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Case study

Comparison of 20% mannitol and 3% hypertonic saline on intracranial pressure and systemic hemodynamics

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ABSTRACT

Mannitol and hypertonic saline (HS) are most commonly used hyperosmotic agents for intraoperative brain relaxation. We compared the changes in ICP and systemic hemodynamics after infusion of equiosmolar solutions of both agents in patients undergoing craniotomy for supratentorial tumors. Forty enrolled adults underwent a standard anesthetic induction. Apart from routine monitoring parameters, subdural ICP with Codmann catheter and cardiac indices by Vigileo monitor, were recorded. The patients were randomized to receive equiosmolar solutions of either 20% mannitol (5 ml/kg) or 3% HS (5.35 ml/kg) for brain relaxation. The time of placement of ICP catheter was marked as T_0 and baseline ICP and systemic hemodynamic variables were noted; it was followed by recording of the same parameters every 5 min till 45 min (Study Period). After the completion of study period, brain relaxation score as assessed by the neurosurgeon was recorded. Arterial blood gas (ABG) was analysed every 30 min starting from T_0 upto one and half hours (T_{90}), and values of various parameters were recorded. Data was analysed using appropriate statistical methods. Both mannitol and HS significantly reduced the ICP; the values were comparable in between the two groups at most of the times. The brain relaxation score was comparable in both the groups. Urine output was significantly higher with mannitol. The perioperative complications, overall hospital stay, and Glasgow outcome score at discharge were comparable in between the two groups. To conclude, both mannitol and hypertonic saline in equiosmolar concentrations produced comparable effects on ICP reduction, brain relaxation, and systemic hemodynamics.

1. Introduction

Increased intracranial pressure (ICP) is a common problem in patients with intracranial space occupying lesions presenting for neurosurgical procedures. To achieve satisfactory operating condition, ICP needs to be reduced by physiological as well as pharmacological means. The most popular pharmacological agent to decrease ICP in intraoperative period is mannitol [1]. However, its administration is associated with various side effects including rebound intracranial hypertension [2,3]. Hypertonic saline (HS) has been used by many researchers to reduce ICP for intraoperative brain relaxation [4,5]. A number of comparative studies on mannitol and HS suggested that the latter is at least as effective as, if not better than the former, for the treatment of intracranial hypertension [6–9]. However, most of these studies included diverse brain pathologies and solutions with different osmolar strengths. Nonetheless, studies which included elective neurosurgical procedure and reported similar brain conditions, used solutions of mannitol and HS with different osmolarity [8,9]. Furthermore, studies where equiosmolar equivolemic solution of mannitol and HS was used; instead of ICP measurement, the brain relaxation score (BRS) which is a subjective measure for the assessment of brain condition, was used by the operating neurosurgeon after opening of duramater [10,11]. Similarly, most of the studies did not monitor the changes in systemic hemodynamics including cardiac parameters such as cardiac output (CO), cardiac index (CI), stroke volume (SV) etc. following administration of mannitol and HS which may change with use of hyperosmolar agents [12–15].

Therefore, the present study was designed to compare the effects of equiosmolar solutions of mannitol (20%) and hypertonic saline (3%) on ICP and systemic hemodynamics in patients scheduled for elective craniotomy for supratentorial tumors. The secondary objective was to compare the effects of these to agents

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on brain relaxation, serum electrolyte changes, urine output, and neurological condition (Glasgow outcome score) at-discharge.

2. Materials and methods

After approval from institutional ethics committee and written informed consent, 40 adult patients belonging to either sex, scheduled to undergo elective craniotomy for supratentorial brain tumors were enrolled for this prospective, randomized double-blinded study. Patients associated with the following conditions were excluded from the study.

- Preoperative Glasgow Coma Scale (GCS) score <14.
- American Society of Anesthesiologists (ASA) physical status IV/V.
- Preoperative hypo- or hypernatremia (serum sodium <135 or >145 mEq/L, respectively).
- History of treatment with hyper osmotic fluids (HS or Mannitol) within 24 hours before surgery.
- History of congestive heart failure, renal function impairment, and diabetes mellitus.
- Patient posted for sellar and suprasellar surgeries.
- Patient with past history of any intracranial surgery.

2.1. Preparation of the study drug

Using computer-generated randomization chart, the patients were assigned to receive equiosmolar solution of either 20% mannitol or 3% hypertonic saline. The osmolarity of 20% mannitol is 1098 mOsm/l and that of 3% HS is 1026 mOsm/l, hence, the conversion factor was calculated as 1.07. To provide equiosmolar strength of both solutions, 5.35 ml/kg of 3% HS solution or 5 ml/kg of 20% mannitol was used.

2.2. Anesthetic management

Routine preoperative check-up was done and investigations were reviewed on the evening before surgery. All the patients received intravenous (IV) phenytoin and dexamethasone on the morning of surgery and intramuscular (IM) glycopyrrolate 0.2 mg 30mins prior to induction of anesthesia. In the operating room (OR), standard monitors like electrocardiograph (ECG), pulse oximeter and non-invasive blood pressure (NIBP) were connected. After preoxygenation for 3 min, anesthesia was induced with fentanyl 2 μg/kg, propofol 2-3 mg/kg, and tracheal intubation was facilitated with rocuronium 1 mg/kg. Infusion of fentanyl 1 μg/kg/hr and vecuronium 0.05 mg/kg/hr was started to ensure adequate analgesia and muscle relaxation. Anesthesia was maintained using oxygen-air mixture and a minimal alveolar concentration (MAC) of 1.0 ± 0.2 isoflurane. The patients were mechanically ventilated to maintain an end-tidal carbon dioxide ($EtCO_2$) of 30 ± 2 mmHg. Ringer's lactate solution was administered as the maintenance fluid at a rate of 2 ml/kg/h. The trigger for blood transfusion was kept at haemoglobin level at or below 8gm/dl.

Additional monitoring modalities included invasive arterial pressure, central venous pressure (CVP), continuous and non-invasive cardiac output monitor (Vigileo, Edwards Life sciences, Irvine, USA), $EtCO_2$ monitor, nasopharyngeal temperature, and urine output. After appropriate positioning of the patient, surgery was started. The neurosurgeon inserted the ICP catheter (Codman MicroSensor Basic Kit, Johnson & Johnson Co, Raynham, MA, USA) through the first burr hole made for craniotomy after raising scalp flap. The catheter was inserted into the subdural space for measurement of ICP and was connected to ICP monitor (ICP Express™ Codman, Johnson & Johnson Professional Inc, Raynham, MA, USA). The time of placement of ICP catheter was marked as T_0 and baseline ICP was noted. Simultaneously, the study drug (mannitol or HS) was infused via the central venous line over 15 minutes using syringe infusion pump.

The systemic and intracranial parameters such as heart rate (HR), systolic arterial pressure(SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), CVP, CO, CI, SV, stroke volume variation (SVV), ICP and cerebral perfusion pressure (CPP) apart from SpO_2 and $EtCO_2$ were recorded at 5 min interval starting from T_0 to 45 min (T_{45}). Neither any surgical stimulus nor any active anesthetic interventions was made during this period. Hypotension (defined as MAP less than 60 mmHg for more than one minute) if occurred, was managed by decreasing dial concentration of inhalational agent, followed by IV mephentermine, if the previous manoeuvre was ineffective. During this period, any change in the systemic hemodynamics and ICP were presumed to be due to the study drug. Arterial blood gas (ABG) analysis was done at every 30 min starting from T_0 to 90 min (T_{90}) and values of various parameters such as hemoglobin, pH, PO_2, PCO_2, electrolytes, base excess, glucose, and lactate were recorded. Urine output was also measured at every 30 min interval from T_0 to 90 min and then on hourly basis.

After the completion of 45 min study period, craniotomy and excision of the tumor was carried out as planned. Brain condition was assessed by the operating neurosurgeon upon opening of duramater using a four-point Brain relaxation scale (BRS) score; [16] 1 – Perfectly relaxed, 2 – Satisfactorily relaxed, 3 – Firm brain, and 4 – Bulging brain. If the brain was found to be bulging; titrated doses of propofol were given. At the end of surgery, the trachea was extubated after reversal of neuromuscular blockade with neostigmine 50 μg/kg and glycopyrrolate 10 μg/kg. The total intake and output of fluids and blood during the surgery was recorded. Immediate postoperative complications such as nausea, vomiting, headache, disorientation, restlessness, convulsion, weakness of limbs, and aphasia were recorded. For postoperative pain, ketorolac 0.6 mg/kg, IM was given every 6 h. Perioperative complications, duration of hospital stay, and neurological condition (Glasgow outcome scale, GOS) of the patients at discharge were recorded.

2.3. Statistical analysis

SPSS version 17 was used for statistical analysis. Data are presented as mean ± standard deviation, median and range or number and percentage. The repeated measures ANOVA and Friedman test was used for analysis of data within the group. Friedman test was used for analysis of base excess within the group. The Fisher's 'Exact T' test was used for analyzing the prevalence of tumour pathology, sex ratio, ASA physical status, requirement for mechanical ventilation and postoperative complications between the two groups. The 'Independent Sample T' test with the equal variance and Wilcoxon rank-sum (Mann-Whitney) test was used for analyzing data between the groups. Mann-Whitney test was used for analyzing volume of the tumour, midline shift, brain relaxation score, base excess, total fluid intake and urine output, blood loss and transfusion, surgical duration, hospital stay and GOS between the groups. P value less than 0.05 was considered significant.

3. Results

A total of 40 patients, 20 in each group were enrolled for this study. There was no significant difference in demographic profiles of the two groups (Table 1). Most of the patients belonged to ASA physical status II (87.5%). The tumor pathology was meningioma in 3 and 6 patients in HS and mannitol groups, respectively; in rest others it was glioma. There was no significant difference in