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Early Postoperative Serum Sodium Level and Urine Output Volume Profile after Endoscopic Endonasal Transsphenoidal Surgery in Macroadenoma Pituitary Tumor

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ABSTRACT

Introduction: Surgery is still the initial treatment of choice to for the majority of date with pituitary tumors. One of the most commonly performed minimally invasive neurosurgical procedures is transsphenoidal endoscopic endonasal surgery (ETS) and microscopic transsphenoidal surgery (MTS), used commonly for the resection of pituitary tumours. Neurosurgical operations for pituitary and suprasellar tumours may result in postoperative complications due to the crucial anatomical location of these tumours. The resulting postoperative complications can manifest as anterior or posterior pituitary dysfunction, particularly sodium disturbances, due to the changes in antidiuretic hormone (ADH) secretion, which remains one of the most frequent postoperative reasons for hospital readmission.
Method: The aim of this study to describe and determine the frequency distribution of patient characteristics who underwent endoscopic endonasal transsphenoidal resection of pituitary adenoma at Universitas Sumatera Utara Hospital between 2021 and 2022.
Result: The findings of this study showed the frequency distribution of patient characteristics who underwentendoscopic endonasal transsphenoidal resection and postoperative sodium serum level profile as well as postoperative urine output profile.
Discussion: The discussion section briefly discusses the findings and their implications. It mentions the high prevalence of headache and visual deficits among the patients, which aligns with previous studies. It also provides an overview of normal water balance and the pathophysiology of water balance disorders after pituitary surgery.
Keywords: Surgery, MTS, ADH

1. Introduction

Surgery is still the initial treatment of choice to date for the majority of patients with pituitary tumors [1,2]. One of the most commonly performed minimally invasive neurosurgical procedures is transsphenoidal endoscopic endonasal surgery (ETS) and microscopic transsphenoidal surgery (MTS), used commonly for the resection of pituitary tumours.

Neurosurgical operations for pituitary and suprasellar tumours may result in postoperative complications due to the crucial anatomical location of these tumours. The resulting postoperative complications can manifest as anterior or posterior pituitary dysfunction, particularly sodium disturbances, due to the changes in antidiuretic hormone (ADH) secretion, which remains one of themost frequent postoperative reasons for hospital readmission [3].

The patterns of water and electrolyte disorders after ETS can be divided into either polyuria or oliguria/hyponatremia, depending on the presence of either low or high levels of ADH, respectively [3].

Some disturbances of water and electrolytes may not reach the level of clinically definedcentral diabetes insipidus (CDI) or syndrome of inappropriate antidiuretic hormone (SIADH). However, they may still require acute or chronic management and are generally divided into six profiles of polyuria or hyponatremia as follows: transient or sustained polyuria, immediate or delayed hyponatremia and biphasic or triphasic diabetes insipidus (DI) [3,4].

2. Method

Patient Selection

We retrospectively reviewed the medical records of 11 patients who undergo transsphenoidal surgery at Sumatera Utara University Hospital. Pituitary tumor is treated at our university medical center via endoscopic transsphenoidal surgery between 2021 and 2022. The inclusion criteria forthis study were participants who had evidence of macroadenoma pituitary tumor based on preoperative brain magnetic resonance imaging (MRI) and postoperative histopathology, as well as a clinical diagnosis of a pituitary tumor. Additionally, participants needed to have a normal level of sodium in their blood, which is also known as normonatremia. Serum sodium was examined preoperatively one day before surgery and were drawn postoperatively on the first postoperative day before discharge. Urine output were examined postoperatively in day 1, day 3, day 5, and day 7. Polyuria and particularly sodium disturbance due to changes in antidiuretic hormone (ADH) secretion may indicate posterior pituitary dysfunction. MRI were performed either in an outpatient setting or inpatient prior to surgery. Tumor sizewas measured on the preoperative MRI and then classifed as macroadenoma (≥10 mm). Histopathology examination after surgery to help diagnose macroadenoma tumor.

All patients underwent endoscopic endonasal transsphenoidal resection of pituitary macroadenoma. The objective of surgery was maximum decompression of the optic apparatus— with maximum care taken not to injure sensitive neural and vascular structures, and to preserve or restore endocrine function.

Method of Data Processing, Analysis, and Measurement

Data will be analyzed descriptively to determine the frequency distribution of patient characteristics whose results will be displayed as a percentage.

Ethics statement

This research will be undertaken after gaining ethical clearance from the Research EthicCommittee of the Sumatera Utara University Hospital.

3. Results

Patient Demographic

This table shows the characteristics of a group of people who are experiencing certain symptoms, categorized by age group, sex, and type of symptoms. Each category has a number of respondents (n) and a percentage of the total number of respondents in that group (%). In the age group category, the majority of the respondents are in the 31-60 years age group, with a percentage of 27.2% for each age category. Only one respondent (9.09%) is in the 21 – 30 years age or over 70 years old. In the sex category, the majority of the respondents are male with a percentage of 63.6%, while female respondents are only 36.3%. In the symptom category, the majority of the respondents reported experiencing headaches (63.6%), followed by visual deficits (54.5%), and other symptoms (percentage not given).

Table 1. Characteristics of Patients

Characteristic	n (%)
Age Group	
0 - 10 year	0 (0.00%)
11 - 20 year	0 (0.00%)
21 - 30 year	1 (9.09%)
31 - 40 year	3 (27.2%)
41 - 50 year	3 (27.2%)
51 - 60 year	3 (27.2%)
61 - 70 year	0 (0.00%)
71 - 80 year	1 (9.09%)
Sex	
Male	7 (63.6%)
Female	4 (36.3%)
Symptoms	
Visual Deficit	6 (54.5%)
Headache	7 (63.6%)
Others	

Postoperative Sodium Serum Level Profile

The table contains the characteristics of patients who have undergone surgery and their postoperative sodium profile results. There were a total of 11 patients involved in this study, with 72.7% (8 patients) showing a normal sodium profile, 9.09% (1 patient) experiencing hyponatremia (low sodium levels), and 18.1% (2 patients) experiencing hypernatremia (high sodium levels)postoperatively.

The table also shows patient characteristics based on age group, gender, adenoma size, and symptoms experienced. It can be seen that there were no patients in 21 – 30 age group and no male patients who experienced hyponatremia. Additionally, all patients with macroadenomas (size >10mm) had either a normal sodium profile or hypernatremia postoperatively. The most common symptoms experienced by patients were headaches and visual deficits.

Table 2. Postoperative Sodium Serum Level Profile

	Postop Sodium Serum Profile		
Characteristic	**Normonatremic (%)**	**Hyponatremic (%)**	**Hypernatremic (%)**
Number of patients (total 11)	8 (72.7%)	1 (9.09%)	2 (18.1%)
Age Group			
0 - 10 year	-	-	-
11 - 20 year	-	-	-
21 - 30 year	1 (9.09%)	-	-
31 - 40 year	2 (18.1%)	-	1 (9.09%)
41 - 50 year	2 (18.1%)	1 (9.09%)	-
51 - 60 year	2 (18.1%)	-	1 (9.09%)
61 - 70 year	-	-	-
71 - 80 year	1 (9.09%)	-	-

Sex			
Male	2 (18.1%)	-	2 (18.1%)
Female	6 (54.5%)	1 (9.09%)	-
Symptoms			
Visual Deficit	5 (45,4%)	1 (9.09%)	1 (9.09%)
Headache	6 (54.5%)	-	1 (9.09%)
Others	-	-	-

Postoperative Urine Output Profile

This table presents data on postoperative urine profiles of patients and their characteristics. The study included 11 patients, with 45.5% (5 patients) having a normal urine profile and 54.5% (6 patients) experiencing polyuria.

The table also shows patient characteristics by age group, sex, adenoma size, and symptoms. Only one patient (9.09%) in the 21-30 age group was included in the study, and no patients in this group experienced polyuria. All patients with macroadenoma (tumor size > 10mm) had a normal urine profile or experienced polyuria postoperatively. The most common symptoms experienced by patients were visual deficit and headache.

In terms of sex, there were more female patients (36.4%) who experienced polyuria compared to male patients (18.2%). Overall, the majority of patients experienced polyuria postoperatively.

Table 3. Postoperative Urine Output Profile

Characteristic	**Postop Urine Profile**	
	Normal (%)	**Polyuria (%)**
Number of patients (total 11)	5 (45.5%)	6 (54.5%)
Age Group		
0 - 10 year	-	-
11 - 20 year	-	-
21 - 30 year	1 (9.09%)	-
31 - 40 year	2 (18.1%)	1 (9.09%)
41 - 50 year	1 (9.09%)	2 (18.1%)
51 - 60 year	-	3 (27.3%)
61 - 70 year	-	-
71 - 80 year	1 (9.09%)	-
Sex		
Male	2 (18.2%)	2 (18.2%)
Female	3 (27.3%)	4 (36.4%)
Symptoms		
Visual Deficit	3 (27.3%)	1 (9.09%)
Headache	2 (18.1%)	5 (45.4%)
Others	-	-

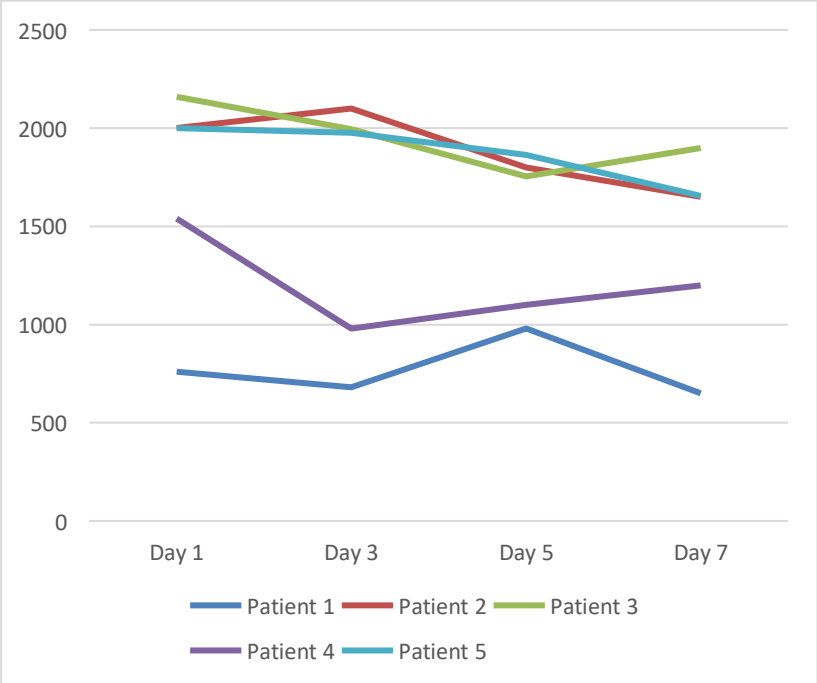

Figure 1. Postoperative urine output profile in patients with normal volume in cc.

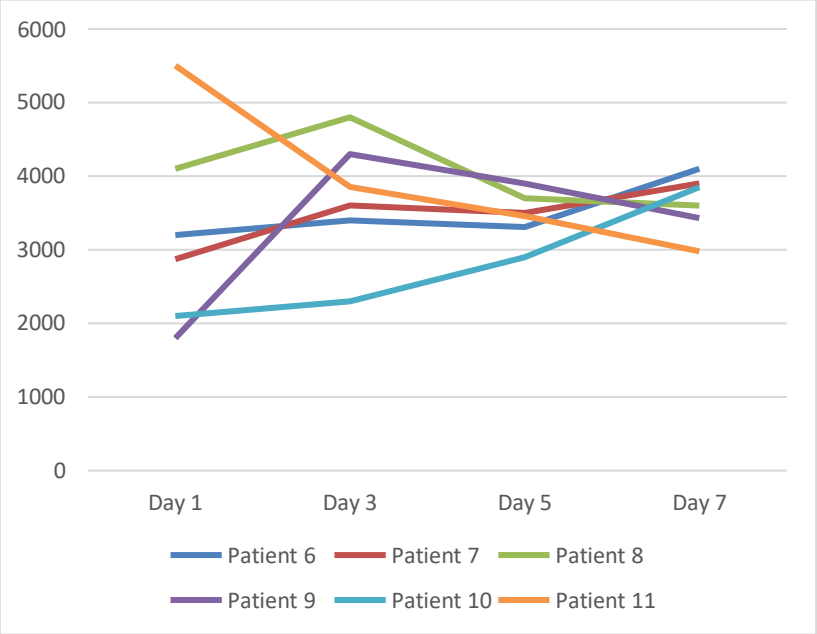

Figure 2. Postoperative urine output profile in patients with polyuria in cc.

4. Discussion

The findings of this study provides information on the characteristics of the participants in the study. The age range of the participants was from 0-80 years old, with the majority of participants within the 31-60 year age group. The majority of participants were male (63.6%), and the most common reported symptoms were headache (63.6%) and visual deficit (54.5%). Based on this information, it is possible to draw some initial observations and hypotheses about the study population and its potential implications. For example, the high proportion of participants reporting visual deficits suggests that this may be a significant health concern in this population. Additionally,the fact that the majority of participants were male may indicate a gender imbalance in health outcomes in this population.

The study conducted by Roka et al showed that headache and visual field defects were the most common clinical symptoms of pituitary adenomas. The study by Tagoe et al further supports these findings, as it revealed that over 33% of patients experienced visual impairment or blindness before and after surgery, and blindness was associated with delayed diagnosis and larger tumor size. However, the study also demonstrated that transphenoidal surgery can be beneficial for patients if the diagnosis is made quickly to prevent irreversible visual impairment or blindness.

Overview of Normal Water Balance

Water homeostasis is predominantly controlled by arginine vasopressin (AVP) [7]. AVP is a 9 amino acid peptide derived from pro-AVP, a 164 amino acid precursor protein consisting of a signal peptide, the AVP moiety, neurophysin 2, and copeptin, a 39 amino acid glycopeptide ([8]. Pro-AVP is synthesized in the paraventricular and supraoptic nuclei of magnocellular neurons in the hypothalamus [7]. Posttranslational processing separates AVP, copeptin, and neurophysin 2 during transport down the infundibulum to axon terminals in the posterior pituitary, where AVP is stored in neurosecretory granules until specific osmotic and nonosmotic stimuli cause secretion into the circulation [7,8].

AVP also has a key role in regulation of the hypothalamic–pituitary–adrenal axis stress response [8,9]. A second neurosecretory pathway transports high concentrations of AVP from parvocellular neurons to the pituitary hypophyseal portal system, where it has a neuroregulatory role in adrenocorticotropic hormone release from the anterior pituitary [8]. In turn, AVP is suppressed by glucocorticoids [10], which increase the osmotic threshold for AVP release [11], while glucocorticoid deficiency increases AVP synthesis and secretion [12].

Pathophysiology of Water Balance Disorders After Pituitary Surgery

Water balance disorders following pituitary surgery are well recognized [1,13]. AVP-D or SIAD can occur in isolation, with incidences up to 45% [14-17) and 28% [1,14,18-23], respectively. Less commonly, a biphasic phenomenon, where an initial polyuric phase is followed by an antidiuretic phase, or a triphasic phenomenon, where a second final polyuric phase follows hyponatremia, can occur, with reported incidences of 1.1% and 3.4% [1].

In the immediate postoperative period (within 24 to 48 hours), AVP-D may develop due to partial or complete pituitary stalk section, which severs the connections between the AVP neuronal bodies in the hypothalamic magnocellular neurons and the nerve terminals in the posterior pituitary, preventing stimulated AVP secretion [1,24] Delayed SIAD can follow early AVP-D or occur in isolation, secondary to uncontrolled release of stored AVP by degenerating nerve terminals in the posterior pituitary [25]

SIAD may or may not be followed by further AVP-D, which can recur after stored AVP in the posterior pituitary has been released if greater than 80% to 90% of AVP neuronal bodies in the hypothalamus have undergone retrograde degeneration. Isolated SIAD occurs following partial pituitary stalk injury, where sufficient nerve fibers connecting the AVP neuronal cell bodies in the hypothalamus to the posterior pituitary nerve terminals are left intact to prevent AVP-D, butdegeneration of injured nerve terminals still results in uncontrolled AVP release [1,25].

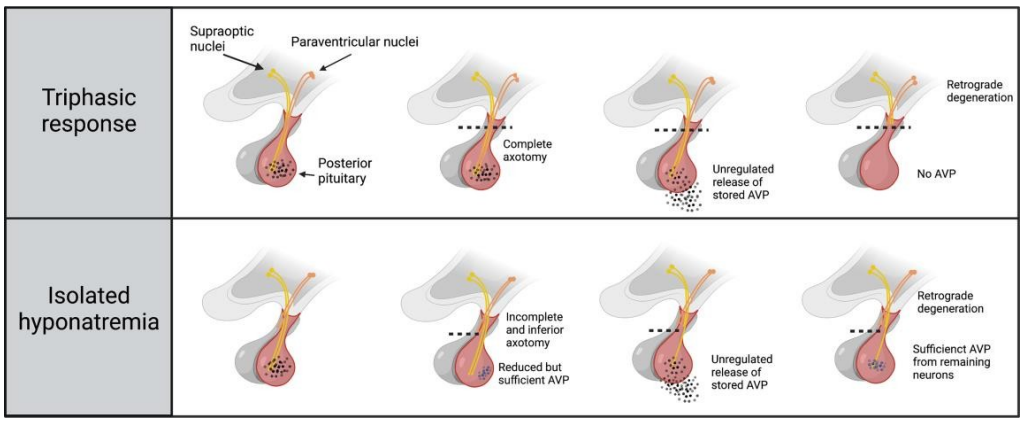

Figure 3. Pathophysiology of water balance disorders following pituitary surgery [26]

Contributing Factors of Electrolyte Disorders in Postoperative Endoscopic Endonasal Transsphenoidal Surgery Patients with Pituitary Gland Disorders

The study provides valuable information about the prevalence of electrolyte disorders, specifically hyponatremia and hypernatremia, in postoperative patients with pituitary gland disorders. However, due to the small sample size, further research is needed to confirm these findings. The studies discussed provide valuable information about the incidence and risk factors associated with electrolyte disorders in postoperative patients with pituitary gland disorders. Cheng Cee Lee et al. conducted a meta-analysis and systematic review to evaluate the incidence and factors associated with delayed postoperative hyponatremia following transsphenoidal surgery for pituitary adenomas. Their analysis showed that delayed postoperative hyponatremia is a relatively rare but serious complication that affects patient outcomes, and identified older age, postoperative diabetes insipidus, longer operation duration, higher intraoperative fluid volume, and faster sodium level increase during the early postoperative period as factors associated with this condition.

Similarly, Yinxin Huang evaluated risk factors for delayed postoperative hyponatremia in patients with non-functioning pituitary adenomas undergoing transsphenoidal surgery. Their study found that delayed postoperative hyponatremia is a common complication, with older age, larger tumor size, longer operation time, intraoperative bleeding, and low preoperative sodium levels as significant risk factors.

Yuen [27] also conducted a study to evaluate the incidence and risk factors associated with electrolyte disorders in postoperative patients with pituitary gland disorders. Their study found that 16% of patients experienced postoperative hyponatremia, while 1.4% experienced hypernatremia, with postoperative diabetes insipidus, intraoperative bleeding, higher intraoperative fluid volume, and longer operation duration as significant risk factors.

Overall, these studies provide further evidence that electrolyte disorders, particularly hyponatremia, are a common issue in postoperative patients with pituitary gland disorders. These findings highlight the importance of careful monitoring and management of electrolyte levels in postoperative patients to prevent serious complications.

Common Urine Profile Changes after Transsphenoidal Surgery for Pituitary Adenomas

The relationship between patient characteristics and urine profiles after transsphenoidal surgery is a significant finding, as shown by the table summarizing the characteristics and urine profiles of 11 patients. The data indicates that older patients and those with macroadenomas have a higher likelihood of experiencing polyuria after surgery. Furthermore, patients with polyuria are more likely to develop headaches compared to those with a normal urine profile.

Table. 4 Diagnostic criteria for different states of fluid imbalances [28]

	Fluid Overload	**Osmotic Diuresis**	**Diabetes Insipidus**	**Adipsic Diabetes Insipidus**
Polyuria	Yes	Yes	Yes	Yes
USG	Normal or low	High	Low	Low
Thirst	Absent to low	Excessive	Excessive	Absent to low
Hyperosmolality /Hypernatremia	No	No	Absent to Mild	Yes, can be severe

Study Hensen [1] findings suggest the importance of closely monitoring patients' water and electrolyte regulation after surgery, as highlighted in a study exploring the prevalence and factors influencing polyuria and hyponatremia after pituitary adenoma removal.

The prevalence of postoperative complications after transsphenoidal surgery for pituitary tumors is an important topic of research. Sane's [29] study highlighted the incidence of postoperative hyponatremia and its association with Cushing's disease. Furthermore, monitoring water and electrolyte regulation after surgery is crucial to avoid complications such as polyuria and headaches. The relationship between patient characteristics and urine profiles is a significant findingthat suggests the need for closer monitoring of high-risk patients. Understanding the factors that influence postoperative complications can help clinicians improve patient care and avoid severe symptoms.

Moreover, a study by Blair [4] explored the mechanisms behind water and electrolyte disturbances after transsphenoidal surgery, which are common and unpredictable. The researchers hypothesized that changing the degree of damage to the pituitary stalk produces a spectrum of water and electrolyte disturbances. To test this hypothesis, the researchers used a mathematical model of physiology called HumMod and simulated pituitary stalk damage at different fractions. The results showed that lower pituitary damage resulted in transient polyuria, while higher levels of damage showed a triphasic pattern of diabetes insipidus. However, the study also suggests that other mechanisms not included in the model may be responsible for postoperative hyponatremia and require further investigation. Overall, the findings of this study provide a plausible mechanistic explanation for some varieties of postsurgical water and electrolyte disturbances, but further research is needed to fully understand the underlying pathophysiology.

In conclusion, the relationship between patient characteristics and urine profiles after transsphenoidal surgery is an important finding, as it indicates that older patients and those with macroadenomas are more likely to experience polyuria after surgery. Patients with polyuria are also more likely to develop headaches compared to those with a normal urine profile. Therefore, it is crucial to closely monitor water and electrolyte regulation after surgery to avoid complications such as polyuria and headaches. Patients with Cushing's disease are at a higher risk of developing both polyuria and hyponatremia after surgery compared to those with acromegaly, indicating the need forclinicians to consider these factors in patient monitoring and treatment. Additionally, Blair et al.'s study suggests that changing the degree of damage to the pituitary stalk produces a spectrum of water and electrolyte disturbances, but further research is needed to fully understand the underlying pathophysiology. Overall, understanding the factors that influence postoperative complications can help improve patient care and avoid severe symptoms]

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None.

Conflict of Interest

The authors declare no conflicts of interest in preparing this article.

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