Prophylaxis versus Treatment against Transurethral Resection of Prostate Syndrome: The Role of Hypertonic Saline

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Abstract

Background: This study aimed at investigating the usage and effects of prophylactic hypertonic saline (HS) to prevent the occurrence of transurethral resection of the prostate (TURP) syndrome. Materials and Methods: Sixty American Society of Anesthesiologists physical status classes I–III candidates for TURP using the monopolar resectoscope were randomized into three groups 20 patients each. Group A received 4 mL.kg⁻¹.h⁻¹ HS 3%; Group B received 2 mL.kg⁻¹.h⁻¹ HS 3%; and Group C received 6 mL.kg⁻¹.h⁻¹ normal saline. Hemodynamics, vasopressors need, electrolytes (sodium, potassium, and chloride), osmolality, and arterial-blood gas (ABG) were recorded. The incidence of transurethral resection syndrome, intensive care unit (ICU) admission, postoperative ventilation, hospital stay as well as any adverse events were noted. Results: Hyponatremia was detected in six patients (P = 0.002) of Group A only, while hyponatremia occurred in five patients (P = 0.009) of Group C alone. Serum sodium in Group C showed a significant decrease starting from T2 (1 h postresection) till Tp3 (48 h postoperative). In Group C, five patients experienced hypotension and bradycardia; hypertensive episodes also occurred in five patients and a hypervolemic state was noted in seven patients. TURP syndrome was confirmed in only five patients, all in Group C (P = 0.009). Postoperative ICU admission was needed for seven patients of C Group, five of which required assisted ventilation. The overall hospital stay was longer for Group C patients. Conclusion: Prophylactic administration of HS during TURP is superior to conventional treatment of an occurred TURP syndrome. Low dose (2 mL.kg⁻¹.h⁻¹ HS 3%) is effective without adverse effects or risk of contrary hyponatremia.

Keywords: Hypernatremia, hypertonic saline, hyponatremia, transurethral resection of the prostate syndrome

Introduction

Transurethral resection of the prostate (TURP) continues to be the gold standard for the surgical treatment of benign prostatic hyperplasia (BPH).¹

The associated adverse effects arising in the cardiovascular and nervous systems are referred to as transurethral resection (TUR) syndrome.² This syndrome consists of a spectrum ranging from asymptomatic hyponatremia to electrocardiogram (ECG) changes, nausea, vomiting, headache, dizziness, convulsions, coma, and death.³ Therefore, spinal anesthesia is often recommended during TURP so that early neurological deterioration signs can be detected.⁴

If circulatory or cerebral signs necessitate active treatment, concurrent administration of hypertonic saline (HS) solution and a loop diuretic can raise serum sodium concentration and osmolality and promote diuresis.⁴

HS infusion raises plasma osmolality, leads to a fluid shift from intracellular to extracellular space, and exerts a positive inotropic effect.⁴ Different HS concentrations were earlier investigated in hemorrhagic, cardiogenic, and refractory hypovolemic shock and for postoperative use. Hence, it can be a suitable fluid for preloading before spinal anesthesia.⁵

In the absence of similarly conducted comparative studies, the main objective of the current one was to investigate the usage and effects of prophylactic HS preloading, with two different concentrations, to combat the expected dilutional hyponatremia induced by irrigating fluid absorption, and to...
prevent the occurrence of TURP syndrome with its potential complications. We hypothesized that low-dose HS prophylaxis would be more beneficial than the awaited conventional TURP syndrome treatment and also superior to the high-dose preloading. The primary outcome was to evaluate the impact of HS infusion on the pattern of intra- and postoperative serum sodium levels. The secondary ones were to assess the operative outcomes in terms of occurring TURP syndrome manifestations or any other related adverse events including the need for the intensive care unit (ICU) admission, mechanical ventilation as well as the overall hospital stay.

**Materials and Methods**

Following approval of the trial protocol by the Institute Local Research Ethics Committee and registration to ClinicalTrials.gov (ID: NCT03428451 on 9 February 2018), a written informed consent form was obtained from all the recruited patients, after being given a full explanation about the experimental procedure.

The study was conducted on 60 American Society of Anesthesiologists (ASA) physical status classes I–III BPH patients, candidates for TURP surgery using the monopolar electric resectoscope, with the exclusion of patients having any condition contraindicating regional anesthesia, electrolyte imbalance, uncontrolled hypertension, congestive heart failure, or being allergic to local anesthetics.

Routine preoperative evaluation, including history taking, general examination, and laboratory investigations, was performed for all patients. After insertion of an 18-G intravenous (i.v.) cannula, each patient was premedicated with Midazolam 2 mg, ranitidine 50 mg, and ondansetron 4 mg.

Using a computer and sealed envelope randomization, eligible patients were allocated into one of three study groups (n = 20 in each). Group A patients received NaCl 3% HS at a dose of 4 mL.kg<sup>-1</sup>.h<sup>-1</sup>; Group B patients received NaCl 3% HS at a dose of 2 mL.kg<sup>-1</sup>.h<sup>-1</sup>; while Group C patients received NaCl 0.9% normal saline (NS) at a dose of 6 mL.kg<sup>-1</sup>.h<sup>-1</sup>. All i.v. infusions were started 30 min before the subarachnoid block and continued all through the procedure at the same specific rate for each infusion.

Upon arrival to the operating theater, all patients were monitored using 5-lead ECG with S-T segment analysis, pulse oximetry, and noninvasive blood pressure (BP). Under local anesthesia with 2 mL of lidocaine 2%. Subarachnoid block was performed using a 27-G pencil-point spinal needle with an introducer (Braun Melsungen, Melsungen, Germany) at the L3–4 or L4–5 intervertebral space. When the correct placement was confirmed by the free flow of clear cerebrospinal fluid, 3 mL of hyperbaric bupivacaine 0.5% (15 mg) in addition to 0.5 mL of fentanyl (25 µg) was injected. Patients were assisted to assume a supine position till the full establishment of the block; then, they were placed in the lithotomy position. A block level at T10 was aimed for. Warm–cold discrimination and pinprick methods were used to determine the block level and the highest dermatomal level of sensory block was noted. If spinal anesthesia was ineffective, the patient was removed from the study.

Maintenance with the study fluid at the specific dose rate for each group was administrated throughout the procedure via the central venous catheter. Criteria for discontinuing the infusion in the HS groups were a serum Na<sup>+</sup> >155 mEq/L or a plasma osmolality >320 mOsm/kg. In patients whose values fit either of these criteria; the infusion of 3% NaCl was changed to Lactated Ringer’s (LR) solution.

TURP was performed with a monopolar electronic resectoscope, using an intermittent irrigation system with distilled water which was kept at room temperature and at 60 cm higher than the level of the resectoscope.

Supplemental oxygen 2–3 L/min was administered through a face mask or nasal prongs. Hypotension (defined as a decrease in mean blood pressure [MBP] >20% of the baseline) was treated with 10 mg i.v. increments of ephedrine. Bradycardia (defined as a heart rate [HR] <50 bpm) was treated with atropine 0.5 mg i.v. Any episode of hypotension or bradycardia was recorded. Nausea and vomiting were treated by additional i.v. administration of 4 mg of ondansetron, 10 mg of metoclopramide, and/or 10 mg of dexamethasone. Blood transfusions and other procedures followed the usual standards.

Vital signs (mean BP, HR, CVP, and oxygen saturation [SpO<sub>2</sub>]) were recorded before (baseline) and after preloading with the study fluid, 10 min after the subarachnoid block, at the end of the procedure, and after the resolution of the block.

Blood samples were obtained from the radial arterial cannula inserted into the radial artery. Baseline plasma electrolytes (sodium, potassium, and chloride), serum osmolality, and ABG analysis were assayed before fluid preloading (T0), in the recovery room (Tr), then 12, 24, 48, and 72 h postoperatively (Tp1, Tp2, Tp3, and Tp4, respectively). In addition, serum Na was measured just after preloading (T1) and at 1 h of resection (T2).
Hyponatremia was defined as a serum Na <130 mEq/L. Hypo-osmolality was defined as plasma osmolality <280 mOsm/kg.

TUR syndrome was defined as the presence of central nervous system disturbances such as nausea, vomiting, restlessness, pain, headache, dizziness, confusion, altered consciousness or even convulsions, and coma with circulatory abnormalities as chest pain, bradycardia, hypertension, or hypotension both intra- and postoperatively. The presence of at least one circulatory disorder and one neurological disorder is necessary for the diagnosis of TUR syndrome.

In case TUR syndrome was suspected, all i.v. fluids were stopped, bleeding points coagulated, and surgery was terminated as early as possible. Frusemide was administered in a dose of 1 mg.kg\(^{-1}\) intravenously. Supplemental 100% oxygen was administered with endotracheal intubation and ventilation if required. Active treatment regime was initiated with 3% HS at a rate of 1.2–2.4 mL.kg\(^{-1}\).h\(^{-1}\) aiming at a rise in serum sodium limited to 1–2 mmol/L/h until symptomatic improvement or serum sodium >125 mmol/L, with a maximum rise of serum Na not exceeding 12 mmol/L in 24 h. Seizures were managed by i.v. administration of midazolam 2–5 mg, thiopental sodium 100–200 mg, or even GA depending on the severity. Bradycardia and hypotension were treated accordingly with i.v. atropine and adrenergic drugs. Persistent hypertension was treated with i.v. infusion of nitroglycerin (0.5–10 μg.kg\(^{-1}\).min\(^{-1}\)) while keeping systolic BP >130 mmHg.

Operative time, weight of the resected prostate, total volume of the irrigation fluid used, doses of ephedrine as well as any intraoperative incidents were recorded.

The study fluid infusion was discontinued with the end of the surgery, and all patients were transferred to a high dependency care unit for observation. Patients were allowed to return to their wards only after confirmation that there were no abnormalities; otherwise, they were admitted to the postoperative ICU. The incidence of occurrence of TUR syndrome, need for ICU admission, postoperative ventilation, and total hospital stay were all noted.

Statistical analysis
The sample size was calculated based on a previous study conducted by Maulana et al.\(^{[6]}\) which stated that the weighted difference between the groups in serum sodium of patients undergoing TURP surgery, the main outcome variable in this study, was 3.3 ± 0.1 mEq/L. Considering a power of 80% and a 5% significance level, 17 patients at least would have been required accordingly for each group. We recruited twenty patients per group to avoid a loss of statistical power as a consequence of patients’ dropout. Sample size calculation was achieved using PS: Power and Sample Size calculation software version 3.1.2 (Vanderbilt University, Nashville, Tennessee, USA).

Data were coded and entered using the IBM SPSS Statistics for Windows, Version 25.0. (Armonk, NY: IBM Corp.). Data were summarized using mean and standard deviation (SD) in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between groups were done using ANOVA with post hoc test in normally distributed quantitative variables, while nonparametric Kruskal–Wallis test and Mann–Whitney U-test were used for nonnormally distributed quantitative variables. For comparison of serial measurements within each group, repeated measures ANOVA was used. For comparing categorical data, Chi-square test was performed. Exact test was used instead when the expected frequency is < 5. \(P < 0.05\) was considered as statistically significant.

Results
Sixty-three patients fulfilled the criteria of the study candidates for TURP at our medical institute. Two patients refused to participate in the study. The remaining sixty-one were randomized into three groups: 20 patients in Group A “4 mL.kg\(^{-1}\) HS group” \((n = 20)\), 20 patients in Group B “2 mL.kg\(^{-1}\) HS group” \((n = 20)\), and 21 patients in Group C “NS group.” one patient in this group was excluded because of protocol violation, \((n = 20)\) [Figure 1].

The three groups were similar with respect to their demographic (age, ASA status, and BMI) and surgical (duration of the procedure, ultrasound estimated prostate size and total volume of irrigating fluid used) data as well as having comparable preoperative laboratory work and hemodynamics (BP, HR, and CVP) \((P > 0.05)\). No patient needed a blood transfusion [Table 1].

The measured serum sodium level in both Groups A and B showed a significant rise only at T1 (postpreload) \((150.60 [2.82] and 145.45 [3.02], respectively) with subsequent statistical insignificance at all following readings compared to their baseline values \((139.65 [3.01] and 139.80 [3.46], respectively) \((P < 0.001)\); whereas in Group C, it showed a significant decline starting from T2 (at 1 h of resection) till Tp3 (48 h postoperative) (baseline: 140.25 [3.67], T2: 133.60 [3.41], Tr: 134.60 [3.23], Tp1: 134.45 [3.00], Tp2: 134.70 [3.02], and

| Procedure | Group A | Group B | Group C | P value |
|-----------|---------|---------|---------|---------|
| Age       | 61.55 (6.00) | 60.55 (6.26) | 61.85 (6.53) | 0.791 |
| BMI       | 28.17 (3.06) | 27.70 (2.96) | 27.89 (2.93) | 0.881 |
| ASA       | 9 (45%) | 7 (35%) | 8 (40%) | 0.945 |
| Procedure duration (min) | 57.00 (6.38) | 54.90 (7.37) | 58.25 (7.31) | 0.321 |
| Irrigation fluid volume (l) | 18.20 (3.21) | 19.40 (3.00) | 18.15 (3.83) | 0.418 |

Table 1: Demographic and surgical data

Data are presented as mean±SD and n (%). SD=Standard deviation, BMI=Body mass index, ASA=American Society of Anesthesiologists
All subjects eligible for TURP  

\( n = 63 \)

2 excluded: refused to participate

Enrolled in the study  

\( n = 61 \)

Randomized  

\( n = 61 \)

Group A (4 ml.kg\(^{-1}\) HS)  

\( n = 20 \)

Group B (2 ml.kg\(^{-1}\) HS)  

\( n = 20 \)

Group C (NS)  

\( n = 21 \)

Protocol violation  

\( n = 0 \)

PP = 20

\( \text{Figure 1: Consort flow diagram} \)

Tp3: 134.60 [2.96]) \((P < 0.001)\). Serum sodium also showed a significantly higher value in Group A compared to both Group B and C only at T1, with significantly lower values in Group C compared to either Group A or B starting from T1 till Tp3 [Table 2].

The plasma osmolality in both Groups A and B showed no significant differences at all reading points compared to their baseline values, whereas in Group C, it showed a significant decline from the baseline (T0: 290.23 [7.58]) starting from Tr (at recovery room) till Tp3 (Tr: 277.01 [10.16], Tp1: 283.20 [3.74], Tp2: 284.47 [3.93], and Tp3: 283.17 [3.48]) \((P < 0.001, 0.038, 0.040, \text{and } 0.002, \text{respectively})\). Plasma osmolality also showed insignificant differences at all points when compared to Groups A and B together, while significantly lower values were detected in Group C compared to either Group A or B starting from Tr till Tp3 [Figure 2-4].

The \( \text{PO}_{2} \) measurements were statistically insignificant either within each group compared with its baseline value or in between the groups at all times, with the exception of a significant decrease in Group C at Tr (102.90 [±7.66]) compared to its corresponding baseline value (113.35 [±17.75]) and to Group A and B values (112.20 [±14.22] and 115.05 [±17.93], respectively) at the same point \((P = 0.003, 0.04 \text{ and } 0.023, \text{respectively})\).

Other ABG parameters (pH, \( \text{PCO}_{2} \), and \( \text{HCO}_{3} \)) did not show significant variations at any of the measuring points. We did not observe differences in all the assessed laboratory work (Complete Blood Count, liver and kidney functions, K, Cl, blood sugar, and anion gap) among the three groups throughout the entire study period.

The hemodynamic variables in Group A and B remained stable and did not show a significant difference, neither in between these two groups nor in comparison with their baseline values, at any of the measuring points, in terms of MBP, HR, and CVP. In Group C, the MBP and CVP declined postblock followed by a notable rise postresection and in the recovery room, accompanied by a decrease in the HR which was detected also postresection and in the recovery room; these Group C hemodynamic changes were statistically significant compared to the baseline values and in relation to either of the other two groups [Figures 2-4].

Hypernatremia was detected in six patients of Group A only, while hyponatremia occurred in five patients of Group C alone [Table 4].

The incidence of hemodynamic instability was higher in Group C. Six patients experienced hypotension and bradycardia, requiring vasopressor treatment; hypertensive episodes occurred in five patients of this group, and a hypervolemic state was noted in seven patients of the same group [Table 4].

Nausea and vomiting occurred more frequently in Group C, while the incidence of shivering was relatively close in between the groups [Table 4].

In respect to the TURP syndrome manifestations (namely headache, dizziness, restlessness, and confusion), they were
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Serum sodium measured in mEq/L. Data are presented as Mean±SD. *Denotes statistical significance. SD=Standard deviation

Table 2: Serum sodium level

|       | Group A     | Group B     | Group C     | A versus B | A versus C | B versus C |
|-------|-------------|-------------|-------------|------------|------------|------------|
| T0    | 139.65 (3.01) | 139.80 (3.46) | 140.25 (3.67) | 1          | 1          | 1          |
| T1    | 150.60 (2.82) | 145.45 (3.02) | 140.55 (3.03) | <0.001*    | <0.001*    | <0.001*    |
| T2    | 141.50 (4.72) | 140.45 (3.47) | 133.60 (3.41) | 1          | <0.001*    | <0.001*    |
| Tr    | 141.15 (4.48) | 138.90 (3.08) | 134.60 (3.23) | 0.198      | <0.001*    | 0.001*     |
| Tp1   | 140.45 (2.82) | 139.00 (2.71) | 134.45 (3.00) | 0.338      | <0.001*    | 0.001*     |
| Tp2   | 140.35 (2.98) | 139.05 (2.65) | 134.70 (3.06) | 0.486      | <0.001*    | 0.001*     |
| Tp3   | 140.70 (3.45) | 139.05 (2.860) | 134.60 (2.96) | 0.294      | <0.001*    | 0.001*     |
| Tp4   | 139.95 (2.70) | 138.90 (2.99) | 138.35 (3.23) | 0.811      | 0.286      | 1          |

Table 3: Plasma osmolality

|       | Group A     | Group B     | Group C     | A versus B | A versus C | B versus C |
|-------|-------------|-------------|-------------|------------|------------|------------|
| T0    | 290.55 (6.95) | 290.40 (5.77) | 290.23 (7.58) | 1          | 1          | 1          |
| Tr    | 293.28 (9.16) | 288.81 (6.88) | 277.01 (10.16) | 0.345      | <0.001*    | 0.001*     |
| Tp1   | 293.32 (7.65) | 289.58 (6.18) | 283.20 (7.34) | 0.171      | <0.001*    | 0.005*     |
| Tp2   | 292.93 (8.09) | 289.44 (6.05) | 284.47 (3.93) | 0.250      | <0.001*    | 0.045*     |
| Tp3   | 293.46 (8.03) | 290.50 (5.81) | 283.17 (3.48) | 0.385      | <0.001*    | 0.001*     |
| Tp4   | 292.17 (6.80) | 290.50 (5.81) | 289.43 (6.24) | 1          | 0.524      | 1          |

Plasma osmolality measured in mOsm/kg. Data are presented as Mean±SD. *Denotes statistical significance. SD=Standard deviation

Figure 2: Mean blood pressure (mean blood pressure). *Denotes statistical significance compared to the baseline values and in relation to either of the other two groups

Figure 3: Heart rate. *Denotes statistical significance compared to the baseline values and in relation to either of the other two groups

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The diagnosis of TURP syndrome was confirmed in only five patients, all were in Group C. Postoperative ICU admission was needed for seven patients of C Group, five of which required temporary assisted ventilation. The overall total hospital stay was longer for Group C patients with a mean (SD) of 3.15 (0.93) days compared to 1.95 (0.39) and 1.8 (0.41) for Group A and B patients, respectively (P < 0.001) [Table 4].

**Discussion**

TURP is regarded as the most common surgical procedure performed on male patients aging more than 60 years.\(^1\) Nonconductive irrigation fluid is necessary for the operating field during the use of a monopolar electric resectoscope.\(^2\) The excessive absorption of this hypotonic, electrolyte-free, distension solution through the opened venous sinuses of the prostatic plexus can cause fluid overload and dilutional hyponatremia.\(^3,7\) TUR syndrome has a multifactorial pathophysiology, which is better understood now but still considered a risk.\(^2\) In general, TUR syndrome is diagnosed with a serum sodium concentration of ≤125 mmol/L with simultaneous clinical cardiovascular and neurological manifestations. However, symptoms of TUR syndrome may experientially occur in patients having serum sodium levels >125 mmol/L.\(^8\) In spite of the current surgical and anesthetic management improvements, 2.5%–20% of TURP patients show one or more TUR syndrome manifestations and 0.5%–5% die perioperatively.\(^9\) It may present early (up to 15 min) after resection starts or late (up to 24 h.) after the operation.\(^11\)
When patients are conscious and alert, the mental status changes may be the first sign of TUR syndrome. Sedation or general anesthesia may mask the symptoms.\cite{10} Spinal anesthesia without sedation (awake TURP) is considered to be the anesthetic technique of choice, permitting the anesthetist to monitor the patient’s conscious level and to early observe any neurological symptoms.\cite{11,12}

Considering that prophylaxis is generally preferable than treatment, we investigated different strategies for the prevention and management of TURP syndrome. We compared preloading with HS instead of conventional NS for patients undergoing TURP endoscopy, and we further investigated the sufficiency and safety of low-dose (2 mL.kg\(^{-1}.h^{-1}\)) infusion rate rather than the high-dose (4 mL.kg\(^{-1}.h^{-1}\)) infusion rate of the hypertonic solution.

Our results showed a far more stable pattern of serum sodium level in both of the HS preloading groups with no statistical difference from the baseline (apart from a postpreloading rise) and without any reported incidence of hyponatremia in either group, compared to five cases in the NS group, which patients also had a statistically significant low sodium level starting 1 h postresection and extending for 48 h postoperatively in relation to the baseline and the other groups. Furthermore, hyponatremia was noted in six patients of the high-dose group, while its incidence in the low-dose group was nil. Plasma osmolality followed the same pattern as serum sodium at all assessment points of its calculation.

Kato and Goto\cite{13} also compared the infusion of 4 mL.kg\(^{-1}.h^{-1}\) of HS 3% (HS group) with 8 mL.kg\(^{-1}.h^{-1}\) of LR’s solution (LR group) during TURP. Plasma sodium, chloride, and osmolality measured in the recovery room were significantly increased in the HS group; however, the day after surgery, all returned to preanesthetic levels. In contrast, plasma sodium decreased significantly in the LR group and this lower value persisted for 1 day.

Serum sodium concentration changes of >7.4 mmol/L and >7% could predict the occurrence of neurological and cardiovascular manifestations. As normal serum sodium concentrations range from 135 to 145 mmol/L, manifestations may clinically develop even in patients with serum sodium levels >125 mmol/L.\cite{8} Dilutional hyponatremia may further be aggravated by electrolyte losses into accumulations of irrigation solution extravasated interstitially in the periprostatic and retroperitoneal spaces.\cite{12,14}

Hemodynamic instability was only found in Group C patients, showing a biphasic pattern, where low MBP and CVP values were observed postblock followed by a postresection and recovery room rise, with a simultaneous drop in HR which was
detected also postresection and in the recovery room. Reported cases of hypotension, bradycardia, hypertensive episodes, or hypervolemia occurred only among this group patients, with a statistically significant incidence.

Despite that hemodynamic effects induced by spinal anesthesia are usually well tolerated in young healthy patients, the prevention of hypotension is commonly achieved using fluid preloading for older ones. Again, the administration of excess free water is to be avoided in patients with cardiovascular restrictions. Isotonic crystalloids, the fluids commonly used to expand the plasma volume, may be ineffective as about 75% of the solution diffuses extravasicularly into the interstitial space within a short time. Colloids have a slightly higher osmotic pressure than Ringer’s solution or saline. A plasma substitute volume ≥500 mL infused during the operation was noted to be a significant risk factor for TUR syndrome in Nakahira et al.’s study. Anaphylactic reactions may also occur with colloids administration; this risk is rare but cannot be acceptable for prophylaxis.

In contrast, HS is more effective, as it can remain in the intravascular space longer than crystalloid solutions and induces instantaneous mobilization of endogenous fluid along the osmotic gradient from the intracellular to the extracellular compartment. In addition, Mouren et al. found that HS increases myocardial contraction and induces vasoconstriction. This effect of a hypertonic solution may explain the improved cardiac output. A previous study showed similar findings, as prehydration with HS during TURP reduced the occurrence of spinal-induced hypotension and reduced the phenylephrine use to maintain BP.

During TURP, irrigation fluid absorption rates can reach 200 mL/min. The rapid absorption of these large volumes can cause hypertension with reflex bradycardia. Moreover, acute hypo-osmolality can cause cerebral edema increasing the intracranial pressure, which results in bradycardia and hypertension by the Cushing reflex. Subsequently, the equilibration of hypertonic fluid with the extracellular fluid compartment may precipitate hypotension in association with hypovolemia. Hypotension and hypovolemia may be compounded by the sympathetic block of spinal anesthesia. This secondary phase may be observed at the end of the operation.

Such fluctuating intravascular fluid volume can explain the intraoperative initial hypervolemia and hypertension followed by the later hypovolemia and severe hypotension, which exactly occurred in our Group C patients. On the other hand, pretreatment with HS was expected to decrease the degree of dilutional hyponatremia. This approach might limit the occurrence of TURP syndrome caused by hypo-osmolality but was feared to promote an increase in the incidence and severity of the syndrome’s hypervolemic manifestations. This eventually did not occur in our Group A and B patients who received HS preloading, proving its safety and efficacy regarding these hemodynamic concerns.

The only significant variation in the ABG analysis was in the measured PO₂, noticed in the NS group at the immediate postoperative reading in the recovery room, demonstrating a relatively lower value compared to the baseline and the other two groups. This can be attributed to the hypervolemia occurring postresection due to irrigation fluid absorption and the accompanying hyponatremia, both leading to an extravascular fluid shift and pulmonary congestion, especially with the recorded higher CVP and lower serum sodium readings, which show a particular statistical significance in Group C compared to the HS groups at that time.

With circulatory overload, the absorbed fluid volume causes dilution of serum proteins decreasing the oncotic pressure of blood. With the concurrent elevation of BP, this drives fluid from the vascular to interstitial space leading to pulmonary and cerebral edema. In Sethi et al. case report, their patient presented with symptoms of chest wall tightness and difficulty in breathing. This could be due to the absorption of hypotonic irrigating fluid into the lungs, resulting in bilateral basal crepitations and SpO₂ drop. Under general anesthesia, the early signs are related to the cardiorespiratory system and include a decrease in SpO₂ and ECG changes.

There is more chance of water intoxication during TURP with the infusion of the isotonic solution in an excess amount to prevent hypotension together with the absorption of irrigation fluid during resection. HS (3% NaCl) has an osmolality of 1026 mOsmol/L, which is about three times that of plasma and its infusion, unlike NS, is not associated with free water intoxication.

Järvelä et al. were concerned with the development of hypokalemia after the rapid expansion of the plasma volume with the potassium-free HS, which might provoke arrhythmia. However, hypokalemia was not seen in any of their study patients, as in none of ours.

At the end of our study, all the diagnosed cases of TURP syndrome (based on the presence of at least one circulatory disorder and one neurological disorder) were only prevalent within Group C patients. Subsequently, higher statistical rates of ICU admission and mechanical ventilation were recorded among the NS group, which eventually lead to a longer hospital stay than Group A and B patients.

Hyponatremia and hypo-osmolality appear to be the principal culprits contributing to the symptomatic changes seen with TURP syndrome. TURP-associated acute hyponatremia should be corrected rapidly to avoid cardiovascular and neurological complications. The incidence of serum sodium concentration lower than 125 mmol/L with TURP may reach 15% with a 40% mortality when hyponatremia becomes symptomatic.

No adverse events attributable to HS or side effects relating to study medications were observed in our trial.
The limitation to our study is the lack of precise neurological scores, which may be explained by the diversity of symptoms and the potential cardiovascular and respiratory compromise, requiring aggressive interventions such as converting from regional to general anesthesia.

CONCLUSION
In summary, our current study concluded that the prophylactic administration of HS, adopted as the pre- and intraoperative fluid infusion during TURP, is superior to the traditional treatment of an occurred life-threatening TURP syndrome, and that the low dose (2 mL.kg$^{-1}$.h$^{-1}$ of 3% HS) is effective and sufficient with no adverse effects or risk of contrary potential hypernatremia that might be encountered by a high-dose regimen. The merits of HS arise from the prevention of occurrence of both the TURP syndrome, the most feared complication of this surgery, and the subarachnoid block-induced hypotension, providing a safer strategy and improving the overall outcome in this clinical situation considering the patients’ particular pathophysiology.

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Conflicts of interest
There are no conflicts of interest.

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