



Original Research Article

## Effect of Prophylactic Ephedrine Infusion versus Crystalloid Preloading on Neonatal Acid-Base Outcome during Spinal Anesthesia for Elective Caesarean Section

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### ABSTRACT

**Background:** Regional anaesthesia has become the preferred technique for caesarean section because general anaesthesia is associated with higher incidence of maternal morbidity and mortality. Ephedrine is the drug of choice to treat spinal-induced hypotension in caesarean patients, but a clinically relevant positive effect on neonatal outcome were not observed in some studies done in the past. So in our study we compared the effect of pretreatment with crystalloid versus ephedrine infusion in neonates during spinal anesthesia for caesarean delivery.

**Objectives:** To assess the safety of prophylactic ephedrine infusion versus crystalloid preloading in neonates.

**Methodology:** 60 subjects were randomly categorized into two groups of 30 each Group I (Crystalloid group) preloaded with 15 ml/kg of Ringer lactate and Group II (Ephedrine group) infusion of 30 mg ephedrine in 500 ml Ringer lactate at a rate of 2 drops/sec was started 5 min before administering spinal anaesthesia. The safety was compared in terms of APGAR score and umbilical cord blood gases in the neonatal outcome.

**Results:** The APGAR score at 1 min and 5 min were good in both the groups. There were no incidence of fetal acidosis. There were no significant ( $p > 0.05$ ) difference in the umbilical blood gas values between Group I and Group II.

**Conclusion:** The study concludes that prophylactic low dose of ephedrine infusion does not cause adverse neonatal outcome.

**Keywords:** acid-base equilibrium, neonate, pH; Crystalloid solution, Ephedrine, Spinal anaesthesia

### INTRODUCTION

Spinal anaesthesia was introduced into clinical practice by German surgeon Karl August Bier in 1898. More than a century has passed and today it is one of the most popular techniques for lower limb and lower abdominal procedures, including

caesarean section.<sup>[1]</sup> It has become the preferred technique for caesarean section because general anaesthesia is associated with higher incidence of maternal morbidity and mortality.<sup>[2,3]</sup>

However spinal anaesthesia is associated with some hazards. The commonest of these

being hypotension with a reported incidence greater than 80%. Maternal hypotension may have detrimental effects on uterine blood flow, fetal well being and ultimately neonatal outcome as measured by umbilical artery pH and APGAR score.<sup>[4-6]</sup>

Treatment of spinal-induced hypotension is best achieved by reversing the underlying physiologic changes like decreased systemic vascular resistance (SVR), preload, and cardiac output. Traditional teaching is that hypotension can be minimized or prevented by intravenous (IV) fluid preloading, positioning of the patient using left uterine displacement, and by the prophylactic and therapeutic use of vasopressors.<sup>[7]</sup> However no method has proved satisfactory.

In terms of neonatal and maternal well-being, prevention of hypotension results in better outcomes than treatment of established hypotension,<sup>[8,9]</sup> and to do this an intravenous fluid preload has for many years been regarded as mandatory before embarking on spinal anaesthesia for caesarean section. But prehydration with a large dose of fluid may result in an increase in the central venous pressure, pulmonary edema and fetal hypooxygenation.<sup>[10]</sup> Among the vasopressors available (ephedrine, phenylephrine and mephenteramine) ephedrine is the vasopressor of choice for spinal-induced hypotension in the parturient because of its ability to maintain uteroplacental blood flow.<sup>2</sup> But an important concern about ephedrine in obstetrics has been the demonstration of an association between its use and a depression of fetal pH.<sup>[4]</sup> Thus in our study we compared the effect of pretreatment with crystalloid versus ephedrine infusion on neonatal acid-base equilibrium.

## **METHODOLOGY**

After obtaining institutional ethics committee approval and informed consent,

60 healthy parturients of ASA I, without fetal compromise scheduled to undergo elective caesarean section under spinal anaesthesia were studied. This prospective randomized controlled study was conducted on patients who were admitted at Father Muller Medical College and Hospital in the Obstetrics and Gynaecology department. Women posted for elective LSCS with singleton pregnancy of 39-41 weeks of gestation between 20-40 yrs of age and weighing 45-70 kg with height between 145-160 cm belonging to ASA I category were included in this study. Parturients with obstetric complications like pregnancy induced hypertension (PIH), obesity, pre-existing hypertension or evidence of fetal anomalies or fetal distress and who were contraindicated for spinal anaesthesia were excluded from the study.

Patients were admitted one day before the surgery. Preoperative evaluation of all the patients were performed with detailed history, physical examination including height, weight, evidence of spinal deformity and mental status of the patient. All the patients were kept nil per oral for 6-8 hours. Aspiration prophylaxis, ranitidine 150 mg and metoclopramide 10 mg was given orally on the night before surgery and also two hours prior to surgery.

On arrival to the operating room all the patients were met by an anesthesiologist other than the one who is in charge of giving spinal anaesthesia. Patients were randomly allocated by means of sealed envelope into either Group I or Group II.

Group I (Crystalloid group): preloaded with Ringer lactate (RL) 15 ml/kg.

Group II (Ephedrine group): infusion of 30 mg ephedrine in 500 ml of Ringer lactate.

Intravenous access was obtained by an 18 G IV cannula. Standard monitors like electrocardiography, pulse oximetry,

noninvasive blood pressure were connected to the patient. The baseline heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and oxygen saturation (SpO<sub>2</sub>) were recorded. Patients in Group I (Crystalloid group) were preloaded with RL at 15 ml/kg over 20 min period prior to spinal anaesthesia, after which the IV infusion was slowed to a minimum rate of 2 ml/kg/hr throughout the study period. Group II (Ephedrine group) patients received infusion of 30 mg ephedrine in 500 ml Ringer lactate at a rate of 2 drops/second (0.48 mg/min), which was started 5 min before administering spinal anaesthesia and was continued throughout the study period.

With the patients in the left lateral position, under strict aseptic precautions, lumbar subarachnoid block was performed at L2-L3 or L3-L4 interspinous space using 23-25 G Quincke Babcock spinal needle by an anesthesiologist who was unaware of the group allocation. After the free flow of CSF was confirmed, 2 ml of 0.5% bupivacaine (heavy) (Sensorcaine, Astra Zeneca Pharmaceuticals, India) was injected slowly over 15 sec. The patients were then immediately turned supine and a wedge was placed under the right buttock to facilitate left uterine displacement. Oxygen at 4 L/min was administered by facemask until delivery of the baby. The time of institution of subarachnoid block was noted. The level of spinal block at various intervals was checked by loss of pinprick sensation and the final level of the block was noted. Surgery was started when the sensory level of block reached T6 dermatome. The time of skin incision, uterine incision and the delivery of the baby were noted down.

Intraoperative monitoring includes maternal heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure. These were recorded at every 2 min interval for the first 10 min then

every 5 min for the next 20 min and thereafter every 10 min till the end of the surgery. Hypotension was defined as a decrease in systolic blood pressure > 30% from the baseline or below 100 mm of Hg and was managed with rescue doses of ephedrine (6 mg). No alteration was made in the rate of IV fluid or ephedrine infusion. Maternal bradycardia was defined as heart rate < 50 bpm and was treated with 0.6 mg of intravenous atropine. The patients were monitored for any palpitation, reactive hypertension (SBP > 30% of the baseline value), nausea, vomiting.

After delivery of the baby, all mothers received 20 IU of oxytocin and a section of umbilical cord was double clamped to allow sampling of the umbilical vein and artery for blood gas analysis. Neonatal condition was assessed by modified APGAR score at 1min and 5 min after delivery by the attending pediatrician.

Statistical analysis of the data was determined with Mann-Whitney U test and Chi square test was used to find out possible associations.

p < 0.05 significant.

p < 0.01 highly significant.

## RESULTS

Sixty healthy parturients without fetal compromise of ASA I who were posted for elective LSCS under spinal anaesthesia were included in the study. Patients were randomly allocated into either Group I (Crystalloid group) or Group II (Ephedrine group). There was no difference between the groups with respect to patient demographics and the time intervals between skin incision (SI) to uterine incision (UI) and uterine incision (UI) to delivery (D). The average upper level of sensory block (T6-T5) was same in both the groups (Table 1). Blood gas values were not available for four Crystalloid group patients and one Ephedrine group patient.

The APGAR score at 1 min and 5 min were good in both the groups. After the blood gases of fifty five neonates were studied, the overall incidence of fetal acidosis (umbilical artery pH < 7.20) was none. There were no significant ( $p > 0.05$ ) difference in the umbilical blood gas values between Group I and Group II. There was no significant ( $p > 0.05$ ) difference in the umbilical vein Pco<sub>2</sub> between the two groups.

Table 1: Maternal characteristics and operative details

	Group I {n=30}	Group II {n=30}
Age (yrs)	26.97 ± 2.79	24.6 ± 3.74
Weight (kg)	60.9 ± 7.9	59.63 ± 6.73
Height (cm)	152.03 ± 6.62	153.22 ± 6.06
Block height(dermatome)	T6 (T6-T5)	T6(T6-T5)
SI – UI (min)	6.63 ± 2.81	5.50 ± 2.17
UI – D (min)	0.67 ± 0.2	0.6 ± 0.24

Values are in mean ± SD or median (range). SI: Skin Incision; UI: Uterine Incision; D: Delivery  
There were no statistically significant ( $p > 0.05$ ) difference between the two groups.

Table 2: Neonatal outcome

		Group I (n=26)	Group II (n=29)
APGAR Score	1 min	8(8-9)	8(8-8)
	5 min	9(9-9)	9(9-10)
Umbilical arterial blood	pH	7.22±.058	7.23±.049
	Po <sub>2</sub>	11.17±5.03	11.43±4.06
	Pco <sub>2</sub>	53.60±7.156	53.23±5.710
Umbilical venous blood	pH	7.27±.050	7.29±.073
	Po <sub>2</sub>	20.53±5.25	22.37±9.45
	Pco <sub>2</sub>	45.60±6.03	44.70±7.94

Values are mean ± SD or median (range)  
There were no statistically significant ( $p > 0.05$ ) difference between the two group

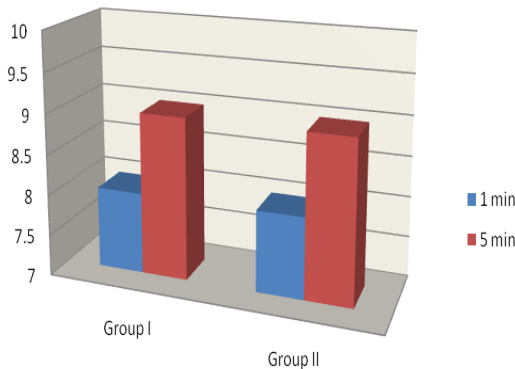


Figure 1 : APGAR score

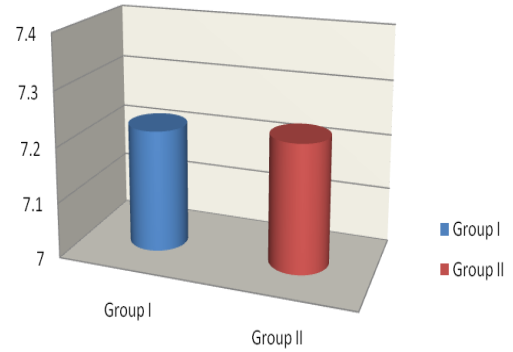


Figure 2 : Umbilical artery pH

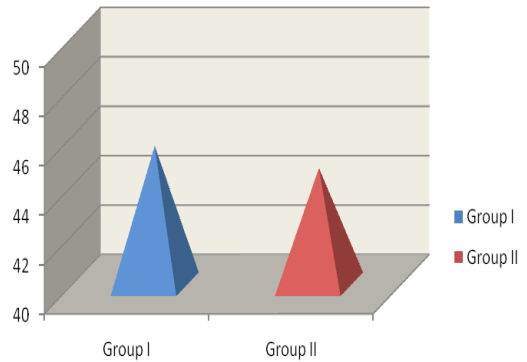


Figure 3 : Umbilical vein pCO<sub>2</sub>

## DISCUSSION

The choice of anaesthesia for any surgery is made by balancing the patient's preference with the risks and the benefits of a particular technique to the patient. The use of regional anaesthesia in obstetrics has increased because it is associated with reduced maternal mortality and morbidity compared with general anaesthesia. Spinal anaesthesia has the advantage of simplicity, rapid onset, low failure rates, minimal drug dose and the provision of excellent muscle relaxation during the surgery.<sup>[5]</sup> But during spinal anaesthesia, sympathetic block causes hypotension to fall due to decreased systemic vascular resistance and cardiac output, the latter being secondary to reduced venous return and sometimes decreased heart rate. It is estimated that 80% of patients who undergo LSCS under spinal

anaesthesia will develop hypotension .<sup>[4]</sup> Hypotension is more frequent and severe in pregnant patients compared with nonpregnant women because of greater sensitivity to local anesthetics resulting in higher blocks, aortocaval compression that decrease the venous return and also change in autonomic balance in favor of a relative increase in sympathetic compared with parasympathetic activity .<sup>[11,12]</sup> Untreated, severe hypotension pose serious risks to both mother and fetus. In the mothers spinal-induced hypotension leads to nausea, vomiting, dizziness, unconsciousness, pulmonary aspiration, apnoea or even cardiac arrest whereas in case of the fetus, maternal hypotension leads to impaired placental perfusion which in turn causes hypoxia, fetal acidosis and neurological injury .<sup>[8]</sup> Hence protocols to prevent hypotension during spinal anaesthesia for caesarean section may result in better outcomes than those designed to treat hypotension once it has occurred. This was demonstrated by Dutta *et al.* who found that patients who received early administration of ephedrine had less nausea and vomiting and better neonatal acid-base status .<sup>[8]</sup>

Clarke *et al.* demonstrated a significant reduction in the incidence of hypotension during spinal anaesthesia for caesarean section after crystalloid administration, from 92% to 57%.<sup>18</sup> Similar results were observed in the study conducted by Rout *et al.*<sup>13</sup> Whereas some of the previous studies .<sup>[14,15]</sup> have found that crystalloid preload confers no advantages in terms of maternal hypotension and neonatal outcome.

Vercauteren *et al.* stated that ephedrine is the vasopressor of choice for spinal hypotension in the parturient because of its ability to maintain uteroplacental blood flow. The appropriate route and dose of ephedrine that should be used to prevent spinal associated hypotension during

caesarean section still remains controversial .<sup>[11]</sup> Regarding the route of ephedrine administration, Rout *et al.* in his study on IM ephedrine stated that it is difficult to predict both absorption and peak effect of IM ephedrine and also observed reactive hypertension, particularly if spinal anaesthesia was unsuccessful .<sup>[16]</sup>

Since many years prophylactic IV ephedrine administered either by infusion <sup>[9, 17]</sup> or bolus doses <sup>[18]</sup> has been considered the gold standard for preventing hypotension. The effect of an IV bolus of ephedrine on arterial pressure is transient and it lasts for only 10 – 15 min as shown by Hollmen *et al.* .<sup>[19]</sup> So we considered ephedrine infusion to prevent spinal-induced hypotension and compared it with crystalloid preloading.

Stephen *et al.*, conducted a randomized study in pregnant females under epidural anaesthesia and showed that the prophylactic administration of 50 mg ephedrine is associated with higher incidence of hypertension and a detectable change in the umbilical artery acid –base status .<sup>[20]</sup> Lee *et al.*, performed a systematic review of seven trials comparing varying doses of ephedrine and phenylephrine for the treatment of spinal hypotension. Neonatal outcome as assessed by apgar scores and fetal acidosis were similar between the phenylephrine and ephedrine groups. Of interest is the fact that patients in the phenylephrine group had neonates with higher umbilical cord blood pH than women given ephedrine .<sup>[20]</sup> This may be clinically important because umbilical cord blood is a sensitive indicator of reduced uteroplacental perfusion. Warwick D *et al.*, studied the vasopressors in obstetrics and concluded that ephedrine may stimulate metabolism in the fetus leading to fetal acidosis .<sup>[11]</sup> Thus in our study we are focusing on the effects of ephedrine on fetus as well by observing the umbilical arterial and venous blood gas.

Neonatal outcome was good in both the groups as assessed by APGAR scoring. On analyzing the data from umbilical cord blood, the umbilical blood gas tensions and acid–base status were similar in both the groups. This may be clinically important because umbilical cord blood is a sensitive indicator of reduced uteroplacental perfusion.

Some of the comparative studies have shown that ephedrine may be associated with increased fetal acidosis, particularly when higher doses were used [4,20]. Although we did not measure uteroplacental flow, our results suggest that, within the range of doses used in our study, the potential vasoconstrictive effects of ephedrine may have a less detrimental effect on uteroplacental blood flow. Thus low dose of prophylactic ephedrine infusion does not cause adverse neonatal effects during spinal anesthesia for elective caesarean section.

However it is difficult to draw conclusion regarding effects of the given prophylactic doses with this small number of subjects, probably larger number of patients may be required to prove it.

## CONCLUSION

The study concludes that prophylactic low dose of ephedrine infusion does not cause adverse neonatal outcome.

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