



The Effects of Pre-Spinal Anesthesia Administration of Crystalloid and Colloid Solutions on Hypotension in Elective Cesarean Section

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Received 2018 April 15; Revised 2018 July 22; Accepted 2018 July 23.

Abstract

Background: Spinal anesthesia is an appropriate alternative for general anesthesia in many operations, particularly in cesarean section. However, the induced hypotension is the main drawback of this method. Therefore, the current study aimed at comparing the effects of crystalloid and colloid solutions used as the preload on the post-spinal hypotension and its complications in females who are candidate for elective cesarean section.

Methods: The current randomized, controlled, double-blind study was conducted on the female candidate of elective cesarean section (n = 96; age range: 20 to 40 years). The patients were in their 37 to 42 weeks of gestational age during the experiments. The systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR) variation, amount of injected ephedrine during surgery, Apgar score at birth, total solution infused after spinal anesthesia, urine output, nausea, and vomiting were comparatively assessed between the two groups.

Results: The percentages of reduction in SBP and DBP variables in the crystalloid solution were higher than those of the colloid group and the differences were statistically significant (P = 0.042 and P = 0.008, respectively). Average percentage of HR changes was more significant in the crystalloid than the colloid group (P = 0.032). In contrary, administration of the two types of solutions did not result in significant differences in the Apgar scores. The prevalence of nausea and vomiting in the colloid group subjects was lower than those of the crystalloid solution group; however, the differences were not significant.

Conclusions: The current study findings recommend colloid solution to prevent hemodynamic instability after spinal anesthesia. However, the costs and availability of the solution and recommendation of anesthesiologist should be considered. Conduction of further clinical trials with larger sample sizes is recommended.

Keywords: Hypotension, Colloid Solution, Crystalloid Solution, Spinal Anesthesia, Cesarean Section

1. Background

The caesarean section (CS) is the most frequent surgical procedure among females worldwide. The proper management of this procedure and anesthetic method for numbing as well as maternal and fetal health during caesarean section is an important issue (1, 2). The selected anesthetic approach for cesarean delivery depends on the type of surgery, urgency of the operation, fetal distress, and anesthetist and patient's decision (3). However, hypotension is the most common side effect associated with this method. The possible mechanism of spinal anesthesia-induced hypotension is associated with spinal nerve sympathectomy, vasodilation of peripheral arteries, decrease of venous return, and consequently decreasing the cardiac output (4). Loss of the circulating fluid decreases venous return and leads to decreased stretch of ventricular muscle, reducing cardiac output, which ultimately results in

hypotension and poor perfusion. To prevent such hypotension, there are two main types of intravenous solutions, crystalloids and colloids, which are used preoperatively (5-7). Crystalloid solutions are released freely within intravascular spaces and interstitial tissues. Therefore, approximately one-third of the injected crystalloid solution usually remains in the intravascular space and the remaining two-thirds directly pass into the tissues. The crystalloid solutions could be used in the isotonic, hypertonic, and hypotonic forms and include normal saline, ringer, balanced salt solution, hypertonic sodium chloride, and dextrose (5%). The main drawback of the crystalloid solutions is that excessive use of these agents causes peripheral and pulmonary edema through decreasing the colloid oncotic pressure of the plasma (8, 9). Colloids are generally better than crystalloids at expanding the circulatory volume, since their larger molecules are retained more easily in the intravascular space and increase osmotic pressure. Col-

loids are also more effective in preventing the hypotension following spinal anesthesia than the crystalloids. However, administration of colloid solutions can cause pulmonary edema as well as anaphylactic shock, resulting in a higher rate of death. Colloids, compared with crystalloids, have longer half-life in blood circulation; therefore, these agents stabilize hemodynamic changes more efficiently (10, 11). Although different approaches are developed to prevent the spinal anesthesia induced hypotension, selection of the right solution for fluid therapy to prevent hypotension is still controversial. Due to the lack of consensus on using appropriate volume expanders for fluid therapy to prevent hypotension following spinal anesthesia, the current study aimed at achieving more accurate results in this area by comparing the application of both crystalloid and colloid solutions and also reducing the hypotension side effects following the surgical operation.

2. Methods

The current randomized, controlled, double-blind clinical trial was conducted on females ($n = 96$) who were candidate for elective cesarean section (age range: 20 - 40 years) in 2017. The patients in the gestational age of 37 to 42 weeks and identified as classes I and II according to the American society of anesthesiologists (ASA) referred to Imam Khomeini hospital of Ahvaz, Iran. All of the experimental procedures of the study were reviewed and approved by the ethics committee of Ahvaz University of Medical Sciences (registration code: IR.AJUMS.REC.1396.887). The exclusion criteria included smoking, alcohol and opioid consumption history, patients using alpha- or beta-blockers, alpha- or beta-agonists, patients with cardiovascular and brain disorders, diabetes, primary (chronic) or secondary (preeclampsia and eclampsia) hypertension, height < 150 and > 180 cm, weight < 50 and > 100 kg, multiple pregnancies, lack of suitable anesthesia level ($< T8$ or $> T4$), and with embryonic abnormalities. After enrollment of the participants and before the start of the study, all of the procedures of the study as well as the main objectives and possible benefits and side effects were clearly explained to the patients. Then, all of the patients read and signed the written informed consent form to participate in the study. The patients were randomly assigned into two groups of crystalloid and colloidal solution groups. The crystalloid group received crystalloid Ringer solution (Samen pharmaceutical Co. Iran) (as Ringer group) and the colloidal group received 6% Voluven® (Fresenius Kabi Deutschland GmbH) (the Voluven group). The experimental procedures in the two groups were as follows: the clinical and vital parameters including electrocardiography (ECG), pulse oximetry and non-invasive blood pres-

sure (NIBP) monitoring, two intravenous (IV) lines were installed using angioquate No.18 and then, the urine outputs were measured. Five to ten minutes before cesarean section the Ringer and Voluven groups respectively received 500 mL Ringer solution and 500 mL 6%Voluven. The patients underwent spinal anesthesia with spinal needle Quinke No.25 in sitting position based on classic midline method with the administration of 10 mg bupivacaine solution 0.5% (AstraZeneca Co., UK). The crystalloid and colloidal solutions were infused as preload, 10 minutes before the spinal anesthesia.

The volume of post-spinal anesthesia infusion of the solution was determined considering the fluid required for maintenance, NPO (nothing by mouth) fasting, amount of blood lost during surgery, and the maintenance of systolic blood pressure (SBP) above 90 mmHg. All pregnant mothers in the current study successfully passed spinal anesthesia after the first attempt. Blood pressure (BP) and heart rate (HR) before spinal anesthesia and every two minutes after that until 10 minutes and then, every five minutes until 30 minutes following spinal anesthesia were recorded. If SBP dropped below 90 mmHg or mean arterial pressure (MAP) dropped $> 20\%$ of pre-spinal MAP, then 5 - 10 mg ephedrine was injected.

The anesthesia level was determined with pinch test. Following these data, the hemodynamic parameters were comparatively assessed in the two groups. The hemodynamic variations assessed in the current study consisted of the SBP, diastolic blood pressure (DBP), HR variation as the mean percentage of variations and were calculated at the predetermined intervals and compared between the two groups. The percentage of variations was calculated as the difference of the two numbers obtained from two consecutive times divided by the number obtained from the previous step multiplied by 100, and the mean of these variations was calculated for each group at the time of evaluation and then compared. In addition, during cesarean section, anesthesia level, prescribed ephedrine dose, nausea, and vomiting in the intervention groups were compared. The infants Apgar scores were recorded at 1 and 5 minutes after the birth. Patients and persons responsible for data collection and analysis were blind to patients groups. The data were reported using descriptive statistics including mean, standard deviation (SD), frequency, and frequency percentage. The statistical analyses were performed with SPSS version 22 using paired t test to compare the means of variables between the two intervention groups. For all statistical analyses the significance level was considered < 0.05 .

3. Results

In [Table 1](#), demographic information of participants is presented.

Table 1. Demographic Characteristics of the Study Participants

| Variable | Group | | P Value |
|----------------------|----------------|----------------|---------|
| | Ringer | Voluven | |
| Age (y) | 30.41 ± 6.152 | 30.15 ± 6.216 | 0.847 |
| Gestational age (wk) | 39.46 ± 1.028 | 39.08 ± 0.971 | 0.766 |
| Height (cm) | 161.11 ± 5.304 | 162.00 ± 5.447 | 0.680 |
| Weight (kg) | 81.69 ± 9.481 | 81.43 ± 11.672 | 0.761 |

According to [Table 1](#), no significant difference was observed in the average age of mothers, gestational age, height and weight of participants between the two intervention groups.

The mean percentage of variation of HR, SBP, and DBP of the patients in each group are presented in [Table 2](#).

The mean percentage of variation of SBP was negative in the intervention groups indicating decreased SBP from the beginning of spinal until 30 minutes after that. The change percentage of SBPs in crystalloid solution group was higher ($P = 0.008$). Also, mean percentage of variation of DBP was negative in the two groups and the percentage of this decrease was higher in the crystalloid solution group ($P = 0.042$).

Average percentage of the HR variations was higher in the crystalloid group than the colloid group and the difference was statistically significant ($P = 0.032$).

The amount of injected ephedrine, total amount of solution infused after spinal, urine output during surgery, and Apgar scores at one and five minutes were recorded in the two groups and average levels were calculated for each group. The results are presented in [Table 3](#).

No significant difference was observed in Apgar score at minutes one and five in the study groups. Average amount of injected ephedrine was significantly lower in the colloid solution group than the other group ($P = 0.005$). The difference in total infused solution after spinal in the study groups was significant ($P > 0.0001$); this amount was lower in the colloid solution group. Also

Table 2. Comparison of the Variation of HR, SBP, and DBP in the Study Groups

| BP | Group | | P Value |
|-----------|----------------|----------------|---------|
| | Ringer | Voluven | |
| Systolic | -4.501 ± 8.120 | -2.008 ± 8.041 | 0.008 |
| Diastolic | -2.991 ± 8.574 | -1.087 ± 7.460 | 0.042 |
| HR | 5.75 ± 6.052 | 2.09 ± 9.008 | 0.032 |

Table 3. Comparison of Average Apgar Score, Injected Ephedrine, Total Solution, and Urine Output in the Study Groups

| Variable | Group | | P Value |
|-----------------------------|-------------------|-------------------|----------|
| | Ringer | Voluven | |
| Apgar score (min 1) | 8.02 ± 0.899 | 7.85 ± 1.648 | 0.784 |
| Apgar score (min 5) | 9.22 ± 0.603 | 9.82 ± 2.118 | 0.368 |
| Ephedrine (mg) | 14.63 ± 8.979 | 7.27 ± 6.045 | 0.005 |
| Total infused solution (mL) | 2526.79 ± 649.613 | 2169.23 ± 706.623 | < 0.0001 |
| Urine output (mL) | 276.55 ± 215.159 | 156.64 ± 100.206 | 0.043 |

urine outputs were lower in the colloid solution group ($P = 0.043$).

The results of the prevalence of nausea and vomiting during operation are presented in [Table 4](#).

Although no significant difference was observed between the study groups in terms of nausea and vomiting, there were fewer patients with nausea in colloid solution group. None of the patients experienced vomiting.

4. Discussion

Spinal anesthesia is an appropriate and effective alternative of general anesthesia in many surgical operations ([12, 13](#)). Different approaches are used to prevent the induced hypotension caused by spinal anesthesia; choosing the right solution for fluid therapy to prevent hypotension is still controversial ([8-11, 14, 15](#)).

According to the current study findings, mean percentages of variation in SBP and DBP were negative in the two interventions indicating decreased values of SBP and DBP from the beginning of spinal injection until 30 minutes follow-up. The difference in the SBP decrease was significant between the two groups where the crystalloid solution showed greater amount of reduction. The study was conducted on pregnant mothers undergoing elective cesarean surgery and their pregnancy had no midwifery risks such as pre-eclampsia, placenta accrete and previa, a few hooks, as well as in females with no illnesses such as renal failure, chronic hypertension, heart disease, and coagulation disorder in the age range. These limitations were ap-

Table 4. The Prevalence of Nausea and Vomiting During Operation in the Study Groups

| Variable | Group | | P Value |
|---------------------------|----------------|-----------------|---------|
| | Ringer No. (%) | Voluven No. (%) | |
| Nausea during operation | 10 (20.83) | 6 (12.5) | 0.335 |
| Vomiting during operation | 0 (0) | 0 (0) | 1 |

plied to some of them due to their risk for mother and baby (if Voluven is prescribed) and some to prevent misunderstandings. The findings of the current study were consistent with those of the studies by ShiQin et al., Alimian et al., and Unlugenc et al., showing that higher PB decreased in the presence of crystalloid solution (16-18). However, the current study findings were inconsistent with the findings reported by Kumar et al., that showed higher BP decline in colloid solution group (19) and with the findings of Cardoso et al., and Osazuwa et al., reporting no significant difference between the two groups regarding BP decline (20, 21). BP decline during operation can be attributed to the vascular expansion due to medication and bleeding during operation where preload infusion during spinal anesthesia can prevent it significantly. However, the general conclusion was that the application of colloid solutions such as Voluven, compared with crystalloid solutions such as Ringer, due to colloidal characteristics, was more effective for hemodynamic stability in operations under spinal anesthesia.

Mean percentage of HR changes showed a significant difference between the intervention groups; the rate of changes was more in the crystalloid group than the colloid group. These findings were not consistent with those of Alimian et al., in which HR changes showed no significant difference between the two groups (17). Average injected ephedrine was significantly lower in the colloid solution group than the other group and this was not consistent with the results of Unlugenc et al., in which injected ephedrine showed no significant difference between the two intervention groups (18). After estimating average Apgar at minutes one and five and according to the results, no significant difference was reported and it was consistent with the findings of Alimian et al., where the Apgar scores showed no significant difference between the two groups. The amounts of the total infused solution after spinal anesthesia were significantly different between the two intervention groups, where the colloid solution showed lower amount (17). This finding was not consistent with that of the study conducted by Unlugenc et al., where the average solution injected after spinal anesthesia did not show significant difference between the two groups (18). It should be noted that the reported differences in the hemodynamic parameters between the crystalloid and colloidal solutions in different studies are partly due to the application of different colloidal and crystalloid solutions. Average urine output showed a significant difference between the two intervention groups; the amount was lower in the colloid solution group. Other complications were nausea and vomiting and comparing their prevalence between the two intervention groups showed no significant difference between the frequencies of nausea and vomit-

ing between the two groups; although the nausea was less frequent in the colloid solution group than the crystalloid group.

4.1. Conclusion

The current study findings showed that colloid solution was more effective in controlling SBP and DBP, compared with the crystalloid solution. In addition, the HR changes, ephedrine, and total solution infused after spinal anesthesia between the two intervention groups showed that colloid solution had better performance in adjusting and controlling these parameters. However, the two solutions did not result in significant difference in Apgar score. Other complications were nausea and vomiting after spinal anesthesia and the current study findings showed that the application of colloidal solution may be more effective to control and prevent these complications.

Acknowledgments

The study was financially supported by Ahvaz Jundishapur University of Medical Sciences and Pain Research Center (grant No.: PAIN-9606).

References

1. Foruzeshfard M, Validad E, Mirmohamadkhani M, Moradan S. [Type of anesthesia chosen by mothers for cesarean section in their first delivery and its related factors in selected hospitals in year 2012]. *Iran J Obstet Gynecol Infertil*. 2013;**15**(39):1-8. Persian.
2. Carvalho B, Cohen SE, Lipman SS, Fuller A, Mathusamy AD, Macario A. Patient preferences for anesthesia outcomes associated with cesarean delivery. *Anesth Analg*. 2005;**101**(4):1182-7. table of contents. doi: [10.1213/01.ane.0000167774.36833.99](https://doi.org/10.1213/01.ane.0000167774.36833.99). [PubMed: [16192541](https://pubmed.ncbi.nlm.nih.gov/16192541/)].
3. Hawkins JL. Epidural analgesia for labor and delivery. *N Engl J Med*. 2010;**362**(16):1503-10. doi: [10.1056/NEJMct0909254](https://doi.org/10.1056/NEJMct0909254). [PubMed: [20410515](https://pubmed.ncbi.nlm.nih.gov/20410515/)].
4. Bishop DG, Cairns C, Grobbelaar M, Rodseth RN. Heart rate variability as a predictor of hypotension following spinal for elective caesarean section: a prospective observational study. *Anaesthesia*. 2017;**72**(5):603-8. doi: [10.1111/anae.13813](https://doi.org/10.1111/anae.13813). [PubMed: [28133720](https://pubmed.ncbi.nlm.nih.gov/28133720/)].
5. Ripolles Melchor J, Espinosa A, Martinez Hurtado E, Casans Frances R, Navarro Perez R, Abad Gurumeta A, et al. 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. [PubMed: [25501602](https://pubmed.ncbi.nlm.nih.gov/25501602/)].
6. Tawfik MM, Hayes SM, Jacoub FY, Badran BA, Gohar FM, Shabana AM, 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):223-4.
7. Fathi M, Imani F, Joudi M, Goodarzi V. Comparison between the effects of Ringer's lactate and hydroxyethyl starch on hemodynamic parameters after spinal anesthesia: A randomized clinical trial. *Anesth Pain Med*. 2013;**2**(3):127-33. doi: [10.5812/aapm.7850](https://doi.org/10.5812/aapm.7850). [PubMed: [24244923](https://pubmed.ncbi.nlm.nih.gov/24244923/)]. [PubMed Central: [PMC3821133](https://pubmed.ncbi.nlm.nih.gov/PMC3821133/)].

8. Orbegozo D, Su F, Santacruz C, He X, Hosokawa K, Creteur J, et al. Effects of different crystalloid solutions on hemodynamics, peripheral perfusion, and the microcirculation in experimental abdominal sepsis. *Anesthesiology*. 2016;**125**(4):744–54. doi: [10.1097/ALN.0000000000001273](https://doi.org/10.1097/ALN.0000000000001273). [PubMed: 27655180].
9. Ekbal NJ, Hennis P, Dyson A, Mythen M, James MFM, Singer M. The anion study: effect of different crystalloid solutions on acid base balance, physiology, and survival in a rodent model of acute isovolaemic haemodilution. *Br J Anaesth*. 2018;**120**(6):1412–9. doi: [10.1016/j.bja.2018.01.026](https://doi.org/10.1016/j.bja.2018.01.026). [PubMed: 29793606].
10. Lotfy ME, Moustafa AM, El Feky EME, Mowafy IA. Colloid versus crystalloid co-load with spinal anesthesia during emergent cesarean section and their effect on hemodynamic changes. *J Am Sci*. 2014;**10**(11):158–63.
11. Loubert C, Gagnon PO, Fernando R. Minimum effective fluid volume of colloid to prevent hypotension during cesarean section under spinal anesthesia using a prophylactic phenylephrine infusion: An up-down sequential allocation study. *J Clin Anesth*. 2017;**36**:194–200. doi: [10.1016/j.jclinane.2016.10.018](https://doi.org/10.1016/j.jclinane.2016.10.018). [PubMed: 28183565].
12. Down JF, Gowrie-Mohan S. A prospective observational study of the subjective experience of caesarean section under regional anaesthesia. *Int J Obstet Anesth*. 2002;**11**(4):242–5. doi: [10.1054/ijoa.2002.0977](https://doi.org/10.1054/ijoa.2002.0977). [PubMed: 15321528].
13. Basques BA, Toy JO, Bohl DD, Golinvaux NS, Grauer JN. General compared with spinal anesthesia for total hip arthroplasty. *J Bone Joint Surg Am*. 2015;**97**(6):455–61. doi: [10.2106/JBJS.N.00662](https://doi.org/10.2106/JBJS.N.00662). [PubMed: 25788301]. [PubMed Central: PMC4357526].
14. Butwick AJ, Columb MO, Carvalho B. Preventing spinal hypotension during Caesarean delivery: what is the latest? *Br J Anaesth*. 2015;**114**(2):183–6. doi: [10.1093/bja/aeu267](https://doi.org/10.1093/bja/aeu267). [PubMed: 25080429].
15. Imani F. Postoperative pain management. *Anesth Pain Med*. 2011;**1**(1):6–7. doi: [10.5812/kowsar.22287523.1810](https://doi.org/10.5812/kowsar.22287523.1810). [PubMed: 25729647]. [PubMed Central: PMC4335751].
16. Xu S, Wu H, Zhao Q, Shen X, Guo X, Wang F. The median effective volume of crystalloid in preventing hypotension in patients undergoing cesarean delivery with spinal anesthesia. *Rev Bras Anesthesiol*. 2012;**62**(3):312–24. doi: [10.1016/S0034-7094\(12\)70132-0](https://doi.org/10.1016/S0034-7094(12)70132-0). [PubMed: 22656677].
17. Alimian M, Mohseni M, Safaeian R, Faiz SH, Majedi MA. Comparison of hydroxyethyl starch 6% and crystalloids for preloading in elective caesarean section under spinal anesthesia. *Med Arch*. 2014;**68**(4):279–81. doi: [10.5455/medarh.2014.68.279-281](https://doi.org/10.5455/medarh.2014.68.279-281). [PubMed: 25568553]. [PubMed Central: PMC4240562].
18. Unlugenc H, Turkkan M, Evruke IC, Gunduz M, Burgut R, Yapicioglu-Yildizdas H, et al. 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. [PubMed: 26860016].
19. Kumar P, Rao S. Role of crystalloids vs. Colloids in preloading in caesarian sections under spinal anaesthesia-a comparative study. *J Evid Based Med Healthc*. 2015;**2**(23):3467–74.
20. Osazuwa IH, Ebague A. Crystalloid preload shows Transient superiority over colloid, or their combination in spinal anaesthesia-induced hypotension prophylaxis for caesarean section. *Niger J Med*. 2015;**24**(2):337–43. [PubMed: 26353424].
21. Cardoso MM, Bliacheriene S, Freitas CR, Cesar DS, Torres ML. [Preload during spinal anesthesia for cesarean section: comparison between crystalloid and colloid solutions.]. *Rev Bras Anesthesiol*. 2004;**54**(6):781–7. [PubMed: 19471789].