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**Research Article**

# Brain relaxation and electrolyte balance during resection of posterior fossa tumors under sitting position: Mannitol versus placebo

**Sherif Abdo Mousa** [a,*], **Tarek Habeeb Ramadan** [a], **Mohamed Kassem** [b]

[a] *Anaesthesia and Surgical Intensive Care Department, Faculty of Medicine, Mansoura University, Egypt*
[b] *Neurosurgery Department, Faculty of Medicine, Mansoura University, Egypt*

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**KEYWORDS**

Brain relaxation;
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**Abstract** *Background:* Mannitol can be negative for outcome, which may explain why we lack scientific support for its use. The purpose of this study was to compare the brain relaxation and electrolyte balance in group of patients with posterior fossa tumor underwent surgery in sitting position with or without mannitol.
*Methods:* Eighty patients scheduled for resection of posterior fossa tumor from April 2009 till April 2012 were enrolled in this prospective, double-blind, randomized study. All cases received general anesthesia and attained sitting position during surgery. Patients were enrolled into two groups, group I received mannitol (20%) 1 gm/kg just before opening the dura. Group II received placebo at the same time. Hemodynamics, duration of surgery, Brain Relaxation Score (BRS) in which surgeons assessed the condition of the brain as 1 = perfectly relaxed, 2 = satisfactorily relaxed, 3 = firm (leveled) brain, 4 = bulging brain were recorded. Blood losses, urine output and serum sodium and potassium levels were assessed. Any operative complications were recorded.
*Results:* No difference in hemodynamics (HR and MBP) whereas CVP with mannitol was higher than with placebo ($p < 0.01$). No difference in brain relaxation score ($p = 0.719$) or operative

* Corresponding author. Mobile: +20 1001637298.
E-mail addresses: S_abdomousa@yahoo.com (S.A. Mousa), dr_tarekhabeeb@yahoo.com (T.H. Ramadan), okassem2000@yahoo.com (M. Kassem).

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complication between both groups. Mannitol was associated with higher urine output ($p < 0.001$), higher serum potassium and osmolarity ($p < 0.001$) and lower serum sodium ($p < 0.001$) than compared with placebo.

*Conclusion:* Surgery for posterior fossa in sitting position could be safely performed without the use of mannitol avoiding its adverse side effects with beneficial effects in terms of preserving hemodynamic, electrolytes balance, reasonable brain relaxation and fewer complications.



## 1. Introduction

Intra operative patient positioning involves balancing surgical comfort, against the risks related to the patient position. Therefore, patient positioning during surgery should be considered during the preoperative evaluation [1].

Since our neurosurgical colleagues frequently require setting up the patients during surgery, its problems should be common knowledge and techniques aimed at their solution should be widely understood. Sitting position is most commonly utilized for posterior fossa surgery and cervical laminectomy. Shapiro and Drummond have demonstrated that the sitting position is still utilized for posterior fossa surgery in about half of practices in USA [2]. Hemodynamic instability is commonly associated with the sitting position during anesthesia, resulting primarily from a sudden decrease in intra thoracic blood volume. Because brain tumors may cause disturbances of cerebral auto regulation and the blood–brain barrier, in addition to the effects of an infusion of mannitol on serum osmolality, systemic hemodynamic, and blood volume; all these effects could possibly have an unfavorable influence on brain condition [3,4]. Moreover, because no previous data on this subject could be found in the relevant literature, we decided to study the effects of undergoing posterior fossa tumor resection during sitting position without the use of mannitol on systemic hemodynamic, blood electrolytes, osmolarity and the brain relaxation versus conventional dose of mannitol.

Mannitol is a sugar alcohol ($C_6H_{14}O_6$) with a molecular weight of approximately 182 kDa, is not significantly metabolized and osmolarity = 1098 mOsm/l, and is excreted unchanged in the urine. It is filtered at the glomerulus and is reabsorbed in the nephron, thereby acting as an osmotic diuretic. The half-life is affected by glomerular filtration rate (GFR) but averages from 39 to 103 min [5]. Osmotherapy, with mannitol is considered the standard of care by most of neuroanesthesiologists. From side effects related to renal and pulmonary system, electrolyte disturbances, and a rebound increase in ICP, osmotherapy can be negative for outcome. These drawbacks, and the fact that the most recent Cochrane meta-analyses of osmotherapy in brain edema could not find any beneficial effects on outcome, make routine use of osmotherapy during the surgery for brain tumor with sitting position is doubtful. In order to counteract this physiologic response, anesthesiologists frequently try to reduce the consumption of the drugs exposing patients to the potential risk of being hemodynamically and metabolic unstable like osmotic diuretics. It is thus important to investigate the brain condition during resection of posterior fossa tumors while the patients attaining the sitting position without the use of osmotic diuretic.

## 2. Patients and methods

In this prospective, double blind and randomized study, we recruited 80 patients, with American Society of Anesthesiologists (ASAs) grades I and II, and diagnosed as infratentorial tumors, into the study from April 2009 till April 2011. Seventy-seven of those patients completed the study. Written informed consent and approval of the hospital ethical committee were taken before starting the study. All patients were admitted in Neurosurgery Department at Mansoura University Hospital for brain tumor resection performed by one of senior staff of the neurosurgeons under general anesthesia in sitting position. None of the patients had a history of cardiopulmonary, renal or liver diseases and none was receiving cardiac medications before operation. Patients with Glasgow Coma Scale score less than 13 and patients with signs of increased intracranial pressure (ICP), were excluded. Tumor characteristics likely to affect the brain relaxation intraoperatively, especially the tumor size, histology, perifocal edema, and midline shift all were well matched for both groups by the preoperative radiological scans. All patients were thoroughly assessed preoperatively by history, physical examination and laboratory evaluations (complete blood picture, liver function and renal function tests). Patent foramen ovale (PFO) was excluded either by transoesophageal echocardiography (TOE) or transthoracic echocardiography and once diagnosed, the patient was excluded for fear of the risk of paradoxical air embolism (PAE). On arrival to the operating theater wide bore intravenous cannula (18 G) was inserted through suitable peripheral vein. I.V. midazolam 0.05 mg/kg and fentanyl 1.5 μg/kg were given and incremental dose of fentanyl was repeated intra operatively according to the hemodynamic state and the anesthesiologist' prescription. After randomization using sealed envelopes, patients were assigned to receive either mannitol (20%) 1 gm/kg just before opening the dura (GI) for intraoperative brain relaxation or normal saline; placebo group (GII), infused through the central line starting with scalp incision at a rate of 20 mL/min in both groups. Both fluids were administered over 15–20 min using an infusion pump with the type of fluid blinded to both surgeon and anesthesiologist.

Preanesthetic monitoring included pulse, ECG, non-invasive blood pressure, and peripheral $O_2$ saturation. After preoxygenation with 100% $O_2$ for 5 min, anesthesia was induced using I.V. thiopental sodium 5–7 mg $kg^{-1}$, with loss of consciousness, the trachea was intubated with a suitable armored cuffed endotracheal tube 2 min after an induction dose of atracurium besylate (0.5 mg/kg) to facilitate intubation, followed by top up doses of 1/5 of the initial dose of atracurium

for maintenance of muscle relaxation. After that, all patients were mechanically ventilated using Drager (Fabius GS-Germany) ventilator with tidal volume of 8–10 ml/kg and $I/E$ ratio 1:2 through closed circuit with fresh gas flow around 3 l. End-tidal $CO_2$ was monitored using Drager (Infinity Kappa, Mexico) monitor with Samsung screen with main stream capnograph and minute ventilation was modified to maintained $EtCO_2$ between 30 and 35 mm Hg to avoid an influence of carbon dioxide on the brain bulk, until it was assessed by the surgeon. Then, if needed, hyperventilation was initiated by the attending anesthesiologist's choice.

''Anesthetic maintenance included 1% sevoflurane in oxygen: air mixture (1:1) combined with IV infusion of propofol (dose range, 1–2 mg/kg/h) and an IV bolus of fentanyl and atracurium, if necessary, which were administered at the attending anesthesiologist's discretion.''

Perioperative fluid requirement was maintained with crystalloid solution (normal saline 0.9% or ringer solution), and it was guided by CVP values and urine volume. No blood was given unless there was severe blood loss (more than 20% of total blood volume) and/or hematocrit value $\leqslant$30%.

A radial artery was cannulated after the induction of anesthesia in non-dominant hand (after performance of modified Allen's test) under aseptic conditions to obtain blood samples. Central venous single lumen catheter (18 G) (Amecath, France) was inserted in the right subclavian vein with strict sterile technique using Sildenger technique. The catheter was then flushed with heparinized normal saline solution and connected to a pressure transducer for central venous pressure monitoring with transducer referenced to the level of ear tragus during the sitting position. The position of the catheter was confirmed by antero posterior chest X-ray just after insertion by C-arm.

Before being placed in the sitting position, patients were dressed in an antigravity elastic bandages wrapped around the calves and thighs to decrease venous pooling in the lower extremities. The patient's head was pinned and fixed with the Mayfield head holder (Mayfield; Integra Life Sciences, USA) before placement in the sitting position. In the sitting position, the patient's upper body was elevated 90–100°, and the patient's head was tilted 20–30° forward to allow the patient to sit firmly with knees slightly flexed on the pillow. The exposure of the infratentorial region requires flexion of the head, but to avoid damage to the spinal cord, a 2-finger breadth distance between the chin and sternum is mandatory. On suspicion of venous air embolism (VAE), a sudden decrease in the $EtCO_2$ of 0.7 kPa (5.25 mm Hg) almost equal to 0.7% [6] without prior change in the ventilation or concomitant decrease in the arterial pressure, the neurosurgeon is immediately notified. Jugular veins were gently compressed manually to help the neurosurgeon to identify the source of air entry. The neurosurgeon closes the leak by applying wax or gel foam in the bone bleeds or surgical closure of the dural sinus bleeds either by suturing or by haemostatic materials. Cautery was used to control muscle bleeder. When the site of the air entry is not found by pressure of the jugular veins, the operative site was covered with compresses soaked in saline for a while; the compresses were slowly removed observing all possible sites of air entry. Aspiration of air from the circulation can be attempted via the central venous catheter. If hemodynamic collapse occurs, the operating table is tilted.

Heart rate (HR), mean arterial blood pressure (MBP), arterial oxygen saturation ($SPO_2$),end tidal carbon dioxide ($EtCO_2$) and central venous pressure (CVP) were recorded before induction (basal) and post-induction, after sitting, 30 min from start of surgery and every 30 min till the end of surgery.

Serum sodium and potassium concentration and serum osmolarity was measured at a basal reading (preoperatively), post-induction, after half dose of mannitol infusion, after full dose of mannitol infusion, 1 h post-infusion, 90 min, 120 min and at recovery room.

Brain relaxation was determined by the surgeon during opening the dura on a four-point scale: 1 = perfectly relaxed, 2 = satisfactorily relaxed, 3 = firm (leveled) brain, 4 = bulging brain immediately after opening the dura [7].

At the end of the surgery, patients were transferred to surgical intensive care for at least 24 h with full monitoring, and any complications were recorded (either intra-operative or postoperative).

For calculation of power analysis, we assumed a difference of 1 point in brain relaxation score between the groups to be clinically significant. A power of analysis based on 95% confidence interval and type-I error protection of 0.05 and an effect size convention of 0.8, a total sample size of 70 patients (35 patients in each group) produced a power of 0.95. But we recruited 80 cases to overcome the possibility of drop out cases.

The statistical analysis of data was done by using excel program for figures and SPSS (SPSS, Inc, Chicago, IL) program statistical package for social science version 16. The t test was used for data proved to be normally distributed (the Kolmogrove Smirnov test). Only significant data revealed to be nonparametric. NB: all tested data revealed to be parametric. The description of the data done in form of mean ($\pm/-$) SD for quantitative data and frequency and proportion for qualitative data. The analysis of the data was done to test statistical significant difference between groups. Chi square test was used for qualitative data. Any difference or change showing probability ($p$) less than 0.05 was considered statistically significant at confidence interval 95%.

## 3. Results

The flow diagram of participation in this study is shown in Fig. 1. One patient of mannitol group had a massive air embolism (requiring correction of the patient's position and resuscitation) and two of placebo group (one exposed to unblinding and the other patient had sever hemorrhage with hemodynamic instability) were excluded from the analysis of the study outcomes (Fig. 1). In this study, there were no significant differences between mannitol group and placebo group with respect to age (20–60 years), weight (55–90 and 55–82 kg, respectively). All patients were ASA I and II (ASA I/ASA II = 21/18 and 23/15, respectively). The duration of surgery and the duration of hospital stay also showed no significant intergroup differences (Table 1).

Estimated blood loss displayed no significant difference between the studied groups (647.250 ± 173.972 ml) in mannitol group versus (650.000 ± 171.389 ml) in placebo group ($p$ value = 0.943) (Table 1) .

The total amount of the urine output, at the end of the procedure reflected a highly significant difference between the

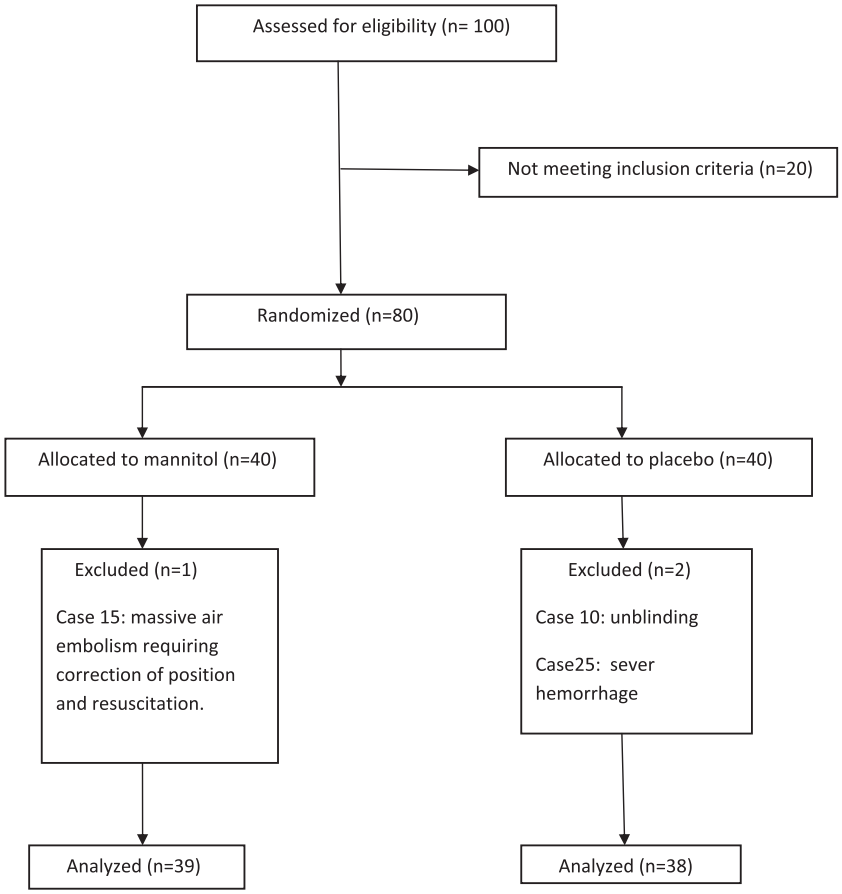


**Figure 1** Consort flow diagram.

**Table 1** Patients characteristics, duration of surgery (min) and total urine output (ml) of the studied groups. Values are presented as mean ± SD, (number) and (%) for ASA classification.

| | GI ($N$ = 39) | | GII ($N$ = 38) | | $p$ Value |
|---|---|---|---|---|---|
| | $N$ | % | $N$ | % | |
| *ASA* | | | | | |
| I | 21 | 53.8% | 23 | 60.5% | 0.62 |
| II | 18 | 46.2% | 15 | 39.5% | |
| Age (years) | 41.90 ± 9.46 | | 42.37 ± 10.19 | | 0.83 |
| *Sex* | | | | | |
| M | 20 | 51.3% | 17 | 44.7% | 0.35 |
| F | 19 | 48.7% | 21 | 55.3% | |
| Wt (kg) | 71.25 ± 8.19 | | 68.55 ± 6.94 | | 0.11 |
| Duration of surgery (min) | 177.37 ± 15.40 | | 177.50 ± 15.48 | | 0.97 |
| Duration of hospital stay (day) | 6.47 ± 1.89 | | 7.05 ± 1.96 | | 0.18 |
| Estimated blood loss (ml) | 647.250 ± 173.972 | | 650.000 ± 171.389 | | 0.943 |
| Total urine output (ml) | 1683.7750 ± 381.237* | | 815.5000 ± 209.724 | | 0.001 |

GI = Mannitol group.
GII = Placebo group.
* Significant difference between GI and GII ($p < 0.05$).

studied groups (1683.7750 ± 381.237) in mannitol group versus (815.5000 ± 209.724) in placebo group ($p$ value < 0.001) (Table 1).

The pathological lesions were located mainly in the posterior fossa and showed no any significant difference between both groups (Table 2).

**Table 2** Type of the lesions. Values are presented as numbers of the patients.

| Type of lesions | GI ($n$ = 39) | GII ($n$ = 38) | $p$ Value |
|---|---|---|---|
| Cerebellopontine angle tumor(CPA) | 13 | 14 | 0.956 |
| Cerebellar tumor | 10 | 8 | |
| Occipital lobe | 8 | 8 | |
| Brain stem lesion | 5 | 4 | |
| Pineal body tumor | 3 | 4 | |

GI = Mannitol group.
GII = Placebo group.

**Table 3** Complications of the studied groups. Values are presented as numbers of the patients.

| Type of complications | GI ($n$ = 39) | | GII ($n$ = 38) | | $p$ Value |
|---|---|---|---|---|---|
| | No. | % | No. | % | |
| Air embolism | 2 | 5 | 2 | 5 | 0.69 |
| Pneumocephalus | 4 | 10 | 1 | 2.5 | 0.17 |
| Neurological deficits | 1 | 2.5 | 1 | 2.5 | 0.75 |

GI = Mannitol group.
GII = Placebo group.

As regard the complications recorded with each group, there were two cases who developed a shower of air embolism in both groups. Although pneumocephalus occurred in four cases in mannitol group and in one case in placebo group, it did not represent significant difference between both groups ($p = 0.17$). Neurological deficit in the form of transient ulnar nerve concussion developed in one case in both groups (Table 3).

Heart rate and mean arterial blood pressure demonstrated no significant difference between both groups throughout the study period (Fig. 2). Heart rate was increased post-induction in both groups compared with the baseline values. Mean blood pressure was decreased significantly after sitting, 30 min, 1 h, 90 min from start of surgery in both studied groups in comparison to the baseline values.

Peripheral arterial oxygen saturation ($SPO_2$) was significantly increased in both groups at 1 h, 90 min and 120 min from the start of surgery ($p < 0.01$) and significantly increased only in placebo group at 30 min compared with basal values ($p \leqslant 0.001$) (Table 4). At the same time, the end tidal carbon dioxide ($EtCO_2$) displayed significant increase in the mannitol group in comparison to the placebo group ($p \leqslant 0.01$ to $p \leqslant 0.02$), where as it showed a highly significant decrease in mannitol group at 30 min from the start of surgery compared with both basal value and the placebo group ($p \leqslant 0.001$) (Table 4).

Regarding central venous pressure in mannitol group, it revealed a significant increase ($p < 0.01$) at 30 min from start of surgery then it returned gradually to nearby the initial basal values (Fig. 3).

Fourteen patients in mannitol group had a brain relaxation score (BRS) 1 versus ten patients in placebo group without significant difference between both groups. Twelve patients in mannitol group versus eleven patients in placebo group had BRS 2. Seven patients in mannitol group versus nine patients in placebo group had BRS 3. Six patients in mannitol group versus eight patients in placebo group had BRS 4. Brain relaxation score displayed no significant difference between the studied groups ($p = 0.719$) (Fig. 4).

Serum sodium level concentration showed a highly significant decrease in mannitol group ($p < 0.001$) compared with placebo group after half dose of mannitol infusion till 90 min post-infusion (Fig. 5). Whereas mannitol group displayed a significant increase of serum potassium level concentration compared with placebo group starting after half dose of mannitol infusion, after full dose of mannitol infusion and at 1 h post-infusion ($p < 0.001$) (Fig. 6). Serum osmolarity showed significant increase in mannitol group ($p < 0.001$) compared with placebo group after half dose of mannitol infusion till 120 min post-infusion (Fig. 7).

## 4. Discussion

In the present study, both groups; mannitol and placebo were compared as regard hemodynamic, brain relaxation score, serum sodium, potassium and osmolarity and any operative complications. Patients in both groups demonstrated comparable both demographic characteristics included the types of lesions and hemodynamic included HR and MBP. Mannitol group displayed significant increase in end tidal carbon dioxide and serum potassium and osmolarity compared with placebo group, whereas it demonstrated a significant decrease in $EtCO_2$ at 30 min from the start of surgery compared with the basal value. Peripheral arterial oxygen saturation was significantly higher in both groups at most of the study periods compared with basal values. Mannitol group displayed significant hyponatremia compared with placebo group. Mannitol group demonstrated significant increase in urine output than placebo group.

Since 1913, when the first surgery with the patient in sitting position was performed, the debate concerning this positioning has continued [8]. The sitting position is thought to be the best for surgical access to the posterior fossa or to dorsally located parietal lesions. In addition to increased risk of venous air embolism, the hemodynamic disturbances following the sitting position were evident [9]. Based on this concept, in the current study, we tried to minimize this hemodynamic and electrolytes derangement associated with the sitting position through avoiding the use of mannitol which might causes a further disturbances in hemodynamics in addition to its unwanted effect on the serum electrolytes with its subsequent effect on such group of patients.

There is a well-documented transient intracranial pressure (ICP) reducing effect of mannitol, but an adverse rebound increase in ICP after its withdrawal has been discussed extensively in the literature and is an expected pathophysiological phenomenon [10].

In our study, although the number of patients in mannitol group with a perfectly and satisfactory brain relaxation were more than those in the placebo group, it did not represent statistical significance between both groups. Also, the number of patients in placebo group with firm and rigid brain was more than those in the mannitol group, but this was not represents significant difference between both groups. Previously, the

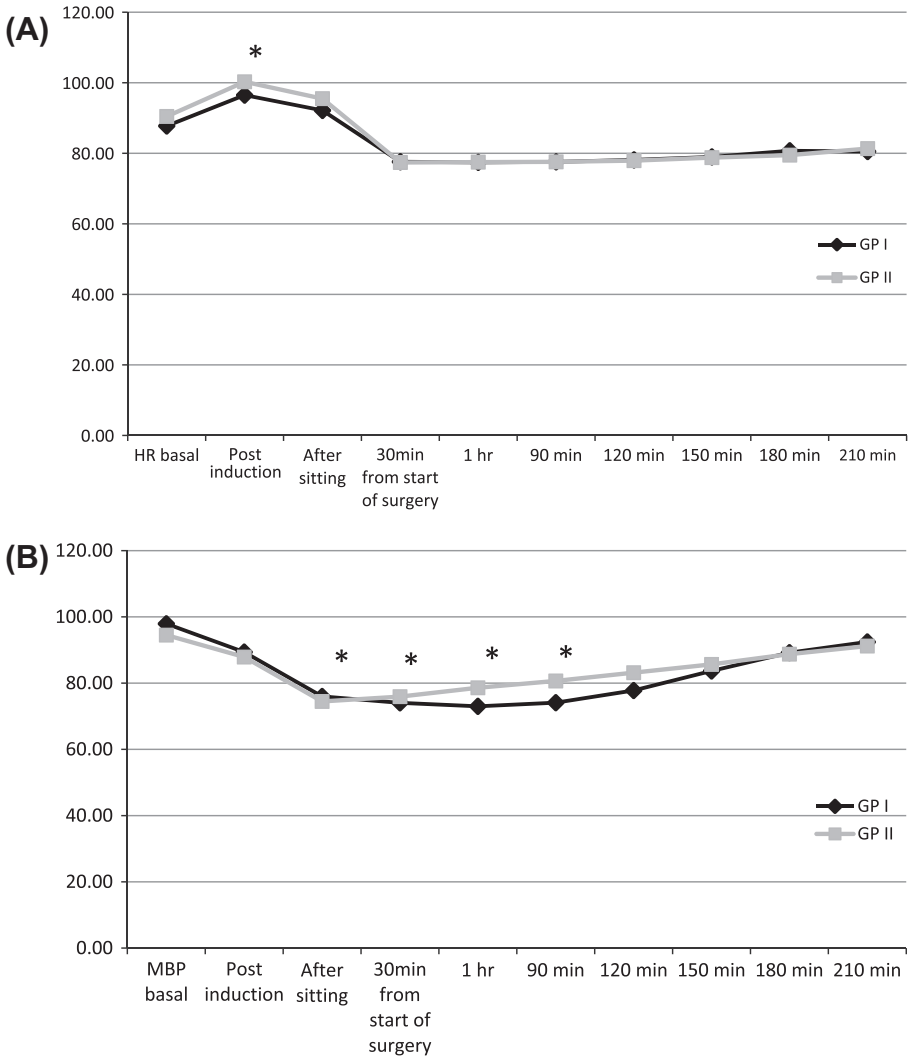


**Figure 2** (A) HR of the studied groups (beat/min); (B) MBP of the studied groups (mm Hg). *Statistically significant compared to the baseline value.

**Table 4** End tidal carbon dioxide $EtCO_2$ (mmHg) and arterial oxygen saturation ($SPO_2$%) of the studied groups. Values are mean ± SD.

| | $EtCO_2$ | | *p* Value | $SPO_2$ | | *p* Value |
|---|---|---|---|---|---|---|
| | GI ($n$ = 39) | GII ($n$ = 38) | | GI ($n$ = 39) | GII ($n$ = 38) | |
| Basal after intubation | 37.25 ± 2.89 | 37.32 ± 2.93 | 0.90 | 98.42 ± 0.98 | 98.40 ± 0.98 | 0.91 |
| After sitting | 33.17 ± 2.61 | 32.70 ± 2.98 | 0.45 | 99.70 ± 0.46 | 99.55 ± 0.55 | 0.19 |
| 30 min from start of surgery | 28.45 ± 3.58** | 33.40 ± 3.63* | 0.001 | 97.60 ± 14.21 | 99.77 ± 0.42** | 0.001 |
| 1 h | 34.92 ± 1.81 | 33.35 ± 2.04* | 0.01 | 99.85 ± 0.36** | 99.25 ± 0.43** | 0.01 |
| 90 min | 36.87 ± 0.79 | 36.00 ± 1.17* | 0.01 | 99.72 ± 0.55** | 99.00 ± 0.32** | 0.01 |
| 120 min | 37.32 ± 0.70 | 36.78 ± 1.13* | 0.02 | 99.17 ± 0.38** | 99.45 ± 0.50** | 0.01 |
| 180 min | 32.55 ± 2.13 | 33.15 ± 2.62 | 0.26 | 99.35 ± 0.62 | 99.30 ± o.46 | 0.68 |
| 150 min | 35.12 ± 1.43 | 35.20 ± 1.84 | 0.84 | 99.02 ± 0.27 | 99.05 ± 0.31 | 0.70 |
| 210 min | 37.50 ± 31.80 | 37.33 ± 0.98 | 0.27 | 99.57 ± 0.50 | 99.45 ± 0.50 | 0.26 |

GI = Mannitol group.
GII = Placebo group.
* Significant difference between GI and GII ($p < 0.05$).
** Significant difference with basal values ($p < 0.05$).

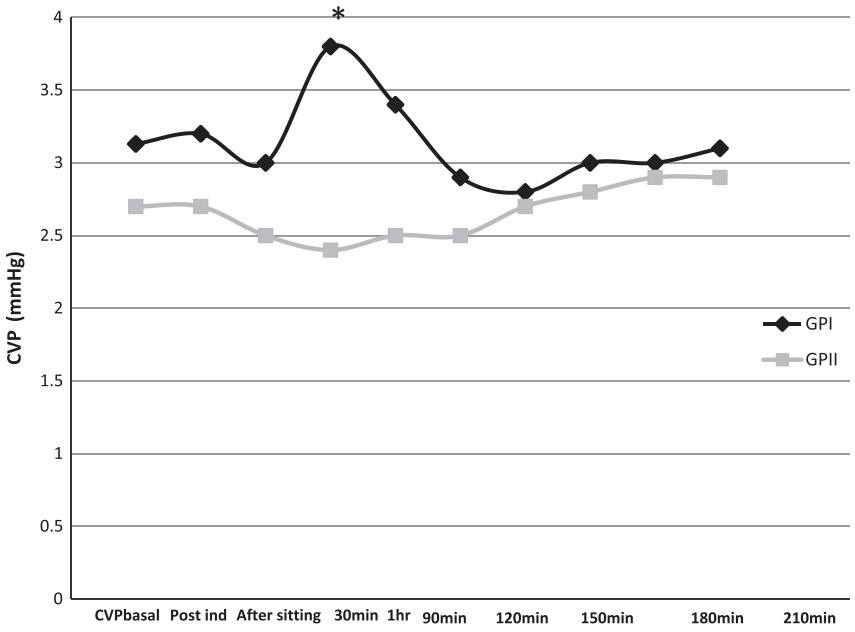


**Figure 3** Central venous pressure (CVP, mm Hg) of the studied groups. Values are in numbers. * = Significant difference between GI and GII ($p < 0.05$). GI = Mannitol group. GII = Placebo group.

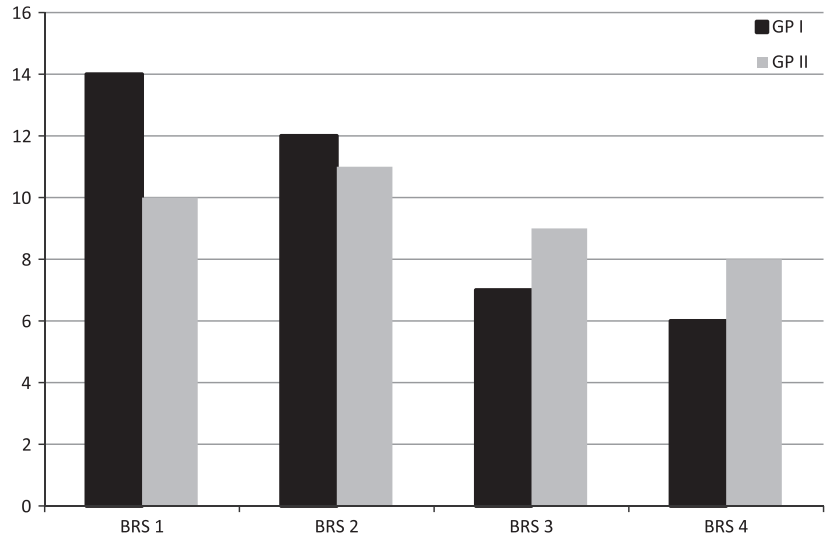


**Figure 4** Brain relaxation score (BRS) of the studied groups. Values are in numbers. Four-point scale score of brain relaxation: 1 = perfectly relaxed, 2 = satisfactorily relaxed, 3 = firm (leveled) brain, 4 = bulging brain. GI = Mannitol group. GII = Placebo group.

effect of mannitol on the brain in patients without increased intracranial pressure has been investigated in two studies in patients undergoing elective craniotomies for various neurosurgical procedures [11,12]. Gemma et al. reported satisfactory brain relaxation in all cases, when a different osmolar load but similar volume of 7.5% HS ($n = 25$) and 20% mannitol ($n = 25$) was given to patients. De Vivo et al. compared three different regimens and combinations of mannitol and HS: (1) 0.5-g/kg bolus of mannitol ($n = 10$) versus (2) 0.25-g/kg bolus of mannitol followed by continuous infusion of 3% HS ($n = 10$) versus (3) bolus of 3% HS followed by continuous infusion of 2% and 1% HS ($n = 10$). Using the scale of brain relaxation similar to ours, the authors did not find any difference between the groups.

The patients in our study displayed no significant hemodynamic difference between the studied groups. It is possible that blood pressure fluctuations were controlled by anesthesia management, masking an acute response to study solutions, but this is considered unlikely because no specific hemodynamic pattern emerged during the study. Another studies proved that the sitting position is often associated with haemodynamic instability, in particular a decrease in mean arterial pressure,

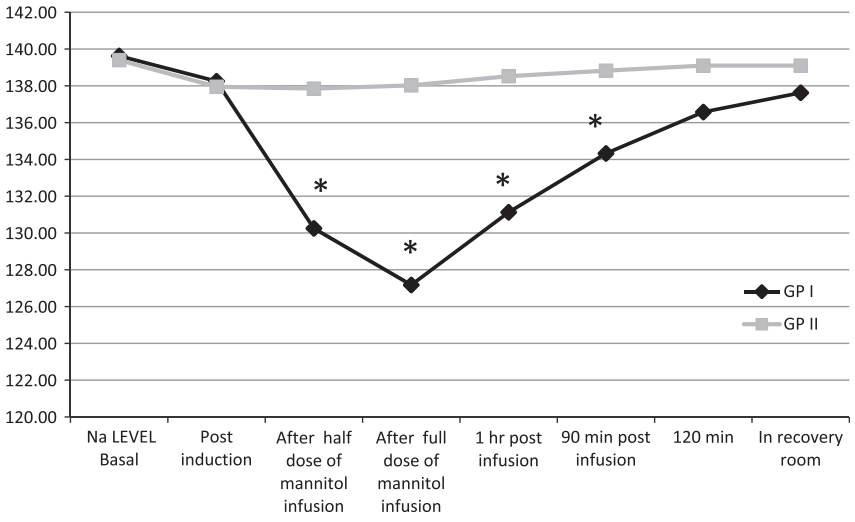


**Figure 5** Serum sodium concentration ($Na^+$) (meq/L) of the studied groups. Values are in numbers.* = Significant difference between GI and GII ($p < 0.05$). GI = Mannitol group. GII = Placebo group.

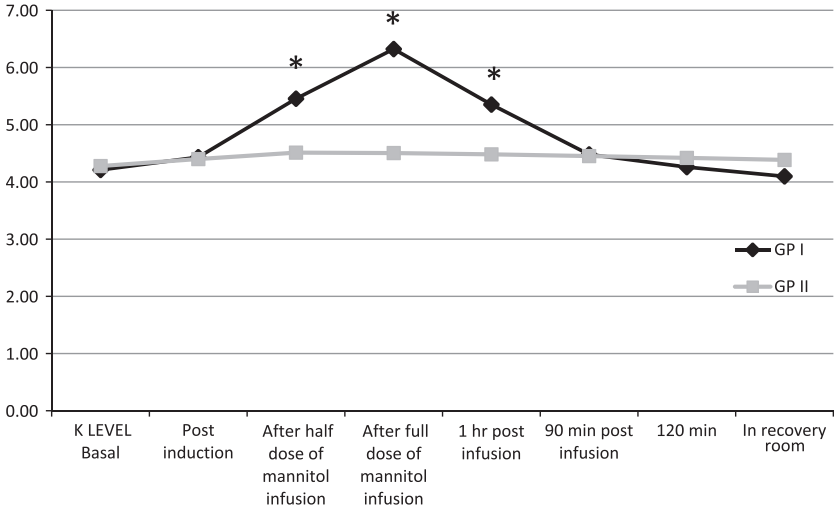


**Figure 6** Serum potassium concentration ($K^+$) (meq/L) of the studied groups. Values are in numbers. * = Significant difference between GI and GII ($p < 0.05$). GI = Mannitol group. GII = Placebo group.

stroke volume index and cardiac index [13,14]. It could be assumed that the cardiovascular effects of the sitting position are caused mainly by a reduction in cardiac preload [15].

The reduction of the mean arterial blood pressure observed in our study in comparison to the baseline values was in accordance to the previous study, in which the arterial hypotension, defined as a decrease in mean arterial pressure of >10% or a decrease in systolic arterial pressure of >20% with an incidence of 5–32% [16].

CVP was increased by mannitol group at 30 min after the start of surgery, consistent with an initial intravascular volume expansion, determined by the increase in serum osmolality. The same result was observed by Rozet et al., in their study on the effect of equiosmolar solutions of mannitol versus hypertonic saline on intraoperative brain relaxation and electrolyte balance [17].

In the current study the significant increase in the level of end tidal carbon dioxide in mannitol group ($EtCO_2$) might be explained by the initial increase in the blood volume that accompanied the mannitol infusion with consequent increase in the pulmonary blood flow. Apart from the quantity and rate of mannitol infused, the duration of the blood volume increase is dependent on both the rate of equilibration of mannitol in the extracellular compartments and the rate of renal excretion of mannitol with the resulting osmotic diuresis [18]. In this study the $EtCO_2$ reached its maximum at the termination of the mannitol infusion and returned gradually to near the control levels later on. At the same time the peripheral arterial oxygen saturation was significantly increased concomitant with the gradual raising of the body to the sitting position which might be attributed to the relieving effect on the thoracic cage away from the abdominal content improving the process of ventilation.

The majority of the cardiovascular effect observed during this study did not occur when patients were placed in the seated position, but rather occurred with infusion of mannitol which might support our hypothesis of lacking interest for the use of mannitol in such group of patients.

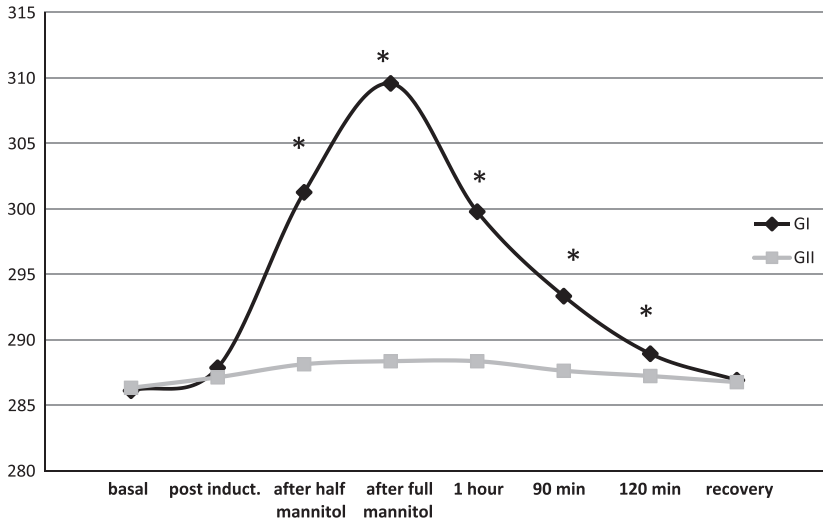


**Figure 7** Serum osmolarity (mmol/L) of the studied groups. Values are in numbers. * = Significant difference between GI and GII ($p < 0.05$). GI = Mannitol group. GII = Placebo group.

Estimated blood loss displayed no significant difference between the studied groups that could be assumed to the sitting position attained in both groups in which, accumulated blood drains out of and away from the operative site, permitting more rapid access to bleeding points, a cleaner surgical field and a technically easier procedure irrespective to the use of mannitol or not.

In this study, surgery was performed by 1 of senior neurosurgeon. Although serious complications were not observed, the prognosis of brain tumor surgery was influenced by many factors, including the size and the location of the tumor, the severity of the adjacent tissue damage, the residual function after tumor excision, and the immune or inflammatory responses to the procedure. The results of hospital stay days in the 2 groups were similar, perhaps because (1) these 2 studied groups were affected mainly by the factors described above, rather than by the effects of mannitol on brain relaxation; (2) significant differences may have been present mainly at the cellular level or at the cognitive function level, which was beyond the scope of our study; (3) even though mannitol yielded a greater effect on brain relaxation, it is very important to note that a reduction in brain volume does not necessarily translate into a better cerebral outcome [19].

Venous air embolism (VAE) is the entrainment of air into the venous system from the operative site or another communication with the environment. Venous air embolism is a frequent event in patients undergoing posterior fossa surgery while in the sitting position, occurring in 45% of patients in the study done by Black and Cucchiara, on the outcome following posterior fossa craniectomy in patients in the sitting or horizontal position [20].

In the current study, the incidence of venous air embolism was not more than 5% in both groups. Really, we depend up on the end tidal carbone dioxide as the only tool for detection of venous air embolism, which might affect the sensitivity of detection. The most commonly used methods are transoesophageal echo (TOE), precordial Doppler, $EtCO_2$, right heart catheterization, and oesophageal stethoscope in decreasing order of sensitivity for air detection [20]. In the current study, the highly significant decrease in the $EtCO_2$ ($p < 0.001$) at 30 min from the start of surgery that observed in mannitol group compared with the basal value might be attributed to the occurrence of shower of venous air embolism (VAE) reflected on the sudden decrease in $EtCO_2$ during the opening of the cranium or the dura. In this study, the unaltered hemodynamics in patients during VAE indicates relatively small VAE. Possible explanations for this are early recognition of air leakage and good cooperation between the surgical and anesthesia teams.

Pneumocephalus occurs due to air entry into the dural or the epidural spaces under pressure and in sufficient volumes to exert dangerous mass effect potential for life threatening brain herniation [21]. In the current study, although the incidence of pneumocephalus showed no significant difference between the studied groups, the number of patients belonged to mannitol group (10%) were more than those in the placebo group (2.5%), which might be attributed to diminution of the brain volume secondary to mannitol administration. This complication has been described in association with posterior fossa tumor resection in the sitting position by many authors [22,23]. In one large study, the incidence of pneumocephalus following posterior fossa surgery in sitting position was 3% [24].

The changes in serum sodium, potassium and osmolality in mannitol group of our study are similar to previous investigations of low dose mannitol [25,26]. In the current study, mannitol caused an immediate decrease in sodium in blood and an increase in potassium and osmolarity over time till 1 h post-infusion where both electrolytes start to return near to the baseline values later on (Figs. 5–7).

Physiologic effects of hyperosmotic fluids on the brain have been compared in multiple animal and human studies with various brain pathologies [27,28]. The principal mechanism of action of mannitol is the creation of an osmolar gradient across the BBB due to impermeability of the BBB to mannitol. Therefore, an intact BBB is required for intravascular water absorption. Indeed, a decrease in intracranial pressure with increased serum osmolality, and decreased brain water content with

hyperosmotic treatment in healthy, but not injured, brain tissue has been shown in animals [29]. In humans, a correlation between an increased concentration in serum sodium and osmolality and a decrease in intracranial pressure and brain water content in noninjured brain areas has been shown in patients with traumatic brain injury and brain tumors, treated with either hypertonic saline (HS) or mannitol [30]. In this regard, our data showing equally effective brain bulk reduction with mannitol was consistent with the classic theory of hyperosmotic therapy. Mannitol caused an acute hyponatremia but a stepwise increase of potassium over time. Different changes of potassium such as hypokalemia and hyperkalemia have been previously reported with mannitol [31]. Hyperkalemia after mannitol administration has been reported [32], but the exact mechanism of this phenomenon is unknown. One of the suggestions includes a cellular potassium efflux with the water, as a result of hyperosmolar condition [33]. Administration of mannitol increases serum sodium concentration or osmolality and decreases ICP and brain water content in non injured brain areas, as shown in human and animal studies [34,35]. The principal mechanism underlying these effects is the induction of a water shift from brain tissues to the intravascular space by the hyperosmolarity of mannitol because the blood brain barrier (BBB) is impermeable to mannitol. At the end of the study, the total urine output was significantly increased with mannitol group indicating an ongoing osmotic diuresis with the risk of accentuating the already disturbed electrolytes state.

## 5. Conclusion

Tumor of the posterior fossa can easily operated without the use of mannitol with accepted hemodynamic condition, reasonable metabolic state and no significant difference in brain relaxation score (BRS), the amount of intraoperative blood loss and the operative complications between both groups.

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