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Hypertonic saline for intraoperative fluid therapy in transurethral resection of the prostate

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Abstract: We tested hypertonic saline solution (HS) to determine its effectiveness in surgical procedures for prostatic hypertrophy. We randomly selected 40 patients undergoing elective transurethral resection of the prostate for either infusion of HS (3% NaCl) at 4 ml·kg^{-1}·min^{-1} (HS group) or lactated Ringer's solution (LR) at 8 ml·kg^{-1}·min^{-1} (LR group). Anesthesiologists regulated the intraoperative infusion rate as needed to maintain blood pressure. There were no differences in systolic blood pressure, heart rate, central venous pressure, or arterial blood oxygenation between the two groups. In the HS group, plasma sodium, chloride, and osmolality, measured in the recovery room, were significantly increased; however, they returned to preanesthetic levels the day after surgery. In the LR group, in contrast, plasma sodium decreased significantly and this lower value persisted for 1 day. An osmolar gap exceeding 10 mOsm·kg^{-1} was observed in 2 patients in the HS group, but plasma sodium remained at normal values. However, in the 1 patient in the LR group whose osmolar gap exceeded 10 mOsm·kg^{-1}, plasma sodium was 115 mEq·l^{-1}. HS, at a low dose, is useful in the intraoperative management of transurethral resection of the prostate.

Key words: Hypertonic saline, Intraoperative fluid therapy, Transurethral resection of the prostate

Introduction

The usefulness of hypertonic saline (HS) solution for the treatment of burns [1], hemorrhagic shock [2], and severe trauma before arrival at hospital [3] has been reported in clinical studies. The primary mechanism underlying the effect of this solution is the volume expansion caused by the osmotic movement of fluid from intracellular and interstitial spaces into the intravascular space [4]. In addition to providing volume expansion, HS may also augment cardiac performance by increasing cardiac contractility [5], reducing afterload [6], and increasing venous return, through a decrease in venous capacitance [7]. These observations suggest that HS could be useful for intraoperative fluid therapy.

Transurethral resection of the prostate (TURP) is a widely used surgical procedure in older male patients. The procedure entails a high risk of water intoxication being induced by absorption of irrigating solution into the circulatory system. Spinal and epidural anesthesia have been commonly used for TURP; however, both these anesthetic methods may lead to hypotensive complications due to sympathetic nerve blockade. It has been reported that older patients undergoing TURP frequently exhibited preoperative circulatory and/or pulmonary complications [8]. Overhydration in these patients increases postoperative complications such as cardiac failure and respiratory disturbances [9].

These findings suggest that HS solution would be more effective than lactated Ringer's solution, the most commonly used agent for intraoperative fluid therapy during TURP, in maintaining blood volume, and that the solution could decrease perioperative complications in TURP, particularly in regard to pulmonary failure and hyponatremia. In this study, we examined the safety and effectiveness of hypertonic saline solution in surgical procedures for prostatic hypertrophy.

Methods

Following approval given by the Institutional Investigational Review Board, informed consent was obtained from 40 patients undergoing elective TURP. There were no criteria excluding the use of hypertonic saline.

All patients were premedicated with diazepam (0.1 mg·kg^{-1}, orally) 3 h prior to surgery. Upon arrival at

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the operating room, patients were randomly selected for either infusion of 3% NaCl at $4 ml \cdot kg^{-1} \cdot min^{-1}$ (HS group, $n = 20$) or lactated Ringer's solution at $8 ml \cdot kg^{-1} \cdot min^{-1}$ (LR group, $n = 20$). Anesthesiologists regulated the intraoperative infusion rate as needed to maintain more than 80% of the preoperative systolic blood pressure. Criteria for discontinuing this infusion in the HS group were: plasma sodium $>155 mEq \cdot l^{-1}$ or serum osmolality $>320 mOsm \cdot kg^{-1}$ [10]. In patients whose values fit either of these criteria, the infusion of 3% NaCl was changed to lactated Ringer's solution.

Epidural puncture was performed at the L_3–L_4 level and 10–12ml of 1%–1.5% mepivacaine was administered through an epidural catheter. Half the dose of the primary injection of mepivacaine was given every 45–60min. After epidural puncture, a 22-G catheter was inserted into the radial artery for arterial pressure monitoring and blood sampling. A central venous pressure (CVP) catheter was inserted via the right antecubital vein. Arterial oxygen saturation (SpO_2) was determined by pulseoxymetry and electrocardiogram (ECG) was monitored. 3% D-Sorbitol solution (Uromatic S, Baxter Healthcare Co., Deerfield, IL, USA) was used for irrigation of the urinary bladder. After surgery, all patients were moved to the recovery room for at least 30min. The HS infusion was discontinued immediately after patients were admitted to the recovery room. When we had confirmed that there were no abnormalities, the patients were returned to their ward and were allowed to drink water 3h later.

Blood samples were obtained in each patient from the radial artery. Plasma electrolytes and serum osmolality (Mosm) were assayed at the time of arterial cannulation (S_1), every 30min during TURP (S_2, S_3, and S_4), in the recovery room (S_{RR}), and 1 day after surgery (S_{P01}). The osmolar gap, i.e., the difference between measured serum osmolality (Mosm) and calculated osmolality (Cosm) was determined [11]. Cosm and the osmolar gap were defined as:

$$\text{Cosm} = 2 \times \text{Na} + \text{glucose}/18 + \text{BUN}/2.8$$
$$\text{Osmolar gap} = \text{Mosm} - \text{Cosm}$$

The osmolar gap serves as an indicator of absorption of the irrigating solution [12].

Plasma aldosterone, anti-diuretic hormone (ADH), and human atrial natriuretic peptide (hANP) were assayed at S_1 and S_{RR}.

Values are expressed as means ± SD. A two-tailed Mann-Whitney test was used to determine differences between the two groups. The rates of vasectomy and the incidence of intraoperative hypotension treated with vasopressors were compared by χ^2 test. Comparison within groups was made by the Friedman test followed by the Wilcoxon test, as indicated. A value of $P < 0.05$ was determined as significant.

Table 1. Demographic data

Group	HS	LR
Number of patients	20	20
Age (years)	70.2 ± 6.8	71.0 ± 7.3
Height (cm)	162.7 ± 7.1	164.5 ± 5.8
Weight (kg)	57.0 ± 12.0	62.2 ± 11.4
Preoperative complications (n)		
Cardiovascular	12	9
Respiratory	4	3
Other	4	1

HS, hypertonic saline solution group; LR, lactated Ringer's solution group.

Table 2. Intraoperative findings

Group	HS	LR
Duration of TURP (min)	54.7 ± 24.2	65.1 ± 31.8
Volume of resected prostate (g)	17.1 ± 7.3	21.0 ± 15.7
Volume of irrigating fluid (l)	22.9 ± 9.5	25.4 ± 12.7
Vasectomy (n)	10/20	13/20
Duration of vasectomy (min)	20.4 ± 14.6	15.7 ± 6.1
Incidence of intraoperative hypotension treated with vasopressors	10/20 (50%)	10/20 (50%)
Volume of intraoperative infusion (ml)		
Start to S_1	230 ± 116§§	440 ± 216
Start to S_{RR}	805 ± 351§§	1620 ± 622
Systolic blood pressure (mmHg)		
At S_1	129.7 ± 34.7	134.2 ± 22.7
At S_2	129.9 ± 32.0	117.6 ± 25.2**
At S_{RR}	130.0 ± 26.2	126.4 ± 25.4

§§ $P < 0.01$ compared with the LR group; ** $P < 0.01$ compared with S_1 value in each group.
HS, hypertonic saline solution group; LR, lactated Ringer's solution group; TURP, transurethral resection of the prostate. S_1, arterial cannulation; S_2, 30min in TURP; S_{RR}, recovery room.

Table 3. Blood chemistry

		C	S_1	S_2	S_{RR}	S_{P01}
Na	HS	141.4 ± 2.1	142.9 ± 2.6§§**	143.5 ± 3.9§§*	145.0 ± 4.4§§**	140.6 ± 2.6§
($mEq \cdot l^{-1}$)	LR	142.3 ± 2.3	139.9 ± 2.4**	138.8 ± 2.2**	136.1 ± 5.8**	138.6 ± 2.4*
K	HS	4.2 ± 0.3§	4.1 ± 0.4	3.9 ± 0.4**	4.1 ± 0.4	4.1 ± 0.5
($mEq \cdot l^{-1}$)	LR	4.0 ± 0.3	4.1 ± 0.2	3.9 ± 0.4	4.0 ± 0.4	4.1 ± 0.4
Cl	HS	105.7 ± 3.4	109.5 ± 3.7§§**	112.8 ± 4.5§§**	114.3 ± 5.1§§**	105.9 ± 3.4§
($mEq \cdot l^{-1}$)	LR	105.1 ± 3.1	106.3 ± 3.7	106.8 ± 3.1*	104.1 ± 4.9	103.3 ± 3.2*
Mosm	HS	—	295.6 ± 7.0§§	298.2 ± 6.1§§	300.7 ± 7.1§§¶¶	289.3 ± 4.2§§¶¶
($mOsm \cdot kg^{-1}$)	LR	—	286.5 ± 4.3	284.3 ± 3.5¶¶	282.6 ± 4.9¶¶	284.1 ± 3.4¶¶

* $P < 0.05$; ** $P < 0.01$, compared with C value in each group; § $P < 0.05$; §§ $P < 0.01$, compared with the LR group; ¶ $P < 0.05$; ¶¶ $P < 0.01$, compared with S_1 value in each group on Mosm.

Mosm, measured serum osmolality; HS, hypertonic saline solution group; LR, lactated Ringer's solution group; C, 1 day before surgery; S_1, arterial cannulation; S_2, 30 min in TURP; S_{RR}, recovery room; S_{P01}, 1 day after surgery.

Table 4. Findings in patients who had an osmolar gap exceeding $10\,mOsm \cdot kg^{-1}$

Patients number and group	No. 16	No. 33	No. 35 (LR)
Duration of TURP (min)	45	40	60
Volume of resected prostate (g)	6	12	20
Volume of irrigating fluid (l)	16	20	26
Systolic blood pressure during study (mmHg)			
Max	155	148	126
Min	112	93	110
Na during study ($mEq \cdot l^{-1}$)			
Max	144	143	141
Min	134	141	115
Measured serum osmolality during study ($mOsm \cdot kg^{-1}$)			
Max	303	306	286
Min	296	293	273
Osmolar gap during study ($mOsm \cdot kg^{-1}$)			
Max	18.0	11.9	34.1
Min	−0.6	−4.9	−9.6

HS, hypertonic saline solution group; LR, lactated Ringer's solution group.

Results

There were no significant differences between the HS and LR groups in age, height, weight, or preoperative complications (Table 1). Many patients had cardiovascular and/or pulmonary diseases (HS group, 13/20; LR group, 12/20). Other complications were diabetes mellitus, renal insufficiency, liver dysfunction, or cerebral infarction.

During surgery, the HS infusion was not discontinued in any patients. Blood sampling was performed every 30 min during TURP; however, most surgery was finished within 60 min. Therefore, we statistically analyzed the data for S_1, S_2, S_{RR}, and S_{P01}.

There were no significant differences between the HS and LR groups in the duration of surgery, weight of resected prostate, or the volume of irrigation fluid (Table 2). There were no significant differences in systolic blood pressure, diastolic blood pressure, heart rate, CVP, or SpO_2 between the two groups. However, in the LR group, systolic blood pressure was significantly decreased at S_2 during surgery compared to S_1 ($P < 0.01$) (Table 2). There were no significant differences between the groups in the number of patients who received vasopressors, ephedrine, and/or dopamine (Table 2).

There was a significant difference in the infusion volume at S_1 between the two groups (Table 2). This is because the fluid infusion was commenced about 20 min before blood sampling at S_1.

In the HS group, plasma sodium increased significantly at S_1, S_2, and S_{RR}, compared to the value 1 day before surgery and it was significantly higher than in the LR group at these three points, but levels were lowered to the value before surgery at S_{P01} (Table 3). In the LR group, plasma sodium decreased significantly throughout the study, compared with the value 1 day before surgery. In the HS group, changes in plasma chloride were similar to those in sodium and there were significant differences between the two groups both during and after surgery.

In both groups, plasma potassium levels at S_2 were significantly lower than at S_1; however, there were no differences between the two groups. Mosm decreased significantly at S_2, S_{RR}, and S_{P01} in the LR group. In contrast, Mosm increased significantly during surgery in the HS group and Mosm values were significantly different for the two groups throughout the study (Table 3).

There was an osmolar gap exceeding $10\,mOsm \cdot kg^{-1}$ in two patients in the HS group and in one patient in the LR group (Table 4). However, plasma sodium remained at normal values in the two patients in the HS group, while, in contrast, plasma sodium was $115\,mEq \cdot l^{-1}$ in the LR group patient. However, these patients showed no complications.

In the HS group, plasma sodium concentration exceeded $150\,mEq \cdot l^{-1}$ (maximum $152\,mEq \cdot l^{-1}$) in three patients. The hypernatremia and hyperosmolality in these patients returned to normal levels 1 day after surgery.

Plasma ADH concentrations in the HS group were significantly higher than in the LR group (Table 5), but there were no significant differences in plasma aldosterone concentrations between the two groups. The value for hANP at S_1 in the HS group was significantly higher than in the LR group.

Arterial pH and HCO^-_3 decreased significantly during surgery and the recovery period, and they were significantly lower in the HS than in the LR group (Table 6). Base excess decreased in both groups, but it was greater in the HS group. The anion gap decreased during surgery in both groups; however, there was no significant difference between the two groups.

Table 5. Antidiuretic hormone (ADH), aldosterone, and human atrial natriuretic hormone (hANP) levels

	Group	S_1	S_{RR}
ADH	HS	8.9 ± 18.7§§	10.7 ± 10.3§
($pg \cdot ml^{-1}$)	LR	5.3 ± 14.7	8.1 ± 12.7
Aldosterone	HS	4.9 ± 3.6	5.4 ± 6.7
($ng \cdot ml^{-1}$)	LR	5.6 ± 4.5	7.0 ± 6.9
hANP	HS	78.9 ± 24.9§	78.5 ± 31.7
($pg \cdot ml^{-1}$)	LR	67.3 ± 35.1	70.9 ± 43.9

§ $P < 0.05$; §§ $P < 0.01$; compared with LR group in each period; HS, hypertonic saline solution group; LR, lactated Ringer's solution group; S_1, arterial cannulation; S_{RR}, recovery room.

Discussion

The patients in whom TURP was performed were older men (overall mean; 70.6 ± 7.0 years) who had a high incidence of preoperative complications (27/40; 67.5%). In such patients, intraoperative overhydration entails a high risk of causing cardiopulmonary complications. In this study, HS group patients required 40% less fluid than LR patients perioperatively, but blood pressure changes and vasopressors requirement were similar in the two groups.

Baraka et al. [13] compared 0.9% isotonic saline ($7\,ml \cdot kg^{-1}$) and 3% HS ($7\,ml \cdot kg^{-1}$) before spinal anesthesia in patients undergoing TURP. They reported that prehydration with HS resulted less in hypotension after spinal anesthesia. In contrast, in this study, there was no beneficial effect on the maintenance of blood pressure with a smaller volume used for prehydration ($1.8\,ml \cdot kg^{-1}$) than in Baraka's study. These different results may reflect differences in anesthesia methods and in fluid volumes. We administered a larger volume of lactated Ringer's solution than of the HS solution. However, a recent study [14] reported that a larger volume of lactated Ringer's solution was required to prevent hypotension associated with central neural block. Accordingly, it appears that 3% NaCl solution $4\,ml \cdot kg^{-1} \cdot h^{-1}$ may be as effective as lactated Ringer's solution $8\,ml \cdot kg^{-1} \cdot h^{-1}$ in TURP.

The absorption of irrigating solutions, known as the TURP syndrome, is one of the major complications of TURP. With the use of osmotically active irrigating solutions, the incidence of severe CNS complications has, consequently, been reduced. However, acute hyponatremia and overhydration are still problems [15]. The osmolar gap, i.e., the difference between measured

Table 6. Acid base and anion gap values

		S_1	S_2	S_{RR}	S_{P01}
pH	HS	7.415 ± 0.049§	7.384 ± 0.042*§§	7.366 ± 0.035**§§	7.425 ± 0.032
	LR	7.426 ± 0.017	7.419 ± 0.045	7.404 ± 0.039**	7.428 ± 0.023
HCO_3^-	HS	25.2 ± 3.2	24.3 ± 3.4*	23.0 ± 3.3**	25.6 ± 2.9
($mEq \cdot l^{-1}$)	LR	25.2 ± 1.8	25.1 ± 1.6	24.2 ± 1.8*	25.4 ± 1.5
Base excess	HS	0.6 ± 2.8	−0.7 ± 2.7**§	−2.1 ± 2.6**§	2.1 ± 2.7*
($mEq \cdot l^{-1}$)	LR	1.2 ± 1.8	0.7 ± 1.4	−0.2 ± 1.5**	1.8 ± 1.4
Anion gap	HS	12.2 ± 2.8	10.2 ± 3.8*	11.8 ± 3.4	13.2 ± 3.3*
($mEq \cdot l^{-1}$)	LR	12.5 ± 2.7	10.8 ± 2.7**	11.7 ± 3.3	13.9 ± 2.8

* $P < 0.05$; ** $P < 0.01$, compared with S_1 value in each group; § $P < 0.05$; §§ $P < 0.01$, compared with LR group.
HS, hypertonic saline solution group; LR, lactated Ringer's solution group; S_1, arterial cannulation; S_2, 30 min in TURP; S_{RR}, recovery room; S_{P01}, 1 day after surgery.

and calculated osmolality, is a useful indicator of irrigating solution absorption [12]. In this study, three patients showed an osmolar gap exceeding $10\,mOsm \cdot kg^{-1}$ (one patient in the LR group, and two in the HS group). Plasma sodium decreased to $115\,mEq \cdot l^{-1}$ in the one patient in the LR group; however, the two patients in the HS group exhibited no plasma sodium changes (Table 4). These findings suggest that HS solution prevented acute hyponatremia following absorption of the irrigating solution.

Several studies have reported using HS solution for intraoperative fluid therapy—in the treatment of intraoperative blood loss [10], in abdominal aortic surgery [16], and in cardiac surgery [17]. Potential limitations of HS therapy include hypernatremia, hyperchloremia, hyperosmolality, and hypokalemia [16]. Severe electrolyte imbalances could result in disorientation, coma, seizures, or cardiac arrhythmia. In this study, maximum elevations of plasma sodium and osmolality in the recovery room were $152\,mEq \cdot l^{-1}$ and $316\,mOsm \cdot kg^{-1}$, respectively. These changes returned to preanesthetic values within 1 day, with no special treatment being given. Holcroft et al. [10] used 3% NaCl ($4\,ml \cdot kg^{-1}$) as a resuscitation solution for intraoperative hemorrhagic shock. In their study, mean serum sodium increased to $152\,mEq \cdot l^{-1}$, but was normalized within 24 h and there were no complications due to hypertonicity of the solution. Shackford et al. [18] demonstrated that increases in serum sodium resolved within 48 h as a result of increased sodium excretion and reduction in free water excretion. The development of central pontine myelinolysis following serum hyperosmolality has been reported [19], but this hyperosmolality was extreme ($362\,mOsm \cdot kg^{-1}$ or more) and prolonged (3 days or more). These values did not occur during perioperative HS infusion in this study.

Dilution acidosis with hyperchloremia occurred in the HS group. This acidosis may be a result of acute hyperosmolality [20]. The acidosis resolved with no treatment on the 1st postoperative day. Wisner et al. [21] reported that HS solution decreased intracellular pH without associated changes in high-energy phosphate, this decrease being a result of cell dehydration rather than of metabolic dysfunction.

In our study, plasma potassium was significantly decreased during TURP in the HS group. Hypokalemia has previously been reported following natriuretic diuresis, which increases potassium excretion [18]. Although we found that changes in serum potassium remained within normal limits, we believe that frequent measurements of serum electrolytes are necessary during TURP.

There are few reports on hormonal changes during HS infusion in surgical patients. In this study, ADH and hANP were higher in the HS group than in the LR group, but aldosterone levels did not change in either group. The release of ADH and hANP could be induced by hyperosmolality and volume expansion. In agreement with our results, Kimura and Takaori. [22] reported that serum ADH level increased significantly in patients undergoing TURP who received hypertonic lactated Ringer's solution. However, these hormonal changes were minor compared with findings in patients who had cardiac surgery [23,24].

In conclusion, the volume of HS infused was half that of isotonic Ringer's lactate solution; however, there were no significant differences in hemodynamics between the two groups. In the LR group, severe hyponatremia was observed in one patient who had an osmolar gap exceeding $10\,mOsm \cdot kg^{-1}$, whereas, in contrast, plasma sodium was within normal levels in the HS group even though the osmolar gap had increased. These findings suggest that 3% hypertonic saline is a safe alternative to isotonic crystalloid therapy in the fluid management of transurethral surgery.

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