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Comparison of the Hemodynamic Effects of Pretreatment with Crystalloids versus Crystalloids plus Ephedrine during Spinal Anesthesia for Caesarean Section.

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Abstract:

Background: Prevention of hypotension during spinal anesthesia for cesarean section avoids maternal and fetal side effects. The aim of this study was to compare the effects of the combination of ephedrine crystalloid and prehydration with crystalloid alone on maternal blood pressure and neonatal outcome during cesarean section under spinal anesthesia.

Method: We enrolled 72 full term women weighing between 50 and 75 Kg, classified as ASA I, scheduled for elective caesarean section under spinal anesthesia. Participants were randomly allocated to either the ephedrine or crystalloid group. After arrival in the operating room and intravenous (IV) access, 10 ml/Kg of ringer solution was infused 10-15 minutes before the initiation of the spinal block, but in the ephedrine group, an additional 10mg of ephedrine was added to the solution for infusion. In the crystalloid group, a placebo was added to the solution.

Results: Hypotension occurred in 55.6% of patients in the crystalloid group and in 25% of patients in the ephedrine group. The difference between the two groups was found to be statistically significant ($P = 0.008$), however, there was no significant difference in mean systolic blood pressure between the two groups (105.61 ± 7.13 in crystalloid group vs. 107.89 ± 9.84 in ephedrine group). Apgar scores in newborns were above 8 in both groups.

Conclusion: Prophylactic ephedrine given by infusion in combination with crystalloid was more effective than crystalloid prehydration in the prevention of hypotension during spinal anesthesia for elective caesarean section.

Keywords: Spinal anesthesia. Ephedrine. Crystalloid. Hypotension.

Introduction:

Spinal anesthesia is often selected for cesarean delivery due to its rapid, reliable and profound sensory and motor blockade. Hypotension and bradycardia are common side effects of spinal anesthesia, with the incidence of hypotension in the supine pregnant patient after spinal anesthesia being as high as 90%.⁽¹⁾ Treatment of spinal hypotension is best achieved by reversing the underlying physiologic causation-decreased systemic vascular resistance, preload, and cardiac output. Ephedrine has mixed direct and indirect actions on α - and β -adrenergic receptors, and is the vasopressor of choice for spinal hypotension in the parturient because of its ability to maintain uteroplacental blood flow.⁽²⁾

Despite the use of prophylactic ephedrine by either intravenous injection or intramuscular injection, several authors have reported an incidence of hypotension between 50% and 70%.⁽³⁾ Prophylactic 50 mg ephedrine given intramuscularly significantly reduced the incidence of hypotension in cesarean section patients who were given a spinal anesthetic.⁽⁴⁾ Another study reported that the minimum effective intravenous ephedrine dose in parturients was 30 mg, yet hypotension still occurred in 35% of these patients and 45% developed reactive hypertension. Therefore, the appropriate route and dose of ephedrine that should be used to prevent spinal associated hypotension during cesarean section still remains controversial.⁽⁵⁾

Prehydration is the administration of 0.5–2 L of intravenous fluid 15–20 minutes

before spinal block. The aim of prehydration is to fill the capacitance vessels and limit hypotension when venodilatation occurs. However, prehydration with a large dose of fluid may result in an increase in central venous pressure, pulmonary edema and hemodilution that may cause fetal oxygenation if hypotension also occurs.⁽⁶⁾

The best prophylaxis of maternal hypotension during cesarean section is still controversial. The aim of this study is to compare the effects of pretreatment with ephedrine and crystalloid with prehydration crystalloid alone on maternal blood pressure, heart rate and Apgar scores of neonates during cesarean section under spinal anesthesia.

Methods:

The present prospectively designed study was approved by the ethics and clinical studies committee at the Zahedan University of Medical Sciences, with informed and signed consent being obtained from all the patients who were enrolled in the study.

We enrolled 72 full term women weighing between 50 and 75 Kg, classified as ASA I and scheduled for elective caesarean section under spinal anesthesia. Parturients who had obstetric complications or evidence of fetal compromise were excluded. All patients were fasted overnight and received premedication with 150 mg of ranitidine taken orally the night before and 2 hours prior to surgery. Participants were randomly allocated into either the ephedrine or crystalloid group. After arrival in the operating room and

intravenous (IV) access, 10 ml/Kg of ringer solution was infused 10-15 minutes before the initiation of the spinal block. Participants in the ephedrine group received 10mg of ephedrine which was added to the solution, while a placebo was added to the solution of those in the crystalloid group by a nurse. Another nurse and an anesthesiologist, neither of whom knew which drug was added to the solution, were jointly responsible for caring for the patient, recording their blood pressure and heart rate and monitoring for adverse reactions and any subsequent treatment of these adverse reactions. Spinal anesthesia was performed in the sitting position with a 25 gauge whitacre needle, using a midline approach at L4-5 interspace. Once free flow of CSF had been recognized the intrathecal anesthetic solution (80 mg of 5% lidocaine) was injected over 15 seconds, aspirating CSF at the end of injection to confirm needle position. After intrathecal injection, the patients were turned in supine position with left uterine displacement. Surgery was started when a sensory block up to T5 dermatome was obtained. Baseline maternal heart rate and arterial blood pressure were measured by an automatic non-invasive monitor and recorded before the induction, as well as every 2 minutes before delivery and every 5 minutes until the patient was discharged from the recovery room. Hypotension, defined as a decrease in systolic blood pressure to less than 90 mm Hg or to less than 30 mm Hg from baseline value, was treated with 5 mg of intravenous ephedrine, and incremental doses were used as required along with additional ringer solution. Maternal bra-

dycardia (defined as heart rate less than 60 beats per min) was treated with 0.5 mg of intravenous atropine. Severe hypotension was defined by a systolic blood pressure less than 85 mm Hg. Nausea was defined as the subjectively unpleasant sensation associated with the awareness of the urge to vomit, while vomiting was defined as the forceful expulsion of gastric contents from the mouth. Retching (the same as vomiting but without expulsion of gastric contents) was considered vomiting. Hypertension in our study was defined as a systolic blood pressure above 145 mm Hg or a diastolic blood pressure above 90 mm Hg.

After intervention for hemodynamics parameters correction, and when nausea unrelated to hypotension occurred, 2mg of intravenous midazolam 2 mg was administered for patient satisfaction. The height of block was recorded as the highest dermatome with a loss of pinprick sensation at 20 minutes post spinal. Times of skin incision, delivery of baby and completion of surgery were also recorded. The surgical technique was uniform for all patients. Apgar scores were obtained at 1 and 5 minutes.

Statistical test were performed using SPSS 11 for Windows. Results recorded include both absolute values and means with standard deviations. Continuous variables were analyzed using a Student's T test. Nominal or ordinal variables were analyzed by a Chi square test, Fisher exact test or a Mann-Whitney U test ($P < 0.05$).

Results:

Hypotension occurred in 55.6% of patients in the crystalloid group and 25% of patients in the ephedrine group, with the difference between the two groups being evaluated to be statistically significant ($P = 0.008$). In addition, there was no significant difference between the mean systolic blood pressure between the two groups (105.61 ± 7.13 in crystalloid group vs. 107.89 ± 9.84 in ephedrine group), and the incidence of nausea was %44.4 (16 patients) in the crystalloid group vs. %16.7 (6 patients) in the ephedrine group ($P=0.011$). Heart rates above 120 were seen in %22.2 (8 patients) in the crystalloid group vs. %19.6

(7 patients) in the ephedrine group ($P=0.127$).

No significant differences were detected in maternal demographic data between the two groups (table 1). Intraoperative data are shown in table 2 and 3. Anesthesia levels were similar in the two groups. No severe hypotension or bradycardia and no episode of hypertension occurred among the patients in our study. Additionally, no patient received more than one dose of ephedrine (5 mg) for treatment of hypotension. Neonatal Apgar scores were similar in the two groups, with all the neonates having Apgar scores ≥ 8 .

Table 1: Characteristics of patients receiving prehydration or ephedrine infusion.

	Crystalloid	Ephedrine and Crystalloid
Age (years)	24 \pm 4.4	25 \pm 3.4
Weight (kg)	67.4 \pm 7.8	66.5 \pm 6.5
Height (cm)	165 \pm 11.9	166.5 \pm 6.5
Gestational age	39.2 \pm 0.25	39.1 \pm 0.3

There were no significant differences between the groups.

Table 2: Intraoperative characteristics of patients receiving prehydration or ephedrine infusion.

	Crystalloid	Ephedrine and Crystalloid	P value
SBP 1-10 min	107.89 \pm 9.84	105.61 \pm 7.13	0.266
SBP 11-60 min	109.39 \pm 6.72	106.20 \pm 8.52	0.083
Maternal heart Rate before OP	84.22 \pm 9.45	80.39 \pm 8.87	0.16
Maternal heart Rate along OP	98.75 \pm 22.67	95.34 \pm 18.32	0.056
Level of sensory block	T5 \pm 1	T5 \pm 1	1.0

SBP: Systolic blood pressure, OP: Operation, * = $P < 0.05$

Table 3: Intraoperative adverse effects of patients receiving prehydration with crystalloid or prehydration with crystalloid and ephedrine infusion.

	Crystalloid		Ephedrine and Crystalloid		P value
	N	%	N	%	
Hypotension	20	55.6	9	25	0.008*
Nausea	6	16.7	16	44.4	0.011*
Tachycardia HR>120	8	22.2	7	19.4	0.127*

* = $P < 0.05$

Discussion:

The current study has shown that prophylactic ephedrine combined with crystalloid was more effective than crystalloid alone for preventing hypotension in healthy parturients undergoing spinal anesthesia for elective cesarean delivery. We demonstrated a higher incidence of hypotension in the prehydration group at 55.6%, compared with 25% in the ephedrine group ($P = 0.008$). This compares well with results observed by Chan and colleagues (1997) who observed that patients in the prehydration group exhibited a hypotension incidence rate of 65% vs. the ephedrine group which saw an incidence of 35%.

Multiple studies have failed to show sustained and predictable blood pressure maintenance after prophylactic crystalloid administration.⁽⁷⁾ Blood pressure and cardiac indices transiently increase, but these effects are short-lived because crystalloid solutions remain intravascular for only a limited period of time.⁽⁸⁾

The debate over the value of crystalloid preloads has been invigorated by the finding that results may be influenced by the volume and speed of the preload.⁽⁹⁾ Crystalloids alone are unable to eliminate hypotension or reduce the incidence of severe hypotension, while the administration of large infusion volumes may cause unwanted delays in urgent cases.⁽¹⁰⁾

Vasopressors have been shown to be more effective at limiting spinal hypotension than crystalloid preloading.⁽¹¹⁾ Despite the use of prophylactic ephedrine

by either intravenous (IV) injection or intramuscular (IM) injection, several authors have reported an incidence of hypotension between 50% and 70%. King and Rosen⁽¹²⁾ failed to show the effectiveness of ephedrine prophylaxis given as an IV bolus (10 mg) or by infusion (20 mg) to reduce maternal hypotension associated with spinal anesthesia for cesarean section. Ephedrine may contribute to maternal tachycardia and hypertension, and could also be responsible for fetal acidemia and electroencephalographic (EEG) abnormalities in newborns.⁽⁴⁻¹³⁾

The appropriate route and dose of ephedrine that should be used to prevent spinal associated hypotension during cesarean section still remains controversial, because treatment of hypotension by ephedrine does not completely restore preanesthetic levels of uterine blood flow even when it restores maternal BP to baseline measurements.⁽¹⁴⁾

Chan et al⁽¹⁵⁾ compared ephedrine infusion and fluid preload for the prevention of spinal hypotension during cesarean section. The hypotension rate was lower and umbilical pH was higher in the ephedrine group. Some authors have compared prophylactic and curative use of ephedrine during spinal anesthesia for cesarean section. These authors also found significantly higher umbilical arterial pH when using prophylactic ephedrine.⁽¹⁶⁾

Some authors have suggested a possible mechanism for fetal acidemia that is not related to uteroplacental or fetoplacental circulation, but to the ephedrine induced by fetal β -adrenergic stimulation

as it crosses the placenta and increases fetal catecholamine levels and fetal heart rate.⁽¹⁷⁾ However, it is possible that fetal catecholamine stimulation before delivery might be beneficial. When a β -adrenergic agonist was administered before elective cesarean section, lower respiratory morbidity, better lung function and reduced risk of hypoglycaemia in the newborn infant were found.⁽¹⁸⁾

None of the patients in our study developed bradycardia. In the ephedrine group, this may have been because of the overriding chronotropic effect of ephedrine when it was given as a vasopressor. Ephedrine maintains SAP mainly by increases in CO and heart rate.⁽¹⁹⁾

Tsen et al reported a nil incidence of hypertension in both ephedrine and control groups in their study designed to evaluate the hemodynamic effects of a 10 mg intravenous ephedrine bolus given simultaneously with spinal anesthesia for cesarean delivery.⁽²⁰⁾ Therefore, it is not surprising that the incidence of reactive hypertension achieved by administering ephedrine as infusion (not the bolus method) was very low as well.

In light of these findings, it seems as if prophylactic ephedrine may be useful during cesarean section to avoid spinal hypotension, which remains a major determinant of fetal acidemia. The results of our study confirm that infusion of ephedrine can be a potent factor for prevention of hypotension during spinal anesthesia for cesarean section.

Conclusion:

Prophylactic ephedrine given by infusion was more effective than crystalloid prehydration in the prevention of hypotension during spinal anesthesia for elective caesarean section.

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