Original Article

Comparative Study of Various Fluid Loading Methods for Elective Cesarean Delivery under Spinal Anesthesia in Phramongkutklao Hospital: A Prospective Randomized Controlled Trial

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Background: The most commonly used anesthetic technique in elective cesarean delivery is spinal anesthesia (SA). However, one drawback of SA is the blocked sympathetic system can induce marked reduction in systemic vascular resistance and mean arterial pressure. In addition, intravenous fluid loading can prevent SA induced systolic hypotension.

Objectives: The present study aimed to compare various fluid loading methods including preload (P), coload (C) and preload combined with coload (PC), to prevent hypotension after SA. The secondary objective was to determine appropriate doses of ephedrine requirement and Apgar score evaluation.

Materials and Methods: The single blind, randomized, prospective, controlled trial was approved by the IRB. The present study was performed among 153 term pregnant patients undergoing elective cesarean delivery with SA. All patients were randomized in three groups, i.e., P (n = 51), C (n = 51) and PC (n = 51). Under SA, noninvasive blood pressure was recorded every minute until delivery. Hypotension was treated with ephedrine intravenously and crystalloid boluses. Apgar scores were recorded at 1 and 5 minutes after delivery.

Results: No significant difference was observed between the groups regarding the incidence of hypotension (P = 66.7%, C = 60.8% and PC = 74.5%, p=0.333). The median time to hypotension was 4 minutes (p=0.619). No significant differences were found in dose of ephedrine (p=0.636) and Apgar score (p=0.302, 0.072 at 1 and 5 minutes) among groups.

Conclusion: No difference was observed in the incidence of hypotension in all patients receiving any timing crystalloid intravenous loading after SA for cesarean delivery.

Keywords: Fluid loading, Spinal anesthesia

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Spinal anesthesia (SA) is the most common anesthetic technique in term pregnant patients undergoing elective cesarean delivery. While easy to perform, it also provides a rapid onset, dense surgical block[1-3]. However, one drawback of SA is the blocked sympathetic system causing a marked reduction in systemic vascular resistance (SVR) and mean arterial pressure (MAP)[4,5]. Hypotension induced by SA is common in 60 to 83.3% of term pregnant women and often presents nausea, vomiting and dyspnea[6-8]. These hemodynamic changes represent the greatest potential hazard for maternal and fetal well-being such as organ ischemia, cardiovascular collapse and utero-placental hypoperfusion[3,4]. Several techniques can prevent SA induced systolic hypotension in pregnancy for women undergoing cesarean delivery such as left uterine displacement (LUD), vasopressor drugs and preload intravenous crystalloid before SA. However, these techniques are not optimal because the incidence of hypotension is still high[6,8]. Regarding the latest spinal anesthesia guidelines, the recommendation is to administer a preload intravenous crystalloid 500 ml, 15 to 20 minutes before SA[9]. From several studies, the technique of intravenous crystalloid loading is preferable in coload more than preload cases because coload can reduce the incidence of maternal hypotension in SA[6,7,10,11]. Because the half-life of intravenous crystalloid is short, about 20 minutes, hypotension would occur[12]. Therefore, the primary objective of the present study was to evaluate

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the administration of intravenous crystalloid among term pregnant patients to prevent hypotension during elective cesarean delivery. The secondary objective was to determine appropriate doses of ephedrine requirement and Apgar score evaluation.

Materials and Methods

After Phramongkutklao Hospital, Royal Thai Army Medical Department IRB approval (ID: S036h/59), a single blind randomized prospective controlled trial was initiated. In addition, the present study was registered under the Thai Clinical Trial Registry (TCTR) http://www.clinicaltrials.in.th (unique trial number: TCTR20180124003). Written consent was provided by all patients after receiving a comprehensive explanation for SA. The intrathecal drugs used in this study included 2.0 to 2.4 ml of 0.5% hyperbaric bupivacaine combined with 0.2 mg morphine. The possible risks and complications that could appear during study were also explained to the patients and their family members.

Subjects

All patients with term, singleton and uncomplicated pregnancy, aged over 20 years undergoing elective cesarean delivery under SA in Phramongkutklao Hospital were enrolled. Patients were eligible for enrollment after categorizing as American Society of Anesthesiologist (ASA) Physical Status (PS) Classification II and exhibiting no clinically significant cardiovascular, pulmonary, renal or endocrine diseases. Exclusion criteria comprised patients undergoing emergency cesarean delivery, elective cesarean delivery under general anesthesia, level of anesthesia below T6 or patient's refusal.

Sample size calculation based on the percentage of maternal hypotension. From related study, maternal hypotension in preload group was 83.3% and in coload group was 53.3%[6]. Fifty-one cases were required for each group.

Study design

Between March and September 2017, 156 patients were enrolled and randomly allocated in three intravascular loading strategies: preload (P), coload (C) and preload with coload groups (PC), 51 patients each, using computer generated random allocation with block randomization (block size 9) (Figure 1). Three patients were excluded; one emergency case and two who refused to participate in the study. Thirty minutes before surgery, all patients received 50 mg ranitidine and 10 mg metoclopramide, intravenously. Venous access was prepared using a 20-gauge intravenous catheter on the left antecubital vein. Standard monitoring included electrocardiogram, noninvasive blood pressure measurement and pulse oximetry. SA was performed at the dorsal of L3-L4 intervertebal level with 2.0 to 2.4 ml of 0.5% hyperbaric bupivacaine combined with 0.2 mg morphine intrathecally by 27-gauge Quincke spinal needle. In the P group, patients received 10 ml/kg of acetate solution over 20 minutes before SA. In the C group, patients received 10 ml/kg of acetate solution over 10 minutes as soon as the CSF was tapped. The patients in the PC group received 5 ml/kg of acetate solution over 20 minutes before SA and 5 ml/kg of acetate solution over 10 minutes as soon as the CSF was tapped. After SA was performed, patients were put in the LUD position with a 15° wedge under the right hip. The height of sensory blockade was assessed every 2 minutes until 20 minutes and until at least the T5 level blockade was achieved. After SA, the following parameters; systolic blood pressure (SBP) and heart rate were recorded every 1 minute throughout the first 20 minutes then every 5 minutes until the end of the surgery. Maternal hypotension was defined as a decrease in SBP to less than 80% of the baseline or SBP <90 mmHg. Hypotension was treated with repeatable 6 mg intravenously and given separately with a maximum dose of 30 mg ephedrine. Also, the crystalloid bolus volume was given when persistent hypotension was observed. After delivery, oxytocin

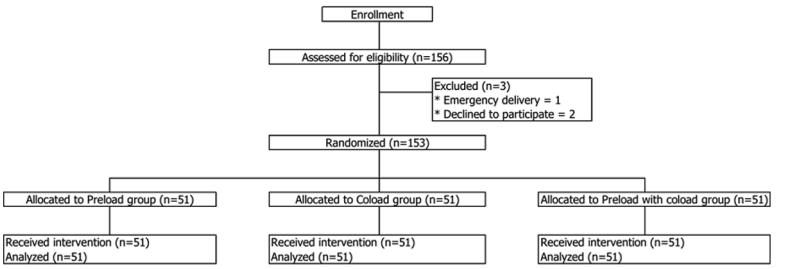

Figure 1. Flowchart of subject's enrollment, allocation and analysis.

was given to all patients with 5 IU bolus followed by 15 IU in an acetate solution intravenous infusion. Apgar scores were recorded at 1 and 5 minutes after delivery.

Statistical analysis

Sample size was determined by power analysis based on pilot data (desired power 0.8, alpha 0.05). Primary outcome was the incidence of maternal systolic hypotension. The Chi-square test was used to determine significant differences. Secondary outcomes were the doses of ephedrine and Apgar score between three groups using Kruskal-Wallis test. Comparisons of the patient baseline characteristics among the three groups was tested using Chi-square, Fisher's exact test, one-way ANOVA and Kruskal-Wallis test for significant p-value <0.05.

Results

No significant differences were observed in demographic data among the P, C and PC groups (Table 1). In addition, no significant differences were found among the groups regarding the incidence of hypotension (P = 66.7%, C = 60.8% and PC = 74.5%, p=0.333). The median time to hypotension was 4 minutes (p=0.619). Moreover, no significant differences were observed among doses of ephedrine (P = 15, C = 12 and PC = 18, p=0.636) and Apgar score (p=0.302, 0.072, at 1 and 5 minutes, respectively) among these groups (Table 2). A trend was noted of less hypotension in the coload than the preload and preload with coload groups but without significance (p=0.364) (Figure 2).

Discussion

The present study demonstrated the role of administering crystalloid to prevent maternal hypotension after SA during cesarean delivery. The result showed the incidence of hypotension was lower

Table 1. Comparison of demographic data and comparative variables among groups

	Preload	Colaod	Preload with Colaod	*p*-value
Gestational age (weeks), mean ± SD	38.75±0.89	38.42±0.85	38.44±0.99	0.120‡
Height (cm), mean ± SD	158.61±4.87	157.73±6.29	158.29±5.63	0.725‡
Weight (kg), mean ± SD	70.55±9.82	69.22±9.71	69.94±8.72	0.775‡
SBP, mean ± SD	123.37±12.68	121.43±10.6	122.78±11.65	0.691‡
DBP, mean ± SD	75.01±10.55	74.77±10.22	74.94±10.94	0.993‡
Intraoperation				
0.5% marcaine, n (%)				0.376†
• 2.0	6 (11.8)	3 (5.9)	2 (3.9)	
• 2.2	30 (58.8)	38 (74.5)	37 (72.5)	
• 2.4	15 (29.4)	10 (19.6)	12 (23.5)	
Loading volume, mean ± SD	691.86±133.88	678.24±113.78	715.76±104.86	0.270‡
Add volume, mean ± SD	128.43±203.53	71.37±118.14	87.94±123.60	0.158‡
Total volume, mean ± SD	820.29±251.08	749.61±129.65	803.71±172.98	0.152‡
Hypotension, n (%)	34 (66.67)	31 (60.78)	38 (74.51)	0.333*
Apgar at 1 minute, median (min-max)	8 (6 to 9)	8 (4 to 9)	8 (7 to 9)	0.302¥
Apgar at 5 minutes, median (min-max)	9 (8 to 9)	9 (8 to 10)	9 (8 to 10)	0.072¥
Postoperation				
Pain score at rest, median (min-max)	1 (0 to 6)	0 (0 to 5)	0 (0 to 5)	0.448¥
Pain score during activity, median (min-max)	4 (0 to 9)	3 (0 to 9)	3 (1 to 8)	0.897¥
Chlorpheniramine, n (%)	14 (27.45)	9 (17.65)	8 (15.69)	0.285*
Ondansetron, n (%)	-	2 (3.92)	-	0.329†
Dimenhydrinate, n (%)	-	1 (1.96)	-	1.000†
Metoclopramide, n (%)	-	-	-	NA
Test level at 20 minutes, median (min-max)	T4 (4 to 6)	T4 (4 to 6)	T4 (4 to 6)	0.212¥

NA = not applicable

* Chi-square test, † Fisher's exact test, ‡ One-way ANOVA, ¥ Kruskal-Wallis test, significant (p<0.05)

Table 2. Comparison of hypotension and ephedrine requirement among groups

	Preload		Colaod		Preload with colaod		*p*-value
	n	Median (min-max)	n	Median (min-max)	n	Median (min-max)	
Time to hypotension	34	4 (1 to 15)	31	4 (2 to 18)	38	4.5 (1 to 16)	0.619
Dose of ephedrine	34	15 (6 to 42)	31	12 (6 to 36)	38	18 (6 to 30)	0.636

Kruskal-Wallis test, significant (p<0.05)

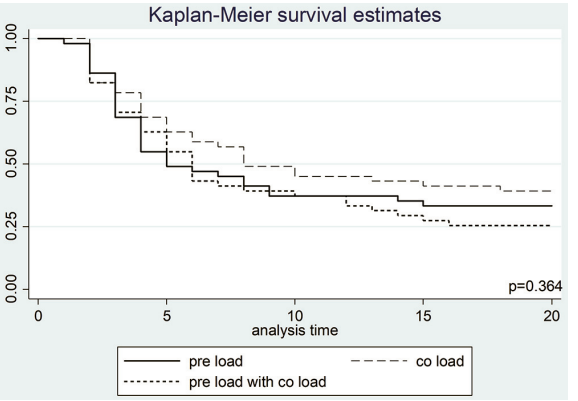

Figure 2. Comparison of mean systolic blood pressure with respect to time to hypotension among groups.

in the coload group (60.8%) than preload (66.7%) and preload with coload groups (74.5%) without significant differences. However, the incidence of maternal hypotension in SA was still high at 60 to 70% in the present study and similar to other studies regardless of the fluid loading strategy used[6-8]. To the authors' knowledge, the combined method between preload and coload method should not be exercised as a substitute for the simple preload method. Several studies have reported that crystalloid preload is the least advantageous in preventing maternal hypotension[5,6,8,11]. The present study determined that duration over 20 minutes before SA and the volume of fluid administration constituted the reasons lowered effectiveness of the preload and the preload with coload methods. One possible reasons for the insignificance of crystalloid solution administration as a prophylaxis against SA induced hypotension is that crystalloid diffuses in the interstitial space and has a short half-life[12]. This suggests that the volume effect may exist in the smaller volume of crystalloid loading. Although crystalloid administration is safe in most patients, evidence suggests that large volumes of crystalloid preload could be counterproductive as an induced hemodilution leading to pulmonary edema. One study reported that the estimated EV50 of the preloaded crystalloid requirement could prevent SA-induced hypotension during a cesarean section. This estimated requirement is about 13 ml/kg[13]. The volume of fluid administration during the intra-operative period still remains indicated including (a) some degree of dehydration causes preoperative fasting and (b) it helps maintain cardiac output during onset of spinal blockade. Several studies have recommended administering a rapid crystalloid infusion after SA as coload[6-8,11]. Crystalloid coload could decrease the ephedrine requirement to maintain maternal blood pressure[6-8,11]. The authors' result was consistent with this finding concerning to the supplement of ephedrine doses was lesser in coload group comparing with the preload and preload with coload groups. The median time to hypotension is 4 minutes after SA. This suggested that hypotension should be treated immediately with intravenous ephedrine. It should be titrated to maintain SBP as closely as possible to the parturient normal baseline value. The optimal dose of prophylactic intravenous ephedrine to prevent maternal hypotension is 12 mg[14]. No evidence exists of any significant difference in Apgar scores. Recent literature has shown that despite the high prevalence of maternal hypotension, term neonates can tolerate this placental blood perfusion challenge without any major negative consequences. The authors' results were consistent with these findings regardless of the fluid loading strategy exercises, producing little effect on the Apgar score.

The present study had a number of limitations. Firstly, because aorto-caval compression will cause hypotension, decreased uterine blood perfusion will occur. This hypotension will be undetected by blood pressure measurement in the upper extremities. Additionally, the one-minute interval measurement is inexact as anticipated. Secondly, the estimated separation of intravenous volume loading would be less than the optimal volume, which the patient required. Therefore, this fact should be taken into account as the cause of marked hypotension in the preload with coload group.

Conclusion

Preload, coload and preload with coload strategies with 10 ml/kg of acetate solution were ineffective in preventing hypotension in the parturient cases with SA. Frequent measurement of the blood pressure at 1 minute intervals for prompt recognition of hypotension and administration of vasopressors to maintain the baseline maternal blood pressure could ensure better neonatal outcomes. Consequently, during the time of intravenous fluid loading, prophylactic or therapeutic ephedrine should also be considered. Prompt administration with ephedrine to the patient is crucial because significant hypotension develops.

What is already known on this topic?

Crystalloid preload is the least advantageous in

preventing maternal hypotension. Several studies have recommended administering rapid crystalloid infusion after SA as coload.

What this study adds?

This present study revealed the median time to hypotension was 4 minutes after SA. This suggested that hypotension should be treated immediately with intravenous ephedrine. Preload with coload with 10 ml/kg of acetate solution was ineffective in preventing hypotension in parturient cases with SA.

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Potential conflicts of interest

The authors declare no conflict of interest.

References

1. Ozden OD, Dogu T, Omaygenc MO, Ozmen F, Albayrak MD, Babur GG, et al. Type of anesthesia affects neonatal wellbeing and frequency of transient tachypnea in elective cesarean sections. J Matern Fetal Neonatal Med 2015;28:568-72.
2. Saracoglu KT, Saracoglu A, Umuroglu T, Eti Z. Neuraxial block versus general anaesthesia for cesarean section: post-operative pain scores and analgesic requirements. J Pak Med Assoc 2012; 62:441-4.
3. Kokovic JT, Radunovic N, Filimonovic D, Nejkovic L, Arsenijevic L, Mirkovic LJ, et al. Maternal hemodynamic influence on uteroplacental oxygen distribution during cesarean section. Clin Exp Obstet Gynecol 2015;42:610-3.
4. Hoefnagel A, Yu A, Kaminski A. Anesthetic complications in pregnancy. Crit Care Clin 2016; 32:1-28.
5. 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.
6. 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.
7. Khan MU, Memon AS, Ishaq M, Aqil M. Preload versus coload and vasopressor requirement for the prevention of spinal anesthesia induced hypotension in non-obstetric patients. J Coll Physicians Surg Pak 2015;25:851-5.
8. Jacob J, Williams A, Verghese M, Afzal L. Crystalloid preload versus crystalloid coload for parturients undergoing cesarean section under spinal anesthesia. J Obstet Anaesth Crit Care 2012;2:10-5.
9. The Royal College of Anesthesiologists of Thailand. Clinical practice guidelines for spinal anesthesia [Internet]. 2015 [cited 2016 Sep 20]. Available from: http://anesthai.org/th/files/documents/4.
10. Mercier FJ. Fluid loading for cesarean delivery under spinal anesthesia: have we studied all the options? Anesth Analg 2011;113:677-80.
11. Mercier FJ, Bonnet MP, De la DA, Moufouki M, Banu F, Hanaf A, et al. [Spinal anaesthesia for caesarean section: fluid loading, vasopressors and hypotension]. Ann Fr Anesth Reanim 2007;26: 688-93.
12. Hahn RG, Lyons G. The half-life of infusion fluids: An educational review. Eur J Anaesthesiol 2016; 33:475-82.
13. 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.
14. Loughrey JP, Walsh F, Gardiner J. Prophylactic intravenous bolus ephedrine for elective Caesarean section under spinal anaesthesia. Eur J Anaesthesiol 2002;19:63-8.