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Research Paper

Changes in Serum Analytics and Biochemical Urinary Parameters Following Brain Tumor Operation

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ABSTRACT

Background: Changes in the body fluid and serum electrolyte status following major operations, such as brain tumor resection, are always expected. These changes can increase post-operation morbidity and mortality.

Objectives: We aimed to evaluate the changes in serum electrolyte levels and renal function parameters in brain tumor patients after operation.

Materials & Methods: This cross-sectional study was performed on 168 patients with supratentorial tumors in Poursina Hospital, Rasht City, Iran, in 2020. The study parameters included patients' demographics, hemodynamic stability, serum sodium, potassium, blood urea nitrogen (BUN) and creatinine levels, urine specific gravity, and urinary output, measured immediately and 12 hours after the operation.

Results: This study revealed statistically significant increases in serum sodium level (from 139.70±5.60 meq/L to 140.34±6.23 meq/L, P=0.002), urinary output (from 1043.70±455.00 mL to 1967.50±661.10 mL, P=0.008), urine specific gravity (from 1.010±0.007 to 1.012±0.008, P=0.011), and in serum BUN level (from 17.46±6.92 to 18.41±6.40, P=0.001), but significant decrease in serum potassium level (from 3.88±0.49 meq/L to 3.78±0.28 meq/L, P=0.017) during the first 12 hours after operation. However, the change in serum creatinine level was not significant (from 1.18±2.08 mg/dL to 1.17±2.08 mg/dL, P=0.787).

Conclusion: Significant changes in serum electrolytes (sodium and potassium) and renal function indicators (urine output, specific gravity, and serum BUN) are expected within the first 12 hours after brain tumor operation.

Keywords: Brain neoplasms, Operation, Electrolytes, Inappropriate ADH syndrome, Diabetes insipidus

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Highlights

- There was an increase in serum sodium level after brain tumor operation, more correlated with male gender, older age, and the two tumor types of oligodendroglioma and glioblastoma.

- The drop in serum potassium level was observed mainly in patients with higher amounts of mannitol consumption.

- An increase was found in urine output and urine specific gravity following brain tumor operation.

Introduction

Currently, non-communicable diseases are considered the leading cause of death in the world [1]. Malignancies are the most prominent cause of death among non-communicable diseases, accounting for about 6.9 million deaths in 2018 [2]. Particularly, 1.6% of all new cancer cases and 2.5% of cancer-related mortalities are related to nervous system tumors [3]. The incidence of central nervous system tumors has risen by 40% in the past 20 years, particularly in adults [4]. Compared to the most common malignancies, such as lung, breast, and prostate tumors, the rate of brain tumors is low. However, many of these tumors exhibit an aggressive clinical course due to direct brain tissue involvement, leading to a poor prognosis and short survival. Since there is no definitive treatment for patients suffering from such brain tumors, palliative therapy aiming to improve the patient's life span and alleviate the patient's symptoms becomes a priority [5]. The treatment plan for most brain tumor patients comprises surgical resection, followed by neo-adjuvant chemo/radiotherapy, if indicated [6], leading to some adverse complications like hemodynamic instability and neurotoxicity, impairing their quality of life [7].

Serum sodium level contributes to various biochemical pathways of the nervous system. Previous studies indicate that hyponatremia can have disruptive effects on the nervous system even in the absence of cerebral edema [8]. Furthermore, one of the disorders noticed by numerous researchers after brain tumor operation is water and electrolyte disturbances, mainly hyponatremia. This condition can be seen in patients with brain tumors due to the damage of antidiuretic hormone (ADH) releasing neurons, called the syndrome of inappropriate antidiuretic hormone secretion (SIADH) [9]. Cerebral salt-wasting syndrome (CSWS) is another hyponatremia-causing condition in these patients. Although the exact mechanism of CSWS in these patients is unknown, releasing natriuretic peptides from damaged brain tissue may cause hyponatremia by affecting the kidneys [10]. Another phenomenon in these patients is suppressing the sympathetic nervous system, which can result in hyponatremia by impacting the kidneys [11].

Moreover, in patients with co-existing brain tumors and brain edema, releasing a variety of chemical mediators such as glutamate, histamine, arachidonic acid, free radicals, or free fatty acids causes brain edema, leading to nerve cell damage. Usual treatments of cerebral edema (e.g. hyperosmolar drugs (such as mannitol), hyperventilation, corticosteroid injection, and diuretics) can cause water and electrolyte imbalance, including hyponatremia [12]. However, the early and timely diagnosis of water and electrolyte disorders, especially sodium imbalance, can prevent unwanted complications [13]. Because a few studies have been done in this regard, we intended to assess the changes in serum levels of electrolytes and urinary parameters in patients with brain tumors during the first 12 hours after operation.

Materials and Methods

This cross-sectional study was performed on 168 patients with supratentorial brain tumors who underwent brain operation in Poursina Hospital, Rasht City, Iran, in 2020. Patients were selected via convenience sampling. Those with a history of renal dysfunction (including renal failure and dialysis), who expired during or immediately after the operation, and patients with craniopharyngioma, pituitary adenoma, or periventricular tumors (due to the direct effect on water and electrolyte status) were excluded from the study. The study parameters included the patient's demographic and hemodynamic parameters (blood pressure and pulse rate), serum sodium, potassium, blood urea nitrogen (BUN), creatinine levels, urine specific gravity, and urine output. The parameters were measured immediately and 12 hours after operation. All laboratory parameters were analyzed in Poursina Hospital's Laboratory. Also, the patients were examined immediately and 12 hours after the operation regarding the medications used, including IV serums (type, dosage, and duration of administration). Besides mannitol, normal saline (10 mL/kg/h) was also administered to all patients.

We analyzed the data using SPSS software, version 26. The quantitative variables are displayed as Mean±SD and the qualitative variables as frequency (percentage). We used the Kolmogorov-Smirnov test to check the assumptions of normality. Using the Wilcoxon test, the statistical differences between the study variables were compared immediately and 12 hours after operation. Using the Kruskal-Wallis test, the statistical differences between the investigated variables at different time points after the operation were analyzed according to age, operation duration, and tumor type. We also examined the differences in study parameters between the genders using the Mann-Whitney U test. P<0.05 were considered statistically significant.

Results

The baseline characteristics of the study population are presented in Table 1. The Mean±SD age of the patients was 46.81±15.45 years, ranging from 9 to 80 years, with slender female predominance (54.8% over 45.2%). The Mean±SD operation duration was 323.99±67.91 minutes, ranging from 80 to 540 minutes. The Mean±SD mannitol usage was 347.56±63.63 mL, ranging from 100 to 500 mL. The most prevalent tumors were oligodendroglioma (32.1%), glioblastoma (25.0%), and meningioma (22.0%).

Table 1. Patient characteristics and laboratory parameters

Variables		No.(%)
Gender	Male	76(45.2)
	Female	92(54.8)
Tumor type	Glioblastoma	61(36.3)
	Meningioma	37(22)
	Oligodendroglioma	54(32.1)
	Astrocytoma	16(9.5)
	Total	168(100)

Variables	Mean±SD (Min-Max)
Age (y)	46.81±15.45 (9-80)
Operation duration (m)	323.99±67.91 (80-540)
Mannitol usage (mL)	347.56±63.63 (100-500)

Variables	Mean±SD		P
	Immediately After Operation	12 h After Operation	
Serum sodium (mg/dL)	139.70±5.60	140.34±6.23	0.002
Serum potassium (mg/dL)	3.88±0.49	3.78±0.28	0.017
BUN (mg/dL)	17.46±6.92	18.41±6.40	0.0001
Urine output (mL)	1043.7±455.0	1967.5±661.1	0.0001
Urine specific gravity	1.010±0.007	1.012±0.008	0.011
Creatinine (mg/dL)	1.18±2.08	1.17±2.08	0.787

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Table 2. Age-adjusted serum analytics

Variables*		Immediately After Operation	12 h After Operation	P
Serum sodium (mg/dL)	<40	141.40±6.17	141.87±7.38	0.281
	40-60	136.80±4.14	137.50±4.48	0.013
	>60	142.40±4.52	143.19±4.76	0.06
Serum potassium (mg/dL)	<40	3.95±0.36	3.74±0.29	0.0001
	40-60	3.81±0.40	3.84±0.22	0.82
	>60	3.87±0.77	3.72±0.33	0.48
BUN (mg/dL)	<40	16.69±5.78	18.24±5.43	0.0001
	40-60	16.86±6.99	17.81±6.59	0.33
	>60	19.95±8.12	19.86±7.45	0.534
Urine output (mL)	<40	1135.4±485	2214.5±663	0.0001
	40-60	966.4±354	1790±642	0.0001
	>60	1036.1±550	1887.5±574	0.0001
Urine specific gravity	<40	1.010±0.006	1.012±0.007	0.038
	40-60	1.010±0.007	1.012±0.008	0.13
	>60	1.010±0.007	1.010±0.009	0.384
Creatinine (mg/dL)	<40	1.25±2.42	1.19±2.43	0.004
	40-60	0.94±0.26	0.95±0.20	0.77
	>60	1.51±3.18	1.58±3.17	0.023

*Classified by age groups (y).

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Regarding the laboratory parameters during the first 12 hours post-operation, the Mean±SD serum sodium levels were 139.70±5.60 meq/L and 140.34±6.23 meq/L (P=0.002), respectively; the Mean±SD serum potassium levels were 3.88±0.49 meq/L and 3.78±0.28 meq/L, (P=0.017), respectively, and the mean serum BUN values were 17.46±6.92 and 18.41±6.40 mg/dL (P=0.001), respectively. There was a significant increase in urinary output from 1043.70±455.00 mL to 1967.50±661.10 mL (P=0.008) and urine specific gravity from 1.010±0.007 to 1.012±0.008 (P=0.011). At the same time, the serum creatinine level changes remained insignificant (1.18±2.08 mg/dL versus 1.17±2.08 mg/dL, P=0.787).

Table 2 presents age-adjusted serum analytics changes; an increase in serum sodium level was evident in ages over 40, while the decrease in serum potassium level occurred in patients younger than 40. Additionally, serum BUN level alteration was significant in those under 60; however, serum creatinine levels remained unaffected between the ages of 40 and 60. The observed change in urine output was independent of the patient's age.

According to Table 3, the change in serum sodium and creatinine levels is associated with the male gender. In contrast, the difference in serum potassium levels correlates more with the female gender. Urinary output and serum BUN levels change occurred equally in both genders.

Table 4 presents that the duration of operation was also directly associated with the changes in serum potassium and BUN levels; the difference in serum sodium level was significant in a 180 to 360 min operation period, though the changes in serum creatinine happened independently from the operation duration.

Table 3. Gender-adjusted serum analytics

Variables*		Immediately After Operation	12 h After Operation	P
Serum Sodium (mg/dL)	Male	137.40±3.64	138.07±5.15	0.01
	Female	141.70±5.55	142.20±6.47	0.073
Serum Potassium (mg/dL)	Male	3.90±0.54	3.83±0.34	0.332
	Female	3.86±0.45	2.73±0.20	0.016
BUN (mg/dL)	Male	19.7±6.64	20.75±6.13	0.003
	Female	15.6±6.62	16.48±5.98	0.001
Urine output (mL)	Male	1008.5±452	1919.7±698	0.0001
	Female	1072.8±457	2007±630	0.0001
Urine specific gravity	Male	1.010±0.007	1.012±0.009	0.153
	Female	1.010±0.007	1.012±0.008	0.034
Creatinine (mg/dL)	Male	0.97±0.25	0.93±0.20	0.05
	Female	1.35±2.80	1.37±2.80	0.091

*Classified by gender.

CJNS

Table 4. Serum analytics adjusted by operation duration

Variables*		Immediately After Operation	12 h After Operation	P
Serum sodium (mg/dL)	<180	137.1±3.38	138.4±3.82	0.273
	180–360	139.2±5.17	139.8±5.8	0.002
	>360	142.4±6.89	143.06±7.77	0.53
Serum potassium (mg/dL)	<180	3.87±0.22	3.75±0.17	0.394
	180–360	3.87±0.53	3.78±0.20	0.109
	>360	3.93±0.34	3.76±0.49	0.049
BUN (mg/dL)	<180	17.28±5.93	16.85±6.17	0.45
	180–360	17.42±7.05	18.23±6.03	0.0001
	>360	17.66±6.77	19.56±7.92	0.044
Urine output (mL)	<180	985.7±259	995.4±340	0.028
	180–360	995.4±340	1926.7±569	0.0001
	>360	1268.3±772	2238.3±923	0.0001
Urine specific gravity	<180	1.000±0.006	1.002±0.009	0.042
	180–360	1.001±0.007	1.001±0.008	0.156
	>360	1.000±0.006	1.001±0.009	0.084
Creatinine (mg/dL)	<180	0.914±0.15	0.914±0.17	0.73
	180–360	1.1±1.68	1.09±1.68	0.736
	>360	1.58±3.48	1.6±3.48	0.731

*Classified by operation duration (min).

CJNS

Table 5. Serum analytics adjusted by mannitol dosage

Variables*		Immediately After Operation	12 h After Operation	P
Serum sodium (mg/dL)	<300	140.8±5.9	141.37±6.70	0.56
	300–450	139.1±5.50	139.81±5.80	0.0001
	>450	139.83±1.40	140.33±6.90	0.513
Serum potassium (mg/dL)	<300	3.87±0.58	3.76±0.29	0.25
	300–450	3.85±0.43	3.78±0.17	0.188
	>450	4.16±0.50	3.83±7.1	0.036
BUN (mg/dL)	<300	18.51±7.88	18.32±7.48	0.468
	300–450	16.72±6.19	17.97±5.49	0.0001
	>450	19.16±8.06	22.58±7.52	0.005
Urine output (mL)	<300	1015.1±415	1871.6±675	0.0001
	300–450	1035.9±417	1947.5±622	0.0001
	>450	1237.5±818	2562.5±684	0.003
Urine specific gravity	<300	1.010±0.005	1.010±0.009	0.0001
	300 – 450	1.011±0.007	1.011±0.007	0.998
	>450	1.010±0.007	1.010±0.010	0.944
Creatinine (mg/dL)	<300	1.70±3.67	1.66±3.67	0.153
	300–450	0.93±0.20	0.94±0.20	0.646
	>450	0.98±0.32	1.06±0.29	0.437

*Classified by mannitol dosage (mL).

CJNS

As indicated in Table 5, the changes in serum BUN and potassium analytics were linked to high-dose mannitol intake, and serum sodium level alteration was found in patients with a 300 to 450 mL dose of mannitol. The change in serum creatinine level was independent of the mannitol dosage.

Furthermore, the tumor type significantly affected the post-operative changes in laboratory indices (Table 6). For example, oligodendroglioma and glioblastoma tumors showed significant changes in serum sodium and BUN levels; conversely, no significant changes were detected in serum potassium and creatinine levels regarding tumor type.

Discussion

Alterations in fluid and electrolytes soon after major operations such as craniotomy for brain tumors are expected owing to various causes, like diabetes insipidus, cerebral salt-wasting syndrome, and improper secretion of antidiuretic hormone. These changes mainly occur within the normal range and, if not so, are eventually reversible. Therefore, additional treatment may not be needed. On the other hand, in some cases, the extreme changes require precise management to reestablish the patient's normal hemodynamic condition.

In this study, we observed an increase in serum sodium level within hours after brain tumor operation, correlated with male gender, older age, and the tumor types: Oligodendroglioma and glioblastoma. Although several studies have indicated the occurrence of acute hyponatremia following brain injury or tumor operation, this study revealed an acute post-operative increase regarding this serum element. The results of the Kiran et al. (2017) study indicated isolated hyponatremia in 11% and concurrent with diabetes insipidus in 9.2% of the sellar/suprasellar

Caspian Journal of Neurological Sciences

Table 6. Serum analytics adjusted by tumor type

Variables*		Immediately After Operation	12 h After Operation	P
Serum sodium (mg/dL)	Glioblastoma	140.8±5.69	140.5±6.18	0.647
	Meningioma	141.2±5.38	140.5±6.49	0.279
	Oligodendroglioma	141.1±5.76	142.6±6.45	0.0001
	Astrocytoma	138.2±4.56	138.5±4.22	0.819
Serum potassium (mg/dL)	Glioblastoma	3.93±0.5	3.79±0.29	0.176
	Meningioma	3.91±0.65	3.73±0.31	0.167
	Oligodendroglioma	3.85±0.47	3.82±0.27	0.879
	Astrocytoma	3.95±0.41	3.87±0.28	0.298
BUN (mg/dL)	Glioblastoma	18.15±5.93	18.68±5.74	0.565
	Meningioma	18.81±7.85	19.05±8.25	0.664
	Oligodendroglioma	19.72±7.3	20.53±6.14	0.008
	Astrocytoma	14.68±4.96	16.18±5.49	0.188
Urine output (mL)	Glioblastoma	856.6±334	2157.8±849	0.0001
	Meningioma	1117.5±570	2010.8±632	0.0001
	Oligodendroglioma	1025±286	2004.6±449	0.0001
	Astrocytoma	978.1±537	1653.1±861	0.001
Urine specific gravity	Glioblastoma	1.010±0.006	1.010±0.009	0.065
	Meningioma	1.010±0.005	1.010±0.007	0.861
	Oligodendroglioma	1.010±0.007	1.010±0.008	0.832
	Astrocytoma	1.000±0.009	1.010±0.009	0.046
Creatinine (mg/dL)	Glioblastoma	1.94±4.38	1.93±4.37	0.891
	Meningioma	1.51±3.13	1.49±3.14	0.73
	Oligodendroglioma	0.95±0.22	0.91±0.2	0.065
	Astrocytoma	0.88±0.12	0.9±0.1	0.571

*Classified by tumor type.

CJNS

brain tumor patients undergone craniotomy [14]. Likewise, Kristof et al. (2009) prospectively studied the incidence, clinical manifestations, duration, and risk factors of water and electrolytes disorder following pituitary adenoma endoscopic operation; 21% of patients showed hyponatremia with 15.7% having coexistent diabetes insipidus [15]. Also, Belzer et al. (2014) investigated the duration and severity of hyponatremia after brain tumor operation in children in the United States. About 43% of patients experienced mild hyponatremia (ranging from 131 to 135 meq/L), 12% a more severe hyponatremia (serum sodium level of 130 or less meq/L), and 45% had normal sodium levels [16]. It can be concluded that hyponatremia is a highly probable complication following brain tumor operation, particularly in elderly male patients. However, other studies demonstrated hypernatremia after brain tumor operation, mainly due to salt excess from subsequent use of saline solutions and mannitol. The increased serum sodium level represents whole-body sodium accumulation and demands targeted hypernatremia treatment to achieve better post-operative outcomes and avoid hypernatremia-related complications such as focal intracerebral and subarachnoid hemorrhages and possibly irreversible neurologic damage.

Moreover, in line with the outcome of our study, Lili You et al. (2017), who investigated the prevalence of hypokalemia after operation for pituitary adenoma tumors, found that only in cases of ACTH-pituitary adenoma, the serum potassium level decrease was significant [17]. Since the drop in serum potassium level was observed mainly in patients with higher amounts of mannitol consumption, the leading cause of observed hypokalemia can be attributed to high doses of mannitol use. Similarly, in the Seo et al. study, the most notable finding was the high occurrence of hypokalemia observed during mannitol administration. Hypokalemia was observed in 22.0% of cases on the first day and constantly increased to 52.3% [18]. It should be noted that even slight changes in the serum potassium level can be associated with severe consequences owing to its narrow normal range, such as cardiac arrhythmias or severe muscle weakness resulting in respiratory failure and even death, which brings the essential need for vigilant monitoring of the element when coming upon major operations.

Besides, the present study revealed an increase in urinary output and urine specific gravity following brain tumor operation, both associated with diabetes insipidus caused by either the tumor or the operation [19]. Although a decrease in urinary output and urine specific gravity is expected immediately after a brain tumor resection, compensatory mechanisms gradually increase both indicators within a few hours post-operation.

Following brain tumor operation, no noticeable changes in serum creatinine levels were observed in this study; however, it should be evoked that kidney function changes following major operations may follow a more gradual course compared to electrolytes. Therefore, long-term follow-up is necessary to accurately trace such changes, specifically in patients with accompanying metastatic kidney disease.

Certain limitations of our study should be acknowledged. Firstly, only 168 patients with supratentorial brain tumors were included in our study. This moderate sample size restricts precise assessment of the effects of clinical characteristics of supratentorial tumors on serum hemodynamics. Secondly, our analysis was performed in Poursina Hospital, which mainly provides services for patients from northern Iran. It may further bring up a heterogenicity concerning the rest of the population in other regions. Further studies are needed to validate our findings, including a larger sample of more ethnically varied patients with supratentorial brain tumors. Also, we recommend further research to be done in the assessment of associations between brain tumor location with serum electrolyte profiles and the prognosis of patients who have undergone supratentorial operation and experienced post-operative electrolyte imbalance.

Conclusion

Based on the findings of our study, the changes in serum electrolytes and urinary laboratory parameters following brain tumor operation are predictable. In this regard, hypernatremia, hypokalemia, increase in urine volume, and specific gravity can be expected during the first 12 hours after the operation. Consequently, monitoring and managing a patient's hemodynamics to track such changes during the very first hours after the operation will be crucial.

Ethical Considerations

Compliance with ethical guidelines

The study was approved by the Ethics Committee at Guilan University of Medical Sciences (Code: IR.GUMS.REC.1399.361). The study process was in compliance with the ethical guidelines of the Declaration of Helsinki 2013.

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Authors contributions

Conceptualization, methodology, supervision, and project administration: Zoheir Reyhanian and Ali Ashraf; Data acquiation: Malihe Mashategan and Zahra Pourhabibi; Validation and revision: Nooshin Zaresharifi; Writing, preparation, review, and editing: Behrad Eftekhari.

Conflict of interest

The authors declared no conflict of interest.

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