Original Article

The Effects of Hydroxyethyl Starch 6% and Crystalloid on Volume Preloading Changes following Spinal Anesthesia

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Abstract

Background: Hypotension is one of the most common complications after spinal anesthesia for cesarean delivery. Normally, preloading with fluids, especially crystalloids, is used to prevention of hypotension. **Methods:** In the present randomized clinical trial study, 120 parturients presenting for elective cesarean section with the American Society of Anesthesiologists Class I and II received either 15 cc normal saline or 7 cc/kg hydroxyethyl starch 6% (Voluven) fluid. Information regarding to systolic, diastolic, mean arterial pressure, and heart rate, incidence of hypotension, adverse effects, the total dose of atropine, and ephedrine were recorded in before and 3, 6, 9, 15, and 20 min after spinal anesthesia. Furthermore, Apgar score of newborn at the 1st and 5th min after birth was recorded. **Results:** There was no significant difference in mean arterial pressure at different stages such as: Exactly after spinal and 3, 6, 15, and 20 min after spinal anesthesia between two groups ($P > 0.05$). Total dose of ephedrine and atropine were similar between groups ($P > 0.05$), respectively. There was no significant difference in Apgar score at the 1st and 5th min after birth between two groups. There were not any adverse effects of drugs in two groups. **Conclusions:** The results of this study show that hydroxyethyl starch 6% compared to normal saline are similar to prevent hypotension during spinal anesthesia for cesarean delivery.

Keywords: *Cesarean section, colloid, crystalloid, hydroxyl ethyl starch, hypotension, Voluven*

Introduction

Hypotension during spinal anesthesia for cesareans section is an important complication which is a potential hazard both to the maternal and fetus with an incidence of up to 80%.[1] Most cesarean delivery is performed under spinal anesthesia. While, general anesthesia is used in urgency patients and regional contraindications under spinal anesthesia. Pulmonary aspiration and failure in intubation are causes to 75% of maternal mortality from anesthesia.[2] The incidence of relevant hypotension was more frequent with spinal anesthesia than with epidural anesthesia. The clinicians have used from various preventive methods such as crystalloids or colloid preloading and uterine displacement along with the fluid and vasopressor to prevent or minimize hypotension after spinal anesthesia for the cesarean delivery.[3,4] However, despite those methods, the favorite method was not approved.[3,4]

Most studies are recommended for the use of colloids compared to crystalloid fluid loading to prevent hypotension following spinal anesthesia for cesarean delivery. However, some studies support the use of crystalloid comparison to colloid is same.[3] Hypotension is generally considered if systolic blood pressure <90–100 mmHg or a 20% fall in blood pressure from the baseline.[5] Unfortunately, there has not been established any fluid therapy alone effectively prevent hypotension after spinal anesthesia for cesarean delivery.[6]

Crystalloids have a shorter half-life intravascular and hence that their ability to expand the intravascular volume is limited and this reason of why hypotension after spinal anesthesia is less successful in the patients that received the preloading with crystalloids. The high volume of crystalloids related to decreased oxygen carrying capacity and increased risk of pulmonary edema and peripheral edema during giving birth. Colloids remain in blood circulation for longer periods and can be a more effective alternative. Hetastarch is colloids which have been used in shock, sepsis, and trauma patients as intravascular

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volume expander.[7,8] The aim of the current study was to compare Hetastarch solution (with Voluven brand) with crystalloids (normal saline) as preloading to prevent hypotension after spinal anesthesia for cesarean section in Iranian healthy women.

Methods

We designed a randomized clinical trial in which 120 healthy term parturients, American Society of Anesthesiologists (ASA) Class I–II that scheduled for elective cesarean delivery under spinal anesthesia from April 2015 to February 2015 were included consecutively. This study was carried out in Baqiyatallah Hospital, Tehran, Iran. This study was approved by the Medical Research Ethics Committee. Ethics committee approval was received along with the informed consent of each patient. Parturients were randomly divided into two groups (control or case group). Randomization was stratified using a random table number. Information regarding subjects' demographics such as age, weight, and stature was recorded. Inclusion criteria were gestational age >31 week, weight between 50 and 110 kg, no history of allergy to local anesthetics drugs, lack of using anticoagulation, no existence of spinal anesthesia contraindications and no history of diabetes, high blood pressure, cardiovascular disease, vascular and kidney diseases, and blood or coagulation disorders. Furthermore, the ages of participants were between 18 and 35 years.

Participants with history of diabetes, hypertension, cardiovascular disease, kidney disease coagulation disorder, and inadequate level of spinal anesthesia that is led to the intervention or acting general anesthetic were excluded in this study.

In each group, 60 participants were included in the study. The control Group (A) received 15 cc/kg normal saline and case Group (B) received 7 cc/kg hydroxyethyl starch 6% (Voluven). In the present study, double blinding was not impossible, for the lack of simulation in Normal saline and Voluven solution with respect to appearance. After the patients lying on the operating bed, systolic, diastolic, mean arterial blood pressure, and heart rates were recorded. The patient in the supine position with the left-leaning angle of 15°.

The control group received 15 cc/kg normal saline and case group received 7 cc/kg hydroxyethyl starch 6% (Voluven made in Fresenius Kabi, factory in Canada) during 15–20 min. Furthermore, before doing spinal anesthesia, vital signs were registered in the questionnaire. Then, placed the parturients in the sitting position and spinal anesthesia has performed with 12–15 mg bupivacaine 0.5% respect to stature. Needle number 26 were used in L3–L4 or L4–L5 levels. The patient immediately placed in the supine position and embedded oxygen with the face mask. Then vital signs were recorded.

Then, all parturients receive normal saline serum as preservative fluid. Surgery was performed after patient anesthesia level assessed with pin prick method that reaching the level of anesthesia to T4–T6 and by removing the inclination of 15°. Vital signs are recorded in 3, 6, 9, 15, and 20 min of after anesthesia. If parturients were hypotensive (systolic pressure <100 mm Hg, or more than 20% systolic pressure falling from initial blood pressure) depending on the severity, were given 5–10 mg Ephedrine. If necessary, the amount of half a milligram of atropine was used in the case of bradycardia did not respond to injections of ephedrine. During Process, total ephedrine or atropine dose was being recorded. The occurrence of every allergy signs, such as itches, hives, or red skin were recorded after doing spinal anesthesia or at the end of recovery. Finally, with the birth of the newborn, Apgar score recorded at the 1st and 5th min. Furthermore, data refer to the hemodynamic condition of the parturients such as heart beat, systolic blood pressure, and diastolic blood pressure and mean arterial pressure was recorded during the operation.

Data analysis

Data were analyzed using SPSS 20 software (SPSS, Chicago, IL, USA). The Mann–Whitney test was used to compare numeric data using analytical test. Repeated measures ANOVA were performed to detect significant differences of groups ($P < 0.05$ were considered statistically significant).

Results

In this study, a total of 120 parturients with ASA Class I and II, who were candidates for the elective cesarean section under spinal anesthesia were included in the study. Sixty participants included to control group (normal saline) and sixty participants included to case group (Voluven).

After 10 min, the sensory level was about T4–T6 for all participants. Systolic and diastolic pressure, mean arterial pressure, and heart rate were recorded in before and 3, 6, 9, 15, and 20 min after spinal anesthesia. Table 1 depicts demographics of the study sample in the participants. There was no significant difference in demographic variables in two groups.

In initiate time of hospitalization, the mean arterial systolic pressure of the control group was 127.76 Mm Hg and in the case group was 122.93 MmHg. The mean arterial diastolic pressure of the control group was 79.1 MmHg and in the case group was 77.50 MmHg. There was no significant difference in the mean arterial

Table 1: Comparison between demographic values (age, length, weight) in two groups

Parameters	Control (*n*=60)	Case (*n*=60)
Age (year)	29.97±3.11	29.60±4.17
Length (cm)	160.77±5.92	157.80±12.30
Weight (kg)	80.43±11.22	79.80±10.15

systolic pressure and mean arterial diastolic pressure between two groups ($P > 0.05$) ($P > 0.05$). Furthermore, the mean arterial blood pressure and heart rates were similar and had no significant difference between two groups ($P > 0.05$). Systolic blood pressure, diastolic blood pressure, the mean arterial pressure, and heart rate falls before spinal anesthesia in control and case group and these are no significant difference in two groups ($P = 0.232$) ($P = 0.616$) ($P = 0.417$) ($P = 0.093$) [Table 2].

Immediately after spinal anesthesia, the mean arterial blood pressure, systolic and diastolic pressure reducing respect to before spinal anesthesia in all participants. There is no significant difference in systolic, diastolic blood pressure, the mean arterial blood pressure in two groups ($P > 0.05$). However, there is a significant difference in heart rate between groups immediately after spinal anesthesia ($P = 0.001$), but it was due to the high initial heart rate in some parturients compared with the initial mean. The mean systolic pressure in all participants was reached to the lowest values in 3, 6, and 9 min after spinal anesthesia but there was no significant difference in two groups [Table 2].

Also, the mean diastolic pressure and the mean arterial pressure in all participants was reached to the lowest values in 3, 6, and 9 min after spinal anesthesia and there was no significant difference in two groups [Tables 3 and 4]. There is a significant difference in heart rate between two groups in 3 and 9 min after spinal anesthesia ($P < 0.05$), respectively [Table 2].

In addition, there is no significant difference in the mean of systolic and diastolic pressure, mean arterial pressure, and heart rate between two groups in 15 and 20 min after spinal anesthesia [Table 2]. In assessment changes of systolic blood pressure respect to times, the lowest hypotension in all participants was recorded in 3, and 6 min after spinal anesthesia [Table 2]. The mean of heart rate respect to different times, the most decelerations in two groups was recorded in 3 min after spinal anesthesia [Table 2]. In the comparison of hypotension prevalence in two group, hypotension was 65% in control group and 60% in the case group and there was no significant difference in two groups ($P > 0.05$) [Table 3].

The mean dose of Atropine in the control group was 0.8 mg and in case group was 0.19 mg ($P = 0.33$) and the mean dose of Ephedrine in the control group was 16.6 mg and in case group was 2.6 mg ($P = 0.55$) [Table 4].

In all newborn babies (except 8 babies in the control group and 10 babies in case group) at least had Apgar score[9] at 1st min and Apgar score[10] at 5th min which there was not significant difference in two groups ($P > 0.05$). Babies who have lower Apgar score had not an Apgar score of <8 at 5th min in two groups ($P > 0.05$).

Table 2: Comparison between variables values at variable times before and after spinal anesthesia for cesarean in case and control groups (n=60)

Variables values	Initiate time of hospitalization		Before anesthesia		Exactly after anesthesia		3 min after anesthesia		6 min after anesthesia		9 min after anesthesia		15 min after anesthesia		20 min after anesthesia		*P*
	Control	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control	Case	
Systolic blood pressure	128±11	123±15	125±13.8	129±14	118±12	119±17	107±16	106±2	97±29	105±16	115±16	116±17	119±16	120±15	119±12	121±14	>0.05
Diastolic blood pressure	76±11	77±12	77±13	79±11	69±13	66±15	60±12	60±14	62±11	60±13	67±12	66±14	69±70	70±13	71±12	71.8±12	>0.05
Mean arterial pressure	93±12	93±9	93±12	96±10	86±12	84±15	76±12	75±14	74±12	75±13	83±11	83±14	85±12	87±12	87±1	88±12	>0.05
Heart rate	89±13	92±11	96±12	100±11	95.5±15	104±15	94±16	99±18	101±2	100±18	102±16	111±22	103±21	106±22	104±18	103±2	<0.05

Table 3: Comparison between two groups related to incidence of hypotension

Groups	Total number	Hypotensive number	Incidence, %	*P*
Control	60	39	0.65	0.306
Case	60	36	0.60	

Table 4: Comparison of the average dose of ephedrine and atropine in two groups

Drugs	Groups	Mean dosage (mg)	*P*
Ephedrine	Control	16.66	0.55
	Case	12.66	
Atropine	Control	0.83	0.33
	Case	0.19	

Discussion

Our results show that hydroxyethyl starch 6% as preloading comparable to normal saline for preventing of hypotension during the spinal anesthesia for the elective cesarean section.

Getika *et al*. reported the prevalence of hypotension after spinal anesthesia in parturients is between 80% and 90%.[5,9-11] Dahlgren *et al*. by applying 1000 cc liquid 3% dextran immediately before spinal anesthesia for elective cesarean section compared to Ringer's lactate reported that the overall incidence of hypotension reduces from 85% to 66%, incidence of clear clinical hypotension reduces from 60% to 30% and Severe hypotension reduces from 23% to 3.6%.[12,13]

Park *et al*. showed that the use of crystalloids before spinal anesthesia (preloading) even when to reach crystalloids to 30 cc/Kg, will not be affected to reduce blood pressure following spinal anesthesia in cesarean section.[14]

Theoretically, the colloidal solution is a better choice for the prevention of hypotension during spinal anesthesia because that colloids for physical properties remain longer time in the vascular spaces. Hydroxyethyl starch 6% in normal saline 9% (Voluven) is a synthetic colloid solution, which has a molecular weight of 450,000 Dalton, PH 5.5, the osmolality of 310 Mmol/L, and similar to blood serum, the oncotic pressure of 34 mm Hg. Its half-life is 25.5 h and has an ability to bulking up plasma volume equivalent to several times the volume injected.[15,16]

In our study, we used of fluids before spinal anesthesia; although, the use of colloidal solution of Hydroxyethyl starch in the amount of 7 cc/kg was effective to reduced pressure compared to not to use fluids before spinal anesthesia (60% of against 85%), but this decline was not significant compared to crystalloid in the amount of 15 cc/kg of body weight (60% vs. 65%).

A study compared colloids as preloading with crystalloids as coloading during spinal anesthesia for elective cesarean section.[17] They concluded that in reduces the hypotension, use of 1000 cc crystalloids as coloading fluid is the same as the application of 500 cc colloid fluid as preloading. Furthermore, none of these techniques cannot reduce hypotension completely and it should be used accompanied with the vasopressor.[17]

Oh *et al*. showed a group of candidate women for elective cesarean section with spinal anesthesia and was received crystalloids as coloading, had less hypotension in compared to a similar group that was received the same amount of fluid as coloading (53% in comparison to 83%). Also, the first group was received less ephedrine (7.5 mg in compared to 15 mg).[1] In a study by Xu *et al*. carried out on 85 candidate parturients for the elective cesarean section with spinal anesthesia. The results showed that the median fluid was estimated about 13 cc/kg for fluid therapy preoperation with crystalloid that it can prevent hypotension following spinal anesthesia. Although, should administer prophylactic vasoconstrictor with the therapeutic dose in the appropriate time.[18]

Other study by Moslemi and Rasooli *et al*. concluded that phenylephrine infusion can reduce effectively hypotension related to spinal anesthesia for cesarean delivery.[19] Moreover, other study showed that integration of precautionary methods would be necessary for reducing hypotension following spinal anesthesia for the elective cesarean section and they mentioned to giving preloading with ephedrine as the best method.[20]

In the present study, we show that vasopressor need to use for protecting mother hemodynamic even in the case group. Although, the mean amount of ephedrine consumption was lower in the case group (the mean of 16 mg of ephedrine was received in the control group compared to the 12 mg in the case group), but there is no significant difference between groups.

Conclusions

Preloading with hydroxyethyl starch is not superior to normal saline for prevention of hypotension in parturients following spinal anesthesia. This research suggests that more studies are needed in related to prevention of hypotension, and look only to the type and effects of preloading liquid cannot effectively remove or prevent the hypotension following spinal anesthesia.

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Conflicts of interest

There are no conflicts of interest.

References

1. 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.
2. Remadevi R, Babu DD, Sureshkumar K, Patil SA. Epidural anesthesia for caesarean section in a pregnant patient with pituitary macroadenoma. J Clin Diagn Res 2014;8:GD01-2.
3. Miller DR, McCartney CJ. Mentoring during anesthesia residency training: Challenges and opportunities. Can J Anaesth 2015;62:950-5.
4. Miller TE, Gan TJ. Total intravenous anesthesia and anesthetic outcomes. J Cardiothorac Vasc Anesth 2015;29 Suppl 1:S11-5.
5. Mitra JK, Roy J, Bhattacharyya P, Yunus M, Lyngdoh NM. Changing trends in the management of hypotension following spinal anesthesia in cesarean section. J Postgrad Med 2013;59:121-6.
6. Jenkins MG, Murphy DJ, Little C, McDonald J, McCarron PA. A non-inferiority randomized controlled trial comparing the clinical effectiveness of anesthesia obtained by application of a novel topical anesthetic putty with the infiltration of lidocaine for the treatment of lacerations in the emergency department. Ann Emerg Med 2014;63:704-10.
7. Jain R, Sharma R. A comparative study of effects of glycopyrrolate and ondansetron on nausea and vomiting in cesarean section under spinal anesthesia. Anesth Essays Res 2015;9:348-52.
8. Mehta N, Gupta S, Sharma A, Dar MR. Thoracic combined spinal epidural anesthesia for laparoscopic cholecystectomy in a geriatric patient with ischemic heart disease and renal insufficiency. Local Reg Anesth 2015;8:101-4.
9. 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;68:279-81.
10. Parida S, Nawaz M, Kundra P. Severe hypotension following spinal anesthesia in patients on amlodipine. J Anaesthesiol Clin Pharmacol 2012;28:408-9.
11. Ranasinghe JS, Birnbach D. Current status of obstetric anaesthesia: Improving satisfaction and safety. Indian J Anaesth 2009;53:608-17.
12. Dahlgren G, Granath F, Wessel H, Irestedt L. Prediction of hypotension during spinal anesthesia for cesarean section and its relation to the effect of crystalloid or colloid preload. Int J Obstet Anesth 2007;16:128-34.
13. 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 Anaesthesiol Scand 2005;49:1200-6.
14. Park GE, Hauch MA, Curlin F, Datta S, Bader AM. The effects of varying volumes of crystalloid administration before cesarean delivery on maternal hemodynamics and colloid osmotic pressure. Anesth Analg 1996;83:299-303.
15. Sharma SK, Gajraj NM, Sidawi JE. Prevention of hypotension during spinal anesthesia: A comparison of intravascular administration of hetastarch versus lactated ringer's solution. Anesth Analg 1997;84:111-4.
16. 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;2:127-33.
17. Tawfik MM, Hayes SM, Jacoub FY, Badran BA, Gohar FM, Shabana AM, *et al.* Comparison between colloid preload and crystalloid co-load in cesarean section under spinal anesthesia: A randomized controlled trial. Int J Obstet Anesth 2014;23:317-23.
18. 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 Anestesiol 2012;62:312-24.
19. Moslemi F, Rasooli S. Comparison of prophylactic infusion of phenylephrine with ephedrine for prevention of hypotension in elective cesarean section under spinal anesthesi: A randomized clinical trial. Iran J Med Sci 2015;40:19-26.
20. Jabalameli M, Soltani HA, Hashemi J, Behdad S, Soleimani B. Prevention of post-spinal hypotension using crystalloid, colloid and ephedrine with three different combinations: A double blind randomized study. Adv Biomed Res 2012;1:36.