid percussion model under general anesthesia other than control group. Following tracheotomy mechanical ventilation was applied to achieve normocapnia. Heart rate, arterial pressure, SpO_2, and temperature were monitored. The abdominal aorta and inferior caval vein was catheterized for monitorization, blood sampling and acute severe bleeding (20% of total blood volume). In normothermic groups active warming of the rats were continued until the end of the study and body temperature targeted to 37, 2-37, 5˚ C. In the hypothermic groups active heating ceased and cold fluid resuscitation applied to keep the rat's temperature between 32-33˚ C. Rats other than Sham group all others were bled for 10ml/kg in 10 minutes. Group HS (Hydroxyethyl starch, n=6 + 4 P- pathology) and Group HypotHS (n= 5+4P) received 10 ml/kg 6**%** hydroxyethyl starch, Group A (Albumin, n=6 +4P) and Group HypotA (n=5+4P) received 10 ml/kg 20 % human albumin, Group TI (Sham group, n=6 +4P) were operated but were not allowed to bleed and did not receive fluid. After fluid replacement mechanical ventilation was continued for 4 hours and blood gasses and oncotic pressures and osmolarity and urine output were recorded. At the end of the study all rats were sacrificed and in some cortical fluid volume were calculated. A blinded pathologist had evaluated rest of the brains histopathologically in regard to intraparenchymal, subarachnoid hemorrhage, hyperemia and edema. These parameters

were scored on a scale of 1-3. Brain water content was also calculated. In statistical analysis one-way ANOVA Dunnett test was performed with post hoc test for brain water content.

Results: Macroscopic hyperemic lesion was observed in all brain samples where lateral fluid percussion was performed. All of these were photographed and recorded. Duramater was observed intact in all enrolled rats. Intraparenchymal hemorrhage score varied between 0-2 in all groups. Subarachnoid hemorrhage and hyperemia scoring varied from 1-3 in all groups. Edema grading was 1-2 in all groups. Brain water content of all groups compared to the control values was not statistically significant ($p=0.054$). In the post hoc test the brain water content was found significantly higher in normothermic albumin and hydroxyethyl starch groups when compared to control ratio.

Summary: Brain water content measurements revealed that hypothermia with colloid resuscitation is a good modality of treatment. Choice of albumin or hydroxyethyl starch does not have any positive effect on the brain edema after traumatic brain injury and severe bleeding.

References

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