Colloid versus Crystalloid Co-load with Spinal Anesthesia during Emergent Cesarean Section and Their Effect on Hemodynamic Changes

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Abstract: Objectives: The study aimed to compare between colloid, crystalloid co-load or combination between them, with spinal anesthesia during emergent cesarean section and their effect on hemodynamic changes. **Background:** Maternal hypotension is the commonest serious problem following spinal anesthesia for Caesarean section, with an incidence up to 83%. Volume preloading has been recommended for prevention of spinal-induced hypotension in this situation. However, controversy regarding the different preloading regimens remains unresolved. **Patients and methods:** the present study was carried out on75 females presented for emergent CS at Menoufia University Hospital. Those females were randomly allocated to one of three equal groups; the first group(A) in which females were co-loaded with crystalloid solution; group(B) in which females were co-loaded with colloid solution and group(C) in which females were co-loaded with both crystalloid and colloid solution. Hemodynamic measurements were obtained just before induction of spinal anesthesia (basal values) and then every 5 minutes after co-loading, till 30 min, then every 10 min til the end of operation. Episodes of hypotension, vasopressors and side effects such as nausea and vomiting were recorded. **Results:** There was no significant difference between studied groups as regards to demographics, basal measurements, heart rate or oxygen saturation at any time, total amount of ephedrine or Apgar score at 1st or 10th minute. On the other hand, there was a significant decrease of SBP, DBP and MAP at group (A) in comparison to either group (B) or group C. First episode of hypotension was reported with significant difference between studied groups. In addition, there was significant difference between studied groups as first bolus of vasopressors. The total number of boluses significantly increased in group A and B in comparison to group C. Nausea and vomiting occurred with a significant increase in group A in comparison to group B and group C .Furthermore, there was significant increase of total fluid volume in group A in comparison to group B and group C. Finally, patient satisfaction was reported as a questionnaire and there was a significant increase of satisfaction in groups C and B when compared to group A . **Conclusion:** Both colloid and crystalloid coload is effective in preventing hypotension associated with spinal anesthesia for emergent CS. In addition it decreases nausea and vomiting and vasopressor usage.
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1. Introduction

The decrease in systemic vascular resistance (SVR) due to preganglionic sympathetic blockade with spinal anesthesia may result in peripheral pooling of blood, which will lead to a decrease in cardiac output and hypotension[1].

Hypotension during spinal anesthesia for cesarean delivery is a common and troublesome complication, both from the maternal and fetal-neonatal point of view. Commonly used methods for the prevention of hypotension, for example, leg wrapping, antithrombo-embolic stockings, patient positioning, and fluid & vasopressor administration have met with mixed success[2]. Traditionally, IV crystalloid fluids are administered in the (20 min) before the induction of spinal anesthesia for cesarean delivery (preload) which may reduce but not eliminate hypotension. This is relatively ineffective since preload is rapidly redistributed[3,4], and also, this method may induce atrial natriuretic peptide (ANP) secretion, resulting in peripheral vasodilatation followed by an increased rate of excretion of the preload fluid[5]. When colloid administration was compared with crystalloid preloading before caesarean section, the incidence of hypotension, although less in the colloid group, was not significantly different[6].

A more rational approach is to administer the fluid bolus at the time that the local anesthetic block is starting to take effect. This might maximize intravascular where volume expansion during vasodilatation from the sympathetic blockade and limit fluid redistribution and excretion. This practice has been termed "coload" [7].

Aim of the work

The study aimed to compare between colloid co-load, crystalloid co-load or combination between them, with spinal anesthesia during emergent cesarean section and their effect on hemodynamic changes.

2.Patients and methods

This study carried out in Menoufia University hospital; after a written informed consent, 75 ASA physical status I and II women with full-term singleton pregnancies who admitted for emergent cesarean delivery under spinal anesthesia were included in the present study.

Exclusion criteria included: chronic or pregnancy- induced hypertension, diabetes on medication, cardiovascular diseases, cerebrovascular diseases, known fetal abnormalities, morbid obesity (BMI>40) and height (<140 cm or >180 cm); and any contraindications to neuraxial anesthesia.

All patients were assessed for concurrent (medical, family, allergy, drugs and previous anesthesia) history. Tow 18-gauge IV canulae which have infusion rate of 80ml/min was inserted to all patient in large veins . All patients did not receive any IV fluids before entering operating room. Ranitidine 50 mg plus metoclopramide 10 mg administered slowly IV just before patient arrival to the operating room (OR). Standard monitors of electrocardiography (ECG), pulse oximetry (Spo$_2$), and noninvasive blood pressure (NIBP) applied on the right arm. The patient sits down and the back was sterilized, local infiltration of the skin and subcutaneous tissues at the level of L3-L4 by 3ml lignocaine 2%. Finally 25-gauge rounded bevel needle used and 2.5 ml bupivacaine 5% was injected intrathecally. Then the patient rapidly directed to left-lateral tilt position.

All patients had the following baseline variables measured in the supine position with 15° of left lateral tilt: base line heart rate (HR), mean arterial blood pressure (MAP), and oxygen saturation (SPO$_2$) before intravenous fluid administration. Hypotension defined as a 20% decrease in mean arterial blood pressure (MAP) or mean arterial blood pressure (MAP) <60 mmHg. Then the patients were assigned into three groups, 25 patients for every group. **Group (A)** co-loaded with 15ml/kg lactated ringer's solution (L.R). **Group (B):** co-loaded with 5ml/kg voluven (hydroxyethyl starch 130/0.4 in 0.9 % sodium chloride). **Group (C):** co-loaded with 7.5 ml/kg lactated ringer's solution (L.R) plus 2.5ml/kg voluven (hydroxyethyl starch 130/0.4 in 0.9 % sodium chloride).

In all groups the IV fluid administrated immediately after intrathecal injection and the patient in supine position with left lateral tilt of the table. All fluids were administrated at room temperature. Vassopressor (ephedrine) was given in boluses (6mg/bolus) if there was hypotension and was repeated if hypotension persist.

Parameters of assessment included Hemodynamic parameters (HR, SBP, DBP, MAP and SpPO$_2$) were measured every 5 min. from spinal injection for 30 min then every 10 min for the completion of surgery. The time from intrathecal injection to the 1st episodes of hypotension (decreased mean arterial blood pressure <60 mmHg), the incidence of hypotension, the number of vasopressor boluses, the total amount of ephedrine administrated, the incidence of nausea and vomiting, neonatal outcome (Apgar score) at 1st and 10 mins and the patient satisfaction were recorded.

Statistical analysis:

Gathered data was processed using SPSS version 16 (SPSS Inc., Chicago, IL, USA). Quantitative data was expressed as means ± SD while qualitative data was expressed as numbers and percentages (%). One way analysis of variance (ANOVA) or t- test were used to test significance of difference for quantitative variables that follow normal distribution. Chi Square (X^2), or Mann Whitney test were used to test significance of difference for qualitative variables. A probability value (*p*-value) < 0.05 was considered statistically significant.

3.Results

In the present work, there was no significant difference between studied groups as regard to age, weight, height, parity, blood pressure, heart rate or oxygen saturation (Table 1). In the present study, there was non-significant difference between studied groups as regard systolic blood pressure at basal, 5, 10, 20, 25, 30, 40, 50 or 60 minutes, while there was significant decrease of SBP at 15 minutes at group A (103.60±21.59) in comparison to either group B (111.48±17.32) or group C (115.52±10.01). In addition, there was non-significant difference between studied groups as regard diastolic blood pressure at basal values, 5, 10, 25, 30, 40, 50 and 60 minutes, while there was significant decrease of DBP in group A in comparison to either group B or C at 15 and 20 minutes. Finally, there was non-significant difference between studied groups as regard Mean arterial pressure at basal values, 5, 10, 25, 30, 40, 50 and 60 minutes, while there was significant decrease of MAP in group A in comparison to either group B or C at 15 and 20 minutes (Figure 1).

In the present work, there was no significant difference between studied groups as regard heart rate or oxygen saturation at any time (data not tabulated).

Regarding first episode of hypotension, it was reported in 48%, 20.0% and 8% in groups A, B and C respectively with significant difference between studied groups. In group A, first episode started to occur at 10 minutes and maximally occurred at 15 minutes, while in group B, it starts to occur at 5 minutes and maximally occurred at 15 minutes and finally in group C it occurred equally at 20 and 30 minutes. In addition, there was significant difference between studied groups as first bolus of vasopressors. The total number of boluses was significantly increased in group A and B in comparison to group C. postoperative nausea and vomiting occurred in 14 cases (18.7%) and there was significant increase in group A (40.0%) in comparison to group B (12.0%) and group C (4.0%). The total amount of fluid ranged from 250 to 1500 with a mean of 783.33±476.35 ml and there was significant increase in group A (1400.0±279.50) in comparison to group B (480.0±100.0) and group C (470.0±131.49). Finally, patient satisfaction was reported in 74.7% of total studied cases, and there was significant increase of satisfaction in groups C and B when compared to group A (the percentage of satisfaction was 92.0%,

80.0% and 52.0% in groups C, B and A successively) (Tables 2,3).

Finally, no significant difference was found between studied groups as regard to total amount of ephedrine, Apgar score at 5th or 10th minute (data not tabulated).
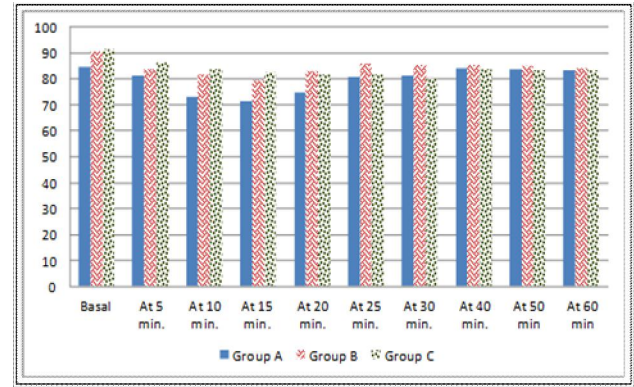

Figure (1): Comparison between studied groups as regards mean arterial pressure at different times

Table (1): Comparison between studied groups as regard to demographic characteristics and basal measurements

	Group A	Group B	Group C	F	P
Age	23.52±2.27	22.76±1.78	23.28±1.86	0.95	0.38
Weight	72.48±4.47	71.32±3.90	72.56±3.57	0.57	0.47
Height	166.16±2.62	166.28±2.07	167.12±2.53	1.16	0.31
Parity	2.28±0.54	2.28±0.73	2.56±0.82	1.29	0.27
Systolic BP	124.04±9.88	124.28±8.98	122.0±6.92	0.52	0.59
Diastolic BP	70.60±8.85	74.80±10.48	73.20±5.37	1.55	0.21
MAP	84.76±13.17	90.80±12.66	91.56±11.13	2.27	0.11
Basal heart rate	98.28±12.49	95.20±14.47	94.44±12.21	0.60	0.55
Oxygen saturation	98.64±0.70	98.84±0.55	98.56±0.50	1.28	0.23

$P > 0.05$: non-significant; $P < 0.05$: significant; $P < 0.01$: highly significant; $P < 0.001$: extremely significant.

Table (2): Comparison between studied groups as regards episodes of hypotension and vasopressor boluses

		Group A	Group B	Group C	test	P
1st episode of hypotension		12(48.0%)	5(20.0%)	2(8.0%)	11.13	0.004*
Time of first episode	5.00	0(0.0%)	1(20.0%)	0(0.0%)	10.26	0.24
	10.00	3(25.0%)	1(20.0%)	0(0.0%)		
	15.00	6(50.0%)	3(60.0%)	0(0.0%)		
	20.00	2(16.7%)	0(0.0%)	1(50.0%)		
	30.00	1(8.3%)	0(0.0%)	1(50.0%)		
First bolus vasopressor		12(48.0%)	5(20.0%)	2(8.0%)	11.13	0.004*
No of boluses	1.0	8(66.7%)	3(60.0%)	2(100.0%)	1.55	0.81
	2.0	1(8.3%)	1(20.0%)	0(0.0%)		
	3.0	3(25.0%)	1(20.0%)	0(0.0%)		
	Total	12	8	2#	9.77	0.008*

Significant decrease in number of boluses in group C in comparison to either group A or group B.

Table (3): Comparison between studied groups as regards outcome and patient satisfaction

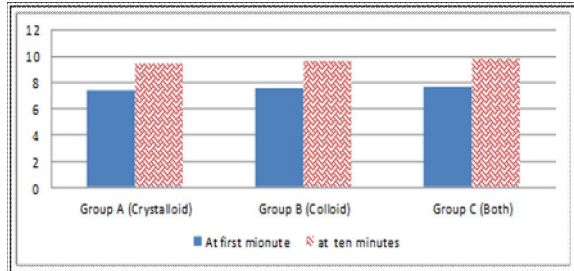|	Group A	Group B	Group C	test	P
PONV	10(40.0%)	3(12.0%)	1(4.0%)	11.76	0.003*
Total amount of fluid	1400.0±279.50	480.0±100.0	470.0±131.49	202.9	<0.001*
Patient Satisfaction	13(52.0%)	20(80.0%)	23(92.0%)	11.13	0.004*

Figure (2): Comparison between studied groups as regards Apgar score at first and ten minutes.

4. Discussion

Since the concept of 'prehydration' was introduced into clinical practice, fluid loading with crystalloid prior to spinal anesthesia has become common practice[14]. However, crystalloid preloading may lead to severe dilutional anemia, resulting in decreased oxygen transport capacity, decreased colloid oncotic pressure, and subsequent pulmonary edema. In addition, the strategy of crystalloid infusion is not affirmed. Crystalloid preloading is more popular in preventing hypotension for patients undergoing cesarean section[7]. On the other hand, colloid preloading has been shown to be more effective in the prevention of spinal anesthesia induced hypotension in Western nations[15].

Despite the advantages of colloid preloading, many are concerned by its costs has been introduced and more importantly, the risk of anaphylaxis[16]. The co-load in undergoing spinal anesthesia, as it is reported that, crystalloid preloading is relatively ineffective for preventing hypotension despite infusing volumes of up to 30 mL/kg[17]. Atrial natriuretic peptide release with subsequent vasodilator and diuretic effects compounded with time-related fluid redistribution are suggested causes of its ineffectiveness[18]. In addition, **Dyer et al.**[7] investigated whether a crystalloid co-load would be more effective than a preload and showed that 20 mL/kg crystalloid co-load reduced hypotension compared with the equivalent preload volume. Volume kinetic studies of RL solution during spinal and general anesthesia by Ewaldsson and Hahn concluded that the arterial pressure is better maintained by a fluid bolus just after the induction of anesthesia than by preloading[18]. It was suggested that loading fluid at the time of administering the intrathecal local anesthetic (coloading) might be a

physiologically more appropriate and rational approach as the maximal effect can be achieved during the time of the block. [19]

Dyer et al. suggested that co-loading might increase intravascular volume expansion during vasodilatation from the sympathetic blockade and limit fluid redistribution and excretion. Rapid crystalloid co-loading soon after induction of spinal anesthesia rather than as preload over 20 min before spinal anesthesia for elective cesarean section was reported to be advantageous in terms of managing maternal blood pressure prior to delivery [7]. The co-loading technique developed after the efficacy of preloading was questioned. It had been found that colloid preload is better than crystalloid preload resulting in increased CO and less hypotension.[20] Crystalloid co-load is better than preload[9]. **Teoh and Sia**[21] found that 15 mL/kg colloid preload but not co-load, significantly increased maternal CO within the first 5 minutes after spinal injection, with no difference in the incidence of hypotension. Paver-Erzen studied the effects of a lactated Ringer's solution co-load compared with preload, or no load on cardiac output after spinal anesthesia. Cardiac output remained elevated above baseline in the co-load group 30 min after induction of anesthesia, whereas it returned to baseline in the preload group and decreased in the group that received no fluid.[22]

As regards blood pressure, incidence of hypotension episodes was 48%, 20.0% and 8% in groups A, B and C respectively. These results were in agreement with **McDonald et al.**[8]. They reported that, at the time of spinal injection, subjects were allocated to receive a rapid 1-L coload of either 6% w/v hydroxyethyl starch solution (HES) or Hartmann (crystalloid) solution (HS). Their results revealed that, the incidence of hypotension from spinal injection to delivery was 60% in the crystalloid group versus 40% in the colloid group, which was in agreement with that of the present study regardless of elevated percentage of occurrence in their study. This elevation could be attributed to different definitions of hypotension and difference in infused amount of both crystalloids and colloids. **Banerjee et al.**[24] in a meta-analysis, retrieved randomized controlled trials that compared a fluid preload with co-load in patients undergoing spinal anesthesia for elective Cesarean delivery. They graded the articles for quality of reporting (maximum score=5) and recorded the

incidence of hypotension, lowest blood pressure, the incidence of maternal nausea and vomiting, umbilical cord pH, and Apgar scores. They combined the results using random effects modeling. They that, in patients undergoing elective Cesarean delivery under spinal anesthesia, the timing of fluid loading did not have an impact on the incidence of hypotension. This was true for both colloid and crystalloid loading. Therefore, it was unnecessary to delay surgery in order to deliver a preload of fluid. Regardless of the fluid loading strategy, either prophylactic or therapeutic vasopressors may be required in a significant proportion of patients especially with crystalloid group. Randomized controlled trials involving healthy term patients undergoing scheduled cesarean delivery that compared the effect of colloid and crystalloid on hypotension, need for vasopressors, cardiac output, neonatal outcomes, and other adverse effects were analyzed. They found that the incidence of hypotension to be 38.7% and 17.3% for crystalloid and colloid respectively. They demonstrated the preventive effect of colloid to be more obvious than that of crystalloid. The also found that, the, vasopressor efficacy for maintaining vascular resistance is important in maintaining maternal blood pressure and in preventing maternal nausea, vomiting, and dizziness. The requirement for vasopressor use reflects the incidence or severity of hypotension. In their study, they showed that colloid effectively reduced the need for vasopressors, as reported in the present work. On the other hand, **Yorozu *et al.*[24]** included sixty-seven patients scheduled for cesarean section under spinal anesthesia were randomly allocated to receive either LR (n= 35) or HES (n= 32) infusion before cesarean delivery. Infusion of the fluid was started immediately after arrival at the operating room, through two fully open i.v. routes of 18 or 16 gauge. The two groups were compared in terms of the incidence of hypotension; ephedrine dose; cord and maternal blood gas, hemoglobin, and glucose; and Apgar scores. They reported that, they could not show a beneficial effect of colloid infusion to prevent spinal anesthesia-induced hypotension compared with crystalloid. These results are in contradiction to the results of the present study and this can be attributed to different inclusion criteria and to amount of fluid infused as they reported that, the intravenous fluid volume administered until delivery in the crystalloid group (1298±503 ml) was significantly greater than that in the colloid group (852±200 ml) in spite of similar periods of intravenous infusion in the crystalloid group and the colloid group (18.1±3.9 and 18.2 ±4.1 min, respectively;

Regarding number of hypotension episode, it was one in 66.7%, 60% and 100% of patients with hypotension in groups, A, B and C. **McDonald *et al.*[8]** reported that, the number of subjects in their study having >1 episode of hypotension was low (7% vs 27% in the colloid and crystalloid groups, respectively), suggesting hemodynamic control is better than the overall incidence of hypotension.

In the present study, colloid co-load was found to decrease total amount of ephedrine, but the difference was statistically insignificant. They results are in contradiction to previous study, where it was reported that, crystalloid co-load has been reported to decrease ephedrine requirement to maintain the maternal blood pressure[7]. Regarding neonatal outcome, there was no significant difference between groups as evidenced by Apgar score. It had been reported that, neonatal outcomes are a major consideration for Cesarean parturients under neuraxial anesthesia due to the threat from hypotension[25]. However, recent literatures show that despite the high prevalence of maternal hypotension, term infants can tolerate this placental blood perfusion challenge without any major negative consequences[26]. Meanwhile, a range of studies also have not found any sequel from the fluid interventions in patients undergoing cesarean section with neuraxial blockade[27,28].

Regarding nausea and vomiting, our results were in agreement with **Smiley[29]** who reported that, the incidence of nausea and vomiting was significantly lower with colloid than crystalloid, suggesting that patients given colloid to increase central blood volume for cesarean section may obtain more clinical benefits. Finally, there was significant increase of satisfaction in groups C and B when compared to group A (the percentage of satisfaction was 92.0%, 80.0% and 52.0% in groups C, B and A successively). This might be due to decreased incidence of side effects (nausea and vomiting) in the colloid co-load group.

In conclusion, results of the present study proved the efficacy of both colloid and crystalloid co-load in preventing hypotension associated with spinal anesthesia for emergent CS. In addition, colloid co-load was better than crystalloid in terms of decreasing incidence of hypotension, decreasing nausea and vomiting and finally small volume of infused fluid.

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