

SPINAL ANAESTHESIA FOR CESAREAN DELIVERY; STUDY OF DIFFERENT DOSES OF IV EPHEDRINE AS PROPHYLAXIS TO PREVENT HYPOTENSION DURING

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ABSTRACT... Objective: To determine the effective dose of intravenous ephedrine for the prevention of hypotension during spinal anesthesia for cesarean delivery. **Design:** A randomized, double-blinded dose finding study. **Place and Duration:** The study was carried out in Combined Military Hospital Gujranwala from March 2009 to March 2010. **Methodology:** Total patients were 80 full term women who were randomly allocated into four groups and were given Ringer lactate 10 ml per kg body weight intravenously. One minute after the spinal injection, patients were given saline control or ephedrine 0.1mg per kg body weight, 0.25mg per kg body weight, or 0.4mg per kg body weight for 30 seconds. The study period started at the time of spinal injection and continued for 15 minutes. Systolic arterial pressure and heart rate were recorded at 1-min intervals. Side effects like hypotension, hypertension, tachycardia, bradycardia, nausea and vomiting were also recorded. Total rescue ephedrine and total dose of used ephedrine in all groups were measured. Neonates were assessed by APGAR score. **Results:** There was less incidence of hypotension in the ephedrine 0.4mg per kg body weight and 0.25 mg per kg body weight group as compared with ephedrine 0.1mg per kg body weight and the control group, 5(25%), 13(65%) vs. 16(80%), 18 (90%) respectively. Systolic arterial pressure (SAP) in the first 15 min after the spinal injection was statistically significant greater in the 0.4mg per kg body weight group compared with other groups ($P < 0.001$). Reactive hypertension occurred in 9(45%) in the 0.4mg per kg group, compared with control group, 0(0%), ephedrine 0.1 mg, 1(5%) and ephedrine 0.25 mg 3(15%) patients. The Heart rate in the first 15 minutes in the ephedrine 0.4mg per kg body weight and 0.25 mg per kg body weight group was statistically significant higher than those of ephedrine 0.1mg per kg body weight and control group ($P < 0.001$). The incidence of tachycardia was more in ephedrine 0.4 mg per kg body weight and 0.25 mg per kg body weight groups as compared to ephedrine 0.1mg per kg body weight and the control group, 9 (45%), 6 (30%) vs. 3 (15%), 2 (10%) respectively. There were significant decrease in total doses of rescue ephedrine required in the ephedrine 0.4mg per kg body weight group as compared to other three groups. Total doses of used ephedrine in all groups were similar. **Conclusion:** We conclude that although ephedrine 0.25 mg per kg body weight reduces the hypotension but the smallest effective dose of ephedrine to reduce the incidence of hypotension significantly was 0.4mg per kg body weight.

Key words: Spinal Anaesthesia, Dose of Ephedrine, hypotension, cesarean section.

INTRODUCTION

Due to fast, profound and high quality sensory and motor block Spinal anesthesia is very popular for cesarean delivery. 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. Because hypotension may have detrimental maternal and neonatal effects, a number of strategies for preventing hypotension have been investigated. These strategies include left lateral uterine displacement, the use of IV fluid preload, gravity (Trendelenburg or leg rising), compression devices on the legs and prophylactic vasopressors².

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 flow³.

Previously, Ngan Kee et al⁴ suggested that ephedrine 30 mg was the most effective IV bolus dose to prevent hypotension, but at the expense of an increased incidence of reactive hypertension. In contrast, a prospective observational study showed that an IV bolus dose of ephedrine 15 or 20 mg decreased the incidence of maternal hypotension without increasing the incidence of reactive hypertension⁵.

Because of the uncertainty about the dose-response relationship for prophylactic IV ephedrine, we studied efficacy and side effects of different doses of IV ephedrine given as a prophylaxis to prevent hypotension during spinal anaesthesia.

MATERIAL AND METHODS

We enrolled 80 full term women weighing between 50

and 80 Kg, classified as ASA I and scheduled for elective caesarean section under spinal anaesthesia. Parturient who had obstetric complications or evidence of fetal compromise were excluded. All patients were fasted over night.

Participants were randomly allocated into saline control, the small dose ephedrine, moderate dose or large dose ephedrine group. After arrival in the operating room, baseline measurements of systolic arterial pressure (SAP) and heart rate were recorded.

10 ml/Kg of ringer solution was infused 10-15 minutes before the initiation of the spinal block. Spinal anaesthesia was administered with the patient in sitting position. After skin infiltration with lidocaine, a 25-gauge needle was inserted at the L3-4 vertebral inter space and hyperbaric 0.75% bupivacaine 1.75 mL was injected intrathecally. The patient was then immediately turned supine with left lateral tilt. Oxygen 4 L/min was given by face mask until delivery.

One minute after the spinal injection, the onset of spinal anaesthesia was confirmed by asking the patient to subjectively verify numbness of the legs; then, saline control or ephedrine 0.1mg per kg body weight, 0.25mg per kg body weight, or 0.4mg per kg body weight was injected intravenously. Each dose was diluted to 10 ml with saline and injected for 30 seconds.

The study period started at the time of spinal injection and study continued for 15 minutes. Upper sensory level of anaesthesia was measured by assessing loss of pinprick discrimination. The baseline Systolic arterial pressure and heart rate were recorded. Then SAP and HR were recorded every minute. Side effects like hypotension, hypertension, tachycardia, bradycardia, nausea and vomiting were also recorded.

Hypotension was defined as 20% decrease in SAP from baseline. Hypertension was defined as 20% increase in SAP from baseline. Maternal bradycardia was defined as heart rate <60 beats/min and treated immediately by using intravenous atropine 0.5 mg. Tachycardia was defined as heart rate >120 beats/min. Hypotension was treated immediately by using rescue intravenous

ephedrine 5 mg every minute until SAP returned to normal values (>80% of base level) Total doses of rescue ephedrine and total dose of used ephedrine in all groups were also recorded.

Neonates were assessed by APGAR scores at 1 and 5 minutes.

RESULTS

There was no difference between the study groups with regard to the age, weight, height, and delivery time shown in (table-I). All patients had adequate surgical anaesthesia. The median upper sensory level 10 min after the spinal injection was T4 (T3-T5) for all the study groups.

Systolic arterial pressure (SAP) in the first 15 min after the spinal injection was statistically significant greater in the ephedrine 0.4mg per kg body weight group as compared to other three groups ($P < 0.001$) (Fig 1).

Fig 1. Changes in systolic arterial pressure in the first 15 min after the induction of spinal anaesthesia

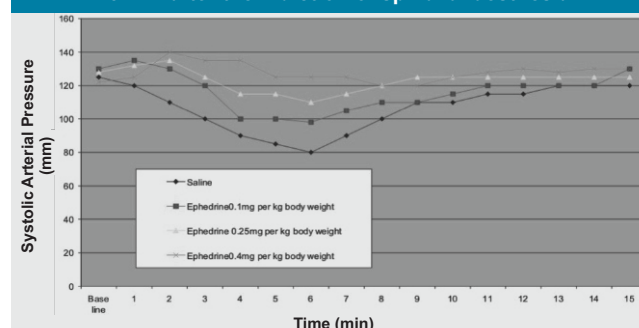


Fig 2. Changes in heart rate in the first 15 min after the induction of spinal anaesthesia

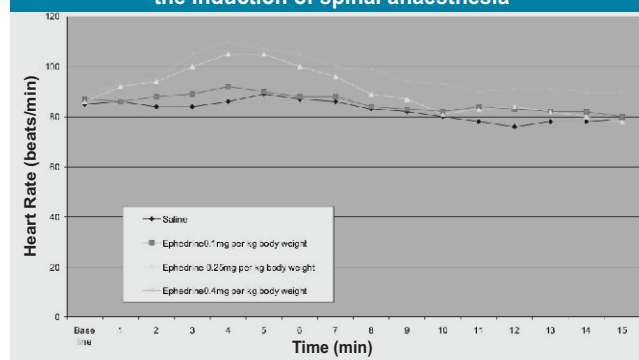


Table-I. Study of different doses of IV ephedrine as prophylaxis to prevent hypotension during spinal anaesthesia for cesarean delivery

Group	Saline	Ephedrine 0.1mg per kg body weight	Ephedrine 0.25mg per kg body weight	Ephedrine 0.4mg per kg body weight
Age (year)	28 (4.8)	27 (5.2)	26 (4.3)	25 (4.5)
Weight (Kg)	66 (5.4)	65 (5.2)	67 (6.2)	64 (5.2)
Height (Inches)	62 (5.2)	63 (6.2)	60 (4.2)	59 (3.2)
Upper sensory level (dermatome)	T4 (T3-T5)	T4 (T3-5)	T4 (T3-5)	T3 (T2-5)
Spinal to delivery time (minutes)	19.8 (2.5)	20 (3.2)	19.7 (2.9)	20 (3.1)

The Heart rate in the first 15 minutes in the ephedrine 0.4mg per kg body weight and 0.25 mg per kg body weight group was statistically significant higher than those of ephedrine 0.1mg per kg body weight and control group ($P < 0.001$) (Fig 2).

The incidences of hypotension, hypertension, tachycardia, bradycardia, nausea or vomiting, the total used ephedrine are summarized in table-II.

There was lower incidences of hypotension in the ephedrine 0.4mg per kg body weight and 0.25 mg per kg body weight group as compared with ephedrine 0.1mg per kg body weight and the control group 5(25%),13(65%) vs. 16(80%), 18 (90%) respectively. There were no significant differences in incidence of nausea and vomiting among four groups. Reactive hypertension occurred in 9(45%) in the 0.4mg per kg group, compared with control group, 0(0%), ephedrine 0.1 mg, 1(5%) and ephedrine 0.25 mg 3(15%) patients. The incidence of tachycardia was more in ephedrine 0.4 mg per kg body weight and 0.25 mg per kg body weight groups as compared to ephedrine 0.1mg per kg body weight and the control group, 9(45%), 6(30%) vs. 3(15%), 2(10%) respectively.

Study of different doses of IV ephedrine as prophylaxis to prevent hypotension during spinal anaesthesia for cesarean delivery.

DISCUSSION

Although crystalloid preloading is a common practice to

prevent hypotension during spinal anaesthesia for caesarian section but vasopressors like ephedrine, phenylephrine and angiotensin II have been shown to be more effective at limiting spinal hypotension than crystalloid preloading⁶. It has been shown that ephedrine is better vasopressor than phenylephrine, or angiotensin II infusions in minimizing hypotension⁷⁻⁸.

Although ephedrine has mixed α - and β -adrenergic activity, it maintains arterial pressure mainly by increases in cardiac output (CO) and heart rate as a result of its predominant activity on β 1-adrenoreceptors¹⁰. King and Rosen⁹ 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.

Kee et al.⁴ investigated the efficacy and optimum dose of intravenous ephedrine for prevention of hypotension during spinal anesthesia for cesarean delivery. They compared the effect of ephedrine 10, 20, or 30 mg intravenous for the prevention of hypotension. They found that a bolus dose of 30 mg intravenous ephedrine was required to reduce the incidence of hypotension during spinal anesthesia for cesarean delivery. They concluded that although the incidence of hypotension was reduced to 35% in the patients who received ephedrine 30 mg compared with the control rate of 95%, this was at the expense of an increased incidence of hypertension, which occurred in 45% of the patients. They suggested that 30-mg intravenous ephedrine may

Table-II. Incidence of hypotension, hypertension, nausea/vomiting and ephedrine requirements

Group	Saline	Ephedrine 0.1mg per kg body weight	Ephedrine 0.25mg per kg body weight	Ephedrine 0.4mg per kg body weight
Hypotension (n)	18 (90%)	16 (80%)	13 (65%)	5 (25%)
Hypertension (n)	-	1 (5%)	3 (15%)	9 (45%)
Tachycardia (n)	2 (10%)	3 (15%)	6 (30%)	9 (45%)
Bradycardia (n)	3	3	2	-
Nausea, vomiting (n)	8	7	6	5
Supplementary ephedrine requirements (mg)	30 (12.5)	23 (7.6)	18 (4.7)	11 (2.1)
Total ephedrine requirements (mg)	30 (12.5)	30 (10.5)	35 (8.6)	37 (5.5)

Values are n or mean (sd)

Table-III. APGAR Score

Time (Minutes)	Saline	Ephedrine 0.1mg per kg body weight	Ephedrine 0.25mg per kg body weight	Ephedrine 0.4mg per kg body weight
01 minute	9 (8-10)	9 (7-10)	9 (7-10)	9 (8-10)
05 minutes	10	10	10	10

not be suitable in some patients such as those with cardiovascular or cerebrovascular disease. Compared with the study of Kee et al,⁴ the incidence of reactive hypertension was lower in other study¹¹ in which ephedrine 0.5mg per kg body weight of patient was used (28.6% VS. 45%).

In our study incidence of hypotension reduced to 25% who received ephedrine 0.4 mg per kg body weight as compared to saline group in which incidence was 90%.but the reactive hypertension was much higher as compared to other groups. Even the patients having ephedrine 0.25mg per kg body weight the incidence of hypotension was reduced to 65%.

More increased heart rate was noted in both above mentioned groups as compared to previous study¹¹.Small dose ephedrine 0.1mg per kg body weight was not effective to reduce the hypotension, was consistent finding with previous studies^{12,13}. In contrast to this in another study small dose ephedrine 10 mg

reduced the hypotension to 25% when it was given as prophylaxis by infusion in combination with crystalloids during spinal anaesthesia for caesarian delivery¹⁴.

In our study less rescue ephedrine was given in 0.4mg per kg group as compared to other three groups but total ephedrine given was similar in all groups because patients were given "rescue" ephedrine as soon as hypotension occurred. This finding resembled with previous study⁴.

Previous studies have shown that the use of ephedrine to prevent or treat hypotension associated with spinal and epidural anesthesia for cesarean delivery may not correct fetal acidosis and may even increase it, especially if hypotension still occurs^{15,16}.

Arterial blood gas facility was not available in our hospital so neonatal outcome was assessed only by APGAR score within 1 minute and 5 minutes interval. There was no difference in neonatal outcome which resembled with

previous study¹¹.

CONCLUSION

We conclude that although ephedrine 0.25 mg per kg body weight reduces the hypotension but the smallest effective dose of ephedrine to reduce the incidence of hypotension significantly was 0.4mg per kg body weight.

Even this large dose did not eliminate the hypotension completely and caused reactive hypertension and tachycardia in some cases. Similarly 0.25mg per kg also increased heart rate in few patients.

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