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Original Article

Effect of Perioperative Fluids on Serum Osmolality and Serum Sodium in Patients Undergoing Transcranial Excision of Craniopharyngioma: A Prospective Randomized Controlled Trial

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Abstract

Background: Electrolyte imbalance and acute diabetes insipidus (DI) are the most common complications in patients undergoing craniopharyngioma excision. Data are sparse regarding the choice of fluid in these patients. We compared the effects of balanced salt solution and 0.45% saline infused perioperatively on serum osmolality and serum sodium levels in these patients. **Methodology:** A prospective randomized double-blinded study was conducted in 30 patients undergoing transcranial excision of craniopharyngioma. The patients received either balanced salt solution or 0.45% sodium chloride solution perioperatively till they were allowed orally. Serum and urine osmolality, serum and urine sodium, urine specific gravity, and total dose of desmopressin required to treat DI were measured in the perioperative period. **Results:** Demographic data were comparable. We observed that there was significantly higher serum osmolality in the intraoperative period at 2nd h ($P = 0.04$), 3rd h ($P = 0.01$), at end of the surgery ($P = 0.034$) and on postoperative day 0 (POD 0) with $P = 0.03$ in patients receiving balanced salt solution. We also observed that the difference in serum sodium levels were significantly higher in patients receiving balanced salt solution as compared to those receiving 0.45% sodium chloride solution intraoperatively, at 3rd h ($P = 0.02$) and at the end of surgery ($P = 0.04$) although the values were comparable in both the groups as measured on POD 0, 1 and 2. **Conclusion:** 0.45% sodium chloride solution has better effect on serum osmolality than balanced salt solution in patients undergoing transcranial resection of craniopharyngioma.

Keywords: *0.45% sodium chloride solution, balanced salt solution, craniopharyngioma, diabetes insipidus, hypernatremia*

Introduction

Craniopharyngioma is a benign tumor that arises from squamous remnant of Rathke's pouch and extends toward the hypothalamus. These patients commonly develop fluid and electrolyte disturbances, notably Central Diabetes Insipidus and Syndrome of Inappropriate Antidiuretic Hormone (SIADH) secretion during perioperative period. The immediate postoperative period, is a state of hyperaldosteronism under the normal hypothalamic pituitary axis.[1-3] Surgery for craniopharyngioma disturbs the normal hypothalamo-pituitary axis resulting in electrolyte abnormalities. The fluid management during intraoperative period has been found to influence the postoperative serum osmolality and serum sodium levels significantly.[4] Hence, the optimal fluid management in perioperative period is essential to ensure better patient outcomes.

Numerous previous studies have been done in animals demonstrating changes in serum osmolality with infusion of large volume of hypo-osmolar fluids but evidence from human studies is lacking. A previous study by Mukherjee *et al.*[5] comparing 0.45% saline, 5% dextrose and 0.9% sodium chloride in patients undergoing craniopharyngioma surgery, reported significantly higher serum sodium levels in the 0.9% sodium chloride group as compared to 0.45% saline in the first 48 h postoperatively. The use of normal saline was associated with higher incidence of hypernatremia, diabetes insipidus (DI), and

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mortality ($P = 0.05$), while the group that received 5% dextrose was associated with hyponatremia, hypoglycemia, and seizures.

There is no study till date which compared the use of balanced salt solution with other fluids in patients undergoing craniopharyngioma excision. As Mukherjee *et al*.[5] have concluded that 0.45% sodium chloride solution is the ideal fluid for perioperative use in patients with craniopharyngioma, so we planned to compare it with balanced salt solution in patients undergoing resection of craniopharyngioma both in intra- and post-operative period hypothesizing that intravenous infusion of balanced salt solution will maintain osmolality better than 0.45% sodium chloride solution.

Methodology

A prospective randomized study was conducted after getting approval from Institute Ethics Committee (NK/1577/MD10079-80) and was registered with Clinical Trials Registry of India (CTRI) with Trial registry number of CTRI/2017/03/008159.

The study was conducted in patients undergoing transcranial resection of craniopharyngioma after getting written informed consent from the patient or nearest kin. The patients were allotted randomly into two groups by computer-generated random number table. Patients in Group S ($n = 15$) received intravenous infusion of 0.45% sodium chloride solution while patients in Group P ($n = 15$) received balanced salt solution (Plasmalyte A) in the intraoperative and postoperative period till patients were started on oral fluids. Patients undergoing transsphenoidal resection of craniopharyngioma, having DI/Diabetes mellitus or renal abnormality before surgery were not included in the study. In the preoperative period, demographic profile, presenting symptoms, neurological and visual deficits, computed tomography (CT) and magnetic resonance imaging findings, thyroid and cortisol level, Glasgow Coma Scale (GCS), serum and urine osmolality, serum and urine sodium, urine-specific gravity, serum blood glucose level were recorded.

A standard anesthetic technique was followed in all the patients. Induction of anesthesia was achieved with Propofol (1–2 mg/kg) with Fentanyl (2 μg/Kg) and muscle relaxation was achieved by vecuronium 0.1 mg/kg. Anesthesia was maintained with isoflurane, oxygen- nitrous oxide mixture (50:50) and intermittent doses of intravenous vecuronium 0.02 mg/kg. Ventilation was maintained with a fresh gas flow rate at 1-2 L/min and keeping end tidal carbon-dioxide of 35–40 mm Hg. Intraoperative analgesia was maintained with intravenous fentanyl infusion 1 μg/kg/h. Intraoperative monitoring also included invasive blood pressure, capnography, central venous pressure (CVP), and urine output. Serum sodium, urine sodium, urine and serum osmolality and urine specific gravity were measured in the preoperative period, thereafter in intraoperative period once every hour for first 3 h and then at the end of the surgery. CVP was maintained around 6–8 mm of Hg and hourly urine output was measured during surgery. Standard anaesthesia protocol for emergence from anaesthesia was followed in patients in whom elective postoperative mechanical ventilation was not planned. The operating surgeon was asked about the extent of tumor resection (partial or near total) at the end of the surgery.

As rescue measures, intravenous 0.45% sodium chloride solution was started in patients who developed hypernatremia (serum sodium >145 mEq/L). Patients were monitored for cerebral edema both clinically and by postoperative CT. Normal saline solution was infused in patients who developed hyponatremia (serum sodium <135 mEq/L) in the intraoperative period.

Patients were followed up in the postoperative period till they started taking fluids and diet orally. They were evaluated daily for GCS, serum and urine osmolality, serum sodium, and urine-specific gravity. Serum cortisol level was assessed on the 3rd postoperative day. Serum and urine osmolality was estimated in the immediate postoperative period to rule out polyuria due to administration of excessive intraoperative fluid. Patients were investigated every day for the development of DI and requirement of vasopressin to treat the same. Blood sugar levels were estimated regularly to exclude the possibility of polyuria due to hyperglycemia.

If patients developed electrolyte disturbance in the postoperative period, it was treated according to the institute protocol and rescue measures taken were noted. According to the protocol if patient developed polyuria (UO >4 ml/kg/h) for two consecutive hours, along with serum sodium >145 mEq/L then initially fluid intake was restricted and serum sodium levels were assessed hourly. If the serum sodium levels still remained high (>145 mEq/L) after 2 h, injection vasopressin 3U was given subcutaneously in patient more than 14 years of age while injection vasopressin 2U (SC) was given to children <14 years. If the patient developed hyponatremia (<135 mEq/L) postoperatively, fluid intake of the patient was completely restricted for 2 h and serum sodium levels was assessed hourly. If serum sodium level did not normalize after fluid restriction, 0.9% sodium chloride solution was administered such that the rise in serum sodium levels did not exceed more than 0.5 mEq/L/h.

Statistical analysis

Statistical analysis was carried out using statistical package for social sciences (SPSS Inc., Chicago, IL, USA, version 21.0). Continuous data were presented as mean ± standard deviation (SD) or median and inter quartile range, as appropriate. For normally distributed data, two groups were compared using Student's *t*-test (unpaired). For all skewed data, two groups distribution was compared using Mann–Whitney U test. All normally distributed data were expressed as mean and SD. Skewed data were expressed as median, interquartile range. Categorical and classified data were compared by Chi-square test or Fischer's exact test. Repeated measure data were analyzed with repeated measures analysis of variance with Bonferroni correction for comparison of two groups. Data correlation was analyzed by Pearson's or spearman's correlation based on distribution of data. A $P < 0.05$ was considered significant.

Results

Thirty patients were enrolled for the surgery. Three patients from group S were excluded from the study after enrolment as the histopathology did not confirm the tumor to be craniophayngioma. Two patients were excluded from group P as they developed intraoperative.

DI as intention to treat analysis. The observations were recorded and the results were statistically analyzed for 13 patients in group P and 12 patients in group S [Figure 1]. The demographic data, hormone status, intraoperative total intravenous fluid infused were comparable in between the groups [Table 1]. The tumor size was comparable between the groups [Table 1]. All patients underwent near total resection of tumor.

Serum osmolality was comparable between the groups in the preoperative period and in the 1st h of surgery but the difference in serum osmolality was significantly different in 2nd and 3rd h intraoperatively and at the end of surgery in between the groups with higher values in patients who received balanced salt solution [Table 2]. We observed that the number of patients with serum osmolality more than 300 mosm/kg were more in group P throughout the intraoperative period [Table 2]. In our study, postoperative day 0 (POD 0) a significant difference in serum osmolality was observed among the two groups [Table 2].

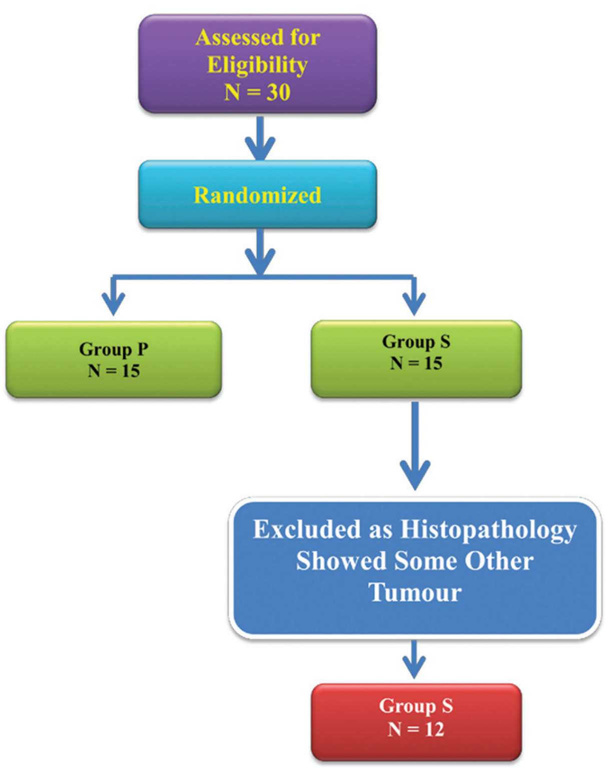

Figure 1: Consort diagram

Serum sodium level in preoperative period was comparable in between the groups. Intraoperatively, the difference in serum sodium levels was significantly higher in group P as compared to group S at 3rd h and at the end of surgery although the values in both the groups were within normal limits. Whereas in the postoperative period, values were higher than in intraoperative period but were comparable in both the groups [Table 2].

Preoperative and intraoperatively urine osmolality and urine specific gravity were comparable and within normal range in both the groups. Although urine osmolality was lower in group S but the difference was not statistically significant. Urine output and dose of vasopressin requirement during study period were recorded. Although the urine output and vasopressin requirement were less in Group S, the difference between the groups was not statistically significant [Table 3]. Time to start oral intake in postoperative period was also comparable in between the groups, although oral intake was earlier in Group S.

In this study, no patient developed any clinical features or had postoperative CT finding suggestive of cerebral edema. Two patients (one adult and one child) from Group P had developed DI in intraoperative period [Table 4]. All patients in both the groups developed DI in the postoperative period. In this study population, one patient from group P died due to complication following intestinal perforation attributed to steroid replacement. Rest all of the patients in this study were discharged and among them, 66.6% in group P and 83.3% in group S had developed chronic DI [Table 4].

Discussion

In this study, infusion of 0.45% sodium chloride (osmolarity-154 mosm/L) was compared to balanced salt solution (osmolarity- 294 mosm/L) in patients undergoing excision of craniopharyngioma. We observed that the serum osmolality was comparable in 1st h of surgery but the difference in serum osmolality was significantly different in 2nd h, 3rd h and at the end of the surgery in between the groups with higher values of serum osmolality in patients receiving balanced salt solution. We also observed that the number of patients with serum osmolality more than 300 mosm/kg were more in patients receiving balanced salt solution. We observed significantly higher serum osmolality on postoperative day 0 in patients receiving balanced salt solution. Though there have been numerous studies in animal model demonstrating changes in serum osmolality with infusion of large volume of hypo-osmolar fluid like ringer lactate but evidence in human beings were lacking.

Table 1: Patient characterstics and intraoperative parameters

Characterstics	Group P (n=13)	Group S (n=12)	*P*
Age (years)	22.46±20.02	15.75±11.22	0.31
Weight (kg)	43.76±26.67	38.75±22.23	0.61
Gender (male/female)$^{\$}$	10/3	9/3	1.00
Duration of surgery (h)	3.8±1.41	4.1±1.1	0.58
Duration of anesth (h)	4.46±1.37	4.7±1.15	0.87
Tumour size (cm^3)	2.7×2.8×1.2	2.8×2.5×1.5	0.75
Hormone levels (%)			
Hypothyroidism$^{\beta}$	3 (23)	4 (33.3)	0.67
Hypocortisolism$^{\beta}$	6 (46.1)	7 (58.3)	0.69
Hypothyroidism and hypocortisolism$^{\beta}$	2 (25)	3 (42.9)	0.60
Urine sodium (mEq/L)	13.2±2.3	13.4±2.1	0.86
RBS (mg/dl)	96.7±10.1	91±10.5	0.23
Intraoperative parameters			
Volume of fluid infused (L)	2.40±1.28	2.23±1.46	0.76

Values expressed as mean±SD. $^{\$}$Presented as number; $^{\beta}$Presented as number. SD – Standard deviation; RBS – Random blood sugar

Table 2: Serum osmolality (mOsm/kg) and serum sodium (mEq/L)

Time period	Group P (n=13)	Group S (n=12)	*P*
Serum osmolality			
Preoperative	299.5±18.29	299±14.1	0.48
Intraoperative (h)			
1	297.3±15.69	293±12.2	0.51
2	295.2±11.8	287.5±5.7	0.04*
3	301.2±13.2	289.9±8.3	0.01*
End of surgery	303.8±13.1	292.4±11.7	0.03*
Postoperative			
POD 0	333.7±32.3	310.17±15	0.03*
Serum sodium (mEq/L)			
Preoperative	138.07±3.8	139.3±2.9	0.37
Intraoperative (h)			
1	139.5±3.74	139.9±3.5	0.77
2	139.11±3.4	138.2±5.7	0.65
3	140.3±3.3	137.2±4.0	0.02*
End of surgery	141.8±3.2	138.5±3.1	0.04*
Postoperative			
POD 0	147.8±5.2	146.6±2.4	0.44

Values expressed as mean±SD. *P<0.05 as statistically significant. POD – Postoperative day 0; SD – Standard deviation

Table 3: Urine output (ml/kg) and dose of vasopressin (units)

Time period	Group P (n=15)	Group S (n=12)	*P*
Urine output (ml/kg)			
Intraoperative (ml/kg/h)	6.35±5.7	4.15±3.08	0.25
Postoperative (ml/kg in24 h)			
POD 0	44.9±14.1	46.4±18.6	0.8
Dose of vasopressin (units)			
Postoperative			
POD 0	7.75±2.9	5.5±2.7	0.1

Values expressed as mean±SD. POD 0: Postoperative day 0

In a study conducted by William *et al.*, a large volume (50 ml/kg) of hypo-osmolar fluid (ringer lactate) and iso-osmolar (0.9% sodium chloride) fluid were given to human volunteers and their effect on serum osmolality was compared. The authors concluded that infusion of hypo-osmolar fluid ringer lactate causes transient decrease in serum osmolality which normalized after 1 h of stopping of the infusion.[6] However, the results of this study done in healthy volunteers cannot be extrapolated to patients with craniopharyngioma.

The difference in serum osmolality in between the two groups depends on the osmolarity of fluids infused in intra- and posto-perative period. The main determinant of serum osmolality is serum sodium that can be affected by sodium content of fluid which is 140 mEq/L and 77 mEq/L respectively in balanced salt solution and 0.45% sodium chloride solution respectively.[7]

In this study, the infusion of 0.45% sodium chloride solution in intraoperative and postoperative period in

Table 4: Complications and patient outcome

	Group P (*n*=15), *n* (%)	Group S (*n*=12) *n* (%)	*P*
Intraoperative DI, *n* (%)	2 (13.3)	0	0.48
Postoperative DI	15 (100)	12 (100)	
Duration of hospital stay (days)$^{\varphi}$	25 (15-31)	21 (14-31)	0.90
Discharge as chronic DI (*n*)	10 (66.6)	10 (83.3)	0.65
Death (*n*)	1 (6.66)	0	1

Values expressed as numbers. $^{\varphi}$Presented as median IQR. IQR: Interquartile range, DI: Diabetes insipidus

patients undergoing craniopharyngioma resection surgery was associated with lesser fluctuations of serum sodium and less episodes of hypernatremia whereas the use of balanced salt solution (plasmalyte A) is associated with higher sodium values in both intra- and post-operative period. Three patients (two adults and one child) who received 0.45% sodium chloride developed hyponatremia and required change of fluid to 0.9% sodium chloride during intraoperative period.

Pratheesh *et al*. compared 0.9% sodium chloride, 0.45% sodium chloride and 5% dextrose as perioperative fluids in patients undergoing craniopharyngioma surgery and observed higher fluctuations in serum sodium levels in patients receiving 0.9% sodium chloride.[8] Mukherjee *et al*. in their study in patients of craniopharyngioma, found serum sodium of 157.8 mEq/L in patients receiving 0.9% sodium chloride compared to 143.4 mEq/L in those receiving 0.45% sodium chloride in the intraoperative period.[5]

In our study, serum sodium levels were higher but comparable in both the groups in postoperative period as measured on POD 0, 1, and 2. We observed sodium levels from 145.6–146.6 mEq/L in patients receiving 0.45% sodium chloride as compared to 149.1–151 mEq/L in patients receiving balanced salt solution in the postoperative period. However, Mukherjee *et al*.[5] observed significantly higher serum sodium levels varying from 148.6 to 159.2 mEq/L in the 0.9% sodium chloride group as compared to 0.45% sodium chloride group varying from 138 to 139 mEq/L in the first 48 h postoperatively. They suggested that the findings may be due to difference in sodium content of the transfused fluids- 0.9% sodium chloride (154 mEq/L), 0.45% sodium chloride (77 mEq/L).

Lehrnbecher *et al*. demonstrated wide fluctuations in serum sodium levels in the intraoperative and postoperative period in patients who underwent resection of craniopharyngioma. The authors used sodium free fluid in patients having polyuria and high sodium containing fluid for patients who received desmopressin.[9] Wide fluctuation in serum sodium levels was not seen in our study as we used rescue measures to manage hyper and hyponatremia including vasopressin to treat DI as compared to this study.[9]

In our study, two patients belonging to balanced salt solution group had intraoperative DI, one adult and one pediatric. Lehrnbecher *et al*. reported no correlation between the extent of tumor resection and the incidence of DI in their study.[9] They explained that in addition to axonal damage by surgery, other factors including alterations in blood flow, metabolic activity and individual variations influence the extent of axonal degeneration which determine the occurrence of DI.[10] In our study, the tumor size in both the groups were comparable and near total excision was done in all the cases, thus the size of the tumor resected may not be the cause of intraoperative DI. However, Bucci *et al*. have observed direct correlation between the incidence of DI with the extent of tumor resection.[11]

Patients undergoing resection of craniopharyngioma classically present with triphasic pattern of DI-SIADH-DI in postoperative period. Classic triphasic pattern seen in craniopharyngioma is characterized by initial phase of DI lasting for 24 h after surgery followed by a second phase of inappropriate vasopressin leading to hyponatremia lasting for 2–14 days and third phase of DI.[12] We could not demonstrate SIADH or triphasic pattern in our study. This could be explained as DI was treated in our patients with vasopressin that induces temporary oliguria.[9] In our study, only 55% of patients who underwent resection of craniopharyngioma, developed DI in the immediate postoperative period. However, in study by Lehrnbecher *et al*., all patients developed DI in postoperative period in <18 h, the reason for which was not clear in their study.[9]

In our study population, only one patient died who belonged to group P. He died due to complication following intestinal perforation attributed to steroid replacement as the patient was hypocortisolic and was on continuous hydrocortisone replacement. Rest all of the patients in our study were discharged and among them, 66.6% in group P and 83.3% in group S were discharged with chronic DI.

Limitations

The number of patients included in our study was less as the study was time bound. Result could be validated better if we could have included more patients of craniopharyngiomas.

Conclusion

We conclude that 0.45% sodium chloride solution is preferred over balanced salt solution as serum osmolality and serum sodium were maintained better with 0.45% sodium chloride solution infused in perioperative period in patients undergoing transcranial excision of craniopharyngioma.

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Conflicts of interest

There are no conflicts of interest.

References

1. Crandell WB. Parenteral fluid therapy. Surg Clin North Am 1968;48:707-21.
2. Desborough JP, Hall GM. Endocrine response to surgery. In: Kaufman L, editor. Anaesthesia Review. Vol. 10. Edinburgh: Churchill Livingstone; 1993. p. 131-48.
3. Hutchin P, Terzi RG, Hollandsworth LC, Johnson G Jr, Peters RM. The influence of intravenous fluid administration on postoperative urinary water and electrolyte excretion in thoracic surgical patients. Ann Surg 1969;170:813-23.
4. Tommasino C. Fluids and the neurosurgical patient. Anesthesiol Clin North Am 2002;20:329-46, vi.
5. Mukherjee KK, Dutta P, Singh A, Gupta P, Srinivasan A, Bhagat H, *et al*. Choice of fluid therapy in patients of craniopharyngioma in the perioperative period: A hospital-based preliminary study. Surg Neurol Int 2014;5:105.
6. Williams EL, Hildebrand KL, McCormick SA, Bedel MJ. The effect of intravenous lactated Ringer's solution versus 0.9% sodium chloride solution on serum osmolality in human volunteers. Anesth Analg. 1999;88:999-1003.
7. Duggal AK, Yadav P, Agarwal AK, Rewari BB. Clinical approach to altered serum sodium levels. J Indian Acad Clin Med 2006;7:91-103.
8. Pratheesh R, Swallow DM, Joseph M, Natesan D, Rajaratnam S, Jacob KS, *et al*. Evaluation of a protocol-based treatment strategy for postoperative diabetes insipidus in craniopharyngioma. Neurol India 2015;63:712-7.
9. Lehrnbecher T, Müller-Scholden J, Danhauser-Leistner I, Sörensen N, von Stockhausen HB. Perioperative fluid and electrolyte management in children undergoing surgery for craniopharyngioma. A 10-year experience in a single institution. Childs Nerv Syst 1998;14:276-9.
10. Verbalis JG, Robinson AG, Moses AM. Postoperative and post traumatic diabetes insipidus. Front Horm Res 1985;13:247-65.
11. Bucci MN, Chin LS, Hoff JT. Perioperative morbidity associated with operative resection of craniopharyngioma: A review of ten years experience. Neurochirurgia (Stuttg) 1987;30:135-8.
12. Ghirardello S, Hopper N, Albanese A, Maghnie M. Diabetes insipidus in craniopharyngioma: postoperative management of water and electrolyte disorders. J Pediatr Endocrinol Metab. 2006;19:413-21.