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Research Article

Comparative study between ephedrine infusion vs. CO/post loading of fluids for prevention of hypotension in emergency cesarean section under spinal anesthesia

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KEYWORDS

Spinal anesthesia;
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Abstract *Introduction:* Maternal hypotension is the most common complication during cesarean section under spinal anesthesia. The aim of this study was to compare the effectiveness of CO/post loading of fluids versus immediate post spinal infusion of ephedrine in prevention of hypotension.
Methods: Ninety healthy pregnant patients ASA I with single term fetus arrived to the operating room with nonlife threatening cause for emergency cesarean section under spinal anesthesia. The patients were allocated randomly into 3 groups, *Group R*: started the CO/post loading at the time of spinal injection and continued after it with 0.5 ml/kg/min Lactated Ringer's solution until delivery of the fetus. *Group V*: started the CO/post loading with 0.5 ml/kg/min Voluven at the same period. *Group E*: started ephedrine infusion at 1 mg/min via the infusion pump immediately after spinal anesthesia until delivery of the fetus.
Results: The systolic blood pressure changes were statistically significant but they failed to reach clinical significant values in the three groups. The total dose of ephedrine was significantly higher in Ephedrine group than the other two groups. Intraoperative heart rate increased in the first 30 min in Ephedrine group without any clinical significance. All fetal data were within normal range and comparable between groups. Apger score of the fetuses was not less than 8 in the three groups. The incidence of nausea and vomiting was higher in group R and group V compared to group E.
Conclusion: Intravenous infusion of ephedrine 1 mg/min immediately after spinal anesthesia for emergency cesarean sections, even if there is no enough time for proper prehydration, can control effectively the hypotension without episodes of hypertension or significant tachycardia, and it had

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no effect on fetal well-being. It could be as effective as CO/post loading of 0.5 ml/kg/min lactated Ringer or Voluven in controlling systolic blood pressure with fewer incidences of post operative complications.

1. Introduction

Spinal anesthesia provides a fast effective and high quality of sensory and motor block in patients undergoing elective or emergency cesarean section (CS) [1,2].

Maternal hypotension is the most common complication during CS under spinal anesthesia with a reported incidence greater than 80% if not prevented [3], and it could be associated with severe nausea and vomiting. It leads to serious risk to the mother (unconsciousness and pulmonary aspiration) and baby (hypoxia, acidosis, and neurological injuries) [4].

The incidence of hypotension and high spinal anesthesia is higher due to a decrease in the amount of cerebrospinal fluid (CSF) in the lumbosacral area and higher cephalad spread of local anesthetics. This is due to compression of inferior vena cava by hypertrophic uterus and developing of collateral venous plexus circulation in the epidural space [5,6].

A number of strategies for preventing hypotension have been investigated; one of these strategies is left lateral uterine displacement [7]. Other strategies have included intravascular volume expansion using intravenous (IV) fluids immediately before spinal injection (preload) [8], or at the time of spinal injection and continued after it (CO/post loading) with colloid or crystalloid solutions [9].

The most effective strategy is prophylactic administration of ephedrine either by the IM route that is very controversial due to high incidence of rebound hypertension [10]. Or the intravenous route that is more effective and controllable, it is more familial and low propensity for utero-placental vasoconstriction [11,12].

So, many investigators try to find the most suitable way to overcome this side effect of spinal anesthesia during CS and only have its benefit as a safe comfortable technique for delivery of a healthy baby.

The aim of this study was to compare the effectiveness of (CO/post loading) of fluids [colloid solutions (Voluvan) or crystalloid solutions (lactated Ringer)] 0.5 ml/kg/min started just before spinal anesthesia and continued until delivery of the fetus versus immediate post spinal infusion of ephedrine 1 mg/min until delivery of the fetus for preventing spinal hypotension during emergency CS. This study measured different variables related to maternal well-being (incidence of hypotension, nausea, and vomiting) and fetal well-being (umbilical artery (pH, PCO2 and base excess) and Apgar score at 1 and 5 min).

2. Material and methods

This study was done in Kasr El-Aini Hospital between May 2010 and October 2011 after approval of the local ethical committee and informed written consent of the patients was obtained, 90 healthy pregnant patients ASA I with single term fetus arrived to the operating room with nonlife threatening cause for emergency CS (prolonged labor or dystocia, failed labor induction or amniotic rupture) under spinal anesthesia. Standard monitors included electrocardiogram (ECG), noninvasive blood pressure monitor, and pulse oximeter was fixed on all patients. Oxygen (4 L/min) was administered to all patients via nasal catheters. The baseline measurements of the heart rate (HR), systolic blood pressure (SBP), and oxygen saturation were recorded in the modified supine position with at least 15° of left lateral tilt.

Exclusion criteria were patient's refusal, fetal distress, known fetal abnormalities, cardiovascular, renal or liver diseases, chronic hypertension or gestation induced hypertension, coagulation disorders, and those with total or partial spinal anesthesia failure.

Intravenous cannula (18G) was fixed in cephalic veins in all patients, and the patients were allocated randomly (by closed envelope) into three groups, 30 patients in each group.

Group R: started the CO/post loading with 0.5 ml/kg/min lactated Ringer's solution (crystalloid solution) using an infusion pump until delivery of the fetus (clamping of umbilical cord).

Group V: started the CO/post loading with 0.5 ml/kg/min Voluven (6% hydroxyethyl starch (HES 130/0.4)) in isotonic sodium chloride solution using an infusion pump until delivery of the fetus (clamping of umbilical cord).

Group E: started ephedrine infusion at 1 mg/min via the infusion pump immediately after spinal anesthesia until delivery of the fetus (clamping of umbilical cord), it was accompanied by infusion of lactated Ringer's solution at minimal intravenous infusion rate required to keep vein open (KVO).

While the patients in sitting position, spinal anesthesia was performed at L2–L3 or L3–L4 interspace using a 9 cm 25 gauge Whitacre spinal needle. 2–2.5 ml (according to the patients height) 0.5% hyperbaric bupivacaine with 25 μg fentanyl was injected through the spinal needle after clear, free flow of CSF was obtained. Patients were then immediately placed in supine position with left uterine displacement. Upper sensory level of anesthesia was detected by assessing loss of pinprick sensation, the surgery started when the block extended to T5 or above.

SBP and HR were recorded at 1 min after spinal anesthesia then every 3 min for the first 30 min then every 5 min until the end of surgery and in the recovery room for at least 90 min from the beginning of spinal anesthesia. Nausea, vomiting, dizziness, and chest symptoms (dyspnea and tachypnea) were also recorded every 10 min. Fetal heart rate was monitored by using cardio-tocography (CTG) continuously until delivery. Hypotension was defined as 20% decrease in SBP from the baseline (it was treated immediately by 5 mg bolus IV ephedrine every 2 min until SBP returned to normal value in all groups), and the maternal bradycardia was defined as HR < 60 beat/min and it was treated immediately by using IV 0.5 mg atropine.

Oxytocin was administered after delivery (10 μ in 500 ml lactated Ringer) in all patients, nausea and vomiting was treated with 10–20 mg IV metoclopromide whether unrelated

to hypotension or not corrected by ephedrine bolus dose alone.

2.1. Data measured

Maternal data: the total volume of fluid intake until delivery of the fetus and the total dose of ephedrine required for all patients were recorded. Changes in SBP, HR, and complications like nausea, vomiting, dizziness, and respiratory distress. Additional data collection included the time interval from spinal anesthesia to delivery of the fetus (clamping of umbilical cord).

Fetal data: Apgar score was assessed at 1 and 5 min by the attending pediatrician, and arterial blood sample was taken from the umbilical cord for blood gases analysis (pH, PCO2) within 2 min after delivery.

2.2. Statistical analysis

Data were presented as mean ± standard deviation, median (range), or percentage as appropriate. Comparison between groups was performed using one way analysis of variance (ANOVA) with post hoc Newman–Keul's test. P values of < 0.05 were considered significant.

3. Results

As regard demographic data (age, weight, and height), they were comparable between the three groups as shown in Table 1. The time from spinal anesthesia until delivery of the fetus was also comparable in the three groups and is represented in (Table 1).

The total volume of fluids was statistically significantly lower in Ephedrine group (group E) 156.8 ± 47.4 ml compared to Ringer group (group R) and Voluven group (group V) 911.06 ± 273.49 ml and 907.68 ± 255.78 ml, respectively (Table 1).

The total dose of ephedrine was statistically significantly higher in Ephedrine group (group E) 31.4 ± 3.9 mg compared to the other two groups. At the same time, Ringer group (group R) needed more ephedrine dose 22.6 ± 9.8 mg than Voluven group (group V) 18.2 ± 7.5 mg but without statistical significant difference (Table 1).

Baseline SBP was comparable between the three groups. Intra and post operative changes were summarized in (Fig. 1). In the 1st 30 min, there were statistical significant drop in SBP as regard the three groups with the max. at 13 min in group E 118 ± 6 mm Hg, 7 min in group R 105 ± 4 mm Hg, and 10 min in group V 109 ± 6 mm Hg. There were 12 patients (36%) in group R, nine patients (27%) in group V compared to three patients (10%) in group E had drop in blood pressure more than 20% of the baseline and needed management with ephedrine.

Intraoperative HR is represented in Fig. 2. In the 1st 30 min, there was statistical significant increase in HR with the max. at 16 min in group E 95 ± 5 beat/min. while there was statistical significant decrease in the HR in the other two groups with the max. at 13 min in group R 73 ± 5 beat/min and 13 min in group V 74 ± 6 beat/min. but also these changes without any clinical significance values.

All fetal data are presented in (Table 2). There were no statistical significant differences in between groups as regard (weight (kg), umbilical artery blood gases, Apger score 1, 5 min).

The incidence of post operative complications is represented in (Table 3) by number of patients and the percentage.

4. Discussion

This study was done on 90 pregnant women undergoing emergency CS for nonlife threatening causes under spinal anesthesia. As a prophylactic to hypotension and due to lack of enough time, we compared CO/post loading of fluids 0.5 ml/kg/min (crystalloid or colloid) with immediate post spinal infusion of 1 mg/min ephedrine until delivery of the fetus, which show a significant control of blood pressure and a decrease in the total IV fluid infusion with no hazards on the fetal well-being.

During emergency CS, the patients are usually admitted to the operating room with short time for anesthetic preparation. Spinal anesthesia is the most familiar choice for those patients but expected hypotension needs adequate management to avoid any maternal or fetal hazards.

Traditionally, preload with fluids has always been performed just before spinal anesthesia [13,14]. Contrary, some investigators found that CO/post loading is more effective when performed after sympathetic block. This is due to higher trend of the body to preserve the fluids (crystalloid) administered in the central compartment, but these phenomena would not be important with colloids as they naturally tend to remain in the intravascular compartment [9,15].

Ueyama et al. and Riley et al. [13,14] showed higher incidence of hypotension in patients preloaded with crystalloids than colloids. These data disagree with Cardoso et al. [8] who found that preload with colloids (modified fluid gelatin)

Table 1 Demographic data.

	R group	V group	E group
Age (years)	30.4 ± 5.1	32.1 ± 4.8	31.6 ± 4.3
Weight (kg)	80.27 ± 9.82	77.25 ± 6.39	81.17 ± 8.6
Height (cm)	164.36 ± 3.5	160.60 ± 4.2	159.56 ± 5.7
Time from spinal anesthesia until delivery (min)	22.7 ± 4.6	23.5 ± 5.1	23.3 ± 3.9
Total volume of fluids until delivery of the fetus (ml)	911.06 ± 273.49	907.68 ± 255.78	156.8 ± 47.4[a]
Total dose of ephedrine (mg)	22.6 ± 9.8	18.2 ± 8.5	31.4 ± 3.9[*]

Data is represented as mean ± SD. Number of patients = 30 in each group.
[a] Statistically significantly lower than the other 2 groups.
[*] Statistically significantly higher than the other 2 groups. $P < 0.05$ is considered statistically significant.

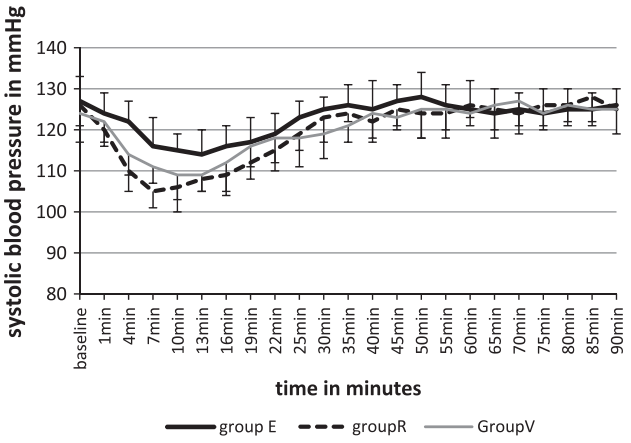

Figure 1 Changes in systolic blood pressure.

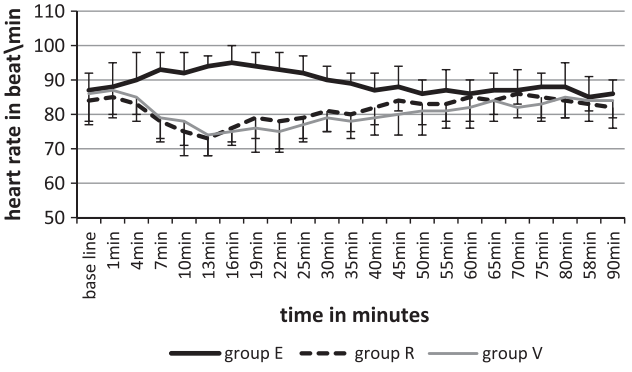

Figure 2 Changes in the heart rate.

was similar to crystalloid (lactated Ringer) in decreasing maternal hypotension incidence after spinal anesthesia for CS. In this study, we could not find a great difference between the effects of colloids and crystalloids in controlling the blood pressure and HR. In the 1st 30 min, there were statistical significant drop in SBP as regard the crystalloid and colloid groups with the max. at 7 min in group R 105 ± 4 mm Hg and 10 min in group V 109 ± 6 mm Hg. But these changes failed to reach clinical significant values. While there was statistical significant decrease in the HR in the crystalloid and colloid groups with the max. at 13 min in group R 73 ± 5 beat/min and 13 min in group V 74 ± 6 beat/min. but also these changes without any clinical significance values.

Table 3 Adverse effects (% of the patients).

	R group	V group	E group
Nausea	11(36.6%)*	9(30%)*	2(6.6%)
Vomiting	5(16.6%)*	3(10%)*	0
Dizziness	2(6.6%)	0	0
Respiratory distress	0	1(3.3%)	0
Post operative headache	1(3.3%)	0	2 (6.6%)

Data is represented as number (%). Number of patients = 30 in each group.
* Statistically significantly higher than the E groups.

The average volume of fluids (0.5 ml/kg/min) was used in this research to avoid the high risk of coagulation disorders and anemia in patients with volume overload and also the large colloidal volumes increase the risk of cardiovascular system overload [8].

Tamilselvan et al. [16] found that the measurement of arterial blood pressure and HR remains the most important monitors in clinical practice. They used a suprasternal Doppler flow technique to measure maternal cardiac output (CO) and corrected flow time (FTc) before and after spinal anesthesia after 3 fluid preload regimens (1.5 L crystalloid (Hartman's solution), 0.5 L of 6% w/v hydroxyethyl starch (HES) solution (HES 0.5), and 1 L of 6% w/v HES solution (HES 1.0). They showed significant increases in maternal CO and FTc compared with baseline values after crystalloid and colloid preload administration, which were maintained until spinal anesthesia was given. After spinal anesthesia, preloading with crystalloid solution failed to maintain any of the variables. Despite the significant increases in the CO, the incidence of clinically significant hypotension remained high in all groups [16]. In our study, we used SBP and HR to monitor and maintain the maternal hemodynamic within normal range to have a good neonatal outcome.

Ephedrine is the vasopressor of choice in obstetric anesthesia. It has a mixed alpha (α) and beta (β) adrenoreceptor activity. It maintains arterial blood pressure mainly by increases in cardiac output and heart rate due to predominant β1 adrenoreceptor activity [17].

Prophylactic intravenous ephedrine administered either by infusion or bolus doses has been the gold standard for preventing hypotension after spinal anesthesia. The use of ephedrine as a continuous infusion has been found to be associated with better control of SBP and HR with fewer patients' side effects compared to bolus doses [18] or intramuscular administration [19].

Table 2 Fetal data.

	R group	V group	E group
Weight (kg)	3.27 ± 0.56	3.35 ± 0.44	3.52 ± 0.39
Umbilical artery:			
pH	7.26 ± 0.05	7.28 ± 0.04	7.27 ± 0.02
PCO2 (mmHg)	45.65 ± 1.88	45.52 ± 1.85	46.45 ± 1.82
Base excess(mEq/L)	−2.4 ± 1.7	−2.3 ± 2.1	−2.5 ± 2.0
Apger score:			
1 min	8(8–10)	9(8–10)	9(8–10)
5 min	10 (9–10)	9(9–10)	10 (9–10)

Data is represented as mean ± SD or median (range). Number of patients = 30 in each group.

Ngan Kee et al. [20] investigated the efficacy and optimum dose of intravenous ephedrine for prevention of hypotension during spinal anesthesia for CS. They compared the effect of ephedrine 10, 20, and 30 mg IV and they suggest that 30 mg IV bolus may not be suitable in some patients with cardiovascular or cerebro-vascular disease. Although the incidence of hypotension was reduced to 35% compared with the control rate of 95%, this was at the expense of an increased incidence of hypertension that occurred in 45% of the patients.

In this study, we used 1 mg/min IV ephedrine infusion immediately after spinal anesthesia until delivery of the fetus (clamping of umbilical cord) and this was significantly effective to control maternal SBP than CO/post loading with 0.5 ml/kg/min lactated Ringer or Voluven at the same period. In addition, there was no clinical significant increase in maternal HR. The total dose of ephedrine was 31.4 ± 3.9 mg in Ephedrine group compared to 22.6 ± 9.8 mg and 18.2 ± 8.5 mg in Ringer group and Voluven group, respectively.

This matched the results of Damevski et al. [21] who found that continuous infusion of ephedrine simultaneously with spinal anesthesia is superior to direct preoperative hydration with crystalloids in preventing the spinal hypotension and its clinical manifestation in parturient delivery with CS. The infusion rate was adjusted according to SBP and the mean quantity of ephedrine given in the Ephedrine group was 30 ± 4.1 mg compared to volume group 25 ± 2 mg, which was preloaded with 20 ml/kg Ringer solution.

Kol et al. [22] determined the efficacy and safety of 0.5 mg/kg prophylactic IV ephedrine shortly after spinal anesthesia for CS in patients preloaded with 15 ml/kg lactated Ringer's solution within 15 min before spinal anesthesia. This could prevent the hypotension without significant maternal tachycardia or hypertension. The same results were given by Desalu and Kushimo [23] who found that the prophylactic ephedrine 30 mg in 1 L of 0.9% saline after spinal block given by standard infusion set was more effective than crystalloid prehydration in the prevention of hypotension during spinal anesthesia for elective cesarean section.

Thiangtham and Asampinwat [24] used small dose (18 mg) of ephedrine added to 100 ml normal saline as a prophylactic infusion over 10 min immediately after spinal anesthesia for hypotension during cesarean sections. And they found that this dose was insufficient for the maintenance of normal blood pressure compared with volume preloaded patients. While Faydaci and Gunaydin [25] concluded that preloading with 20 ml/kg of Ringer lactate prior to spinal anesthesia followed by constant ephedrine infusion 3 mg/min after spinal block until umbilical cord clamping reduce the incidence of hypotension and postoperative nausea and vomiting but the total amount of ephedrine was high (38.4 ± 8.5 mg) and not suitable for many cases. So, during our study, we used lower dose which gave better results without affecting the maternal or fetal well-being.

The well-being of the fetuses of obstetric patients under regional anesthesia is more dependent on the prevention of prolonged hypotension periods than on the type of solution used for preload or even on the choice of the vasopressor to be used to prevent and treat such complication [8].

However, many investigators have reported lower umbilical pH values after prophylactic maternal ephedrine administration. This was most evident when large dose of ephedrine $\geqslant$50 mg was administered IM or 3–4 mg/min IV were used [26,27].

In this study, there was no significant difference in neither Apger score at 1, 5 min nor umbilical artery blood gases data between the three groups in spite of the difference in the incidence of hypotension. This probably reflects the early recognition and restoration of hypotension with rescue ephedrine.

5. Conclusion

Intravenous infusion of ephedrine 1 mg/min immediately after spinal anesthesia for emergency cesarean sections, even if there is no enough time for proper prehydration, can control effectively the hypotension without episodes of hypertension or significant tachycardia, and it had no effect on fetal well-being. It could be as effective as CO/post loading of 0.5 ml/kg/min lactated Ringer or Voluven in controlling systolic blood pressure with less incidence of postoperative complications in the form of nausea and vomiting.

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