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ORIGINAL ARTICLES

Ephedrine Infusion with Rescue Ephedrine Boluses versus Rescue Boluses alone for Preventing Hypotension during Spinal Anesthesia for Cesarean Delivery.

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Abstract

Background: Maternal hypotension is an unwanted consequence of the physiologic onset of spinal blockade, and causes both maternal and fetal effects. Maternal symptoms include nausea, vomiting, and a sense of ''impending doom'' from inadequate cerebral perfusion. Inadequate treatment of hypotension can ultimately end with the loss of consciousness and cardiovascular collapse.

Materials and methods: We included 80 full term parturient (ASA I or II) with uncomplicated pregnancies. The patients were prospectively randomized into two groups. 80 patients received 1000 mL NaCl 0,9 % solution before the initiation of spinal anesthesia. Maternal systolic blood pressure was measured every 1 minutes (for first 10 minutes) and then every 3 minutes. One group received ephedrine infusion (1 mg/min) with rescue ephedrine boluses (10 mg), (usually defined as a maternal blood pressure < 30% above baseline), (40 patients) and the other received rescue boluses alone (10 mg) , (usually defined as a maternal blood pressure < 30% above baseline), (40 patients).

Results: Gr 1 (Ephedrine infusion with rescue ephedrine boluses). The incidence of hypotension was at 8 patients (8/40 [20%]), (when an absolute value of less than 90 mmHg).

Gr 2 (rescue boluses ephedrine alone). The incidence of hypotension was at 32 patients (32/40 [80%]), (when an absolute value of less than 90 mmHg).

Group 2 had a higher incidence of hypotension compared with group 1 (32/40 [80%]) vs (8/40 [20%]).

Neonatal outcomes were not different between the 2 groups.

Conclusion: Prophylactic variable rate ephedrine infusion and rescue ephedrine bolus dosing is more effective than relying on rescue ephedrine bolus dosing with respect to limiting clinician workload and maternal symptoms during spinal anesthesia for cesarean delivery.

Keywords: Maternal hypotension, spinal anesthesia, ephedrine.

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Abbreviations

SC - Caesarean Section; CSF - Cerebrospinal Fluid; AS - Spinal anesthesia; IV – Intravenous; ECG - Electrocardiogram; FC - Heart Rate, PA - Systolic Blood Pressure; Sp O2 - Oxygen Saturation; CTG – Cardiotocography;

Introduction

In patients undergoing elective or emergency caesarean section (SC), spinal anesthesia provides a rapid and high-quality motor and sensory block [1,2].

Maternal hypotension is the most common complication during SC under spinal anesthesia, with a reported incidence of more than 80% if not prevented [3], and it can be accompanied by severe nausea and vomiting. It puts both the mother (loss of consciousness and pulmonary aspiration) and the baby (hypoxia, acidosis, and neurological injuries) at risk [4].

Because of the decreased amount of cerebrospinal fluid (CSF) in the lumbosacral area and the greater cephalic spread of the local anesthetic, the incidence of hypotension and high spinal anesthesia is higher.

Because of the decreased amount of CSF in the lumbosacral area and the greater cephalic spread of the local anesthetic, the incidence of hypotension and high spinal anesthesia is higher. This is due to the hypertrophic uterus compressing the inferior vena cava and the development of collateral venous plexus circulation in the epidural space [5, 6].

A number of strategies for preventing hypotension have been investigated, one of which is the pregnant woman's left supine positioning by shifting the uterus to the left [7]. Other approaches have included intravascular volume expansion with intravenous (IV) fluids immediately before the spinal injection (preload) [8, 9], or at the time of the spinal injection and continuing afterward (post load) with colloid or crystalloid solutions.

The most effective strategy is prophylactic ephedrine administration, which is highly controversial due to the high incidence of rebound hypertension [10]. Alternatively, the intravenous route is more effective and controllable, is more familiar, and has a low proclivity for utero-placental vasoconstriction [11, 12].

The purpose of this study was to compare the efficacy of ephedrine, as a vasopressor used to treat hypotension caused by spinal anesthesia in caesarean deliveries, applied in perfusion and with small immediate doses, to the use of ephedrine only in immediate doses. Several variables related to maternal well-being (incidence of hypotension, reactive hypertension, nausea and vomiting) and fetal well-being (as measured by Apgar score) were measured in this study.

These variables were compared in two groups, and the ANOVA test was used to determine significance at p 0.05. In addition, the frequency of hypotension, reactive hypertension, nausea, vomiting, and lower Apgar scores was compared between the two groups.

Materials and methods

It is a randomized controlled trial. Participants in the study and anesthesia personnel involved in surgery were blinded to group assignment.

This study was carried out at American Hospital 2 in Tirana from March 2021 to December 2021. The study included 80 patients in full-term labour (ASA I or II) with uncomplicated pregnancies. Previously, the patients were divided into two groups at random. Before spinal anesthesia, all 80 patients received 1000 mL of 0.9% NaCl solution and were not premedicated. All patients received standard monitoring, which included an electrocardiogram (ECG), non-invasive blood pressure monitoring, and pulse oximetry.

Oxygen (4 L/min) was administered to all patients via nasal catheters. Baseline measurements of heart rate (FC), systolic blood pressure (PA), and oxygen saturation (Sp O2) were recorded in the modified supine position with at least 15° lateral tilt to the left before the application of spinal anesthesia.

Spinal anesthesia was performed in the L2-L3 or L3-L4 intervertebral space in the sitting position, using a G 26 pencil tip spinal needle, and 15mg (3ml) of hyperbaric bupivacaine 0.5% was applied after a clear and free flow of CSF. Patients were immediately placed in the supine position with left uterine displacement. The upper level of anesthesia was evidenced by assessing the loss of pinprick sensation, the operation started when the block extended to T5 or above.

PA and HR were recorded every 1 min after spinal anesthesia, for the first 15 min after application of spinal anesthesia, then every 3 min for the first 30 min, and then every 5 min until the end of the operation and in the recovery room for at least 90 minutes from the start of spinal anesthesia. Nausea, vomiting, dizziness, and chest symptoms (dyspnea and tachypnea) were also recorded every 10 minutes. Fetal heart rate was monitored using cardiotocography (CTG) continuously until delivery.

Oxytocin was administered postpartum (10 IU in 500 ml sol NaCl 0.9%) to all patients, nausea, and vomiting were treated with 10–20 mg IV metoclopramide if unrelated to hypotension or when not corrected by dose alone bolus ephedrine.

Conceptual definition of terms

Hypotension was characterized as a drop in systolic blood pressure > 30% of baseline and was treated with an additional bolus of 10 mg ephedrine as in Gr 1 in the study, who received 10 mg ephedrine perfusion, also in Gr 2, who did not there is ephedrine in perfusion after application of spinal anesthesia. Reactive hypertension was defined as blood pressure 20% higher than baseline before the use of vasopressors. A heart rate below 60 beats per minute has been described as bradycardia when associated with hypotension and has been treated with 0.5 mg atropine. Tachycardia would be considered an FC higher than 120 beats.

Apgar was investigated in the 1st and 5th minutes of all newborns and the evidence of scoring 8 points and below was called low. [13,14].

Inclusion criteria

(1) Physical status ASA I or II (2) Full pregnancy (at term) of a single fetus; (3) planned cesarean delivery; (4) 19-40 years old.

Exclusion criteria

(1) To refuse inclusion in the study; (2) Female patients under 19 years of age; (3) previous or pregnancy-induced systemic hypertension; (4) occurrence of cardiovascular or cerebrovascular diseases; (5) fetal disorders; (6) allergy to drugs used in the study and contraindications for spinal anesthesia; (7) pregnant woman with a blood pressure of 140/95 mmHg or higher before anesthesia; (8) pregnant woman who has chronic hypertension; (9) pregnant woman who has heart rate <60/min and >120 beats per minute before anesthesia.

Group 1

To this group was applied ephedrine infusion (1 mg/min) as well as immediate (bolus) ephedrine (10 mg), (usually when arterial pressure decreased below 30% of the baseline value), (40 patients).

Group 2

To this group was applied only immediate (bolus) ephedrine (10 mg), (usually when arterial pressure decreased below 30% of the baseline value), (40 patients), and this dose was repeated several times until PA stabilized.

Below, the demographic data of both groups of patients will be presented in tables, as well as the evidence of the variables that were in the study:

	Gr 1 (n = 40)	Gr 2 (n = 40)	P value
Age	28.1 ± 4.54	28.4 ± 4.16	0.382
Weight (kg)	74.6 ± 12.42	73.8 ± 12.16	0.534
Pregnancy (weeks)	38.4 ± 1.26	38.3 ± 1.28	0.582
Time of birth from the application of AS (min)	14.5 ± 2.78	13.8 ± 3.26	0.644
Time of end of operation from the application of AS (min)	76..4 ± 8.16	75 ± 9.36	0.728

Values are mean±SD or median (min-max). AS=Spinal anesthesiap-value <0.05 is significant

Table 1: Demographic data of patients

Sensor block level	Gr 1 No (%)	Gr 2 No (%)	P value
T4	24 (60%)	23 (57.5%)	0.847
T5	12 (30%)	13 (32.5%)	
T6	4 (10%)	4(10%)	
Total	40 (100%)	40 (100%)	

p-value<0.05 is significant

Table 2: Sensor block level

Parameter	Gr 1 (n =40)	Gr 2 (n = 40)	P value
FC (Cardiac Frequency/min)	94.2 ± 6.82	95.5 ± 5.84	0.267
PA mmHg	122.4 ± 6.86	121.8 ± 7.16	0.364
Hypotension Nr (%)	8 (20%)	18(45%)	<0.05*
Reactive hypertension Nr (%)	0 (0%)	3(7,5%)	<0.05*
I/V bolus application Ephedrine Nr (%)	10 (25%)	23(57.5%)	<0.05*

*p-value<0.05 is significant

Table 3: Hemodynamic data

Ephedrine application (mg)	Gr 1 No (%)	Gr 2 No (%)	P value
No patient	10 (25)	23 (57.5)	<0.001*
10mg	6 (15)	4 (10)	
20mg	3 (7.5)	9 (22.5)	
30mg	1 (2.5)	10(25)	
Total	10 (25)	23 (57.5)	

* p-value<0.05 is significant

Table 4: Ephedrine bolus application for the treatment of hypotension

Parameter	Gr 1 No (%)	Gr 2 No (%)	P value
Nausea	6(15%)	14(35%)	<0.001*
Vomiting	3 (7.5%)	11(27.5%)	<0.005*
Apgar score after1 min (<7)	2 (5%)	2 (5%)	0.847
Apgar score after 5 min (<8)	1 (2.5%)	2 (5%)	0.264

* p-value<0.05 is significant

Table 5: Adverse effects and neonatal outcomes

Results

From the data obtained, expressed according to the tables, it would result: From table no. 1, we note that there are no significant differences between the two groups included in the study in terms of age, weight, weeks of pregnancy, time of delivery after spinal anesthesia, and the duration of the intervention, p >0.05

From table no. 2 we also find that the level of the sensory block established after spinal anesthesia has no significant differences between the two groups, p >0.05.

Table no. 3 shows that there are no significant differences between the two groups in terms of PA and FC, but there are significant differences in terms of hypotension after spinal anesthesia.

In Group 1 receiving ephedrine infusion, the incidence of hypotension is lower, in 8 patients (20%), compared to Group 2, which is found in 18 patients (45%), p<00.5. Reactive hypertension was found only in 3 patients in Gr 2 who received only immediate (bolus) ephedrine.

The application of bolus doses of ephedrine is found only in 10 patients in Gr 1 (25%), a low figure compared to Gr 2, where we find it in 23 patients (57.5%). Taking bolus doses of ephedrine in Gr 1 is significantly lower than in Gr 2, p<0.05

From the data in table no. 4, we can see that the number of patients receiving repeated bolus ephedrine, but also as a quantity, for the treatment of hypotension after spinal anesthesia, in Gr 1 is significantly lower compared to Gr 2, $p<0.05$

From the data in table no. 5, we can see that the side effects of spinal anesthesia, mixed and vomiting, are lower in Gr 1, 6(15%) and 3(7.5%) patients, compared to Gr 2, where found in 14 (35%) and 11 (27.5%) of patients, $p<0.05$

Regarding the neonatal data, according to the Apgar scale, no significant differences are evident between the two groups under study, $p>0.05$.

Discussions

A current systematic review of a large number of publications on hypotension after spinal anesthesia in cesarean deliveries has shown that the use of vasopressors, prophylactic phenylephrine and ephedrine, was more effective in controlling and preventing hypotension in healthy pregnant women undergoing spinal anesthesia for cesarean delivery. However, this effect did not translate into a significant reduction in nausea and/or vomiting or any change in neonatal outcome.

In some countries, but especially Canada, ephedrine, and phenylephrine are the two most commonly used vasopressors to treat hypotension caused by spinal anesthesia during cesarean delivery. Traditionally, phenylephrine was used only as a second-line agent, as there were concerns about its pronounced vasoconstrictor action, which could result in a reduction in local uteroplacental perfusion and compromise fetal health. However, many studies showed that the administration of ephedrine in cesarean deliveries resulted in fetal acidosis more than phenylephrine [15]. They showed a significant decrease in pH, BE (base excess) and partial oxygen pressure, as well as an increase in neonatal PaCO2 (partial pressure of carbon dioxide), if large doses of ephedrine were applied.[16]

Regarding the administration of preoperative fluids to prevent hypotension from caesarean section, studies are contradictory. According to Rout et al., which presents spinal anesthesia in childbirth, the administration of crystalline solutions before anesthesia in doses of 20 mL/kg, did not result in a significant decrease in the incidence of hypotension [17].

However, other later studies on the strategy that should be used to prevent hypotension after spinal anesthesia in cesarean deliveries, suggest that the use of crystalloid or colloid solutions before spinal anesthesia, reduces the incidence of hypotension [18, 19].

Regarding the effect of obesity (Body mass index BMI) on the incidence of hypotension after spinal anesthesia in cesarean births, studies show that there is no special effect. Also, in emergency cesarean births, the frequency of hypotension is lower [20]. Obese pregnant women (pre-pregnancy BMI ≥30 kg/m2), have a higher risk of cesarean delivery, difficulty in performing spinal anesthesia, higher risk of incorrect intubation, more difficult ventilation, increased incidence of wound infection, diabetes, thromboembolism and higher mortality in cesarean delivery, but not higher incidence of hypotension [21].

Regarding nausea and vomiting, numerous studies estimate that their incidence is not significantly reduced by the use of vasopressors, and especially by ephedrine and spinal anesthesia in cesarean births, they have a higher frequency than in non-obstetric operations since their origin is multifactorial [22].

Regarding neonatal effects, there was no association between ephedrine use and fetal acidosis in our study. This is in contrast to the observational study by Shearer [23] who reported a significant association, with a threefold greater incidence of fetal acidosis in the ephedrine group compared to the control (no ephedrine). The authors hypothesized that the reduction in uteroplacental perfusion resulting from hypotension may be further compromised by the α-agonist vasoconstrictive properties of ephedrine [23], but this was not confirmed by studies that assessed uterine vascular resistance using ultrasound (Doppler). [24, 25]

Ephedrine, as a mixed α and β adrenergic agonist, became the drug of choice in obstetric anesthesia after several studies found it to be the best vasopressor for maintaining uterine blood perfusion in a sheep model of induced hypertension. medications [26].

However, further studies are required to confirm the safety and efficacy of prophylactic ephedrine in cases where there is compromised uteroplacental perfusion.

In summary, there is evidence that prophylactic ephedrine perfusion combined with immediate doses in cases of hypotension not controlled with perfusion ephedrine alone has satisfactory efficacy in preventing hypotension during spinal anesthesia for cesarean delivery, and we found no substantial evidence that ephedrine was associated with an improved neonatal outcome.

Conclusions

The application of ephedrine perfusion at a dose of 1 mg/min immediately after spinal anesthesia for cesarean births, accompanied as appropriate by immediate small doses of ephedrine i/v, can effectively control hypotension without episodes of hypertension or significant tachycardia and there was no effect on the well-being of the fetus. We did not have an appreciable decrease in the frequency of nausea and vomiting.

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