

## EVALUATION OF CHANGES IN SERUM CONCENTRATION OF SODIUM IN A TRANSURETHRAL RESECTION OF THE PROSTATE

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### Abstract

*Introduction and objectives:* The purpose of this study was to evaluate changes in serum electrolytes during Transurethral resection of the prostate (TURP) and to evaluate the degree of correlation of hyponatremia and the factors that affect the incidence of TURP syndrome and to show the impact of the duration of the procedure on the severity of hyponatremia due to absorption of irrigation fluid in the systemic circulation.

*Materials and Methods:* This study examined 60 male patients planned for elective TURP. The level of serum electrolytes are determined by taking venous blood samples preoperatively and Postoperatively and when the duration of the operation was longer than 60 minutes, the level of serum electrolytes was determined intraoperative. The amount of used irrigation fluid, the weight of resection prostate, and duration of surgery, were also followed.

Patients were divided in two groups according to the length of the surgical procedure: Group 1 (30–60 min) and Group 2 (> 60 min).

*Results:* Statistically significant reduction of serum sodium and the elevation of the potassium level in serum observed postoperatively and was directly proportional to the volume of of the used irrigation fluid, the duration of the procedure and volume of the resected prostate.

*Conclusions:* To evaluate changes in serum electrolyte during TURP is simple and economical method for the indirect estimation of irrigation fluid absorption into the systemic circulation during TURP and opportunity for early identification of TURP syndrome.

**Key words:** TURP, TURP syndrome, hyponatremia, hyperkalemia.

### Introduction

Benign prostatic hyperplasia (BPH) is a common disease in men over 40 years. It is characterized by urinary frequency, urgency, incontinence, nocturnal, a weak urine flow, intermittency [1].

The exact mechanism for the occurrence of BPH is still unknown. It is believed that while the long-term affects the synthesis of testosterone, while some authors believe that there is a hereditary hypothesis [2].

The normal size of the prostate is approximately up to 20 g, so BPH is considered when

the size of the prostate is bigger than this and associated with obstructive and/or irritative symptoms [3].

Transurethral resection of the prostate (TURP) is the endoscopic urological intervention used in the treatment of BPH [4]. The name indicates that this technique allows visualization of the prostate through urethra and its removal [5].

TURP technique is significantly more secure and effective replacement for open prostatectomy in most cases [6]. This endoscopic intervention is a gold standard in 95% of simple prostatectomy [7].

Large triple lumen catheter is used for irrigation and drainage (flushing) of the bladder after the intervention [8].

TURP may be carried out under spinal or general anesthesia.

TURP procedures have specific characteristics due to the use of irrigation fluid filling the bladder, dilating the mucosal surfaces, the removal of blood, cleaning and rinsing of pieces in resected prostatic tissue and enabling better visualization.

Various irrigation solutions used for TURP: distilled water, glycine, sorbitol, and mannitol [9].

A possible complication of TURP procedure is systemic absorption of hypotonic irrigation fluid directly into the vascular system through the prostatic venous plexus or indirect absorption of retroperitoneal or perivesical space [10].

The driving force is the pressure of the irrigation fluid, which should exceed the venous pressure of 1.5 kPa [11].

Other clinical manifestations that occur due to absorption of a larger quantity of irrigation fluid during TURP together are known as TURP syndrome.

TURP syndrome is described in more than 20% of patients in the TURP [12].

It is rare, but a potentially fatal syndrome with a multifactor and complex pathophysiology, so that it requires a multidisciplinary management [13]. TURP syndrome is iatrogenic form of water intoxication, the combination of increased fluid intake and hyponatremia, which can be seen in endoscopic operating procedures, but mostly in TURP.

TURP syndrome can occur in the first 15 min of resection (early TURP syndrome), up to 24 hours postoperatively [14].

TURP syndrome is characterized by systemic manifestations (cardiovascular, CNS changes and changes in metabolism). The clinical picture varies and is influenced by the type of irrigant which is used, from the patient and surgical factors. There isn't a classic presentation of TURP syndrome. Signs and symptoms are vague and variable, the sensations on the face and neck, lethargy, fear, fatigue, headache, dizziness, nausea, vomiting, dyspnea, arrhythmia, hypertension, bradycardia, restlessness, confusion. If not treated early symptoms, the clinical picture is exacerbated by the onset of cyanosis, hypotension, cardiac arrest and death [11].

Almost at every TURP procedure is absorbed certain amounts of irrigation fluid through the prostatic venous sinuses (20 ml/min to several L). Penetration of one liter irrigant in circulation for a period of 1 hour match with an acute reduction in serum sodium concentration of 5–8 mmol/L, and it suggests that there is a risk of symptoms associated with absorption [15].

Acute hyponatremia with serum concentration of sodium (115–120 mEq/L) is a potentially serious condition [16].

Hyponatremia and plasma hypoosmolality, may result in intravascular hemolysis leading to increase in serum potassium [17].

Hyperkalemic cardio toxicity increases with hyponatremia and acidosis [18].

Cardiovascular changes during TURP syndrome is due to a combination of hyponatremia and hyperkalemia [18].

Despite advanced surgical and anesthetic techniques which are used for prevention of TURP syndrome, as well as a better understanding of its pathophysiology, there is still a risk of occurrence of TURP syndrome, so the responsibility should be shared by the anesthesiologist and the urologist. The best prevention would be the adoption of proper surgical technique and preoperative evaluation, preparation of patients and to take the appropriate therapeutic measures.

This study analyzed the changes in electrolyte status with TURP, which indirectly reveals absorption of the irrigant in the systemic circulation, and early diagnosis and development of TURP syndrome.

## Objectives

To evaluate the changes in serum electrolytes during TURP.

To evaluate the degree of correlation of hyponatremia and the factors that affects the incidence of TURP syndrome (duration of the procedure, the weight of resected prostatic tissue, the amount of irrigation fluid used).

To determine which of the factors that can lead to TURP syndrome have the greatest impact on the degree of hyponatremia in TURP.

### Motive

The motivation for this research comes from the need to evaluate the impact of the duration of the TURP procedure the degree of hyponatremia, and therefore timely to recognize the greater absorption of irrigation fluid volume in the systemic circulation.

Timely recognition and treatment of electrolyte misbalances, especially prevention is essential to reduce the possible occurrence of TURP syndrome, and thus morbidity and mortality in patients treated with TURP procedure.

### Materials and methods

This study studied 60 male patients, 50–80 years of age and ASA classification I–III, scheduled for elective transurethral resection of the prostate. The study did not include patients who have heart or lung disease, renal failure, metastases lumbar level medulla spinalis, patients undergoing emergency transurethral procedures, patients with severe electrolyte disorders, diuretic therapy, diarrhea and or vomiting.

All patients were underwent pre anesthesiology assessment and preoperative routine examinations.

After successfully setting an i.v. line before the intervention and before applying an i.v. fluid, venous blood sample was taken for determination of serum sodium and potassium concentration. This sample was considered as a control value. Second sample of blood was taken after the intervention and was considered as a study value. All patients were applied 10 ml/kg Ringer lactate before spinal anesthesia, and then continue with the application rate according to the needs of patients. The choice of Ringer lactate was due to the similarity of the sodium concentration and osmotic pressure in the serum.

With standard monitoring of the monitored heart rate, pulse, ECG, noninvasive blood pressure and saturation of blood oxygen.

Central neuroaxial block was performed in aseptic conditions the level between third and four lumbar vertebra and between four and fifth intravertebral space, in a sitting position and was achieved successfully analgesia to the level of T 8–10 Dermatome.

Patients were placed in litotomy position and a conventional monopolar TURP (M-TURP) procedure was began by inserting the resectoscope into the bladder. Sterile water was used as irrigation fluid, using a cylindrical glass vessel at a height of 60 cm, measured from the level of the pubic symphysis to the patient on the operating table (Richard Wolf Sterile Water System).

Patients were monitored for: the duration of the surgical procedure in minutes (the time of insertion of the resectoscope in the bladder until the end of the intervention); the volume of resected prostatic tissue (gr); volume of irrigation fluid used during the procedure (L).

Perioperative patients were monitored for the possible occurrence of early symptoms of TURP syndrome and the appropriate measures were taken to prevent further complications.

Serum sodium and potassium were determined preoperatively and postoperatively.

Changes in serum sodium and potassium levels were correlated with the volume of the used irrigation fluid, the duration of the procedure and volume of the resected prostate.

### Statistical Methods

Statistical series according to definite variable are shown in tabular and graphical formats:

- Structure of numerical series is analyzed using measures of central tendency (average) and measures of dispersion (standard deviation);
- Testing of significance of differences between the two arithmetic environments with independent samples (between groups N1 and N2) is done with nonparametric Mann-Whitney U Test (there is an irregular distribution);

Analysis of the relationships between the number statistical series, is made with Pearson's correlation coefficient ( $r$ );

- The level of significance ( $p < 0.05$ ) is taken as statistically significant.

### Results

Clinical manifestation of fully developed TURP syndrome did not occur in any patient

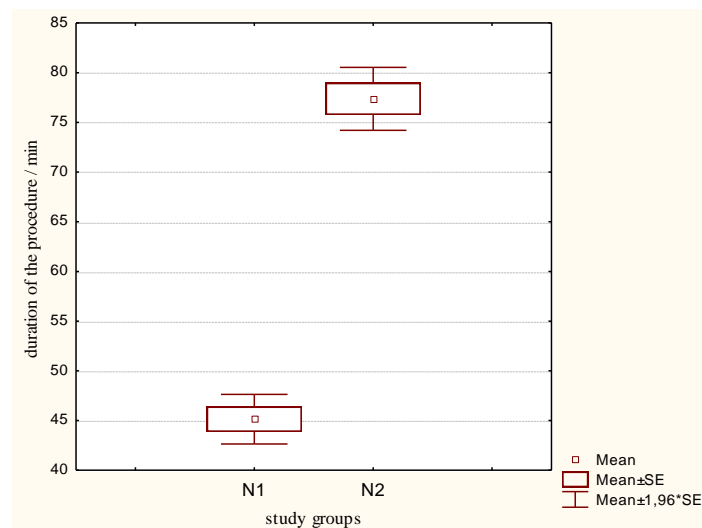
due to the taken precautions intraoperatively. In 7 patients (8.13%) anxiety and bradycardia appeared when the duration of TURP exceeded 60 minutes, which corresponds to a reduction of serum sodium and increased serum potassium confirmed intraoperatively by taking venous blood samples using a gas analyzer. Between both groups there is significant statistical

difference in the mean values of the duration of the Procedure / min (Mann-Whitney U Test:  $Z = -6.65$   $p = 0.0000$ ), the volume of the used irrigation fluid/L ( $Z = -6.63$   $p = 0.000000$ ) and volume of resected prostatic tissue/gr ( $Z = -6.58$   $p = 0.000000$ ). For all three parameters mean values are significantly lower in the first study group (Table 1 and Chart 1A, 1B and 1C)

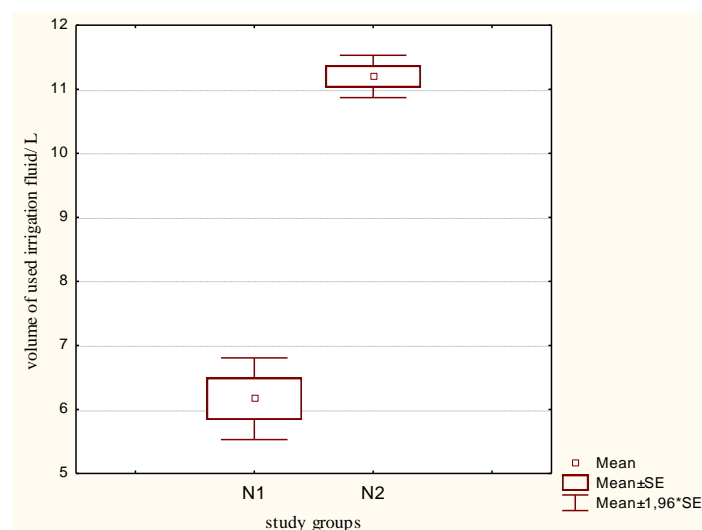
Table 1

*Average values of the duration of the procedure / min, volume of irrigation fluid used / L and volume of the resected prostate / gr in both groups*

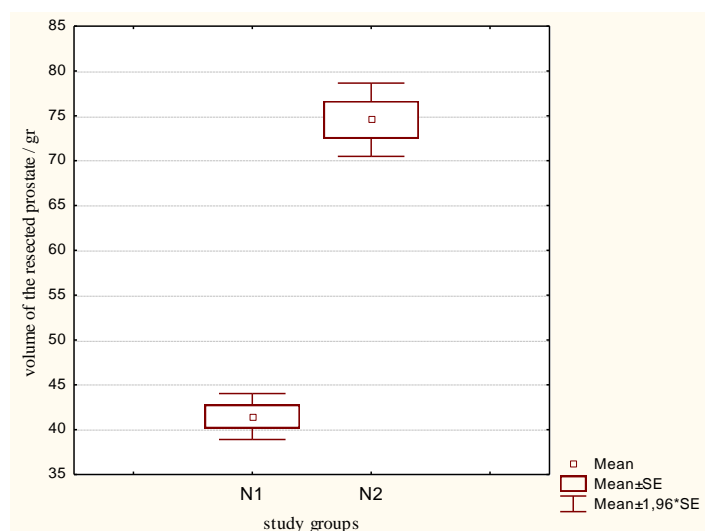
Parameters	N1 = 30		N2 = 30		Significance level (p)
	average	CD	average	CD	
Duration of procedure / min	45.13	6.97	77.37	8.84	$p = 0.000\ 000$
Volume of used irrigation fluid / L	6.17	1.78	11.20	0.92	$p = 0.000\ 000$
Volume of the resected prostate / gr	41.46	7.16	74.57	11.42	$p = 0.000\ 000$



Graph. 1A – Average values of the duration of the procedure / min in both study groups



Graph. 1B – Average values in the volume of used irrigation fluid / L in both study groups



Graph. 1C – Average values of the volume of the resected prostate / gr in both groups

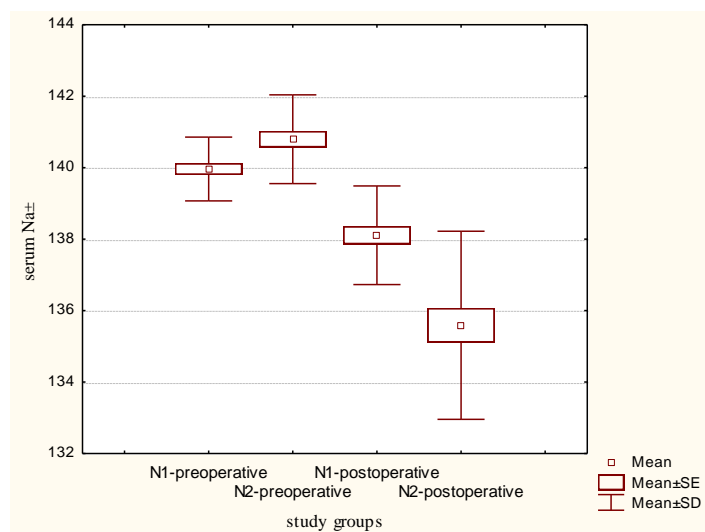
There was significant statistical difference between both groups in the mean values of preoperative (Mann-Whitney U Test:  $Z = -2.74$   $p = 0.00596$ ) and postoperative serum  $\text{Na}^+$  ( $Z = 4.41$   $p = 0.000010$ ). Differences between

the two groups are statistically significant in terms of preoperative (Mann-Whitney U Test:  $Z = -2.81$   $p = 0.00485$ ) and postoperative  $\text{K}^+$  ( $Z = -4.62$   $p = 0.000004$ ). (Table №. 2 and Chart. 2A and 2B)

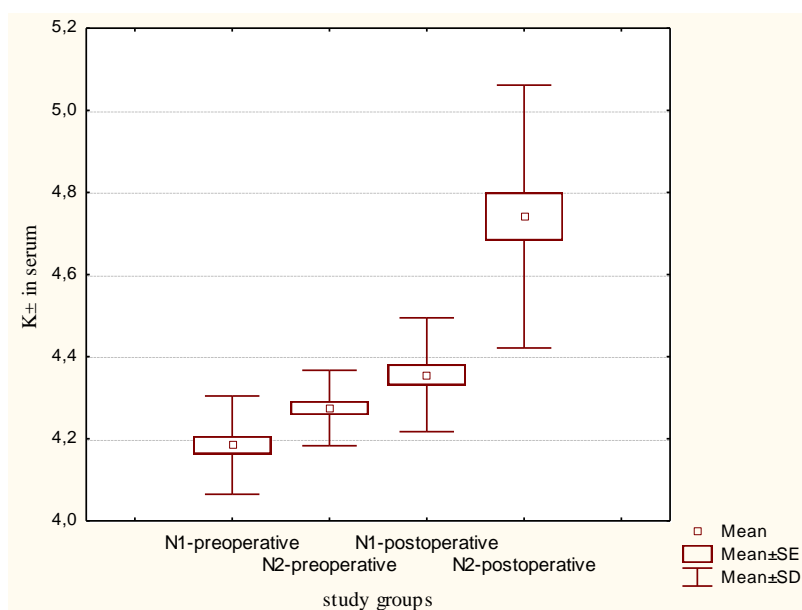
Table 2

Average values of  $\text{Na}^{\pm}$  and  $\text{K}^{\pm}$  in serum preoperative and postoperative in both study groups

Parameters	N1 = 30		N2 = 30		Significance level (p)
	average	CD	average	CD	
Preoperative Na	139.96	0.89	140.80	1.24	596 $p = 0.00$
Postoperative Na	138.11	1.38	135.59	2.63	$p = 0.0000\ 10$
Preoperative K	4.18	0.12	4.27	0.09	485 $p = 0.00$
Postoperative K	4.35	0.14	4.74	0.32	$p = 0.0000\ 04$

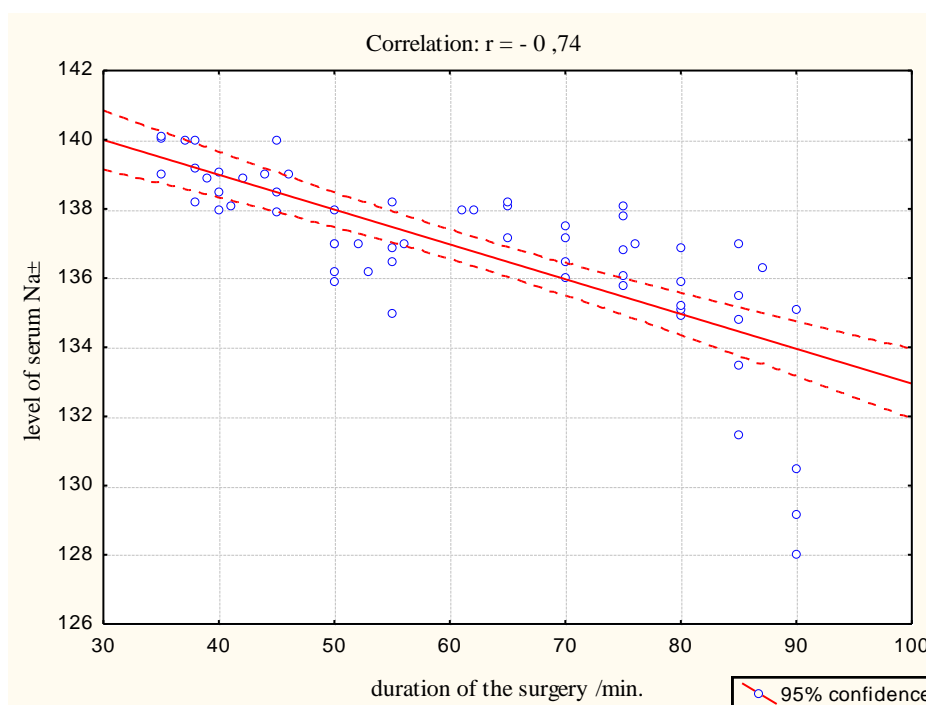


Graph. 2A –Average values of serum  $\text{Na}^{\pm}$  preoperative and postoperative in both study groups



Graph. 2B – Average values of  $K^{\pm}$  in serum preoperative and postoperative in both study groups

Among the duration of operation and level of serum  $Na^{\pm}$ , there is strong negative correlation ( $r = -0.74$ ). The longer the intervention, the more reduced the level of  $Na^{\pm}$  in serum. (Figure 3)

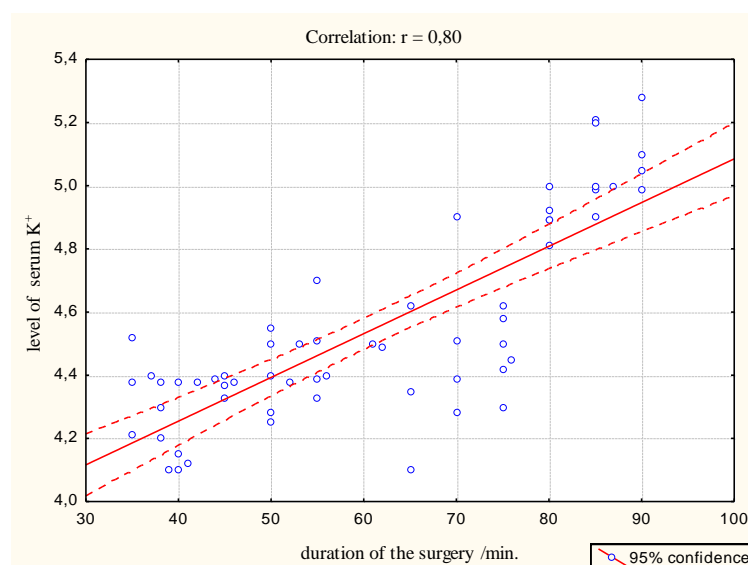


Graph. 3 – Correlation between the duration of the surgery and the level of serum  $Na^{\pm}$

There is strong negative correlation between the volume of the used irrigation fluid / L and  $Na^{\pm}$  levels in the serum ( $r = -0.68$ ). The larger the volume of the used irrigation fluid is lower the level of serum  $Na^{\pm}$  is. Regarding the volume of the resected prostate tissue and  $Na^{\pm}$  levels in the serum, there is also a strong negative correlation ( $r = -0.78$ ).

The larger the volume of the resected prostate, the lower the  $Na^{\pm}$  level in the serum 1 hour after surgery.

Concerning the duration of operation and level of  $K^{\pm}$  serum there is a strong positive correlation ( $r = 0.80$ ). The longer the intervention, the more it increases the level of  $K^{\pm}$  serum (Chart №. 4)



Graph. 4 – Correlation between the duration of the surgery and the level of serum  $K^+$

Between the volume of the used irrigation fluid / L level of  $K^{\pm}$  serum is strong positive correlation ( $r = 0.72$ ). By increasing the volume of the used irrigation fluid, increases the level of  $K^{\pm}$  in serum. Between the volume of the resected prostate / g and the level of  $K^{\pm}$  in serum, also there is a strong positive correlation ( $r = 0.79$ ). The larger the volume of the resected prostate, the greater the level of  $K^{\pm}$  in serum.

### Conclusion

Pathophysiological mechanism of TURP syndrome consists of pharmacological and volume effects of irrigation fluid, and serum electrolyte changes, so it is difficult to avoid occurrence of complications. The best preventive method is selecting the proper surgical technique and optimize the condition of patients preoperative.

Therefore our study emphasized the need for evaluation of serum levels of sodium and potassium preoperative at patients scheduled for TURP procedure and optimization of serum electrolytes to prevent serious complications.

Normal decrease in serum sodium at TURP is 5–8 mEq/L. However cardio toxic effects of hyponatremia will depend on simultaneous variation of serum potassium during the procedure. In proceeding lasting more than 60 minutes, and the weight of the prostate is more than 60 g, the ability to call more com-

plications is greater. By limiting the height of the column of irrigation fluid to 60 cm, can ensure optimum vision of the surgeon and reduce the complications of the absorption fluid. Sterile water, although it is hypotonic, used for irrigation has good optical properties, it isn't the cathode and prevents spreading diathermia electricity during resection.

Early identification of TURP syndrome and its treatment by administration of hypertonic saline, decreases or prevents further adverse effects.

Laser TURP and bipolar procedures, modern techniques in urology, can help minimize the absorption of fluids And its complications, especially at patients with heart diseases and critically ill patients.

This provides an opportunity for further investigation and monitoring of serum electrolyte changes in patients who performed TURP procedures.

### Discussion

Transurethral resection of the prostate is a common surgical intervention at men over 60 years. Patients who are undergoing TURP are often elderly and suffer from heart, lung, kidney and endocrine disorders.

Occasionally these patients become dehydrated and have a lack of essential electrolytes like sodium, calcium and potassium, when using a diuretic with a limited consumption of fluids.

Endourology surgery is associated with intraoperative complications such as bleeding and adverse effects due to systemic absorption of intravesical irrigation fluid.

Water intoxication and hyponatremia postulated by Han et al in 1990. a primary cause of the genesis of TURP syndrome [19]. TURP syndrome is characterized by a change of the intravascular volume and plasma osmolar effects. The absorption of small amounts of fluid gives dilutional hyponatremia and patients begin to complain of dizziness, headache, nausea, dyspnea, etc. However, other side effects due to absorption of more liquid.

Hyponatremia may cause weakness, muscle spasms and seizures. Hard changes are associated with the absorption of more than 3 L of fluid.

In our study, we found significant changes in serum sodium (hyponatremia) by changing the volume of sterile water which we used as irrigant, the duration of the procedure and the volume of the resected prostate.

Serum potassium was transient increasing in response to irrigant absorption, probably related to intracellular, penetration of irrigant.

Clinical manifestations of hyperkalemia occur when the level of potassium in the plasma was more than 6 mmol/L, with ECG changes, high and sharp T wave, PR prolongation, QRS widening and arrhythmias. Hyperkalemic cardio toxicity was increasing with hyponatremia and acidosis.

Our study showed that hyponatremia and hyperkalemia happens during TURP and the most dependent duration of the procedure.

Han and associates also found a significant elevation of serum potassium during absorption of sterile water intraoperative. The cause of hyperkalemia was the inability of the sterile water to hold isotonicity of the plasma [16,20].

Madsen et al in 1973. showed another important factor that will also determine rate absorption liquid, which actually is the hydrostatic pressure in the prostate area, the dependence of the amount of irrigation cylindrical vessel and the pressure inside the bladder during the operation. The ideal height of the irrigation fluid is 60 cm, so that about 300 ml of liquid flow per minute in resection and provides good visibility [21].

For this study, we set the irrigation fluid at a height of 60 cm.

Regional technique neuroaxial central block was preferred over general anesthesia as possible observation of the early symptoms and signs of TURP syndrome. Regional anesthesia reduces the incidence of postoperative venous thrombosis. Clinical studies haven't shown difference in blood loss, postoperative cognitive function and mortality between regional and general anesthesia [22].

Blood loss was difficult to assess because of the use of irrigation fluid, so it was necessary to rely on clinical signs of hypovolemia.

Irrigation fluid was heated to body temperature to prevent hypothermia during TURP.

Electrolyte solutions can't be used for irrigation during TURP, because the transfer of power of the electrocauter.

Water provides better visibility for hemolysis, but significant absorption will cause acute water intoxication.

1.5% glycine, endogenous amino acid is considered adequate irrigation fluid, given its advantages, including low cost, its tendency to cause less hemolysis and renal failure. 2.2% glycine is isotonic with plasma, but the side effects are greater. Transient blindness can occur by absorption of glycine because it is inhibitory neurotransmitter in the retina [23].

A mixture of sorbitol, 2.7% and mannitol 0.54% (195 mOsm/L) are also used in most countries. Less frequently used solutions which comprised 3.3% include sorbitol, mannitol 3%, 2.5–4% dextrose and 1% urea.

These fluids are hypotonic so significant water absorption can occur, especially when irrigation fluid is pressurized. The use of large amounts of sorbitol or dextrose may lead to hyperglycemia. Utilizing 3% of mannitol causing intravascular volume expansion more than 1.5% glycine, and sorbitol, mannitol occupies an intermediate position [10].

Morbidity and mortality is higher when the operation takes more than 90 minutes [24, 25].

Several methods have been proposed to reduce the risk of absorption of liquid, but none is appropriate (sufficient) to remove complications.

Monitoring the extent of absorption of fluid during operation allows control fluid balance in each patient.



Methods for monitoring the absorption are ethanol monitoring and gravimetric measurement [26].

Newer techniques, such as bipolar resectoscope and vaporization of tissue instead resection, reduce the absorption of fluid and its consequences [27].

Mamoulakis et al in their study evaluated evidence by a meta-analysis, based on the randomized controlled trials (RCTs) comparing bipolar TURP (B-TURP) with M-TURP for benign prostatic obstruction.

They concluded that there was no clinically relevant differences in short – term efficacy exist between the two techniques, but B-TURP is preferable due to a more favorable safety profile (lower TUR syndrome and clot retention rates) and shorter irrigation and catheterization duration [28]. "With B-TURP, dilutional hyponatremia of TURP syndrome is a historical event in the 21st century" [29]. Bipolar technology does not prevent fluid absorption, which can still happen, therefore it should always be kept in mind [30].

In retrospective study [31] even unexpected hyponatremia and pulmonary edema was reported in one case and was attributed to secondary fluid shifts between intra and extravascular compartments unrelated to the saline irrigation.

One of the major complications of M-TURP is intra or preoperative bleeding, which is clinically significant mainly if it causes clot retention or necessitates blood transfusion or reoperation. Although transfusion rates in M-TURP series have been significantly reduced over time, clot retention incidence ranges between 2–5% and bleeding still remains a concern [4]. The hemostatic capacity of bipolar current has been reported to be superior in a number of ex vivo studies, possibly as to the "cut-and-seal" effect of plasma created by bipolar energy [32, 33].

Reuter and his colleagues showed in 1978 that the low pressure irrigation during TURP, will limit the risk of the intravascular absorption [34].

The surgeon should be informed about the current absorption of fluids, when it exceeds 1L. This allows taking steps to prevent excessive absorption.

Proper care remains the most important therapeutic approach for managing complica-

tions. Treatment for dilutional hyponatremia should be based more on the administration of hypertonic saline and it's more common than the use of diuretics. The administration of calcium, alkalization and even hemodialysis in severe cases, can go over the toxicity of potassium [35].

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## Резиме

### ЕВАЛУАЦИЈА НА ПРОМЕНИТЕ ВО СЕРУМСКАТА КОНЦЕНТРАЦИЈА НА НАТРИУМ ПРИ ТРАНСУРЕТРАЛНА РЕСЕКЦИЈА НА ПРОСТАТА

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*Вовед и цели:* Целта на оваа студија е да се евалуираат промените во нивото на серумските електролити при трансуретрална ресекција на простата (TURP) и да се евалуира степенот на корелација на хипонатремијата и факторите што влијаат на појавата на TURP-синдромот, како и да се докаже влијанието на времетраењето на постапката врз сериозноста на хипонатремијата поради апсорпција на иригационата течност во системската циркулација.

*Материјал и метод:* Во оваа студија се испитувани 60 машки пациенти планирани за TURP-простата. Евалуирана е корелацијата меѓу

големината на хипонатремијата и факторите што влијаат на појавата на TURP-синдромот. Нивото на серумските електролити се одредуваше со земање венски примероци на крв предоперативно и постоперативно, а кога траењето на операцијата беше подолго од 60 мин., нивото на серумските електролити се одредуваше интраоперативно. Се следеа и количината на употребена иригациона течност, тежината на ресецираната простата, како и времетраењето на хируршката интервенција. Пациентите беа поделени во две групи според должината на хируршката процедура: група 1 (30–60 мин.) и група 2 (> 60 мин.).

*Резултати:* Статистички значајна редукција на нивото на серумски натриум и елевација

на нивото на калиум во серумот се забележани постоперативно и беше директно пропорционално со волуменот на користената иригациона течност, времетраењето на постапката и волуменот на ресецираната простата.

*Заклучоци:* Да се евалуираат промените на серумските електролити за време на TURP е едноставен и економичен метод за индиректна проценка на апсорпција на иригационата течност во системската циркулација за време на TURP и можност за рана идентификација на TURP-синдромот.

**Клучни зборови:** TURP, TURP-синдром, хипонатремија, хиперкалемија.