

Original Article

The Effects of 6% Hydroxyethyl Starch Compared with Normal Saline on Controlling Undesirable Hemodynamic Changes Following Spinal Anesthesia in Patients Undergoing Orthopedic Surgery: a Randomized Clinical Trial

Siamak Yaghobi¹, Amir Hesam Alirezaei², Mahmood Bakhtiyari^{3,4}, Marzieh-Beigom Khezri¹, Nilofar Massoudi⁵✉

Abstract

Background: The aim of the current study was to compare the effects of normal saline solution and 6% hydroxyethyl starch (HES/HAES) solution on hemodynamic changes after spinal anesthesia in patients undergoing lower limb orthopedic surgery.

Materials and Methods: This randomized clinical trial was performed on 50 patients undergoing surgery, aged 20-60, with physical status of ASA I, II. Before surgery, the hemodynamic status of each patient including systolic and diastolic blood pressure, heart rate, and central venous pressure was measured. Then, the patients were randomly divided into two groups and for the control group, 7 ml/kg 9% (or normal) saline and for the experimental group 6% hydroxyethyl starch were administered. Hemodynamic indices were re-measured after the completion of infusion, and then spinal anesthesia was performed. After anesthesia, hemodynamic indices were measured every 5 minutes for 1 hour and then every 10 minutes for 2 hours. The analysis of variance (ANOVA) for repeated measures was used to evaluate the significant changes in hemodynamic indices.

Results: The mean and standard deviation of systolic and diastolic blood pressure, heart rate, and central venous pressure in the control group were 113.0 (7.3), 73.0 (6.0), 95.6 (5.7), and 5.8 (0.9), respectively, and in the intervention group were 104.8 (5.5), 66.1 (4.2), 95.8 (8.2), and 4.3 (0.9). ANOVA for repeated measures showed that the incidence of decreasing changes in systolic and diastolic blood pressure, heart rate, and central venous pressure of the patients for whom hydroxyethyl starch was prescribed was significantly less than that of the patients for whom normal saline was prescribed.

Conclusion: Hydroxyethyl starch has a more effective role in controlling hemodynamic changes before spinal anesthesia than normal saline.

Keywords: Hydroxyethyl starch, Normal saline, Hemodynamic, Randomized clinical trial.

1. Department of Anesthesiology, School of Medicine, Qazvin University of Medical Sciences, Iran
2. Clinical Research Development Center at Shahid Modarres Hospital, Department of Nephrology, Shahid Beheshti University of Medical Sciences, Tehran, Iran
- 3 PhD, Department of Community Medicine, School of Medicine, Alborz University of Medical Sciences, Karaj, Iran
4. Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
5. Clinical Research Development Center at Shahid Modarres Hospital, Department of Anesthesiology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

✉ **Corresponding Author:** Nilofar Massoudi (MD), Clinical Research Development Center at Shahid Modarres Hospital, Department of Anesthesiology, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Tel/Fax: (+98) 21 22360635.

Email: Massodi@sbmu.ac.ir

Please cite this article as: Yaghobi S, Alirezaei AH, Bakhtiyari M, Khezri MB, Massoudi N. The Effects of 6% Hydroxyethyl Starch Compared with Normal Saline on Controlling Undesirable Hemodynamic Changes Following Spinal Anesthesia in Patients Undergoing Orthopedic Surgery: a Randomized Clinical Trial. *J Cell Mol Anesth.* 2017; 2(4):180-8.

Introduction

Spinal anesthesia, except for contraindications, is the preferred method of performing numbness in lower limb surgery (1). Spinal anesthesia's benefits such as reduction in blood loss, infection rates, need for transfusion, and thromboembolic events compared with those of general anesthesia have been confirmed in numerous studies (2).

Despite being safe and having many benefits, this anesthetic technique has side effects such as hemodynamic changes, headaches, cauda equine syndrome, and radiculopathy. Among the complications of this anesthetic technique, hypotension is very common in 95% of the patients in line with findings of some researchers (3). The main reason for this event is the block of the sympathetic nervous system following cardiac output reduction and/or vascular resistance reduction. This complication is considered to be a very important and serious complication because it can lead to the limitation of blood supply to vital organs such as the heart and brain (4).

To reduce the adverse effects of hemodynamic changes following spinal anesthesia, especially hypotension, various therapeutic approaches have been studied (5-7). Comparing the effects of three different doses of dihydroergotamine—a family of ergot alkaloids—on hemodynamic changes following spinal anesthesia, Sahmedini et al. (4) Revealed that intravenous injection of this drug at a dose of 5-10 mcg/kg was effective in the treatment of spinal anesthesia-induced hypotension. Baygmohammadi et al. (8), in a double-blind clinical trial, compared the effect of atropine and placebo (normal saline) on hemodynamic changes following spinal anesthesia. The results of this study demonstrated that hemodynamic changes in the atropine-receptor group were significantly lower than those in the placebo-receptor group. McDonnell et al (9), also performed a randomized double-blind clinical trial and determined that both metaraminol and phenylephrine had the same advantages in preventing hypotension due to spinal anesthesia.

In general, one of the recommended methods for preventing hypotension following spinal anesthesia is the administration of crystalloid solutions, including Ringer's solution (10). However, owing to the fact that

the administration of high volumes of these solutions can lead to a peripheral edema in cardio-pulmonary patients and then a reduction in oxygen-carrying capacity, it seems that the administration of colloid solutions is the best choice (11). Hydroxyethyl starch (HES) is a colloidal, synthetically adapted polymer of amylopectin, a waxy starch derived from maize or sorghum (Figure 1). Clinically, HES is used for volume alternate to keep on or improve tissue perfusion in patients with sepsis, trauma, shock, or surgical stress (10, 12, 13). In addition to its consequence on continuation of stability of hemodynamic parameters, latest studies have shown that HES may decrease capillary leakage in many pathological circumstances that increase capillary permeability (14).

Neuraxial block is one of the methods that can be used to perform spinal anesthesia in lower limb surgeries. This technique, like any other medical technique, has complications, one of which is hypotension due to decreased intravascular volume of hypovolemia because of patients fasting (15). Therefore, in order to prevent this complication, the use of a solution that can produce more intravascular volume, such as colloidal solutions, is more effective than crystalloid solutions (16). Since there is not enough information about the effect of prescribing colloidal solutions prior to spinal anesthesia in preventing hemodynamic changes in patients undergoing lower limb orthopedic surgery, the aim of the present study was to compare the effects of normal saline and 6% hydroxyethyl starch solutions on hemodynamic changes after spinal anesthesia in patients undergoing lower limb orthopedic surgery.

Methods

This study was a double-blind randomized clinical trial being performed on 50 patients undergoing lower limb orthopedic surgery with spinal anesthesia in Shahid Rajai Hospital in Qazvin. The inclusion criteria of the study included:

- the patient should be a candidate for lower limb orthopedic surgery with spinal anesthesia,
- the age of the patient should be between 20 and 60 years of age, and
- ASA I and II physical status class

The exclusion criteria included:

- the age of the patient should be less than 20 years or more than 60 years,
- the patient should have prohibition of spinal anesthesia, and
- the patient should have hypotension or hypertension

Patients who had undergone a spinal anesthesia in a sequential manner due to lower limb trauma and had inclusion criteria were included in the study, if they were satisfied. Patients were randomly divided into two groups of normal saline and hydroxyethyl starch recipients using colored cards. The procedure of the study was that first before the surgery a CVP cannula (14 gauge) which was positioned into the right antecubital area and in the supine position using regional anesthesia was used to measure systolic and diastolic blood pressure, heart rate, and central venous pressure of each patient (i.e., baseline measurements). Then, the patients were randomly divided into two groups. For control group, 7 ml/kg normal saline and for the experimental group 6% hydroxyethyl starch was administered. These solutions were infused from the peripheral vein and within 10 minutes. After the completion of infusion, systolic and diastolic blood pressure, heart rate, and central venous pressure were measured and then spinal anesthesia at the L3.4 level was performed using a 22-gauge needle and 3 cc of 0.5% Marcaine. After anesthesia, the anesthesia level was measured using the pin-prick technique and systolic and diastolic blood pressure, heart rate, and central venous pressure values were measured every 5 minutes for 1 hour and then every 10 minutes for 2 hours. To describe the results, the mean \pm standard deviation and number (percent) were used. An analysis of variance for repeated measures was used to examine the existence of significant changes in these variables over time.

Results

The number of participants in this study was 50 (i.e., 25 participants in the intervention group and 25 participants in the comparison group). 34 (68%) participants were male and the rest were female. The mean (SD) age of the patients was 45.3 (9.07). The gender composition of the participants in the intervention and control group was completely similar

(50% male and 50% female). The mean (SD) age of the participants in the intervention and control group was 44.24 (8.81) and 46.36 (9.38), respectively. The independent t-test did not show a significant difference between these means ($P = 0.414$).

The mean (SD) systolic blood pressure at baseline in the intervention and control groups was 104.8 (5.5) and 113.0 (7.3), respectively ($P < 0.001$). The mean (SD) diastolic blood pressure at baseline in the intervention and control groups was 66.1 (4.2) and 73.0 (6.0), respectively ($P < 0.001$). The mean (SD) heart rate at baseline in the intervention and control groups was 95.8 (8.2) and 95.6 (5.7), respectively (P -value 0.921). The mean (SD) central venous pressure at baseline in the intervention and control groups was 4.3 (0.9) and 5.8 (0.9), respectively ($P < 0.001$).

The mean systolic and diastolic blood pressure, heart rate, and central venous pressure based on measurement time are presented in Table 1. To determine the existence of significant changes in these variables over time, the analysis of variance for repeated measures was used. According to Mauchly's test of sphericity, for each of the four outcomes examined, the coefficients of continuous measurements were significantly different, so the Greenhouse-Geisser correction was used to check for significant changes in each of the four outcomes. In addition, due to the significant differences in baseline values of the two groups, these values were considered as covariate in the equation to modify their effect in the comparison of changes between the two groups. In this way, the analysis of variance for repeated measures with the Greenhouse-Geisser correction of sphericity and modulation of the effects of age, gender, and basic parameters of the outcome variables was performed. In the following sections, the results of these tests are presented separately for the outcome variables.

Systolic Blood Pressure: The mean systolic blood pressure based on measurement time and intervention group type (i.e., normal saline and hydroxyethyl starch groups) are presented in Table 1. According to this table, the mean systolic blood pressure significantly increased in both groups after completion of infusion compared with the baseline values and 5 minutes after

Table 1: The status of hemodynamic changes (SBP&DBP) over time in the groups treated with Hydroxyethyl starch and normal saline.

Measurement times	Systolic blood pressure			Diastolic blood pressure		
	Intervention group (Hydroxyethyl starch)	Control group (normal saline)	P-value	Intervention group (Hydroxyethyl starch)	Control group (normal saline)	P-value
	Mean±SD	Mean±SD		Mean±SD	Mean±SD	
After the completion of infusion	124.92 ± 4.77	116.17 ± 6.68	<0.001	82.16 ± 5.15	76.58 ± 5.84	0.001
20 th minute after spinal anesthesia	110.88 ± 6.66	91.75 ± 5.50	<0.001	70.64 ± 4.67	60.17 ± 5.34	<0.001
40 th minute after spinal anesthesia	117.16 ± 3.75	97.50 ± 5.99	<0.001	75.88 ± 4.08	64.42 ± 4.34	<0.001
60 th minute after spinal anesthesia	120.74 ± 3.02	104.79 ± 6.29	<0.001	52.78 ± 4.33	67.54 ± 2.84	<0.001
80 th minute after spinal anesthesia	122.08 ± 2.84	109.13 ± 5.29	<0.001	80.08 ± 3.52	69.67 ± 3.21	<0.001
100 th minute after spinal anesthesia	120.44 ± 4.16	110.08 ± 4.77	<0.001	79.56 ± 5.29	69.75 ± 2.80	<0.001
120 th minute after spinal anesthesia	121.00 ± 2.63	112.42 ± 4.89	<0.001	79.04 ± 3.90	71.83 ± 4.92	<0.001
140 th minute after spinal anesthesia	121.96 ± 2.85	115.25 ± 5.41	<0.001	80.56 ± 4.10	73.96 ± 5.62	<0.001
160 th minute after spinal anesthesia	124.92 ± 4.18	116.88 ± 5.24	<0.001	81.22 ± 5.50	74.71 ± 6.23	<0.001
180 th minute after spinal anesthesia	125.64 ± 3.93	116.71 ± 5.29	<0.001	85.20 ± 5.09	75.79 ± 5.59	<0.001

spinal anesthesia significantly decreased. Then, from the fifth minute to the end of the study, there was a slowdown increase (despite slight reductions at some time points). In Figure 1, changes in mean systolic blood pressure are presented for both groups (i.e., hydroxyethyl starch and normal saline groups). The analysis of variance for repeated measures revealed the following issues:

- 1) The changes in mean systolic blood pressure of the participants were not statistically significant (P value: 0.082 and F=1.84),
- 2) The effect of the prescribed drug on the changes in systolic blood pressure was statistically significant (P<0.001 and F=15.36); in other words, in patients treated with hydroxyethyl starch, the systolic blood pressure drop was significantly lower than that of those for whom normal saline was prescribed,
- 3) Gender had a significant effect on the changes in the mean systolic blood pressure of the participants during the study period (P-value 0.026 and F=2.34); in other words, the decreasing changes in mean systolic blood

pressure in females were significantly higher than that of males (P-value: 0.052 and F=1.85);

4) Age had no significant effect on the changes in the mean diastolic blood pressure of the participants during the study period (P-value: 0.532 and F=0.86); and

5) There was no significant interaction between gender and prescribed drugs; in other words, the effect of hydroxyethyl starch on systolic blood pressure changes in males and females did not significantly differ (P value: 0.625 and F=0.752).

Diastolic Blood Pressure: The mean diastolic blood pressure based on measurement time and intervention group type (i.e., normal saline and hydroxyethyl starch groups) are presented in Table 1. According to this table, the mean diastolic blood pressure significantly increased in both groups after completion of infusion compared to the baseline values, and 5 minutes after spinal anesthesia significantly decreased.

Table 2: The status of hemodynamic changes (HR&CVP) over time in the groups treated with Hydroxyethyl starch and normal saline.

Measurement times	Heart Rate			CVP		
	Intervention group (Hydroxyethyl starch)	Control group (normal saline)	P-value	Intervention group (Hydroxyethyl starch)	Control group (normal saline)	P-value
	Mean±SD	Mean±SD		Mean±SD	Mean±SD	
After the completion of infusion	85.16 ± 6.61	91.96 ± 4.93	<0.001	8.24 ± 0.60	4.96 ± 0.81	<0.001
20 th minute after spinal anesthesia	88.40 ± 5.02	85.48 ± 12.49	0.28	6.36 ± 0.64	5.75 ± 0.61	0.001
40 th minute after spinal anesthesia	86.16 ± 5.35	85.72 ± 9.97	0.84	6.24 ± 0.52	5.75 ± 0.85	0.012
60 th minute after spinal anesthesia	83.80 ± 4.09	85.00 ± 6.75	0.45	6.12 ± 0.60	5.75 ± 0.74	0.06
80 th minute after spinal anesthesia	82.48 ± 3.39	85.16 ± 5.77	0.051	6.04 ± 0.68	6.17 ± 0.70	0.68
100 th minute after spinal anesthesia	81.72 ± 4.86	84.80 ± 6.03	0.052	6.08 ± 0.57	6.13 ± 0.74	0.99
120 th minute after spinal anesthesia	81.12 ± 4.18	85.28 ± 4.86	0.002	6.08 ± 0.70	5.83 ± 0.82	0.20
140 th minute after spinal anesthesia	79.00 ± 4.58	84.68 ± 5.58	<0.001	6.04 ± 0.54	6.13 ± 0.90	0.85
160 th minute after spinal anesthesia	76.78 ± 4.68	84.12 ± 4.76	<0.001	5.80 ± 0.76	6.25 ± 0.99	0.08
180 th minute after spinal anesthesia	76.80 ± 3.88	83.40 ± 4.59	<0.001	5.72 ± 0.68	6.33 ± 1.05	0.019

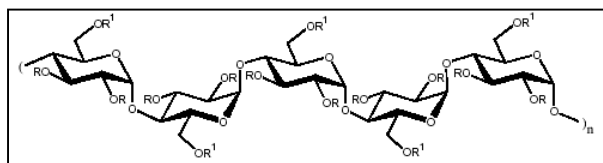


Figure 1. The structural formula of 6% hydroxyethyl starch.

Then, from the fifth minute to the end of the study, there was a slowdown increase (despite slight reductions at some time points). In Figure 2, changes in mean diastolic blood pressure are presented for both groups (i.e., hydroxyethyl starch and normal saline groups). The analysis of variance for repeated measures depicted the following issues:

- 1) The changes in mean diastolic blood pressure of the participants during the study period were not statistically significant (P value: 0.084 and F=1.89),
- 2) The effect of the prescribed drug on the changes in diastolic blood pressure was statistically significant (P=0.001 and F=4.05); in other words, in patients treated with hydroxyethyl starch, the diastolic blood

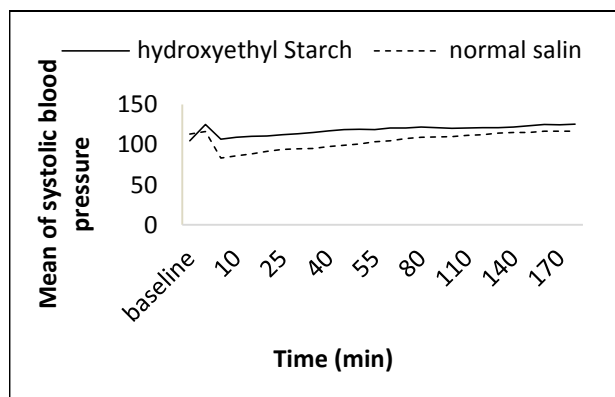


Figure 2. Changes in Mean Systolic Blood Pressure of Groups under Investigation (i.e., hydroxyethyl starch and normal saline groups).

- pressure drop was significantly lower than that of those for whom normal saline was prescribed,
- 3) Gender had no significant effect on the changes in the mean diastolic blood pressure of the participants

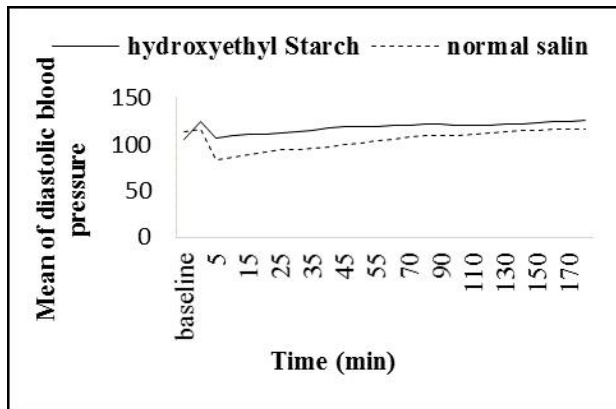


Figure 3. Changes in Mean Diastolic Blood Pressure of Groups under Investigation (I.E., Hydroxyethyl Starch and Normal Saline Groups).

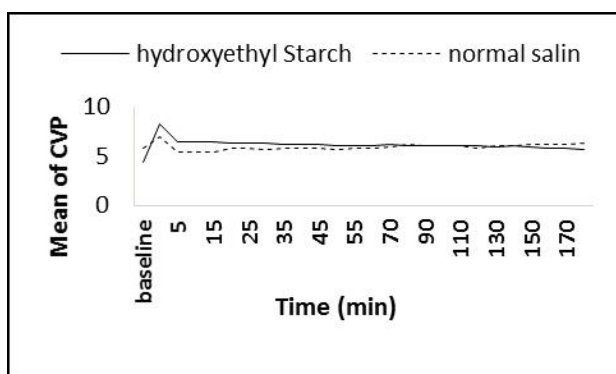


Figure 5. Changes in Mean Central Venous Pressure (CVP) of Groups under Investigation (i.e., hydroxyethyl starch and normal saline groups).

during the study period (P-value = 0.464 and F=0.94); in other words, the changes in mean diastolic blood pressure in males and females did not significantly differ,

4) Age had no significant effect on the changes in the mean diastolic blood pressure of the participants during the study period (P-value: 0.287 and F = 1.26), and

5) There was no significant interaction between gender and prescribed drugs; in other words, the effect of hydroxyethyl starch on diastolic blood pressure changes in males and females did not significantly differ (P value: 0.629 and F = 0.72).

Heart Rate

The mean heart rate based on measurement time and intervention group type (i.e., normal saline and hydroxyethyl starch groups) is presented in Table 1. According to this table, the mean heart rate significantly increased in both groups after completion of infusion compared to the baseline values, and 5

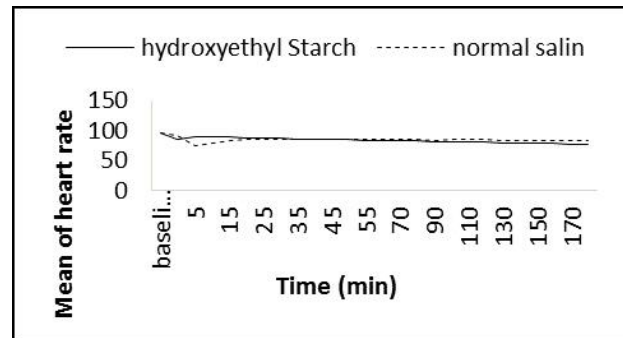


Figure 4. Changes in Mean Heart Rate of Groups under Investigation (I.E., Hydroxyethyl Starch and Normal Saline Groups).

minutes after spinal anesthesia significantly decreased. Then, from the fifth minute to the end of the study, there was a slowdown increase (despite slight reductions at some time points). In Figure 3, changes in mean heart rate are presented for both groups (i.e., hydroxyethyl starch and normal saline groups). The analysis of variance for repeated measures found out the following issues:

- 1) The changes in mean heart rate of the participants during the study period were not statistically significant (P value: 0.497 and F=0.89),
- 2) The effect of the prescribed drug on the changes in heart rate was statistically significant (p<0.001 and F=16.58); in other words, in patients treated with hydroxyethyl starch, the heart rate drop was significantly lower than that of those for whom normal saline was prescribed. As it is depicted in the figure, until the thirty-fifth minute, the mean heart rate in the hydroxyethyl starch group was higher than that of the normal saline group, from the 40th minute to the fifty-fifth minute, it was similar in the two groups, and after 50th minute the mean heart rate in the hydroxyethyl starch group was lower than the normal saline group.
- 3) Gender had no significant effect on the changes in the mean heart rate of the participants during the study period (P-value = 0.394 and F=1.01); in other words, the changes in mean heart rate in males and females did not significantly differ,
- 4) Age had no significant effect on the changes in the mean central venous pressure of the participants during the study period (P-value: 0.704 and F=0.50), and
- 5) There was no significant interaction between gender and prescribed drugs; in other words, the effect of hydroxyethyl starch on heart rate changes in males and

females did not significantly differ (P value: 0.101 and $F=2.05$).

Central Venous Pressure (CVP)

The mean central venous pressure based on measurement time and intervention group type (i.e., normal saline and hydroxyethyl starch groups) is presented in Table 1. According to this table, the mean central venous pressure significantly increased in both groups after completion of infusion compared to the baseline values, and 5 minutes after spinal anesthesia significantly decreased. Then, from the fifth minute to the end of the study, there was a slowdown increase (despite slight reductions at some time points). In Figure 4, changes in mean central venous pressure are presented for both groups (i.e., hydroxyethyl starch and normal saline groups). The analysis of variance for repeated measures revealed the following issues:

- 1) The changes in mean central venous pressure of the participants during the study period were not statistically significant (P value: 0.596 and $F = 5.72$),
- 2) The effect of the prescribed drug on the changes in central venous pressure was statistically significant ($P < 0.001$ and $F = 5.72$); in other words, in patients treated with hydroxyethyl starch, the central venous pressure drop was significantly lower than that of those for whom normal saline was prescribed.
- 3) Gender had no significant effect on the changes in the mean central venous pressure of the participants during the study period (P-value = 0.710 and $F = 0.74$); in other words, the changes in mean central venous pressure in males and females did not significantly differ,
- 4) Age had no significant effect on the changes in the mean central venous pressure of the participants during the study period (P-value: 0.656 and $F = 0.80$), and
- 5) There was no significant interaction between gender and prescribed drugs; in other words, the effect of hydroxyethyl starch on central venous pressure changes in males and females did not significantly differ (P value=0.462 and $F=0.985$).

Discussion

In the current study, the effects of hydroxyethyl starch and normal saline on hemodynamic changes after spinal anesthesia in patients undergoing lower limb orthopedic surgery were investigated. The two main options for controlling hemodynamic changes

following spinal anesthesia are colloids and crystalloids(17). The role of colloids in improving the hemodynamic changes resulted from spinal anesthesia compared with crystalloids has been confirmed in several studies(18-20).

In this study, hydroxyethyl starch—as one of the known colloidal solutions—was significantly more effective than normal saline—as a standard treatment—in controlling the hemodynamic changes including changes in systolic and diastolic blood pressure, heart rate, and central venous pressure. The mean systolic and diastolic blood pressure drop in patients for whom hydroxyethyl starch was prescribed was significantly lower than that of those for whom normal saline was prescribed. Karinen et al. (21), comparing the effects of crystalloid (lactated Ringer's) and colloidal (hydroxyethyl starch) solutions on hemodynamic changes during spinal anesthesia in cesarean section, showed that the incidence of hypotension after spinal anesthesia in mothers receiving hydroxyethyl starch was lower than mothers receiving lactated Ringer's (38% vs. 62%). In another study, it was demonstrated that immediate infusion of hydroxyethyl starch instantly after spinal anesthesia not only prevented hypertension but also had much more stable effects than lactated Ringer's solution (22). In a clinical trial, Romdhani et al. (23) also compared the effects of hydroxyethyl starch and normal saline on the changes in systolic, diastolic, and arterial blood pressure and heart rate in women who chose cesarean delivery for delivery. In their study, the two groups had just a significant difference in the incidence of hypotension; hence, the incidence of this disorder was significantly lower in the hydroxyethyl starch group than in the other group. However, there was no significant difference between the two groups in terms of preventing heart rate reduction. In a study conducted by Donati et al. (24), there was also no significant difference between the changes in heart rate of the patients receiving hydroxyethyl starch and the control group (no treatment). They attributed this between-groups similarities in heart rate changes to the substantial cardiovascular stability resulted from the selective spinal anesthesia which did not activate a compensatory vagal effect. Meanwhile, in the present study, hydroxyethyl starch was significantly better than normal saline in preventing heart rate reduction.

According to Cook (25), the weaker effect of normal saline in preventing heart rate loss compared with hydroxyethyl starch can be attributed to the weaker ability of this crystalloid solution in maintaining the balance of sympathetic and vagal activity.

The mean of reduction of central venous pressure was also significantly different in the two groups; the hydroxyethyl starch group had totally a lower loss in the mean central pressure. Marhofer et al. (26) also observed that central venous pressure loss of elderly patients, who had been hydrated before spinal anesthesia with hydroxyethyl starch to undergo hip surgery, was significantly less than that of the control group. According to Pollard, one of the reasons for the reduction in central venous pressure after spinal anesthesia is blood loss. For instance, with 10 mL/kg withdrawal blood, the decrease in central venous pressure during spinal anesthesia may be 66% on average. On the other hand, observing the absence of significant changes in the mean central venous pressure during spinal anesthesia, Poon et al. (27) concluded that a significant drop in blood pressure during spinal anesthesia was not due to blood loss during surgery. Based on the results of these two studies and considering the findings of the present study, the mean systolic and diastolic blood pressure drop in the normal saline group was higher than the hydroxyethyl starch group; thus, it can be concluded that the decrease in blood pressure in the normal saline group compared with the hydroxyethyl starch group was probably due to a greater blood loss during surgery.

Conclusion

With regard to the consistency of the results of this study with available sources, it can be determined that the administration of hydroxyethyl starch prior to spinal anesthesia can play a more effective role in controlling hemodynamic changes.

Acknowledgment

The authors would like to thank Clinical Research Development Center at Shahid Modarres Hospital for his financial support.

Conflicts of Interest

The authors declare that they have no conflict of interest.

References

- Rai A, Bhutia MP. Dexmedetomidine as an Additive to Spinal Anaesthesia in Orthopaedic Patients Undergoing Lower Limb Surgeries: A Randomized Clinical Trial Comparing Two Different Doses of Dexmedetomidine. *Journal of clinical and diagnostic research. J Clin Diagn Res.* 2017 Apr; 11(4): UC09–UC12.
- Park, Y.B., et al., Comparison of Short-Term Complications of General and Spinal Anesthesia for Primary Unilateral Total Knee Arthroplasty. *Knee Surg Relat Res.* 2017 Jun 1;29(2):96-103.
- Ahmad, M., M. Ahmad, and N. Atif, haemodynamic preservation in cesarean sections by low dose 0.5% hyperbaric bupivacaine. *Journal of Ayub Medical College Abbottabad.* 2017;29(2):211-4.
- Bergenswald L, Eklund B, Kaijser L, Klingenström P, Westermarck L. Haemodynamic effects of dihydroergotamine during spinal anaesthesia in man.. *Acta Anaesthesiol Scand.* 1972;16(4):235-9.
- Ngan Kee WD, Lee SW, Ng FF, Tan PE, Khaw KS. Randomized double-blinded comparison of norepinephrine and phenylephrine for maintenance of blood pressure during spinal anesthesia for cesarean delivery. *Anesthesiology.* 2015 Apr;122(4):736-45.
- Marashi SM, Soltani-Omid S, Soltani Mohammadi S, Aghajani Y, Movafegh A. Comparing Two Different Doses of Intravenous Ondansetron With Placebo on Attenuation of Spinal-induced Hypotension and Shivering. *Anesth Pain Med.* 2014 Mar 18;4(2):e12055.
- Pearse RM, Harrison DA, MacDonald N, Gillies MA, Blunt M, Ackland G, Grocott MP, Ahern A, Griggs K, Scott R, Hinds C, Rowan K; OPTIMISE Study Group. Effect of a perioperative, cardiac output-guided hemodynamic therapy algorithm on outcomes following major gastrointestinal surgery: a randomized clinical trial and systematic review. *JAMA.* 2014 Jun 4;311(21):2181-90.
- Lim HH, Ho KM, Choi WY, Teoh GS, Chiu KY. The use of intravenous atropine after a saline infusion in the prevention of spinal anesthesia-induced hypotension in elderly patients. *Anesth Analg.* 2000 Nov;91(5):1203-6.
- McDonnell NJ, Paech MJ, Muchatuta NA, Hillyard S, Nathan EA. A randomised double-blind trial of phenylephrine and metaraminol infusions for prevention of hypotension during spinal and combined spinal-epidural anaesthesia for elective caesarean section. *Anaesthesia.* 2017 May;72(5):609-617.
- Feliu J, Ventura JL, Segura R, Rodas G, Riera J, Estruch A, Zamora A, Capdevila L. Differences between lactate concentration of samples from ear lobe and the finger tip. *J Physiol Biochem.* 1999;55(4):333-9..
- Davis AL, Carcillo JA, Aneja RK, Deymann AJ, Lin JC, Nguyen TC, Okhuysen-Cawley RS, Relvas MS, Rozenfeld RA, Skippen PW, Stojadinovic BJ, Williams EA, Yeh TS, Balamuth F, Brierley J, de Caen AR, Cheifetz IM, Choong K, Conway E Jr, Cornell T, Doctor A, Dugas MA, Feldman JD, Fitzgerald JC, Flori HR, Fortenberry JD, Graciano AL, Greenwald BM, Hall MW, Han YY, Hernan LJ, Irazuza JE, Iselin E, van der Jagt EW, Jeffries HE, Kache S, Katyal

- C, Kissoon NT, Kon AA, Kutko MC, MacLaren G, Maul T, Mehta R, Odetola F, Parbuoni K, Paul R, Peters MJ, Ranjit S, Reuter-Rice KE, Schnitzler EJ, Scott HF, Torres A Jr, Weingarten-Abrams J, Weiss SL, Zimmerman JJ, Zuckerberg AL. American College of Critical Care Medicine Clinical Practice Parameters for Hemodynamic Support of Pediatric and Neonatal Septic Shock. *Crit Care Med.* 2017;45(6):1061-1093.
12. Madhusudan P, Tirupakuzhi Vijayaraghavan BK, Cove ME. Fluid resuscitation in sepsis: reexamining the paradigm. *Biomed Res Int.* 2014;2014:984082.
13. Nicholson Jp, Wolmarans Mr, Park Gr. The role of albumin in critical illness. *Br J Anaesth.* 2000 Oct;85(4):599-610.
14. Kaplan SS, Park TS, Gonzales ER, Gidday JM. Hydroxyethyl starch reduces leukocyte adherence and vascular injury in the newborn pig cerebral circulation after asphyxia. *Stroke.* 2000;31(9):2218-23.
15. Heesen M, Klimek M, Hoeks SE, Rossaint R. Prevention of Spinal Anesthesia-Induced Hypotension During Cesarean Delivery by 5-Hydroxytryptamine-3 Receptor Antagonists: A Systematic Review and Meta-analysis and Meta-regression. *Anesth Analg.* 2016;123(4):977-88.
16. Oh AY, Hwang JW, Song IA, Kim MH, Ryu JH, Park HP, Jeon YT, Do SH. Influence of the timing of administration of crystalloid on maternal hypotension during spinal anesthesia for cesarean delivery: preload versus coload. *BMC Anesthesiol.* 2014 16;14:36.
17. Terkawi AS, Larkin SK, Tsang S, Sheeran JS, Tiouririne M. Effects of hydroxyethyl starch 6 % (130/0.4) on blood loss during cesarean delivery: a propensity-matched analysis. *J Anesth.* 2016 Oct;30(5):796-802.
18. Upadya M, Bhat S, Paul S. Six percent hetastarch versus lactated Ringer's solution - for preloading before spinal anesthesia for cesarean section. *Anesth Essays Res.* 2016; 10(1):33-7.
19. Unlugenc H , Turktan M , Evruke IC , Gunduz M , Burgut R , Yapicioglu-Yildizdas H , Isik G. Rapid fluid administration and the incidence of hypotension induced by spinal anesthesia and ephedrine requirement: the effect of crystalloid versus colloid coload. *Middle East J Anaesthesiol.* 2015; 23(3):273-81.
20. Ripollés Melchor J, Espinosa Á, Martínez Hurtado E, Casans Francés R, Navarro Pérez R, Abad Gurumeta A, Calvo Vecino JM. Colloids versus crystalloids in the prevention of hypotension induced by spinal anesthesia in elective cesarean section. A systematic review and meta-analysis. *Minerva Anesthesiol.* 2015; 81(9):1019-30.
21. 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(6):1571-6.
22. Zorko N, Kamenik M, Starc V. The effect of Trendelenburg position, lactated Ringer's solution and 6% hydroxyethyl starch solution on cardiac output after spinal anesthesia. *Anesth Analg.* 2009 Feb;108(2):655-9.
23. Romdhani C, Trabelsi W, Lebbi A, Naas I, Elaskri H, Gharsallah H, Rachdi R, Ferjani M. Lower incidence of hypotension following spinal anesthesia with 6% hydroxyethyl starch preload compared to 9 % saline solution in caesarean delivery. *Tunis Med.* 2014; 92(6):406-10.
24. Donati A, Scarcella M, Nardella R, Zompanti V, Sinkovetz L, Iuorio S, Pelaia P. Fluid challenge in patients submitted to spinal block. *Minerva Anesthesiol.* 2007; 73(4):213-8.
25. Cook PR, Malmqvist LA, Bengtsson M, Tryggvason B, Löfström JB. Vagal and sympathetic activity during spinal analgesia. *Acta Anaesthesiol Scand.* 1990 May;34(4):271-5.
26. Marhofer P, Faryniak B, Oismüller C, Koinig H, Kapral S, Mayer N. Cardiovascular effects of 6% hetastarch and lactated Ringer's solution during spinal anesthesia. *Reg Anesth Pain Med.* 1999; 24(5):399-404.
27. Poon KS, Wu KC, Chen CC, Fung ST, Lau AW, Huang CC, Wu RS. Hemodynamic changes during spinal surgery in the prone position. *Acta Anaesthesiol Taiwan.* 2008; 46(2):57-60.