

ORIGINAL PAPER

doi: 10.5455/medarch.2019.73.44-48

MED ARCH. 2019 FEB; 73(1): 44-48

RECEIVED: DEC 30, 2018 | ACCEPTED: FEB 16, 2019

¹Anesthesiology, Critical Care and Pain Management Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

²Physiology Department, Faculty of medicine, Hormozgan University of Medical Science, Bandar Abbas, Iran

³Critical Care nursing, Operation Room Department, Paramedicine Faculty, Hormozgan University of Medical Science, Bandar Abbas, Iran

Corresponding author: Hashem Jarineshin, Associate Professor of Anesthesiology, Anesthesiology, Critical Care and Pain Management Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran. E-mail: hjarineshin@yahoo.com. ORCID ID: <https://www.orcid.org/0000-0001-9269-1205>.

A Comparison Between the Effects of Preloading with Ringer's Solution and Voluven on Hemodynamic Changes in Patients Undergoing Elective Cesarean Section Under Spinal Anesthesia

Fatemeh Khosravi^{1,2}, Mojgan Alishahi¹, Yaser Khanchemehr³, Hashem Jarineshin¹

ABSTRACT

Introduction: The most common complications after spinal anesthesia for Cesarean section is hypotension. Administration of intravenous crystalloid or colloid fluid before the induction of anesthesia is a way to prevent it. **Aim:** The aim of this study was to compare the effects of preloading with ringer's solution and Voluven on hemodynamic changes in patients underwent elective Caesarean section under spinal anesthesia. **Methods:** This study was conducted on 70 pregnant women. They were randomly divided into two groups of 35. Group I received 10 ml/kg Ringer's solution (R group) and group II received 10 ml/kg Voluven (V group) over 15 min before spinal anesthesia. Mean SBP, DBP, MAP, HR, SPO₂, mean Apgar of newborn at 1 and 5 minutes after birth, mean blood pH and analysis of umbilical venous blood gases of newborns, prevalence of nausea and vomiting, and the rate of shivering and its severity were recorded in the both groups. **Results:** Blood pH and analysis of blood gases and Apgar of newborn at 1 and 5 minutes after birth were similar in both groups. Shivering did not differ significantly between the two groups. Level of anesthesia and the incidence of nausea and vomiting in the R group were significantly higher than those in the V group (P=0.041 and P=0.029, respectively). **Conclusion:** The administration of both crystalloid and colloid fluids were effective in preventing the hypotension, although the use of Voluven was preferred to Ringer with respect to the level of the blockade and the incidence of nausea and vomiting.

Keywords: Spinal Anesthesia, Preload, Ringer's Solution, Voluven Solution, Hemodynamic changes.

1. INTRODUCTION

General anesthesia and spinal anesthesia (SA) are acceptable methods for a Cesarean section (C-section). SA is often selected by anesthesiologists as a more acceptable and less risky method due to its speed, reliability and deep sensory and motor blockade. Today, for a variety of reasons, including an increased awareness of patients and getting a good feeling for mother and fetus, pregnant women may prefer SA rather than general anesthesia. Despite the benefits of SA, this method has side effects such as cardiovascular complications, hypotension, etc. The sympathetic nervous system blockade after SA may lead to a decrease in maternal blood pressure during Caesarean delivery, which is one of

the most common and dangerous complications of this method (1). A decrease in blood pressure may boost the risk of cardiovascular complications such as ischemia and heart failure. As a result of hypotension, blood flow to the uterine vascular bed decreases leading to hypoxia, acidosis, fetal distress, reduced Apgar, and risk to baby's health. Studies have shown that this response is more intense in patients who are not well hydrated before anesthesia (2). Therefore, proper monitoring of a delivery and the appropriate anesthetic technique, and more importantly, fetal and maternal health are very important during C-section (3).

Many studies have been conducted to prevent hypotension after SA. Some studies have suggested various

© 2019 Fatemeh Khosravi, Mojgan Alishahi, Yaser Khanchemehr, Hashem Jarineshin

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

methods to prevent the hypotension, such as compression bandage of patient's legs, the use of elastic stockings, positioning of the patient, prescription of vasopressors (e.g. ephedrine or phenylephrine), and infusion of colloid and crystalloid fluids as preload /or coload, that each of them has some degree of effect, but there is still no specific method to eliminate maternal hypotension (4–6).

The aim of fluid infusion prior to anesthesia is to neutralize the hypovolemia induced by SA. For this purpose, various fluid infusion protocols, including crystalloids and colloids, have been used for preloading before spinal anesthesia. Several studies have shown that administration of colloid or crystalloid fluids approximately 20 min before administration of an anesthetic drug can prevent hypertension after SA (7, 8). In spite of some procedures for the prophylaxis, the incidence of hypertension during spinal anesthesia for C-section is approximately 80%. Accordingly, numerous studies have been conducted on the type of fluid infusion (crystalloid and colloid), fluid infusion time (pre-load or during spinal anesthesia), and fluid infusion volume (8, 9). In the meantime, several studies have been able to show that colloid solutions as preloading infusion are effective in the prevention of the hypotension after SA (10, 11). Colloid fluids remain in the blood vessels for long periods of time, and a volume that they require is equal to the lost volume. However, one of the disadvantages of colloids is their deleterious effects on the hemostatic system, which is not worry about Voluven (Hydroxyethyl starch (HES) due to low molecular weight. HES is a non-ionic starch derivative. Different compounds of HES have been produced based on molecular weight and hydroxylation rate, which one of them called Voluven is used to compensate for vascular volume loss. Voluven is a new HES with fewer side effects. With regard to the physicochemical properties, Voluven with the help of the extracellular fluid can improve hemodynamic disorders using higher quality and speed (12–14).

On the other hand, many studies have been able to show that crystalloids, especially Ringer solution and Ringer's lactate solution (RL), are effective in the prevention of hypotension during SA (15). Of note crystalloids are significantly cheaper than colloids and easier to access, but they must be administered in large amounts and for a longer time. Crystalloids can also cause complications, such as edema and electrolyte disturbances. Crystalloids by entering extravascular space may not completely replace intravascular space. Some studies have demonstrated that administration of Voluven and crystalloid fluids showed no significant difference between the two groups of the patients in the hemodynamic parameters (10, 16). Considering the importance of hemodynamic stability during SA, especially in pregnant women, and the presence of the contradictory results from earlier studies.

2. AIM

The aim of the present study was to compare the effects of preloading with ringer's solution and Voluven solution

on hemodynamic changes in patients underwent elective Caesarean section under spinal anesthesia.

3. METHODS

A randomized, double-blind clinical trial was conducted on seventy term Singleton Pregnancy women aged of 18-45 years old in ASA (American Society of Anesthesiologist) I-II candidate for elective cesarean section under spinal anesthesia. This study was approved by the Ethics Committee of Hormozgan University of Medical Sciences (Code: HEC-REC-1395.033). After obtaining the written informed consent, seventy subjects were randomly divided into two groups (n=35), based on the random allocation software. Group I received 10 ml / kg Ringer's solution (Samen pharmaceutical CO, Mashad, Iran) (R group) and group II received 10 ml / kg Voluven (6% HES 130/0.4)(Voluven, 500ml, Fresenius Kabi Deutschland GmbH, D-61346 Bad Homburg v.d.h Germany) (V group) over 15 min before spinal anesthesia. Spinal anesthesia was performed with a 25-G Quincke needle in the sitting position at the L4-5 intervertebral spaces after preparation of anesthetic area. After observing a free cerebrospinal fluid (CSF), 2.5 ml of 0.5% bupivacaine and hyperbaric was injected by an anesthesiologist. Immediately after anesthesia, the patients lied in the supine position with a slight left tilt and the patients' blood pressure and heart rate were measured immediately after the blockade, then every 2-10 min, and then every 5 min until the end of surgery and recorded in the questionnaire. The levels of sensory and sympathetic blockade were also checked in the first 3-5min after the blockade and surgery was allowed when an anesthetic level was between T4 and T6. When the systolic pressure dropped below 90 mm Hg there was a decrease in Blood pressure more than 20% from baseline values, 5mg ephedrine was injected. Moreover, if there was symptomatic bradycardia (HR <60), 0.6 mg atropine was administered. The total doses of ephedrine and atropine used and the level of sensory blockade in both groups were recorded.

Both groups had received the same quantity of fluids, which included the administration of a balanced salt solution in accordance with rule 4: 2: 1. The umbilical cord blood PH and Apgar score of newborns at 1 and 5 minutes after birth in both groups were measured and recorded. Presence of nausea and vomiting in the patients of both groups were recorded. Nausea is defined as an unpleasant sensation associated with the awareness of the possible vomiting, while vomiting is described as the forceful ejection of stomach contents up through the mouth. The severity of nausea is also classified into (17): mild (sensation of unease / discomfort that does not interfere with the persons' normal activity), moderate (sensation of unease / discomfort that reduces normal activity), severe nausea (no doing the normal daily activity). Vomiting is also classified according to VAS (visual analogue scale), VAS scoring is performed as follows:

0: No vomiting, 1: episode vomiting, 2: episode vomiting, 3≤:episode vomiting.

If there was an interval of less than 5 minutes, vomiting were recorded as one episode. Ondansetron 4mg

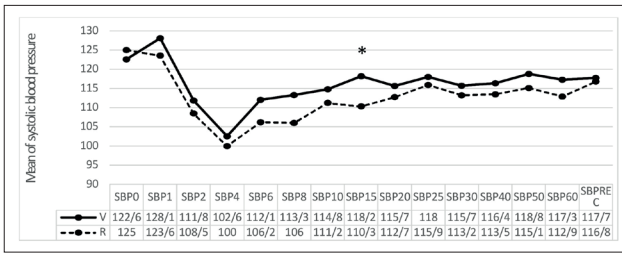


Figure 1. Comparison of Mean Systolic Blood Pressure Changes

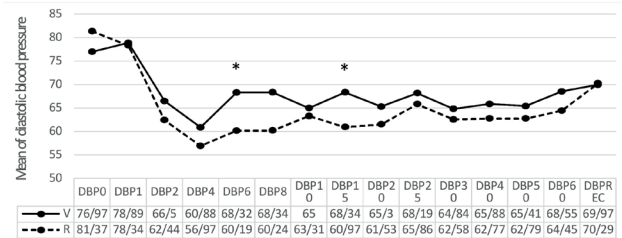


Figure 2. Comparison of Mean Diastolic Blood Pressure Changes

was administered intravenously to treat the patients with moderate to severe nausea or vomiting ≥ 2 times, without hypotension. According to a five-point scale similar to the study of Chu and Tsai (18), the incidence of shivering and its severity in the patients were recorded and evaluated as follows: No shivering, 1: piloerection or peripheral vasoconstriction but no visible shivering, 2: muscular activity in only one muscle group, 3: muscular activity in more than one muscle group but not generalized, and 4: shivering involving the whole body. Grade 0 to 2 was defined to mild shivering and grade 3 and 4 was defined for severe shivering, in case of severe shivering over Grade 2, 25 mg pethidine was administered intravenously.

Patients who had complications during surgery, such as excessive bleeding and required blood transfusion, and atony with the need for hysterectomy, as well as an incomplete block or block failure with the need for anesthesia supplementation, were excluded from the study.

Statistical analysis

Data were collected in a questionnaire which was composed of the two parts. The first part of the questionnaire included the demographic data such as age, weight, height and ASA class, and the second part included the initial hemodynamic findings during surgery. All data were analyzed by descriptive statistics (mean \pm standard deviation) and independent test, one way analysis of variance (ANOVA), repeated measures ANOVA and Chi-square test using SPSS version 19. The value of $p < 0.05$ was considered to be statistically significant.

4. RESULTS

Two groups consisted of 70 patients with 35 patients in each group were examined in this study. No significant differences were observed in the mean of weight, age, height, Body mass index (BMI) between the two groups (Table 1). Moreover, there was no significant difference in mean systolic blood pressure at different times between the two groups ($P > 0.05$), except at 15 minutes, which indicated a significant difference between the two group ($P = 0.04$), and patients in the V group had higher systolic blood pressure (Figure 1). No significant dif-

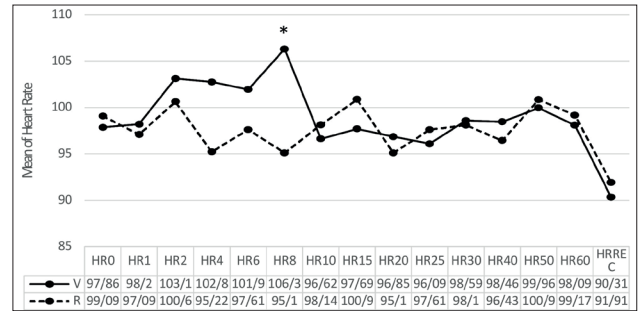


Figure 3. Comparison of Mean Heart Rate Changes

ference was observed in mean diastolic blood pressure between the two groups at different times studied ($P > 0.05$), except at 6 and 15 min, which showed a significant difference between the two groups ($P = 0.028$ and $P = 0.023$), respectively, and patients in the V group had higher diastolic blood pressure (Figure 2).

Characteristics	R group	V group
Age(year)	29.15 \pm 6.41	29.40 \pm 4.96
Weight(kg)	71.31 \pm 10.77	70.91 \pm 10.31
Height(cm)	160.50 \pm 6.63	163.43 \pm 7.20
BM (Kg/m ²)	27.78 \pm 3.77	26.14 \pm 3.75

Table 1. Demographic Characteristics of Patients in Both Groups based on Mean \pm Standard Deviation

Apgar Score	R group	V group	P value
1st minute Apgar	8.77 \pm 0.49	8.83 \pm 0.38	0.721
5th minute Apgar	9.86 \pm 0.36	9.74 \pm 0.44	0.235
PH	7.28 \pm 0.11	7.31 \pm 0.7	0.516
Pco2(mmHg)	49.37 \pm 13.41	48.12 \pm 11.53	0.812
Po2(mmHg)	46.82 \pm 26.21	53.58 \pm 25.13	0.534
HCO3(meq/Lit)	23.02 \pm 2.28	23.18 \pm 1.61	0.850

Table 2. Comparison of Mean and Standard Deviation of Apgar Score of Newborns at 1 and 5 minutes, Mean Blood PH and Analysis of Umbilical Venous Blood Gases in the Infants of Two Groups

Complication	R group	V group	P value
Vomiting	19(54.3%)	10(28.6%)	0.029*
Number of vomiting			
1	16 (84.2%)	10 (100%)	
2	3 (15.8%)	0 (0%)	0.530
≥ 3	0 (0%)	0 (0%)	
Shivering	18 (51.4%)	16 (47.1%)	0.717
Severity			
Mild	16 (88.9%)	13 (81.3%)	0.648
Severe	2 (11.1%)	3 (18.8%)	

Table 3. Incidence and Severity of Nausea and Vomiting, and Incidence and Severity of Shivering

No significant difference was observed in mean arterial blood pressure between the two groups at different times studied ($P > 0.05$), except at 15 min, which showed a significant difference between the two groups ($P = 0.015$), and patients in the V group had higher arterial blood pressure. No significant difference was observed in the mean heart rate between the two groups at different times ($P > 0.05$), except at 8 min, which showed a significant difference between the two groups ($P = 0.024$) and the patients in the V group had higher heart rate (Figure 3). There was no significant difference in the mean arterial oxygen saturation level between the two groups at different times studied ($P > 0.05$), except at 6 minutes and recovery, which showed a significant difference between the two groups ($P = 0.049$ and $P = 0.023$, respectively). At 6 min, the arterial oxygen saturation value was higher in R group and at recovery time, the arterial oxygen saturation value was greater in the V group.

Information regarding mean Apgar at 1 and 5 minutes, mean blood CO₂ pressure, mean blood oxygen pressure, and mean bicarbonate in the blood has been shown in Table 2. The mean level of anesthesia in the V group was 4.47 ± 0.86 and in the R group was 4.12 ± 0.48 ; according to Mann-Whitney test, there was a significant difference between the two groups ($P = 0.041$). About nausea and vomiting, 10 subjects in the V group (28.6%) and 19 in the R group (54.3%) had vomiting. According to the chi-square test, there was a significant difference between the two groups in the incidence of vomiting ($P=0.029$). Regarding severity of vomiting, all subjects in the V group vomited once, but 84.2% of subjects in the R group vomited once and 15.8% vomited twice, which this difference was not statistically significant ($P=0.530$). Shivering was seen in 16 (47.1%) subjects of V group and 18 (51.4%) ones in R group that according to the Chi-square test, no significant difference was observed between the two groups ($P=0.717$). In the V group, 13 (81.3%) subjects had mild shivering and 3 (18.8%) had severe shivering, and in the R group, 16 (88.9%) subjects had mild shivering and 2 (11.1%) had severe shivering, which this difference was not statistically significant. ($P = 0.648$) (Table 3).

5. DISCUSSION

The present study was conducted on 70 pregnant women underwent elective Cesarean section under spinal anesthesia. The results of the study indicated that there were no significant differences in demographic parameters such as age, weight, height, BMI, and ASA class between the two groups, which were consistent with the results of other studies (8, 9, 19). Moreover, the results obtained from this study demonstrated that there were no significant differences in hemodynamic changes, so that no significant changes in systolic and diastolic blood pressure, arterial mean blood pressure, heart rate and arterial oxygen saturation level were observed in patients who received Ringer (R group) and those who received Voluven (group V) at different times, which were consistent with the results of studies conducted by Marciniak and Tawfik (9, 19). Although the results of the present

study were not consistent with studies by Young-oh and Madi-Jebara (5, 8), in the study of Young-oh, only Hartmann's crystalloid solution was used as preload and coload at two different times, and hemodynamic changes were also measured over time. It also utilized 8 mg bupivacaine and 15 µg fentanyl to produce the blockade, which this study was different from our study. Moreover, the study of Madi-Jebara was different from our study in terms of infusion fluid volume and the dose of anesthetic medication administered. In the study, a constant volume containing 1 liter of Ringer's solution and 500 cc of Voluven solution was utilized and 10 mg bupivacaine plus 0.1 mg morphine and 2.5 µg sufentanil were used for spinal anesthesia. In addition, in terms of heart rate and blood oxygen saturation level, our results were consistent with those of the study of Mandal, but our results contrasted with those of this study for systolic blood pressure and mean arterial blood pressure. The Mandal's study used a constant volume containing 1 liter of Ringer's solution and 500 cc of Voluven solution, which could be a reason for contrasting with our results (4).

In the present study, there were no statistically significant differences between the two groups with respect to the overall incidence of hypotension and bradycardia, as well as the dose of ephedrine and atropine used, which were consistent with the Mearny's study, while contrasting with the results of other studies (2, 3, 20), which in these studies, the incidence of hypotension and dose of vasopressors (phenylephrine and ephedrine) used in the Voluven group were significantly lower compared to the Ringer group, which possible causes for these differences might be expected between the amount of the preloaded fluid infused and local anesthetic dose used for spinal anesthesia. In the present study, the neonatal outcomes, including Apgar score of newborns at 1 and 5 minutes after birth and the analysis of umbilical venous blood gases of newborns (PH, po₂, pco₂ and bicarbonate) were assessed between the two groups and the results showed no significant difference between the two groups, which were consistent with the results of other studies (3, 5, 6). It is noteworthy to mention that even the results of studies that were different from our results for hemodynamic changes, but for neonatal outcomes were consistent with our results (2, 5, 8). In the present study, the level of anesthesia induced in the patients of two groups was evaluated, although the level of anesthesia induced in the R group was slightly higher than that in the V group, this difference was also statistically significant. In this regard, only one study evaluated the relationship between the fluid therapy before spinal anesthesia and the level of blockade (21), which there was no significant difference in the mean level of anesthesia between the R and V groups, however, in contrary to our study, the level of anesthesia in the V group was slightly higher than that in the R group ($T9/94 \pm 2/15$ versus $T8/32 \pm 1/16$). However, it is important to note that this study was different from our study in term of the volume of infused colloid fluid, local anesthetic dose used and the type of surgery in patients who underwent elective lower limb surgery, which might be the possible cause of the difference between the

results. Furthermore, in our study, complications such as nausea and vomiting and their severity, shivering and its severity in the patients of both groups were evaluated, which the results indicated that the incidence of nausea and vomiting increased significantly in the R group compared to the V group, but for other cases, there was no statistically significant difference between the groups studied. Regarding nausea and vomiting, findings from the present study were consistent with those of the studies conducted by Mercier and Shahriyari (3, 22), but contrasted with the results of other studies (5, 9). Regarding shivering and its severity, unfortunately we could not find any literature that was relevant to our research.

6. CONCLUSION

The results from the present study demonstrated that using Voluven or Ringer as preload before spinal anesthesia for Cesarean section showed no differences in hemodynamic parameters during surgery and recovery, incidence of hypotension and bradycardia, ephedrine and atropine used, Apgar score, pH of arterial blood gases, and incidence of shivering between the two groups of patients and both crystalloid and colloid fluids of Voluven could be used for this purpose. Although the use of Voluven is preferred to Ringer with respect to the level of the blockade and the incidence of nausea and vomiting, the availability and lower cost of the Ringer's solution makes it easier to use.

- **Acknowledgments:** We would like to thank Hormozgan anesthesiology, critical care, and pain management research center staff, Farnoosh Towfighi and Nina Heydari for writing assistance, Esmaeel Alimolaei who contributed to the editing of the manuscript.
- **Author's contribution:** K.F., A.M. and K.Y. participants in the acquisition, analysis and interpretation of data for the work. J.H. gave substantial contribution to the conception or design of the work, drafting the article, and final approval of the version to be published.
- **Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms.
- **Financial support and sponsorship:** This study was supported by the vice-Chancellor for research, Hormozgan University of Medical Science, Bandar Abbas, Iran. The grant number is 94100.
- **Conflict of interests:** There are no conflicts of interest.

REFERENCES

1. Jarineshin H, Fekrat F, Kashani S. Effect of Ondansetron in Prevention of Spinal Anesthesia-Induced Hypotension in Pregnant Women Candidate for Elective Cesarean Section. *Journal of Current Research in Science*. 2016; 4(1): 57-62.
2. Alimian M, Mohseni M, Safaeian R, Faiz SHR, Majedi MA. Comparison of hydroxyethyl starch 6% and crystalloids for preloading in elective Cesarean section under spinal anesthesia. *Med Arch*. 2014; 68(4): 279.
3. Mercier FJ, Diemunsch P, Ducloy-Bouthors AS, Mignon A, Fischler M, Malinovsky JM, et al. 6% Hydroxyethyl starch (130/0.4) vs Ringer's lactate preloading before spinal anaesthesia for Caesarean delivery: the randomized, double-blind, multicentre CAESAR trial. *British journal of anaesthesia*. 2014; 113(3): 459-467.
4. Mandal M, Chattopadhyay S, Bagchi T, Chakrabarti S. Comparison of crystalloid and colloid preload on maternal hemodynamics in elective Cesarean section under spinal anaesthesia. *International Journal of Research in Medical Sciences*. 2017; 4(6): 2428-2435.
5. Madi-Jebara S, Ghosn A, Sleilaty G, Richa F, Cherfane A, Haddad F, et al. Prevention of hypotension after spinal anesthesia for cesarean section: 6% hydroxyethyl starch 130/0.4 (Voluven) versus lactated Ringer's solution. *Lebanese medical journal*. 2008; 56(4): 203-207.
6. Matsota P, Karakosta A, Pandazi A, Niokou D, Christodoulaki K, Kostopanagiotou G. The effect of 0.5 L 6% hydroxyethyl starch 130/0.42 versus 1 L Ringer's lactate preload on the hemodynamic status of parturients undergoing spinal anesthesia for elective cesarean delivery using arterial pulse contour analysis. *Journal of anesthesia*. 2015; 29(3): 352-359.
7. Masoudifar M, Hadi MR, Koushki AM. A Comparison between Preloading with Voluven or Lactated Ringer's Solution on Hemodynamic Status during Lower Extremity Orthopedic Procedures. *Journal of Isfahan Medical School*. 2013; 31(224).
8. 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 anesthesiology*. 2014; 14(1): 36.
9. Tawfik MM, Hayes S, Jacob FY, et al. Comparison Between Colloid Preload and Crystalloid Coload in Cesarean Section Under Spinal Anesthesia: A Randomized Controlled Trial. *Obstetric Anesthesia Digest*. 2015; 35(4): 223-224.
10. Teoh WH, Sia AT. Colloid preload versus coload for spinal anesthesia for cesarean delivery: the effects on maternal cardiac output. *Anesthesia & Analgesia*. 2009; 108(5): 1592-1598.
11. Karinen J, Räsänen J, Alahuhta S, Jouppila R, Jouppila P. Effect of crystalloid and colloid preloading on uteroplacental and maternal haemodynamic state during spinal anaesthesia for Caesarean section. *British journal of anaesthesia*. 1995; 75(5): 531-535.
12. Liu FC, Liao CH, Chang YW, Liou JT, Day YJ. Hydroxyethyl starch interferes with human blood ex vivo coagulation, platelet function and sedimentation. *Acta Anaesthesiologica Taiwanica*. 2009; 47(2): 71-78.
13. Tiryakioğlu O, Yıldız G, Vural H, Goncu T, Ozyazicioglu A, Yavuz Ş. Hydroxyethyl starch versus Ringer solution in cardiopulmonary bypass prime solutions (a randomized controlled trial). *Journal of cardiothoracic surgery*. 2008; 3(1): 45.
14. Dahlgren G, Granath F, Pregner K, Rösblad PG, Wessel H, Irestedt L. Colloid vs. crystalloid preloading to prevent maternal hypotension during spinal anesthesia for elective cesarean section. *Acta anaesthesiologica scandinavica*. 2005; 49(8): 1200-1206.
15. Carpenter RL, Caplan RA, Brown DL, Stephenson C, Wu R. Incidence and risk factors for side effects of spinal anesthesia. *Anesthesiology*. 1992; 76(6): 906-916.
16. Masoumi K, Forouzan A, Darian AA, Navaii AR. Comparison of the effectiveness of Hydroxyethyl Starch (Voluven) solution with normal saline in hemorrhagic shock treatment in Trauma. *Journal of clinical medicine research*. 2016; 8(11): 815.
17. Bendre R, Karthik S, Potli S, Madhusudhana R. A comparative study of ondansetron with dexamethasone and granisetron with dexamethasone for prevention of postoperative nausea and vomiting following abdominal surgeries under general anaesthesia. *WJPPS*. 2015; 4(3): 605-620.
18. Sagir O, Gulhas N, Toprak H, Yucel A, Begec Z, Ersoy O. Control of shivering during regional anaesthesia: prophylactic ketamine and granisetron. *Acta anaesthesiologica scandinavica*. 2007; 51(1): 44-49.
19. Marciniak A, Wujtewicz M, Owczuk R. The impact of colloid infusion prior to spinal anaesthesia for Caesarean section on the condition of a newborn - a comparison of balanced and unbalanced hydroxyethyl starch 130/0.4. *Anesthesiology intensive therapy*. 2013; 45(1): 14-19.
20. Matsota P, Karakosta A, Pandazi A, et al. The effect of 0.5 L 6% hydroxyethyl starch 130/0.42 versus 1 L Ringer's lactate preload on the hemodynamic status of parturients undergoing spinal anesthesia for elective cesarean delivery using arterial pulse contour analysis. *Journal of anesthesia*. 2015; 29(3): 352-359.
21. Memary E, Mirkheshti A, Moghaddam MJ, Abtahi D, Yaseri M, Kamali F. Comparison of the Effects of Pre-Anesthetic Administration of Normal Saline, Ringer and Voluven on the Spread of Sensory Block With Hyperbaric Bupivacaine Spinal Anesthesia. *Anesthesiology and pain medicine*. 2014; 4(2).
22. Shahriari A, Khooshideh M, Heidary M. Prevention of Hypotension during Spinal Anesthesia for Caesarean Section: Preload with Crystalloids or Hydroxyethyl Starch. *Medical Hypothesis, Discovery & Innovation Interdisciplinary Sciences Journal*. 2014; 1(1).