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ORIGINAL RESEARCH REGIONAL ANESTHESIA

The hemodynamic effects of hypertonic saline preload versus co-load measured by non-invasive cardiometry in patients undergoing TURP surgery: a randomized controlled trial

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ABSTRACT

Background & objective: Transurethral resection of prostate (TURP) is usually performed under spinal anesthesia. To control spinal hypotension intravenous fluids are infused. We evaluated the effect of timing of hypertonic saline infusion as a preload or a co-load on hemodynamic parameters in patients undergoing TURP using non-invasive cardiometry.

Methodology: A randomized controlled study was conducted. A total of 100 ASA physical status I-III patients planned for TURP under subarachnoid block were randomly assigned to either a preload of 4 ml/kg of hypertonic saline (NaCl 3%) over 15-20 min before spinal anesthesia (Group P, n = 50) or a co-load at the maximum rate at the moment of cerebrospinal fluid identification (Group C, n = 50). Cardiometry was used to measure cardiac output and systemic vascular resistance; and mean arterial blood pressure, systolic blood pressure, heart rate, and the requirement for ephedrine and serum sodium levels were recorded.

Results: There was a rise in cardiac output readings at 5, 10 and 15 min in both groups, but Group P showed a significantly more rise compared to Group C after spinal anesthesia and compared with their baseline values. As for the systemic vascular resistance, a substantial drop occurred in Group P at 5, 10, and 15 min when compared to Group C, as well as when compared to their baseline levels. Except for considerably lower systolic blood pressure readings at 5 min after spinal block in Group P, in both groups, systolic blood pressure and heart rate changes were comparable. The median dose of ephedrine required for Group P patients was significantly greater.

Conclusion: Hypertonic saline co-loading is more effective than its preloading in decreasing hypotension occurring with subarachnoid anesthesia for TURP surgery.

Abbreviations: CO: Cardiac Output; HR: Heart Rate; SBP: Systolic Blood Pressure; SD: Standard Deviation; SV: Stroke Volume; SVR: Systemic Vascular Resistance; TURP: Transurethral Resection of the Prostate.

Key words: Hypertonic Saline; Co-load; Preload; Cardiometry; Subarachnoid Anesthesia; TURP

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1. INTRODUCTION

Benign prostatic hyperplasia is widespread in elderly men, and this population is typically associated with a variety of comorbidities, notably those of the cardiovascular system, placing them at risk of a variety of intraoperative complications. Transurethral resection of the prostate (TURP) syndrome refers to the adverse consequences of the procedure on both the cardiovascular and nervous systems.[1] As a result, TURP patients require meticulous hemodynamic monitoring and fluid management.

Electrical cardiometry (Electrical velocimetry) is a non-invasive, always-on method of measuring cardiac output (CO), stroke volume (SV), and other hemodynamic parameters. Many studies indicate that its use as a continuous CO monitor is more reliable than other well-established methods such as transthoracic echocardiography[2, 3] and transesophageal echocardiography.[4]

Spinal anesthesia is a frequent procedure in clinical use. One of the most common adverse effects is a reduction in systemic vascular resistance, which leads to systemic hypotension.[5, 6]

Isotonic fluid administration is routinely used to avoid this occurrence, and it is typically well tolerated by healthy young people. Excess free fluid administration, on the other hand, is not desirable in individuals with cardiovascular compromise who require more concentrated hypertonic saline with a reduced fluid burden.[7]

One technique for decreasing hypotension is to rapidly infuse crystalloid solution at the start of anesthesia (co-load), as the co-load provides more intravascular fluid at the peak of vasodilation.[8, 9]

Hypertonic saline increases plasma osmolality and causes fluid to migrate from the intracellular to extracellular space.[10] This induces an increase in intravascular volume, which improves hemodynamics.[11] Hypertonic solution has been used in a variety of procedures and populations to treat hypotension produced by subarachnoid block, as well as to treat dilution hyponatremia caused by absorption of the irrigating fluid following trans-urethral resection of the prostate.

The primary goal of this study was to investigate the effect of timing hypertonic saline infusion as a preload or a co-load on hemodynamic parameters in TURP patients. The major goal was to see how hypertonic saline (preload versus co-load) affected post-spinal hypotension utilizing cardiometry for hemodynamic monitoring. The secondary outcomes were to assess the requirement for the necessary dose of vasopressor, post-operative serum Na level, and any adverse events that occurred.

2. METHODOLOGY

The trial obtained approval from the Ethics Committee of the Faculty of Medicine, Cairo University, Egypt (N-14-2016), and it was registered at the clinicaltrials.gov (NCT03324477; October 27, 2017; https://clinicaltrials.gov/ct2/show/NCT03324477).
After full explanation of the study procedure, all recruited patients signed a written informed consent form.

The study was conducted at Cairo University's Kasr Al-Ainy Hospital on 100 ASA class I-III patients, aged 40 to 80 years, who were candidates for TURP surgeries under subarachnoid block, with the exclusion of those who had any condition contra-indicating regional anesthesia, electrolyte imbalance, or were allergic to any of the study drugs.

Study design

Our study is a single-blind study (where the patients are unaware of their allocation to which of the two study groups).

All patients had routine pre-operative assessment, which included a history, general examination, and laboratory tests. Each patient was given Ranitidine 50 mg and Ondansetron 4 mg as a pre-medication. Patients were randomly assigned to receive 4 ml/kg of hypertonic saline (NaCl 3%) either pre-operatively over 15-20 min before spinal anesthesia induction [Group P: (n = 50)] or at the maximum possible rate at the time of cerebrospinal fluid identification [Group C: (n = 50)].

A 5-lead electrocardiogram with S-T segment analysis, pulse oximetry, and non-invasive blood pressure were used for routine monitoring.

After taking the approval of the patient and signing a consent, a central venous catheter was inserted to

monitor the readings of the central venous pressure – the anesthetist - after washing the hands and wearing sterile gown and gloves, skin of the patient's neck was prepared with sterile antiseptic and dressings, a local anesthetic was infiltrated at the anatomical triangle of insertion between the two heads of the sterno-mastoid muscle where the entrance was at the apex of this triangle, skin at this area was infiltrated by a local anesthetic (lidocaine 2%) till the patient felt numbness at the site of infiltration, Seldinger needle attached to syringe was inserted slowly into the internal jugular vein angled 30 ºC, blood was freely aspirated by the syringe then Seldinger wire was passed easily through the needle that was then removed, then the dilator was passed over the wire gently but firmly to dilate a tract through to the internal jugular vein. The dilator was then removed and the central line passed over the Seldinger wire that was lastly removed. All lines were aspirated and flushed and caps applied then the line was fixed and dressed with sterile dressings.

Patients were then allocated in either groups; Group P receiving hypertonic saline volume 4 ml/ kg over 15 – 20 min before spinal anesthesia or Group C receiving hypertonic saline at the induction of spinal injection.

Following total sterilization, spinal anesthesia was given by a 25G spinal needle at the level of L3/4 or L4/5. To obtain an anesthetic dose up to the T10 dermatome, a mixed solution of 3-3.5 ml of 0.5% hyperbaric bupivacaine hydrochloride hydrate and 25 µg fentanyl in 0.5 ml was utilized.

Cases in which spinal anesthesia failed and patients switched to general anesthesia were excluded from the study. TURP was conducted using an intermittent irrigation system of distilled water held at room temperature and 60 cm above the level of the resectoscope. Throughout the surgical operation, all patients were given an oxygen (3-4 L/min) face mask.

A modest sinusoidal current was delivered to two standard electrocardiography electrodes at the base of the neck and inferior aspect of the thorax using non-invasive ICON cardiometry. Two additional electrodes 5 cm within the stimulating electrodes measured the changing impedance throughout the thorax.

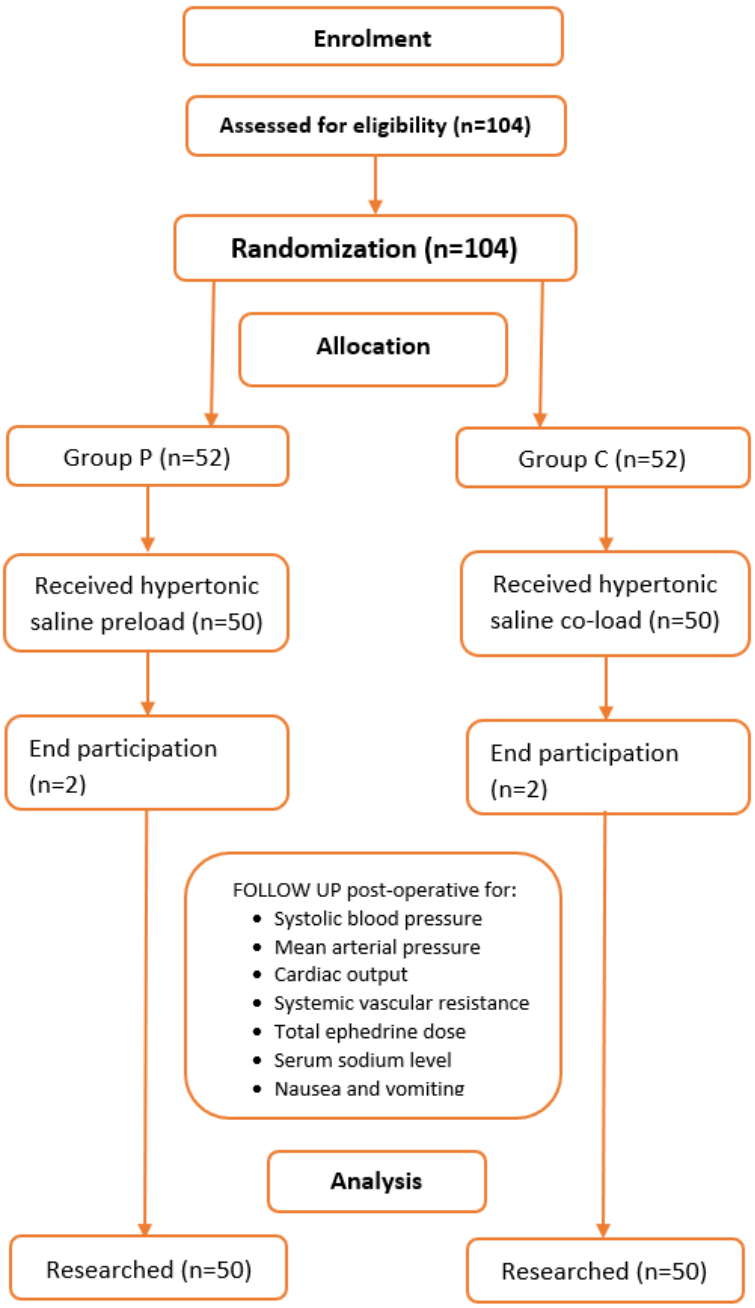

Figure 1: CONSORT flow diagram of the study

Two gel pad sensors were carefully put on each side of the thorax at the mid-axillary line, and two sensors were placed on each side of the neck just above the clavicle after the skin was cleaned with alcohol.

If the systolic blood pressure (SBP) was ≤ 80% of the baseline or ≤ 100 mm Hg, an IV bolus of ephedrine 10 mg was given. Atropine (0.3-0.6 mg) was used to treat

Table 1: Comparing the two groups according to different parameters

Parameters		Group P (n = 50)	Group C (n = 50)	Test of sig	P
Age (y)		64.1 ± 6.5	65.6 ± 7.1	t = 1.160	0.249
Weight (kg)		79.7 ± 6.4	80.5 ± 9.1	t = 0.458	0.648
Height (m)		1.7 ± 0.1	1.7 ± 0.1	t = 0.635	0.527
BMI (kg/m^2)		28 ± 3.2	27.8 ± 3.2	t = 0.163	0.871
ASA	○ I	19 (38%)	21 (42%)	χ^2 = 1.000	0.607
	○ II	19 (38%)	21 (42%)		
	○ III	12 (24%)	8 (16%)		
BSA		1.93 ± 0.08	1.95 ± 0.13	t = 0.613	0.541
Size of prostate (ml)		59.7 ± 8.8	64.8 ± 11	t = 2.561*	0.012*
Duration of surgery (min)		56.2 ± 6.8	56.2 ± 6.8	t = 0.000	1.000

Data presented as mean ± SD; t: Student t-test; χ2: Chi square test
P: p value for comparing between the two studied groups
**: Statistically significant at P ≤ 0.05*

bradycardia (heart rate [HR] ≤ 50). If the hypotension persisted or recurred, the vasopressor medication was repeated. Smaller reductions in BP (SBP falls ≤ 20%) were treated similarly whether accompanied by nausea, vomiting, or dizziness.

If the patient got at least one dosage of a vasopressor, hypotension was considered to be present. At the moment of hypotension, an extra fast bolus infusion of Ringer's solution was given.

Patients were observed for signs and symptoms of TURP syndrome (e.g., DCL, headache, hypertension, bradycardia, pulmonary edema, seizures), which were treated appropriately.

Before the hypertonic saline was delivered, a baseline set of hemodynamic measures [HR, SBP, mean arterial pressure, CO, systemic vascular resistance (SVR), and cardiac index] were taken. Following the onset of spinal anesthesia, these measures were taken every 5 min for the first 30 min, and subsequently every 15 min until the procedure was completed.

Trans-rectal ultrasonography estimated prostate size, operation duration, total volume of irrigating fluid used, number of ephedrine doses necessary, incidence of any adverse events, and post-operative plasma Na level were all documented.

Sample size

We believed that a shift of 35% (11 mmHg) using hypertonic saline as a co-load would be clinically meaningful based on a prior research[12] that demonstrated a drop in SBP of 31 mmHg in patients having TURP surgery after receiving preload with hypertonic saline (with a standard deviation of 19 mmHg).

So, using Medcalc software, we computed our sample size based on an assumption of mean differences of 11 mmHg between the two groups and a standard deviation of 18 mmHg. With a research power of 80% and a P value of 0.05, each group required a minimum of 48 patients. To account for any drop-outs, a total of 100 patients (50 in each group) were included.

Statistical analysis

Means and standard deviations were used to display all normally distributed continuous data. The median (range) was used to express non-normally distributed continuous and ordinal data. Categorical data were presented as the number of patients and the incidence rate. To compare continuous data in the two groups, the unpaired t-test was utilized. To examine changes in continuous variables in relation to baseline preoperative values, such as HR and blood pressure, repeated measure ANOVA with post-hoc Dunnets test were utilized within each research group. To compare categorical data, the Chi square or Fisher Exact test were utilized. A $P < 0.05$ was considered significant for all statistical comparisons. The Statistical Package for Social Sciences SPSS software was used for all data analysis and graphical displays.

3. RESULTS

One hundred and four patients fulfilled the criteria of the study candidate for TURP at Kasr AL-Ainy hospital, Cairo University; in the period from November 2017 till June 2018. Three patients refused to participate in the

Table 2: Comparing the two groups according to systemic vascular resistance

Systemic vascular resistance	Group P (n = 50)	p0	Group C (n = 50)	p0	t	p
Intra operative						
Baseline	1529.3 ± 7.9		1528.2 ± 2.0		0.938	0.350
5 min	581.7 ± 5.5	< 0.001*	1030.0 ± 2.8	< 0.001*	509.84*	< 0.001*
10 min	627.9 ± 2.7	< 0.001*	1027.7 ± 2.1	< 0.001*	811.0*	< 0.001*
15 min	725.8 ± 1.7	< 0.001*	1373.6 ± 16.2	< 0.001*	280.35*	< 0.001*
20 min	1529.4 ± 1.7	1.000	1528.8 ± 1.73	1.000	1.762	0.081
25 min	1528.4 ± 1.6	1.000	1528.9 ± 1.22	1.000	1.890	0.062
30 min	1528.2 ± 1.6	1.000	1528.3 ± 1.3	1.000	0.068	0.946
45 min	1528.3 ± 1.7	1.000	1528.2 ± 1.4	1.000	0.502	0.617
60 min	1528.5 ± 1.8	1.000	1528.1 ± 1.6	1.000	1.143	0.256
90 min	1528.8 ± 1.4	1.000	1529.1 ± 5.1	1.000	0.376	0.708

Data presented as mean ± SD; t: Student t-test

p0: P value for Post Hoc test (adjusted Bonferroni) for ANOVA – comparing with Baseline readings in each group; P: P value for comparing between the two studied groups in each period

**: Statistically significant at P ≤ 0.05*

0

Table 3: Comparison between the two studied groups according to cardiac index

Cardiac index (L/min/ m²)	Group P (n = 50)		Co-load group (n = 50)		t	P
	Mean ± SD	p_0	Mean ± SD	p_0		
Intra operative						
Baseline	2.31 ± 0.11		2.30 ± 0.15		0.437	0.663
5 min	3.34 ± 0.16	< 0.001*	3.08 ± 0.22	< 0.001*	6.696	< 0.001*
10 min	3.32 ± 0.20	< 0.001*	3.10 ± 0.21	< 0.001*	5.424	< 0.001*
15 min	3.36 ± 0.16	<0.001*	2.30 ± 0.16	1.000	32.668	< 0.001*
20 min	2.33 ± 0.10	1.000	2.32 ± 0.16	1.000	0.643	0.522
25 min	2.32 ± 0.11	1.000	2.34 ± 0.16	0.060	0.711	0.479
30 min	2.31 ± 0.11	1.000	2.31 ± 0.15	1.000	0.144	0.885
45 min	2.32 ± 0.11	1.000	2.30 ± 0.16	1.000	0.571	0.570
60 min	2.32 ± 0.10	1.000	2.30 ± 0.16	1.000	0.814	0.418
90 min	2.33 ± 0.10	1.000	2.31 ± 0.15	1.000	0.919	0.361

Data presented as mean ± SD; t: Student t-test

p0: P value for Post Hoc test (adjusted Bonferroni) for ANOVA – comparing with Baseline readings in each group; P: P value for comparing between the two studied groups in each period

**: Statistically significant at P ≤ 0.05*

study. The remaining one hundred and one were randomized into two groups: 51 patients in Group P; one patient in this Group was excluded because of protocol violation (n = 50) and 50 patients in Group C (n = 50) (Figure 1).

In terms of demographic (age, ASA status, and body mass index) and surgical statistics (length of the surgery, U/S estimated prostate size, and total amount of irrigating fluid utilized), the two groups were comparable (Table 1).

Hemodynamics recordings revealed a significant difference between both groups showing the Group P with a lower HR compared to the Group C at 5 and 15 min readings with a P ≤ 0.05 (0.018 and <0.001) respectively, even comparing the HRs to the baseline

Table 4: Comparison between the two groups according to different parameters

Parameter	Group P (n = 50)	Group C (n = 50)	Test of Sig.	p
Ephedrine needed [n (%)]	41 (82)	6 (12)		< 0.001*
Total ephedrine use (mg)	12.1 ± 2.1	3.6 ± 1.1	t = 15.598*	< 0.001*
Serum Na level (mEq/L)	139.9 ± 3	140.3 ± 3.1	t = 0.557	0.579
Irrigation fluid volume (L)	22.1 ± 3.7	21.4 ± 3.7	t = 0.921	0.359
Side effects				
Nausea and vomiting	7 (14.0%)	4 (8.0%)	$\chi 2 = 0.919$	0.338
Bradycardia	6 (12.0%)	4 (8.0%)	$\chi 2 = 0.444$	0.505

Data presented as mean ± SD; t: Student t-test; $\chi 2$: Chi square test
*P: p value for comparing between the two studied groups; *: Statistically significant at p ≤ 0.05*

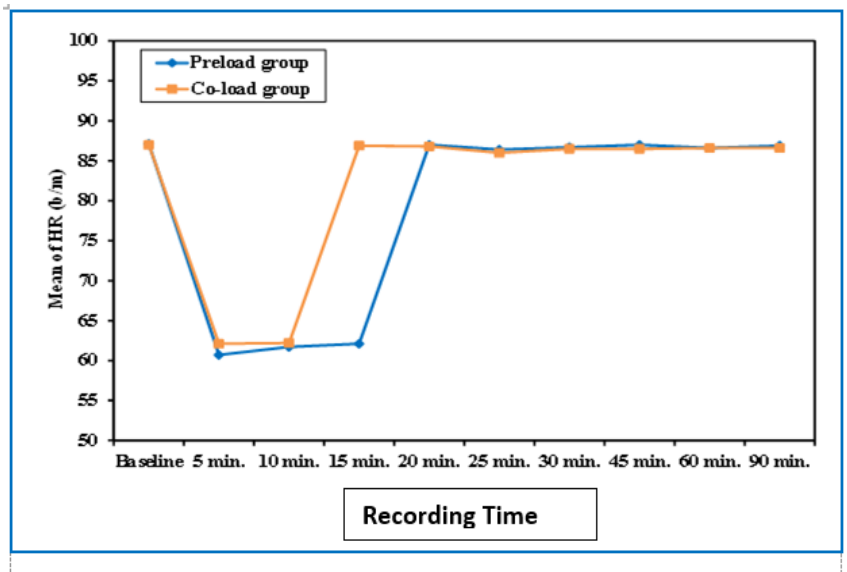

Figure 2: Comparative heart rates in the two groups

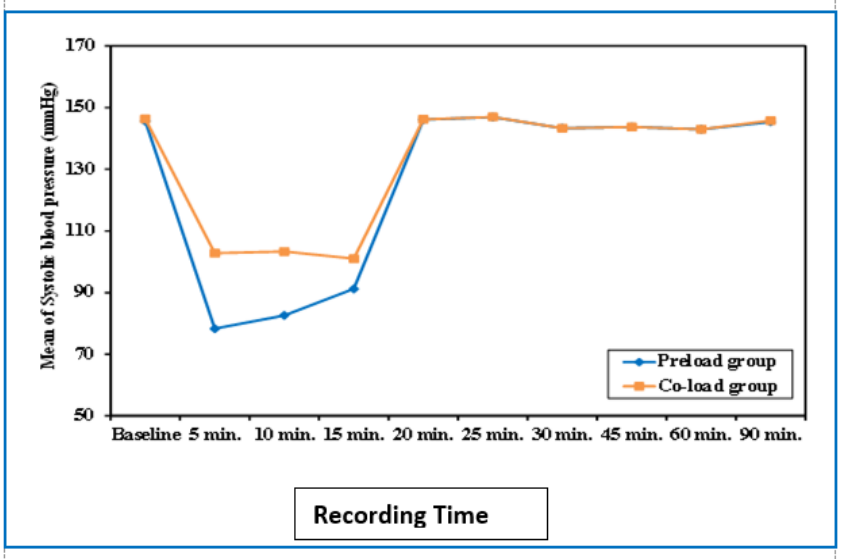

Figure 3: Comparative systolic blood pressures in the two groups

readings in each group also showed lower rates at 5, 10 and 15 min with a P < 0.001 (Figure 2).

Systolic blood pressure readings also revealed a significant drop in the Group P compared to the Group C at 5, 10 and 15 min with a P < 0.001 where SBP dropped 78 – 91 mmHg; whereas Group C recorded 100 – 104 mmHg - in addition – comparing the readings in each group to the baseline readings also revealed a significant P <.001 (Figure 3).

The mean arterial blood pressure in both groups showed a marked drop compared to the baseline readings in each group separately - the Group P dropped to a mean of 54 – 67 mmHg related to their baseline readings (93 mmHg) at 5, 10 and 15 min with a P < 0.001 – whereas the Group C readings dropped till 83-84 mmHg at the same timings (5, 10 and 15 min) with a P < .001 (Figure 4) – creating a significant difference between both groups also with a P <0.001.

The central venous pressure readings were higher in the Group C with an average of 8 mmHg compared to the Group P 7 mmHg at the 15th minute reading showing a higher intravascular fluid volume in the Group C with a P < 0.001 (Figure 5) – showing that the rate of infusion of the hypertonic saline may have a great effect on

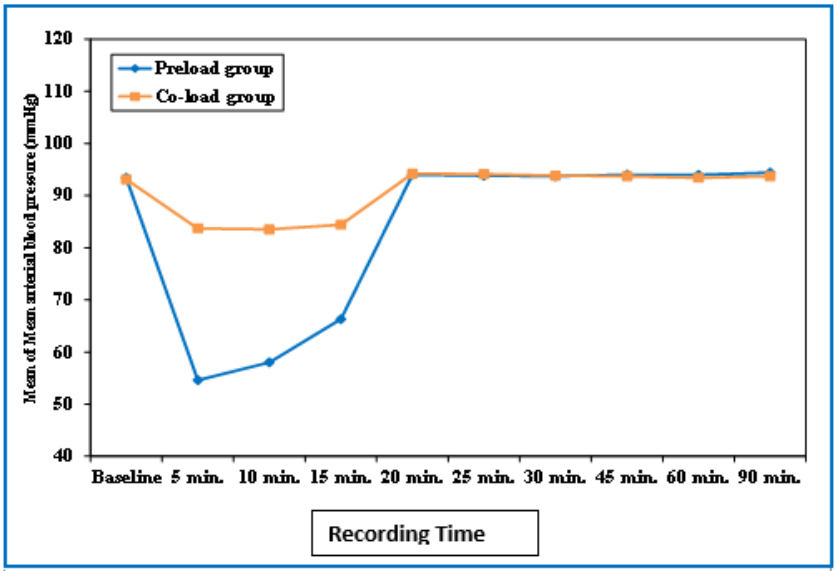

Figure 4: Comparative mean arterial blood pressures in the groups

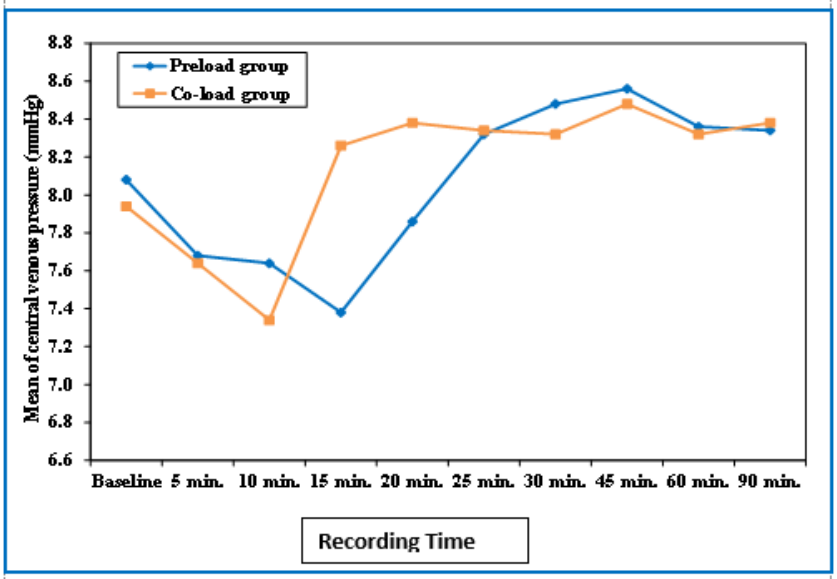

Figure 5: Comparative central venous pressures in the groups

replenishing the intravascular volume and motivating the movement of fluid from the intracellular space to the intravascular lumen.

Our systemic vascular resistance readings dropped significantly in the Group P when compared to the Group C at 5, 10 and 15 min with a mean of (581 – 726 dynes/sec/cm-5) and (1027- 1374 dynes/sec/cm-5) respectively with a P value <0.001 (Table 2).

Inversely, the CO readings have risen in both groups trying to maintain the hemodynamic stability and that rise was higher in the Group P that recorded CO readings of 6.5- 6.4 L/min at 5, 10 and 15 min were as the Group C recorded 5.9- 6 L/min at their maximum rise with a significant difference between both groups and even with their baseline readings showing a P < 0.001– though that rise was significant mainly in the Group P but I didn't maintain a stable systolic or even mean arterial blood pressure. That was explained by the marked drop in the systemic vascular resistance due to the impact of vasodilatation performed by the spinal block causing the pooling of blood in the venous system that was more powerful than the rise in the CO antagonizing its effect.

The cardiac index readings were also higher in the Group P at 5, 10 and 15 min with a significant difference between both groups P < 0.001 (Table 3).

The effect of co-loading of hypertonic saline was dramatically powerful in maintaining the patients' hemodynamic stability that was revealed also by the marked difference between both groups in the use of ephedrine that was mainly in the Group P of patients where 41 patients out of 50 required the administration of at least 12 mg of ephedrine while in the Group C only 6 patients needed lower doses of ephedrine 3-4 mg (Table 4).

Serum Na levels were comparable in both groups, with no significant difference, irrigation fluid volume was also comparable in both groups, with no significant difference (Table 4), and there were no significant differences in the occurrence of side effects (Table 4).

4. DISCUSSION

Spinal anesthesia for TURP allows patients to remain awake during the surgery, which can help detect early signs of TURP syndrome. During the surgical procedure, there is a danger of circulatory overload owing to excessive absorption of irrigation fluid through open prostatic venous sinuses, which may be aggravated by increased venous return due to lithotomy posture. Because the majority of TURP patients are elderly and may have cardiac impairment, they are more prone to volume overload.[12]

The use of spinal anesthetic reduces the danger of circulatory overload caused by peripheral vasodilation,

which causes blood to pool in peripheral vessels. Postoperative analgesia and a lesser risk of deep vein thrombosis are two additional advantages of spinal anesthesia.[12]

Nonetheless, because sympathetic suppression is a key source of vasodilation, it causes reduced venous return and hypotension that is reversed by intravenous fluids and vasopressors.[13]

Preload and co-load are the most often used methods for avoiding hypotension. As preload and co-load, both crystalloid and colloid are used. Crystalloid is preferred over colloid because it is less costly and has less of an influence on coagulation and renal function; however, because crystalloid has a half-life of 15 to 20 min, its usefulness in avoiding hypotension is questionable. Colloids have a long half-life, which allows them to maintain intravascular volume and avoid hypotension. Colloids, on the other hand, are costly, difficult to get, and have been associated with allergic responses. Several researches have revealed that a higher number of colloids is required to keep intravascular volume stable for more than thirty min[14]

Because osmolality governs volume distribution, hypertonic saline causes fluid transfer from intracellular to intravascular and interstitial spaces.[15] As a result, it expands plasma volume more than its own. As a result of irrigation fluid systemic absorption, patients undergoing TURP may suffer dilutional hyponatremia. The quantity of absorption varies with the length of the resection procedure, the amount of bleeding, and the type, volume, and pressure of the irrigating fluid.[16] Hypertonic saline prehydration may minimize dilutional hyponatremia.

The purpose of this study was to investigate the effect of timing hypertonic saline infusion as a preload or a co-load on hemodynamic parameters in patients having TURP procedures.

The current study found that administering hypertonic saline as a co-load reduces spinal induced hypotension significantly more than preload administration, as evidenced by the fact that the Group C required lower doses of vasopressor ($p< 0.001$) than the Group P. In our investigation, using hypertonic saline as a preload or co-load significantly enhanced CO at 5, 10, and 15 min after spinal anesthesia induction, relative to baseline measurements; - This rise in CO for both groups was sustained until the 15-min interval following spinal anesthesia induction.

Teoh et al.[17] studied the impact of colloid preload versus co-load on CO in 40 ASA I and II women undergoing elective caesarean section. Patients were allocated at random to Group P (15 ml/kg HES preload) or Group C, administered when cerebrospinal fluid was detected). Preload significantly increases CO at 5 min after spinal induction but not at 10 or 20 min However, as compared to the Group P, the rise in CO in the Group C was not significant at the specified interval. In this study, 90% of patients who received a colloid preload and 75% of those who received a colloid co-load had a reduction in SBP and hypotension with no data showed about systemic vascular resistance.

In our current investigation, there was a substantial reduction in systemic vascular resistance following spinal anesthesia in the Group P ($p <0.001$) at 5, 10 and 15 min compared to the Group C. In comparison to baseline values, there was a substantial drop in SVR at 5, 10 and 15 min in the Group P, with a bigger amplitude than in the Group C.

By combining our data, we discovered that preloading increased CO at 5, 10, and 15 min intervals in response to the significant decrease in SVR induced by spinal anesthesia at these times, which was greater than the compensatory increase in CO in the Group P, resulting in a decrease in SBP at these times with a higher incidence of hypotension. Co-loading, on the other hand, induced a rise in CO at 5, 10, and 15 min while retaining a greater SVR at these intervals, resulting in a lower incidence of hypotension compared to the Group P.

McDonald et al.[18] looked at the effect of crystalloid vs colloid co-loading on CO. They discovered an increase in CO at 5 and 10 min after spinal induction as compared to baseline measurements, with no statistical significance between both groups, which contradicts our findings at the same time periods.

Some studies looked at the use of preload in spinal anesthesia and its influence on post-spinal hypotension, and they discovered that colloid preload is superior to crystalloid preload in terms of increased CO and decreased hypotension.[19] Several research[8] recommend employing crystalloid co-load because it has a greater influence on CO than preload and the results are comparable to our current investigation.

In terms of the effect of hypertonic saline on SBP and post spinal hypotension in TURP procedure, hypertonic saline solution enhances cardiac contractility.[20] This effect is most likely responsible for the increased CO following hypertonic saline infusion, since it improves organ perfusion by increasing plasma volume, tissue oxygenation, and myocardial function. We noticed that our findings are often congruent with the trends reported in the same population when using hypertonic saline.[21]

In Islam et al.[22] research, sixty patients with ASA grades I and II were randomly allocated to one of two groups, thirty in each, to compare the use of hypertonic saline preloading to normal saline preloading. Group A got 15ml/kg of 0.9% NaCl solution as a preload, while

Group B received 4ml/kg of NaCl solution (3%). Hypertonic saline had the upper hand in terms of minimizing the incidence of post-spinal hypotension.

Functional sympathetic denervation causes hypotension following spinal anesthesia, which occurs not only in the arterial and arteriolar circulations, but also in the venous reservoir. Venodilation causes blood to pool in capacitance vessels, lowering the venous return.[23] The fast mobilization of endogenous fluid via the osmotic gradient from the intracellular to the extracellular space is the primary mechanism by which hypertonic saline counteracts hemodynamic changes during spinal anesthesia.[24] Furthermore, hypertonic saline can elicit both direct cardiac stimulation and venoconstriction.[25, 26]

Many recent studies have been undertaken to study the effects of preload and co-load on hemodynamics, with a focus on the role of crystalloid co-load in the prevention of post-spinal hypotension and its superiority over preload.[27-29]

Khan et al.[28] divided sixty patients into preload and Group Cs of thirty each. Individuals with ASA 1 - 3 between the ages of 20 and 60 who were undergoing any surgery using spinal anesthesia were eligible. All patients in the Group P got 10 ml/kg crystalloid before spinal anesthesia induction, and all patients in the Group C received it at the time of spinal anesthesia. At different time intervals, there was no statistically significant difference between the groups in HR, systolic and mean arterial pressure. Diastolic blood pressure was significantly different in both groups 6 - 15 min after spinal anesthesia. Spinal induced hypotension occurred in 21 (70%) and 15 (50%) patients in the preload and Group Cs, respectively (P = 0.187). The quantity of ephedrine required for spinal induced hypotension was significantly larger (P = 0.017) in the Group P.

Kulkarni et al.[29] studied the effectiveness of co-loading versus preloading in preventing post-spinal hypotension following elective caesarean section. A total of 100 parturients aged 18-35 years were randomly allocated to two groups of fifty each for elective caesarean section in this research. Group P received a preload of 20ml/kg of ringer's lactate solution administered over a 20-min period prior to spinal anesthesia, whereas Group C received a co-load of 20ml/Kg of ringer's lactate solution administered at the maximum possible rate via pressurized administering set at the time of spinal anesthesia administration. They came to the conclusion that co-loading crystalloids during spinal anesthesia for elective caesarean delivery lowers the occurrence of hypotension (23%) more than preloading (72%).

The use of crystalloids as preload or co-load revealed no significant difference in obstetric patients in Farid et al.[27] study evaluating the efficacy of crystalloid preload against co-load on the prevention of post-spinal hypotension. Nonetheless, Oh et al.[30] study indicated that in the same cohort as Zainab Farid et al, the Group C had a lower incidence of spinal induced hypotension and required far fewer vasopressors than the Group P.

In our investigation, there were no significant differences in the incidence of nausea, vomiting, and bradycardia after spinal anesthesia between the two groups. In both groups, there were no significant changes in postoperative serum Na levels compared to baseline values.

5. LIMITATIONS

There were some limitations to our investigation. The lack of a control group made determining an absolute reduction in the incidence of hypotension impossible. We elected not to include it since withholding fluids would be unethical in practical practice. Second, we did not record CO, SVR, SBP, or HR after hypertonic saline preloading and before the start of spinal anesthesia since it was irrelevant to our investigation of post-spinal hypotension. Third, we did not collect diastolic blood pressure readings which is more likely related to the vasodilating impact of spinal anesthesia, although we assessed SVR directly using cardiometry instead.

6. CONCLUSION

We conclude that the hypertonic saline co-load is more effective in decreasing post spinal hypotension compared to its preload use, as co-loading significantly maintained the cardiac output and systemic vascular resistance after induction of spinal anesthesia for TURP surgery

7. Data availability

The numerical data generated during this research is available with the authors.

8. Acknowledgement

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9. Conflict of interest

The authors report no conflict of interest. The study utilized the hospital resources only, and no external or industry funding was involved.

10. Authors' contribution

NS: Concept, conduction of the study work, data analysis and manuscript drafting

ME: Concept, data interpretation and manuscript editing

ME: Design, conduction of the study work, data interpretation and manuscript drafting

SW: Concept, conduction of the study work, data analysis and manuscript drafting

VJ: Design, data interpretation and manuscript editing

11. References

1. Nakahira J, Sawai T, Fujiwara A, Minami T. Transurethral resection syndrome in elderly patients: a retrospective observational study. BMC Anesthesiol. 2014;14:30. PMID: 24782656 DOI: 10.1186/1471-2253-14-30
2. Noori S, Drabu B, Soleymani S, Seri I. Continuous non-invasive cardiac output measurements in the neonate by electrical velocimetry: a comparison with echocardiography. Arch Dis Child Fetal Neonatal Ed. 2012;97:F340-343. PMID: 22933092 DOI: 10.1136/fetalneonatal-2011-301090
3. Rauch R, Welisch E, Lansdell N, Burrill E, Jones J, Robinson T, et al. Non-invasive measurement of cardiac output in obese children and adolescents: comparison of electrical cardiometry and transthoracic Doppler echocardiography. J Clin Monit Comput. 2013;27:187-193. PMID: 23179019 DOI: 10.1007/s10877-012-9412-7
4. Schmidt C, Theilmeier G, Van Aken H, Korsmeier P, Wirtz SP, Berendes E, et al. Comparison of electrical velocimetry and transoesophageal Doppler echocardiography for measuring stroke volume and cardiac output. Br J Anaesth. 2005;95:603-610. PMID: 16155037 DOI: 10.1093/bja/aei224
5. Hartmann B, Junger A, Klasen J, Benson M, Jost A, Banzhaf A, et al. The incidence and risk factors for hypotension after spinal anesthesia induction: an analysis with automated data collection. Anesth Analg. 2002;94:1521-9. PMID: 12032019 DOI: 10.1097/00000539-200206000-00027
6. Hofhuizen C, Lemson J, Snoeck M, Scheffer GJ. Spinal anesthesia-induced hypotension is caused by a decrease in stroke volume in elderly patients. Local Reg Anesth. 2019;12:19-26. PMID: 30881108 DOI: 10.2147/LRA.S193925
7. 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. PMID: 11094001 DOI: 10.1097/00000539-200012000-00031
8. Dyer RA, Farina Z, Joubert IA, Du Toit P, Meyer M, Torr G, et al. Crystalloid preload versus rapid crystalloid administration after induction of spinal anaesthesia (coload) for elective caesarean section. Anaesth Intensive Care. 2004;32:351-7. PMID: 15264729 DOI: 10.1177/0310057X0403200308
9. Mojica JL, Meléndez HJ, Bautista LE. The timing of intravenous crystalloid administration and incidence of cardiovascular side effects during spinal anesthesia: the results from a randomized controlled trial. Anesth Analg. 2002;94:432-437. PMID: 11812714 DOI: 10.1097/00000539-200202000-00039
10. Onarheim H. Fluid shifts following 7% hypertonic saline (2400 mosmol/L) infusion. Shock. 1995;3:350-354. PMID: 7648336
11. Tølløfsrud S, Noddeland H. Hypertonic saline and dextran after coronary artery surgery mobilises fluid excess and improves cardiorespiratory functions. Acta Anaesthesiol Scand. 1998;42:154-161. PMID: 9509195 DOI: 10.1111/j.1399-6576.1998.tb05101.x
12. Bhattacharyya S, Bisai S, Biswas H, Tiwary MK, Mallik S, Saha SM. Regional anesthesia in transurethral resection of prostate (TURP) surgery: A comparative study between saddle block and subarachnoid block. Saudi J Anaesth. 2015;9:268-271. PMID: 26240544 DOI: 10.4103/1658-354X.158497
13. Rooke GA, Freund PR, Jacobson AF. Hemodynamic response and change in organ blood volume during spinal anesthesia in elderly men with cardiac disease. Anesth Analg. 1997;85:99-105. PMID: 9212130 DOI: 10.1097/00000539-199707000-00018
14. Lewis SR, Pritchard MW, Evans DJ, Butler AR, Alderson P, Smith AF, et al. Colloids versus crystalloids for fluid resuscitation in critically ill people. Cochrane Database Syst Rev. 2018;8:CD000567. PMID: 30073665 DOI: 10.1002/14651858.CD000567.pub7
15. Järvelä K, Koskinen M, Kööbi T. Effects of hypertonic saline (7.5%) on extracellular fluid volumes in healthy volunteers. Anaesthesia. 2003;58:878-881. PMID: 12911361 DOI: 10.1046/j.1365-2044.2003.03332.x
16. Hahn RG. The transurethral resection syndrome. Acta Anaesthesiol Scand. 1991;35:557-567. PMID: 1785231 DOI: 10.1111/j.1399-6576.1991.tb03348.x
17. Teoh WH, Sia AT. Colloid preload versus coload for spinal anesthesia for cesarean delivery: the effects on maternal cardiac output. Anesth Analg. 2009;108:1592-8. PMID: 19372341 DOI: 10.1213/ane.0b013e31819e016d
18. McDonald S, Fernando R, Ashpole K, Columb M. Maternal cardiac output changes after crystalloid or colloid coload following spinal anesthesia for elective cesarean delivery: a randomized controlled trial. Anesth Analg. 2011;113:803-810. PMID: 21890886 DOI: 10.1213/ANE.0b013e31822c0f08
19. Ueyama H, He YL, Tanigami H, Mashimo T, Yoshiya I. Effects of crystalloid and colloid preload on blood volume in the parturient undergoing spinal anesthesia for elective Cesarean section. Anesthesiology. 1999;91:1571-6. PMID: 10598596 DOI: 10.1097/00000542-199912000-00006
20. Mouren S, Delayance S, Mion G, Souktani R, Fellahi JL, Arthaud M, et al. Mechanisms of increased myocardial contractility with hypertonic saline solutions in isolated blood-perfused rabbit hearts. Anesth Analg. 1995;81:777-782. PMID: 7574010 DOI: 10.1097/00000539-199510000-00021
21. Mazzoni MC, Borgström P, Arfors KE, Intaglietta M. Dynamic fluid redistribution in hyperosmotic resuscitation of hypovolemic hemorrhage. Am J Physiol. 1988;255:H629-637. PMID: 2458047 DOI: 10.1152/ajpheart.1988.255.3.H629
22. Islam A, Siddique MRU, Kamal M, Banik D, Akhtaruzzaman AKM, Hye MA. Effects of hypertonic saline preloading in sub arachnoid blockade for transurethral resection of prostate - A comparative study. J Bangladesh Soc Anaesthesiologists. 2014;22:66-71. DOI: 10.3329/jbsa.v22i2.18145
23. Ferré F, Martin C, Bosch L, Kurrek M, Lairez O, Minville V. Control of Spinal Anesthesia-Induced Hypotension in Adults.

Local Reg Anesth. 2020;13:39-46. PMID: 32581577 DOI: 10.2147/LRA.S240753

24. Latif FS, Ibraheem DA, Alansary AM, Salama MGM. Comparison between Hypertonic Saline (3%) and Normal Saline (0.9%) as a Preload before Spinal Anaesthesia in Caesarean Section. Egypt J Hosp Med. 2018;72:5513-6. DOI: 10.21608/ejhm.2018.11388

25. Magalhães DMS, Zanoni FL, Correia CJ, Simas R, Soares RGF, Sannomiya P, et al. Hypertonic Saline Modulates Heart Function and Myocardial Inflammatory Alterations in Brain-Dead Rats. J Surg Res. 2019;235:8-15. PMID: 30691854 DOI: 10.1016/j.jss.2018.09.058

26. Pascual JM, Watson JC, Runyon AE, Wade CE, Kramer GC. Resuscitation of intraoperative hypovolemia: a comparison of normal saline and hyperosmotic/hyperoncotic solutions in swine. Crit Care Med. 1992;20:200-210. PMID: 1371098

27. Farid Z, Mushtaq R, Ashraf S, Zaeem K. Comparative efficacy of crystalloid preloading and co-loading to prevent spinal anesthesia induced hypotension in elective caesarean section. Pak J Med Health Sci. 2016;10:42-45. [FreeFullText]

28. Khan MU, Memon AS, Ishaq M, Aqil M. Preload Versus Coload and Vasopressor Requirement for the Prevention of Spinal Anesthesia Induced Hypotension in Non-Obstetric Patients. J Coll Physicians Surg Pak. 2015;25:851-855. PMID: 26691355

29. Kulkarni AG, Asai O, Tarkase AS. Comparative evaluation of co-loading versus preloading for prevention of post-spinal hypotension in elective caesarean section. Indian J Clin Anaesth. 2016;3:335-341. DOI: 10.5958/2394-4994.2016.00059.7

30. Oh AY, Hwang JW, Song IA, Kim MH, Ryu JH, Park HP, et al. Influence of the timing of administration of crystalloid on maternal hypotension during spinal anesthesia for cesarean delivery: preload versus coload. BMC Anesthesiol. 2014;14:36. PMID: 24920942 DOI: 10.1186/1471-2253-14-36

