Efficacy and Safety of Preoperative Administration of Half Molar Hypertonic Sodium Lactate during Transurethral Resection of Prostate (TURP)

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Abstract

***Background*: Water irrigation during transurethral resection of prostate (TURP) often caused hyponatremia, hypoosmolality, and decreasing of pH called TURP syndrome. Current standard fluid therapy in TURP still could not prevent or correct TURP syndrome. This study was aimed to assess the efficacy and safety of preoperative hypertonic sodium lactate (HSL) infusion in maintaining plasma sodium level, osmolality, arterial pH and hemodynamic parameters during TURP compared to normal saline (NS).**

***Methods*: In this prospective randomized controlled double blind study, 22 patients underwent TURP surgery under spinal anesthesia were assigned into 2 groups with 11 patients in each group. HSL or NS were administered before spinal anesthesia with loading dose 4 mL.kgBW^{-1} within 20 minutes. During procedure NS with 2-4 mL.kgBW^{-1}.hr^{-1} were infused as maintenance in both groups.**

***Result*: Postoperative mean of sodium level and osmolality in HSL group was significantly different compared to NS group (142.2±2.0 mEq/L vs 138.9±2.1 mEq/L, p<0.05, and 294.6±3.5 mOsm/kg vs 290.6±3.2 mOsm/kg, p<0.05) respectively. Postoperative pH in HSL group was 7.433±0.04, whereas in NS group was 7.356±0.05 (p<0.05). Evolution of hemodynamic parameters was better in HSL group. Five of 11 patients in NS group need ephedrine injection due to decreased of blood pressure >30% after spinal anesthesia, whereas none of patients in HSL group need ephedrine.**

***Conclusion*: Preoperative administration of hypertonic sodium lactate in TURP was better in maintaining plasma sodium level, osmolality, arterial pH and also hemodynamic parameters than normal saline.**

Key words: TURP syndrome, hyponatremia, hypoosmolality, acidosis, hemodynamic, hypertonic sodium lactate.

Introduction

Transurethral resection of prostate (TURP) is a gold standard for the treatment of benign prostate hyperplasia (BPH). Absorption of water irrigation during TURP may disturb circulatory and neurological system and lead to TURP syndrome. Incidence rate of TURP syndrome is about 0.5-7% (1) and its mortality rate is 0.2-0.8%. (2,3)

Significant hyponatremia during TURP occurs in 11-41% of patients. The incidence of plasma sodium level less than 125 mmol.L^{-1} after TURP may reach up to 15% with mortality rate of 40%. (4) Severe hyponatremia results in hemolytic and renal failure, respiratory compromise, electrocardiogram

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changing and cardiovascular depression, seizure, coma, and death. (5) Absorption of water irrigation also causes hypoosmolality which could cause cerebral and pulmonary edema. (6) Dilution of sodium concentration in plasma also decreases strong ion difference (SID) and causes acidosis known as TURP acidosis. (7)

Some studies have been conducted to find out the proper solution that could maintain hemodynamic status and prevent hyponatremia, hypoosmolality, and arterial pH during TURP. Efficacy of hypertonic saline solution with varying osmolarity during TURP procedure has been widely investigated. Baraka et al investigated the efficacy of hypertonic saline 3% to maintain stable hemodynamic during TURP under spinal anesthesia. (8) Kato used hypertonic saline 3% to prevent the decrease of sodium level and osmolality during TURP. (9) Veroli investigated the effect of 2 mmol.kgBW^{-1} of hypertonic saline 5% as preloading solution before epidural anesthesia in TURP (10) and Jarvela investigated the similar dose of hypertonic saline 7.5% as preloading solution before spinal anesthesia. (11) In these studies, hypertonic saline was able to maintain hemodynamic status during spinal anesthesia and prevented the decrease of plasma sodium level. However, high concentration of chloride in hypertonic saline, according to Stewart, will cause dilutional acidosis named hyperchloremic acidosis (12) that would worsen the acidosis that already happened during TURP.

Replacement of chloride with lactate in hypertonic sodium lactate may prevent acidosis because lactate will immediately metabolized in Cory cycle in the liver and remained sodium as strong positive ion which will cause mild alkalosis. (13,14) This effect, in addition to high sodium content in hypertonic sodium lactate, may maintain plasma sodium level and serum osmolality, therefore will prevent TURP syndrome. The effect of hypertonic sodium lactate has been investigated in several studies during and after cardiac surgery. Hypertonic sodium lactate has been proven to increase cardiac index and oxygen delivery, decrease systemic and pulmonary vascular resistance index, induce much higher negative fluid balance, and also attenuate metabolic acidosis. (15-17)

This study aimed to evaluate the efficacy and safety of hypertonic sodium lactate with dose of 4 mL.kgBW^{-1} as preoperative solution in maintaining sodium concentration, osmolality and acid base homeostasis during TURP procedure.

Methods

This prospective randomized controlled double blind study was conducted in the operating theater of Hasan Sadikin Hospital, Bandung, Indonesia, and has been approved by local ethical committee and signed informed consent has been obtained from each patient enrolled. Twenty two patients with age of 60–75 year-old (American Society of Anesthesiologist [ASA] physical statuses II–III) underwent TURP under spinal anesthesia has been enrolled in this study. All patients had no cardiac disease, no renal or hepatic impairment, no pulmonary edema, no preexisting diabetic or metabolic acidosis and had sodium level at 135-155 mEq/L. Eligible patients were randomly assigned for either infusion of half molar hypertonic sodium lactate solution, which were provided by Innogene Kalbiotech Pte.Ltd, (HSL group, n=11) or normal saline solution (NS group, n=11).

In the operating theater, the patients were continuously monitored for consciousness level, blood pressure, heart rate, respiratory rate, ECG, and oxygen saturation (Life Scope 14, Nihon Kohden 2000, Tokyo, Japan). After an overnight fasting, all patients were premedicated with midazolam at a dose of 0.04 mg.kgBW^{-1} intravenously. An 18-Gauge intravenous catheter was inserted to the left radial vein for fluid administration and an arterial line was then inserted to the right radial artery to obtain arterial blood sample. Lactated Ringer's solution (RL) with a dose of 10 mL.kgBW^{-1} was infused within 10 minutes to replace the preoperative fasting fluid deficit. After that, patients in HSL group received hypertonic sodium lactate with a loading dose of 4 mL.kgBW^{-1} within 20 minutes and patients in NS group received normal saline with a loading dose of 4 mL.kgBW^{-1} within 20 minutes. After the study fluid infusion finished, spinal anesthesia was performed using a 27-Gauge Quinke-type spinal needle (Spinocan, B.Braun, German) at the level L3-4 intervertebral space. All patients received 2-2.5 mL of 0.5% bupivacaine (5 mg/ml, hyperbaric). The TURP procedure was started when the level of blockade has reached T8. During TURP procedure normal saline were

continuously infused with a dose of 2-4 $mL.kg^{-1}.hr^{-1}$ for fluid maintenance in both groups. The TURP procedure was performed using distilled water, with height of water irrigation 60 cm from the patient body and duration of resection was limited to less than 90 minutes. After the TURP procedure finished, the patients were referred to the recovery room. Blood sample were obtained from arterial cannula inserted in radial artery. Plasma electrolytes (sodium, potassium, chloride), blood lactate, serum osmolality (mOsm) and arterial blood gas analysis were assayed at the end of fasting fluid replacement (baseline/T1), immediately after the end of study fluid infusion (T2), at the first 30 minute during TURP (T3), and immediately after the patients were in the recovery room (T4) with I-Stat Analyzer 200 series (provided by Innogene Kalbiothech Pte. Ltd.). Plasma osmolality parameters were calculated using standard formula (Os molality=2Na+(glucose/18)+(urea/2.8). Hyponatremia was defined if plasma sodium level less than 130 mEq/L. Hypoosmolality was defined if serum osmolality less than 280 mOsm/kg. Acidosis was defined if arterial pH was less than 7.35. Statistical assessment was carried out either through unpaired student t-test or Chi-Square test, or through Mann-Whitney test to determine differences between two groups with significance level (α) of 95% with $p<0.005$ were considered as statistically significant and $p<0.01$ were considered as statistically very significant. Statistical analysis was performed using the SPSS for windows (version 15).

Results

Patient's characteristics

Twenty two patients underwent TURP procedure were participated in this study and analyzed. There were no differences of baseline characteristics between two groups. Duration of resection and total volume of irrigating water used during procedure was insignificantly higher in HSL group (**Table 1**). Baseline plasma electrolyte levels (sodium, potassium and chloride), serum osmolality, and blood gas analysis were not different between two groups. None of the patients in both groups needed blood transfusion during and after procedure.

Effect of hypertonic sodium lactate infusion on biological parameters

Changes of sodium concentration after study fluid infusion were significantly different between HSL and NS group (**Figure 1a**). Plasma sodium concentration increased very significantly with time in HSL group compared to the preoperative value (T1) (**Table 1**, $p<0.01$), whereas in NS group the sodium concentration continuously decreased. Plasma sodium concentration at first 30 minutes of procedure (T3) and at recovery room (T4) in NS group decreased very significantly compared to preoperative value ($p<0.01$). Sodium concentration at the end of study fluid infusion (T2) was significantly different between both groups ($p<0.05$) and even the difference became very significant at recovery room (T4) ($p<0.01$). Potassium concentration of two groups did not much change in each time of assessment. Plasma chloride concentration decreased very significantly in both groups after study fluid infusion (T2), at first 30 minutes of procedure (T3) and at recovery room (T4) compared to preoperative value (T1). The decrease of chloride concentration after study fluid infusion (T2) and at first 30 minutes of procedure (T3) was significantly different between two groups ($p<0.05$) (**Table 2**).

Evolution of serum osmolality after study fluid infusion was significantly different between HSL group and NS group (**Figure 1b**). Serum osmolality in HSL group significantly increased with time compared to baseline value (T1) (**Table 2**, $p<0.01$). Otherwise, serum osmolality in NS group continuously decreased during surgery even though the decrease of osmolality in each time of assessment was not different compared to baseline value. Serum osmolality at recovery room (T4) in HSL group were significantly higher compared to NS group ($p<0.05$) (**Table 2**).

Blood lactate level increased after HSL infusion however it decreased to nearly baseline level at the recovery room (T4). Blood lactate level in NS group did not change with time. Changes in blood lactate level at the end of study fluid infusion (T2) and at first 30 minutes of procedures (T3) were very significantly different between two groups ($p<0.01$) (**Table 2**).

Arterial pH, $PaCO_2$, base excess (BE), and HCO_3 in HSL group increased significantly in each time of assessment

compared to baseline value; however, the value of all parameters were still in normal range. Evolution of arterial pH was significantly different between two groups (**Figure 1c**). Arterial pH in NS group decreased with time and very significantly decreased to mild acidosis at first 30 minutes of procedure (T3) compared to preoperative ($p<0.01$). Arterial pH in HSL group increased with time; however, the pH was still in normal range. Changes of pH at the end of fluid infusion (T2) was significantly different between two groups ($p<0.05$) and even the difference became very significantly at first 30 minutes of surgery (T3) and at recovery room (T4) (**Table 2**, $p<0.01$). $PaCO_2$ in each time of assessment increased very significantly in both groups compared to baseline value, however the changes of $PaCO_2$ in both group were not different ($p>0.05$). Base excess in HSL group became more positive in each time of assessment, whereas in NS group base excess did not change and remained negative until at recovery room (T4). Changes of arterial HCO_3 value in each time of assessment were significantly different between two groups ($p<0.01$). Arterial HCO_3 increased very significantly in each time of assessment in HSL group compared to preoperative value, whereas in NS group this parameters did not change significantly. Infusion of hypertonic sodium lactate increased SID and this increase became very significant at first 30 minutes of TURP procedure and at recovery room, whereas in NS group this parameter did not change (**Table 2**).

Hemodynamic parameters

Evolution of mean blood systolic and diastolic pressures in both groups were not significantly different in which blood pressure decreased after spinal anesthesia. However, mean of blood pressure were still in normal range in both groups. The decrease of systolic and diastolic blood pressures in HSL group were insignificantly lower compared to NS group. Mean arterial pressures were significantly lower in NS group at minute 20 and 30 of procedure compared to HSL group (**Figure 2**). Per patients observation showed that 5 patients in NS group needed ephedrine injection due to the decrease of blood pressure >30% from baseline, whereas none of the patients in HSL group required ephedrine injection.

Discussion

The absorption of irrigating solution used in TURP procedure leading to hyponatremia, hypoosmolality and acidosis, known as TURP syndrome, is one of the major complications of TURP and remains unsolved problem. Previous trial showed that the use of hypertonic saline which has similar sodium load with hypertonic sodium lactate as intraoperative fluid therapy could maintain plasma sodium level and serum osmolality in TURP procedure. (8-11)

Our study showed that sodium concentration was significantly different between HSL group and NS group. Preoperative hypertonic sodium lactate administration in TURP procedure could maintain plasma sodium concentration throughout the procedure and prevent hyponatremia, whereas preoperative normal saline administration was followed by continuously decrease of sodium concentration. The lowest concentration of plasma sodium in NS group was at recovery room.

Decrease of serum osmolality occurred during TURP, caused by absorption of irrigating solution which has less osmolarity than plasma. Hypoosmolality could induce the increase of intracranial pressure and results in bradycardia, hypertension and pulmonary edema. (6) As we can not use isoosmolar irrigating solution during TURP, the use of hypertonic solution preoperative or intraoperative might be a choice to prevent the occurrence of hypoosmolality. In this study we found that preoperative hypertonic sodium lactate administration during TURP could maintain serum osmolality throughout the procedure and could prevent hypoosmolality until the end of procedure, whereas in normal saline serum osmolality continuously decreased with the lowest level was at recovery room (T4). However, the sodium concentration and serum osmolality in normal saline group were also still in normal range due to short time of procedure and also the usage of limited water irrigation.

Acid base balance could be changed during TURP procedure due to absorption of irrigating water which will dilute plasma sodium concentration and decreasing SID and further, according to Stewart, (12) would lead to acidosis. Evidence showed that metabolic acidosis occurred during TURP related to duration of resection and water irrigation used in procedure. (7) In this study we found that hypertonic sodium lactate administration increased arterial pH, base

excess and SID and the increases of all parameters were still in normal range. After infusing hypertonic sodium lactate to the patients, lactate will be immediately metabolized and the remained Na will lead to increase SID that resulted in mild alkalinization. (13,14) In normal saline groups the arterial pH, base excess and SID decreased and at first 30 minutes of procedure the acid base balance was shifted to mild acidosis.

Hemodynamic status evolution (blood pressure and MAP) showed similar pattern in both groups in which blood pressure and MAP decreased. However, hypertonic sodium lactate could maintain both parameters better than NS because the decrease of both parameters was lower in HSL group. The most interesting finding was that none of patients in HSL group required ephedrine injection due to decreased of blood pressure >30% of baseline level. In contrast, 5 of 11 patients in NS experienced hypotension and required ephedrine IV. Previous study also showed similar finding that hypertonic saline prehydration during TURP reduced the occurrence of spinal hypotension and reduced the use of phenylephrine to maintain blood pressure. (8)

No adverse events were found in this study relating to study medication. Hypertonic sodium lactate increased plasma lactate level, however lactate will be metabolized and the lactate level returned to nearly baseline value at the end of TURP procedure. No electrolyte imbalance occurred during the study.

Conclusion

Preoperative hypertonic sodium lactate administration was better in maintaining plasma sodium concentration, serum osmolality, and arterial pH during TURP than isotonic saline. Preoperative hypertonic sodium lactate administration could reduce the occurrence of spinal hypotension and the use of ephedrine. Hypertonic sodium lactate might be a choice of preoperative fluid regimen during TURP procedure.

Table 1. Baseline Characteristics of the Patients and Surgical Procedure

Characteristic	HSL	NS	P value
Age (year)	68.9±3.0	68.7±3.5	0.897
Weight (kg)	57.1±4.0	56.5±4.4	0.765
Height (cm)	161.0±4.3	159.9±4.4	0.562
Prostate weight (g)	42.9±9.3	44.3±12.7	0.777
Prostate resected (g)	17.3±3.4	16.5±5.0	0.696
Resection time (min)	61.4±9.2	54.5±8.5	0.087
Water irrigation (L)	19.2±2.5	17.6±2.5	0.158

Patients underwent TURP procedure were randomized to receive either HSL (n=11) or NS (n=11) before spinal anesthesia. Values are mean±SEM. No significant difference was observed between the HSL and NS groups.

Table 2. Effect of HSL or NS on Biological Parameters

Parameters	Group	T1	T2	T3	T4
Na^+	HSL	139.9±2.4	142.3±1.9[bc]	141.4±2.0[bc]	142.2±2.0[bd]
	NS	140.1±2.5	139.9±2.5	139.4±2.0[b]	138.9±2.1[b]
K^+	HSL	3.5±0.6	3.4±0.7	3.3±0.4	3.5±0.6
	NS	3.3±0.3	3.3±0.3	3.3±0.2	3.5±0.3
Cl^-	HSL	107.0±2.6	103.5±1.8[bc]	103.5±2.2[bc]	104.6±2.2[b]
	NS	108.1±3.1	107.5±3.4[b]	106.6±3.4[b]	106.7±3.1[b]
Lactate	HSL	1.2±0.5	5.5±2.2[bd]	2.2±0.8[bd]	1.9±1.5
	NS	0.8±0.4	0.8±0.3	0.7±0.3	0.9±0.6
Osmolality	HSL	290.2±3.7	294.5±3.1[b]	293.3±4.3[b]	294.6±3.5[bc]
	NS	291.3±4.0	291.4±4.2	290.8±2.9	290.6±3.2
pH	HSL	7.399±0.03	7.423±0.04[bc]	7.441±0.05[bd]	7.433±0.04[bd]
	NS	7.381±0.04	7.358±0.07	7.335±0.06[b]	7.356±0.05[a]
$PaCO_2$	HSL	35.0±6.1	40.8±7.2[b]	43.7±7.4[b]	42.2±6.3[b]
	NS	34.7±5.4	38.4±7.4	40.3±5.1[b]	39.2±5.7[b]
BE	HSL	-3.2±3.7	2.1±3.6[bd]	4.8±3.1[bd]	3.7±3.1[bd]
	NS	-4.4±5.1	-3.7±4.9[a]	-3.1±4.9[b]	-3.2±4.8
HCO_3	HSL	21.9±3.6	26.6±3.1[bd]	29.1±3.2[bd]	28.2±3.1[bd]
	NS	21.1±4.6	21.7±4.1	22.6±4.4[a]	22.3±4.1
SID	HSL	35.2±1.8	36.3±1.9	38.8±0.9[bd]	39.1±2.3[bd]
	NS	34.5±2.5	34.9±2.2	35.4±2.8[a]	34.8±2.4

T1: before HSL or NS infusion; T2: immediately after HSL or RL infusion; T3: at first 30 minutes after HSL or NS infusion; T4: at recovery room.

Sodium (Na^+), potassium (K^+), chloride (Cl^-), lactate and bicarbonate are in $mmol.L^{-1}$; PCO_2 are in torr and osmolality is in $mOsm.kg^{-1}$. Data are mean±SEM. Statistical comparison was carried out through a two-way ANOVA for repeated measures: 1) effect of time ($p<0.05$); 2) effect of group (HSL vs NS, $p<0.05$). When the difference was significant, a Man Whitney analysis was performed: [a] significantly different from T1 (paired student's t test, $p<0.05$); [b] very significantly different from T1 (paired student's t test, $p<0.01$); [c] significantly different from NS ($p<0.05$); [d] very significantly different from NS ($p<0.01$).

Figures 1a, 1b and **1c**. Effect of HSL versus NS on Plasma Sodium Concentration, Osmolality and Arterial pH

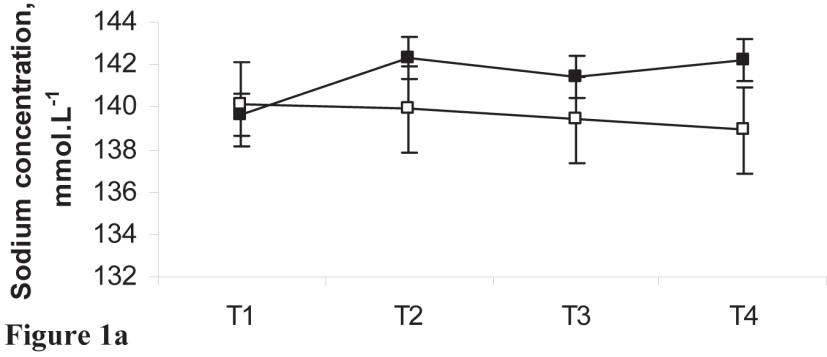


Figure 1a

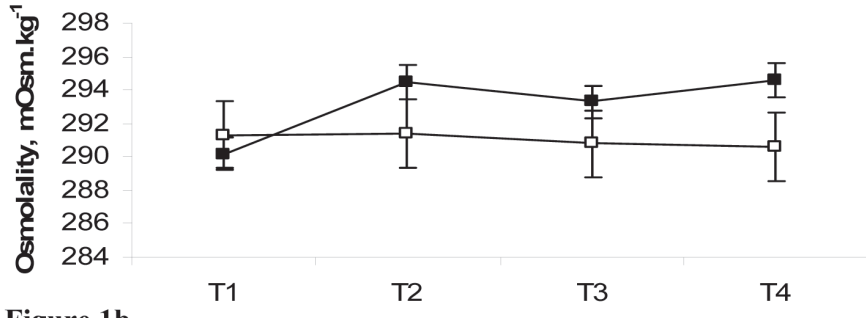


Figure 1b

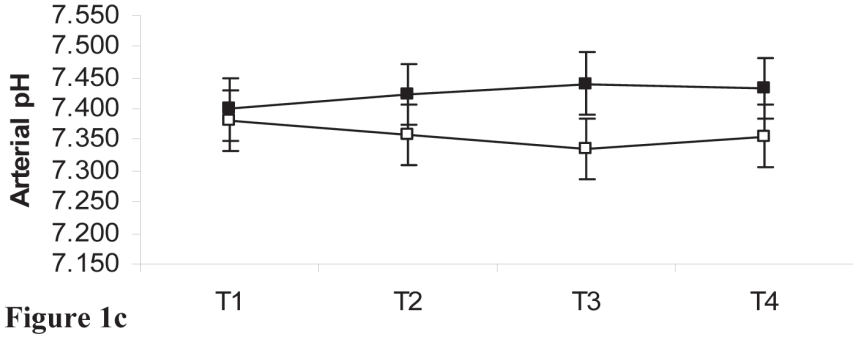
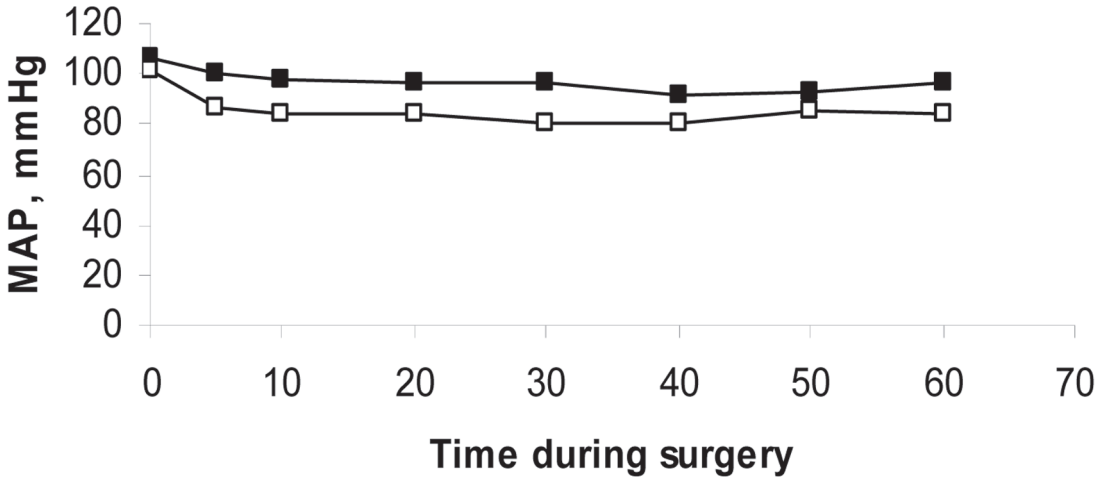


Figure 1c

Legend: Opened symbols: NS; closed symbols: HSL; T1: Baseline; T2: immediately after HSL or NS infusion; T3: at first 30 minutes during TURP; T4: at recovery room. Results were expressed as mean±SEM, statistical comparison between NS and HSL by unpaired student's t test for sodium concentration ($p<0.001$), osmolality ($p<0.011$) and arterial pH ($p<0.001$).

Figure 2. Effect of HSL versus NS on Mean Arterial Pressure



Legend: Opened symbols: NS; closed symbols: HSL; MAP: mean arterial pressure (mmHg). Result was expressed as mean±SEM; no significant difference was noted between two groups.

References

1. Weis N, Jorgensen PE, Bruun E. "TUR syndrome" after transurethral resection of the prostate using suprapubic drainage. Int Urol Nephrol 1987;19:165-9.
2. Chilton CP, Morgan RJ, England HR, Paris AM, Blandy JP. A critical evaluation of the result of transurethral resection of the prostate. Br J Urol 1978;50:542-6.
3. Estey EP, Mador DR, McPhee MS. A review of 1486 transurethral resections of the prostate in a teaching hospital. Can J Surg 1993;36:37-40.
4. Goel CM, Badenoch DF, Fowler CG, Blandy JP, Tiptaft RC. Transurethral resection syndrome. A prospective study. Eur Urol 1992;21:15-7.
5. Shido A, Kasai M, Hashimoto T, Nomura T, Sakura S, Saito Y. Two cases of TURP syndrome with severe cardiovascular depression. Masui 2003;52:512-4.
6. Gravenstein D. Transurethral resection of the prostate (TURP) syndrome: a review of the pathophysiology and management. Anesth Analg 1997;84:438-46.
7. Scheingraber S, Heitmann L, Weber W, Finsterer U. Are there acid base changes during transurethral resection of the prostate (TURP)?Anesth Analg 2000;90:946-50.
8. Baraka A, Taha S, Ghabach M, Sibaii A, Nader A, Matta M. Hypertonic saline prehydration in patients undergoing transurethral resection of the prostate under spinal anaesthesia. Br J Anaesth 1994;72:227-8.
9. Kato S, Goto F. Hypertonic saline for intraoperative fluid therapy in transurethral resection of the prostate. J Anesth 1996;10:170-5.
10. Veroli P, Benhamou D. Comparison of hypertonic saline (5%), isotonic saline and Ringer's lactate solutions for fluid preloading before lumbar extradural anaesthesia. Br J Anaesth 1992;69:461-4.
11. Järvelä K, Honkonen SE, Järvelä T, Kööbi T, Kaukinen S. The comparison of hypertonic saline (7.5%) and normal saline (0.9%) for initial fluid administration before spinal anesthesia. Anesth Analg 2000;91:1461-5.
12. Stewart PA. Modern quantitative acid-base chemistry. Can J Physiol Pharmacol 1983;61:1444-61.
13. Gladden LB. Lactate metabolism: a new paradigm for the third millennium. J Physiol 2004;558:5-30.
14. Aduen JF, Burritt MF, Murray MJ. Blood lactate accumulation: Hemodynamics and acid base status. Intensive Care Med 2002;17:180-5.
15. Mustafa I, Leverve XM. Metabolic and hemodynamic effects of hypertonic solutions: sodium-lactate versus sodium chloride infusion in postoperative patients. Shock 2002;18:306-10.
16. Mustafa I, Roth H, Hanafiah A, Hakim T, Anwar M, Siregar E, et al. Effect of cardiopulmonary bypass on lactate metabolism. Intensive Care Med 2003;29:1279-85.
17. Leverve XM, Boon C, Hakim T, Anwar M, Siregar E, Mustafa I. Half-molar sodium-lactate solution has a beneficial effect in patients after coronary artery bypass grafting. Intensive Care Med 2008;34:1796-803.