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Original Article

Correlation between Volume of Glycine Used as Irrigating Fluid and Serum Sodium Level during Transurethral Resection of the Prostate [TURP]

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ABSTRACT

Background: Benign prostatic hyperplasia causes bothersome lower urinary tract symptoms like urinary frequency, urgency, intermittency and weak urine flow due to symptomatic bladder outlet obstruction. Transurethral resection of the prostate is the second most common surgery performed in men over 65 years of age. Endoscopic procedures in the urinary system require the use of irrigating fluids.

Aim of the Study: The aim of this study was to evaluate changes in serum sodium levels with the use of 1.5% glycine solution as the irrigating fluid during transurethral resection of the prostate as the primary outcome. Secondary outcomes included hemodynamic changes like blood pressure (systolic and diastolic) and heart rate.

Patients and Methods: This prospective analytical study included 50 male patients aged 45-70 years scheduled for elective transurethral resection of the prostate at Al-Azhar Hospitals in Damietta and Cairo, Egypt after obtaining written informed consent.

Results: The median age was 50 years and median weight was 68 kg. The median resected prostate volume was 50 gm, median surgery duration was 100 minutes, and median total volume of irrigation fluid was 2085 ml. There was a statistically significant positive correlation between the total volume of glycine irrigation fluid and sodium levels intraoperatively and postoperatively, especially at 2.5 and 3.5 hours postoperatively ($p=0.038$, 0.024 respectively). Statistically significant decreases were seen in systolic blood pressure, diastolic blood pressure, and heart rate from preoperative to postoperative parameters. Postoperative hemoglobin, hematocrit, and platelet counts were also significantly lower ($p<0.001$).

Conclusion: Sodium levels significantly decreased intraoperatively during transurethral resection of the prostate when using glycine as the irrigation fluid, with subsequent hemodynamic and neurological manifestations related to hyponatremia.

Keywords: Glycine; TURP; Hyponatremia; Prostate.

INTRODUCTION

Transurethral resection of prostate [TURP] is the second most frequently performed surgical procedure in men over 65 years old. During endoscopic procedures in the urinary system, fluids are used to expand the mucosal spaces, clear blood and debris from the operating area, and improve visibility. Although efforts have been made to understand and prevent complications, some complications remain unchanged [1].

Numerous commercially available irrigating fluids make it challenging to determine the appropriate one to use. Typically, the decision is based on tradition, although factors such as the fluid's price and properties [such as stickiness and transparency] also influence the choice [2].

Glycine is an amino acid that naturally occurs in the body and does not have the potential to cause an allergic reaction. It is relatively inexpensive and has a transparent appearance. Nevertheless, the fluid is not physiologically balanced since it lacks electrolytes, and excessive absorption is a known complication [3].

If a significant amount of irrigating fluid is absorbed, it can quickly increase the volume of blood and lead to dilutional hyponatremia. This condition can be severe and result in a shift in osmotic pressure, causing cerebral edema and increased pressure within the skull [4].

AIM OF THE WORK

The present study aims at evaluating the changes in serum sodium with use of 1.5% glycine solution as irrigating fluid during TURP.

Primary outcome: correlation between glycine volume used and serum sodium level intra and post-operatively.

Secondary outcomes: Detection of neurological symptoms as changes in conscious level and irritability. Hemodynamic changes including blood pressure [SBP, DBP] and heart rate [HR].

PATIENTS AND METHODS

This prospective analytical correlational clinical study included 50 male patients aged 45 to 70 years with ASA physical status I and II, who were scheduled for elective transurethral resection of the prostate. The study was carried out at Al-Azhar University Hospitals [Damietta and Cairo] from December 2021 to May 2022 after approval by the local Medical Ethics Committee and obtaining written informed consent from each patient.

Exclusion criteria: Patients who refuse to participate in the study, patients with complicated heart or lung disease, contraindications to spinal anesthesia, chronic kidney disease [CKD], sodium-losing nephropathy, any disease affecting sodium levels, patients with severe electrolyte disorders, those on diuretic therapy, and those experiencing diarrhea and vomiting.

Calculation of Sample Size: The sample size was determined using the "MedCalc® version 12.3.0.0 program from Ostend, Belgium." A statistical calculator was utilized to determine the sample size, with a 95% confidence interval, a study power of 90%, and an alpha error of 5%. Based on the formula, at least 17 patients were required to detect a significant difference at an α value of 0.05 and a study power of 90%.

Preoperative management

Preoperative assessment was conducted through history taking, clinical examination, and laboratory investigations including complete blood count (CBC), sodium, potassium levels, bleeding time, clotting time, INR, liver function tests (AST, ALT), and kidney function tests (urea and creatinine).

Following the assessments, fasting instructions were provided to the patient, requiring 8 hours of fasting for solids and 2 hours for fluids and electrolytes.

Before administering intravenous fluids, a venous blood sample was obtained to establish the baseline serum sodium concentration, serving as the control value. Additional blood samples were collected every 30 minutes during the operation. All patients received a 10 ml/kg hystril infusion before undergoing spinal anesthesia.

Anesthetic techniques

Patients were regularly monitored for heart rate, pulse, ECG, noninvasive blood pressure, and oxygen saturation using standard monitoring techniques.

A central neuroaxial block was performed in a sterile environment at the third and fourth lumbar vertebrae or the fourth and fifth

intervertebral space while the patient was seated. This procedure successfully achieved analgesia up to the T8-10 dermatome level.

Following this, the patients were positioned in lithotomy, and a conventional monopolar Transurethral Resection of the Prostate (M-TURP) procedure was initiated by inserting the resectoscope into the bladder.

Intra-operative management

Glycine was utilized as the sole irrigating fluid during the procedure at a height of 60 cm and a pressure of 60-70 cm H2O. Glycine volume used and blood samples were collected every 30 minutes to measure the sodium concentration level, correlating them with the volume of irrigation fluid (glycine) employed.

Additionally, changes in blood pressure (SBP, DBP) and heart rate were monitored and recorded every 15 minutes. Observations for irritability and consciousness level were also conducted.

Post-operative assessment

Evaluation of serum sodium levels every half hour up to 6 hours postoperatively and observation of neurological symptoms of hyponatremia were conducted. The correlation between serum sodium levels and glycine volume was also evaluated.

Post-operative laboratory analysis included: hemoglobin (Hb), hematocrit (Hct), platelets (PLT), prothrombin time (PT), partial thrombo-plastin time (PTT), international normalized ratio (INR), alanine aminotransferase (ALT), urea, creatinine, and potassium.

Statistical analysis

The data that were gathered were entered into a computer and analyzed statistically using the SPSS program [Statistical Package for Social Science], specifically version 24. The data underwent the Shapiro Walk test to determine if they had a normal distribution. The difference between qualitative variables was calculated using the Chi-square test [$\chi 2$] and Fisher exact test, as appropriate. The Wilcoxon test was employed to compare the changes over time for non-normally distributed variables. All statistical comparisons were two-tailed, and a significance level of P-value $\leq$ 0.05 was considered significant, while a P-value > 0.05 indicated a non-significant difference.

RESULTS

In the present study, the median age was 50 years [range 45-75 years] and the median weight was 68 kg [range 58-78 kg].

Regarding operative data, the median volume of resected prostate was 50 gm [range 40-78 gm], the median duration of the surgery was 100 minutes [range 85-125 minutes], and the median total volume of irrigation fluid was 2085 ml [range 1610-3770 ml] as shown in Table [1].

Regarding correlations between the total glycine volume of irrigation fluid and sodium levels intra- and post-operatively, there is a statistically significant positive correlation between the volume of used glycine and sodium levels, especially at 2.5 hours and 3.5 hours post-operatively, with p-values of 0.038 and 0.024, respectively, as shown in Table [2].

Regarding intraoperative changes in SBP, there is a statistically significant decrease in SBP with a p-value of <0.001 as shown in Table [3].

Regarding intraoperative changes in DBP, there is a statistically significant decrease in DBP with a p-value of <0.001 as shown in Table [4].

Regarding neurological symptoms suggestive of hyponatremia among the included TURP patients who used glycine as an irrigation fluid; 28% had irritability and 26% had impaired consciousness level as shown in Table [5].

Table [1]: Studied Patients' Operative Data

	Median [Range]
Volume of resected prostate [gm]	50 [40-78]
Duration of surgery [min]	100 [85-125]
Total volume of irrigation fluid [ml]	2085 [1610-3770]

Table [2]: Correlations between total glycine volume of irrigation fluid and sodium level intra and post-operative

Sodium level	Total Glycine volume of irrigation fluid	
	Correlation coefficient	P value
Baseline	0.145	0.213
After 1/2 hour	0.189	0.189
After 1 hour	-0.070	0.63
After 1.5 hour	0.070	0.63
After 2 hours	0.172	0.232
After 2.5 hours	0.294	0.038
After 3 hours	0.245	0.087
After 3.5 hours	0.320	0.024
After 4 hours	-0.063	0.665
After 4.5 hours	0.095	0.51
After 5 hours	-0.107	0.458
After 5.5 hours	-0.229	0.11
After 6 hours	-0.248	0.083

Table [3]: Intraoperative changes in SBP [mmHg]

Time	Median [Range]	Friedman Test	P
Baseline SBP	110 [90-120]	**273.3**	**<0.001**
After 15 minutes	115 [90-130]		
After 30 minutes	100 [85-120]		
After 45 minutes	90 [80-110]		
After 60 minutes	90 [80-98]		
After 75 minutes	87 [80-96]		
After 90 minutes	85 [78-90]		
After 105 minutes	78 [67-90]		
After 120 minutes	80 [70-90]		

Table [4]: Intraoperative changes in DBP [mmHg]

Time	Median [Range]	Friedman Test	P
Baseline SBP	80 [70-84]	**296**	**< 0.001**
After 15 minutes	80 [70-87]		
After 30 minutes	76 [70-80]		
After 45 minutes	75 [65-80]		
After 60 minutes	75 [70-80]		
After 75 minutes	70 [60-80]		
After 90 minutes	64 [50-70]		
After 105 minutes	50 [35-70]		
After 120 minutes	58 [50-75]		

Table [5]: Neurological symptoms of hyponatremia of the studied patients

		No.	%
Irritability	**Yes**	14	28.0%
	No	36	72.0%
Impaired consciousness	**Yes**	13	26%
	No	37	74%

DISCUSSION

Transurethral resection of the prostate [TURP] is a frequently performed urological surgery for symptomatic benign prostatic hyperplasia [BPH], and it remains the preferred treatment due to its excellent outcomes and decreased morbidity and mortality rates [5].

During transurethral resection of the prostate [TURP], significant amounts of irrigation fluids are utilized to distend and irrigate the bladder. However, the systemic absorption of irrigation

fluids can result in various complications, such as volume overload, pulmonary edema, hyponatremia, and hypothermia. Additionally, some of the commonly used fluids, such as glycine and sorbitol, have negative effects [6].

Glycine has negative impacts on both the heart and kidneys. After absorption, glycine is metabolized in the liver to ammonia, which can lead to hyperammonemia and neurological symptoms such as tremors and seizures. Ingestion of large amounts of glycine can also result in hyperglycemia and lactic acidosis [7].

This prospective analytical correlational clinical study was conducted on 50 patients who underwent TURP and used glycine as an irrigation fluid with their median age 50 years [45-75] years and median weight 68 Kg [58-78] kg. The median duration of the surgery is 100 minutes [85-125] minutes.

The amount of time considered acceptable is crucial, as fluids are absorbed at a rate of 20 ml per minute. Any physiological changes resulting from excessive fluid absorption usually become evident within 30-60 minutes following the completion of surgery [8].

In our study there is statistically significant decreased of intraoperative SBP, DBP and HR with p-value <0.001. this goes in run with Nandita **Adlakha *et al.*** study which was conducted on to evaluate and revealed statistically significant intraoperative decreased SBP and DBP in TURP with p-value <0.001 [9].

There is statistically significant decreased sodium level intraoperative during TURP using glycine irrigation fluid especially after 2 hours and after 6 hours postoperatively with p-value <0.001.

If a substantial amount of irrigating fluid is absorbed, it can quickly increase the volume of blood and lead to dilutional hyponatremia. Severe hyponatremia can cause a shift in osmotic pressure, resulting in cerebral edema and an increase in pressure within the skull [10].

Several strategies can be employed to reduce fluid absorption during transurethral resection of the prostate [TURP]. These techniques include performing alternative procedures such as open prostatectomy or Holmium Laser Enucleation of the Prostate [HoLEP] for prostates larger than 80 grams, avoiding deep resection, limiting the operative time to 60 minutes, maintaining the height of the irrigating fluid at 60 cm, and using an isotonic solution [11].

Similarly, another study by **Ibrahim *et al.*** [1] was conducted on 50 patients who underwent TURP and reported statistically significant decreased sodium level with p-value <0.001.

Another study by **Mithani *et al.*** [12] found TURP using glycine irrigation fluid shows statistically significant decreased sodium level which was significantly with volume of irrigation fluid >40 L with –value <0.001.

In the current study, neurological symptoms suggestive of hyponatremia was detected among the included TURP patients who used glycine as an irrigation fluid; as 14 of 50 patients [28%] had irritability and 13 of 50 patients [26%] had impaired conscious level.

Another study by **Ishio *et al.*** [13] was conducted on 229 patients needed TURP and found that the neurological symptoms significantly correlated with sodium level and duration of the operation >90 minutes.

Conclusion Sodium level significantly decreased intraoperatively during TURP using glycine irrigation fluid especially after 2 hours and after 6 hours postoperatively. Neurological manifestations related to hyponatremia in our study included irritability [28%] and impaired conscious level [26%].

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