Prevention of Hypotension Following Spinal Anaesthesia for Caesarean Section: Comparison between Crystalloid Preloading & Prophylactic Ephedrine Bolus & Infusion

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Summary:
This study was conducted to compare the efficacy of crystalloid administration with prophylactic ephedrine infusion for reducing the incidence of hypotension during spinal anesthesia for elective caesarean section.

Studies have shown that ephedrine prevents decrease in uterine blood flow & prevents fetal acidosis & hypoxia associated with hypotension. Thus, the maternal & neonatal outcomes are better, compared to other agents. Even though ephedrine remains the drug of choice to treat spinal hypotension intraoperatively in caesarean patients, only a few studies are there to show its prophylactic efficacy in preventing hypotension. In the present study, the role of prophylactic ephedrine infusion in preventing spinal hypotension in caesarean patients has been evaluated.

Key words:
Hypotension, crystalloid, ephedrine, Anesthetic technique: Spinal anesthesia Obstetrics

Introduction:
Regional anaesthesia has become the preferred technique for caesarean section because general anaesthesia is associated with higher maternal morbidity & mortality. However, spinal anaesthesia is also 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 & ultimately neonatal outcome as measured by umbilical artery pH & Apgar scores.

Various techniques have been devised to prevent the occurrence of hypotension. The use of lateral uterine displacement is routine. Other strategies have included the use of intravenous fluid preload, trendelenberg position, compression stockings on the legs & prophylactic vasopressors. However, no method has proved satisfactory. Of the available vasopressors like Mephaseramine, Ephedrine & Phenylephrine, Ephedrine is most commonly used & is the drug of choice for the purpose.

Studies have shown that ephedrine prevents decrease in uterine blood flow & prevents fetal acidosis & hypoxia associated with hypotension. Thus, the maternal & neonatal outcomes are better, compared to other agents. Even though ephedrine remains the drug of choice to treat spinal hypotension intraoperatively in caesarean patients, only a few studies are there to show its prophylactic efficacy in preventing hypotension. In the present study, the role of prophylactic ephedrine infusion in preventing spinal hypotension in caesarean patients has been evaluated.

Materials & methods
This study was undertaken in the department of Anaesthesiology, Goa Medical College, after obtaining approval from the ethical committee of the Institution.

In this prospective single blind randomized controlled study, 150 inpatients, between age group of 20-40 years, weighing 45-65 kg with height between 145-160 cm, of ASA grade I who were undergoing elective caesarean sections were selected. Informed, valid written consent was obtained from each of the 150 patients for participation in the study.

A thorough preoperative evaluation of all these patients was performed with detailed history, physical examination including height, weight, evidence of spinal deformity or any neurological disease and mental status of the patients.

The basal heart rate & blood pressure was recorded prior to surgery, with the patients lying in the left lateral position on three occasions. The average of these values was noted down as the baseline recording. Large bore IV line was secured.

The patients were randomly divided into 3 groups.

Group 1: - Preloading with Ringer Lactate @ 20ml/kg 20 minutes prior to spinal anaesthesia.

Group 2: - No preloading. 6mg Intravenous bolus ephedrine when spinal anaesthesia is given followed by 24 mg ephedrine in 500 ml Ringer Lactate as infusion @ 2 drops/sec (0.384 mg/min).

Group 3: - No preloading. 30 mg ephedrine in 500 ml Ringer Lactate as infusion @ 2 drops/sec (0.48 mg/min) which is started 5 minutes before administering spinal anaesthesia.

All patients were kept nil by mouth for 6-8 hrs. Anti-aspiration prophylaxis was given which included Ranitidine 150 mg & metoclopramide 10 mg orally on the night before surgery and also on the morning of surgery.

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### Anaesthetic Technique:
The patients were shifted to the operation theatre on a trolley maintaining left lateral position. An intravenous line was started. Cardioscope, Pulse oximeter and blood pressure cuff attached and baseline values recorded. Patients were placed in left lateral decubitus position. Under strict aseptic precautions, lumbar subarachnoid block was performed at L2 – L3 or L3 – L4 interspinous space using 23 – 25G spinal needle. 1.8 to 2 ml of 0.5% Bupivacaine (heavy) was injected slowly after careful aspiration of cerebrospinal fluid. The time of institution of subarachnoid block was noted down. The patients were then immediately turned supine and a wedge was placed under the right buttock to facilitate left uterine displacement. Oxygen @ 4-5 L/min. was given using a clear facemask. One minute after the spinal injection, the onset of spinal anaesthesia was confirmed by asking the patient to subjectively verify numbness of the legs. Surgery was started when the sensory level of the block reached T6. The level of spinal block at various intervals and the final level of the block were noted down. The time of skin incision, uterine incision and the delivery of the baby were noted down. Neonatal condition was assessed by modified Apgar score (APGAR) at 2 and 5 minute interval after delivery. The heart rate and blood pressure were recorded manually every 1 minute up to 5 minutes and thereafter every 5 minutes till the end of the surgery. Hypotension was defined as a decrease in the Systolic BP > 20% from the baseline value or below 90 mm of Hg and was managed with rescue doses of ephedrine (6mg). No alteration was made in the rate of intravenous fluid or ephedrine infusion. The total dose of intravenous rescue ephedrine was noted in all the 3 groups.

### Statistical Analysis:
The data thus obtained was statistically analyzed using the following test.
1. ANOVA test.
2. The p value of < 0.05 was considered to be statistically significant & p value < 0.01 were considered highly significant.

The adjoining graph 1 shows that the mean baseline HR was comparable in the three groups. Thereafter the HR in group II & III, where prophylactic Ephedrine was given, remained on the higher side as compared to group I, where no prophylactic Ephedrine was given. This was seen to be statistically highly significant (p < 0.001).

Graph 2 shows the comparison of the changes in the SBP in the 3 groups. The baseline SBP in the 3 groups was comparable. A highly significant difference was noted in the SBP in groups II & III between 2-7 minutes as compared to group I (p < 0.001). The fall in SBP was maximum in group I as compared to groups II & III between 2-7 minutes, but after this, the SBP in the 3 groups were almost similar because of rescue ephedrine given to counteract hypotension.

The bar diagram (graph 4 & table 1) shows that the percentage of fall in SBP was maximum in group I & the least in group II. These observations were found to be statistically highly significant (p < 0.001).

The graph 3 shows that the maximum fall in the DBP was seen in group I between 4-7 minutes after the spinal anaesthesia, which is statistically significant. The DBP in groups II & III also decreased but the fall was comparatively less. After 7-10 minutes there was no much difference in the DBP of the 3 groups.

Dose of Rescue Ephedrine (Table 2 & graph 5)
The bar diagram shows that the mean dose of rescue Ephedrine required was maximum in group I followed by group III. It is the least in group II, which is highly significant (p < 0.001).

### Discussion:
Spinal anaesthesia is the most common anaesthetic technique used for caesarean section, and is safer than general anaesthesia. But the disadvantage of spinal anaesthesia is spinal hypotension which may have detrimental effects on mother and fetus. Frequent occurrence and rapid onset of hypotension during spinal anaesthesia has encouraged anesthetists to try and prevent or minimize the associated maternal symptoms of nausea and vomiting during the establishment of the block.

Untreated, severe hypotension can also pose serious risks to both mother (unconsciousness, pulmonary aspiration, apnoea or even cardiac arrest) and baby (impaired placental perfusion leading to hypoxia, fetal acidosis and neurological injury) Even mild hypotension can reduce the uteroplacental blood flow and can contribute to fetal acidosis. Hence protocols that aim to prevent hypotension during spinal anaesthesia for caesarean section may result in better outcomes than those designed to treat hypotension once it has occurred, as proved by Dutta et al. 11

It was found that the incidence of hypotension was more in the preloading group where patients received no prophylactic ephedrine. In most studies, hypotension is defined as a decrease in the systolic arterial pressure (SAP) more than 25% from the baseline reading or a decrease of SAP to less than 90–100 mm Hg as absolute values. In the present study hypotension is defined as systolic blood pressure less than 30% of the baseline value or less than 90 mmHg.

The incidence of hypotension following spinal anaesthesia was 80% in the preloading group (40/50), 12% in group II (6/50) and 22% in group III (11/50). This difference is statistically significant and it is evident that 6mg bolus ephedrine followed by infusion is more effective than ephedrine infusion alone for the prevention of hypotension when compared to preloading. The peak incidence of hypotension...
occurred between 4 minutes to 6 minutes of administration of the intrathecal drug. The rescue doses of ephedrine (6 mg) required to treat hypotension was higher in the preloading group (6.12mg) compared to 0.72mg in group II and 1.32mg in group III.

Thus prophylactic administration reduces the incidence of hypotension as well as the total dose of ephedrine required to treat hypotension. This minimum dose reduces the side effects due to higher doses of ephedrine such as fetal acidosis, fetal tachycardia, reactive hypertension and other subjective symptoms in the mother like palpitation, headache etc.

Prophylactic efficacy of a single dose of 5 mg ephedrine given immediately after the induction of spinal anesthesia was studied in prehydrated caesarean patients by Marcel P. Vercauteren, Hilde C. Coppejans, Vincent H. Hoffmann, 50 parturients undergoing cesarean delivery were divided into two groups and received either ephedrine 5 mg or intravenous saline in a double-blinded fashion.

<table>
<thead>
<tr>
<th>GROUP</th>
<th>Mean</th>
<th>SD</th>
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<tr>
<td>1</td>
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<td>6.24</td>
</tr>
<tr>
<td>2</td>
<td>11.52</td>
<td>3.52</td>
</tr>
<tr>
<td>3</td>
<td>12.77</td>
<td>5.67</td>
</tr>
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Table 1: Comparison of percentage of fall (%FALL) in SBP

<table>
<thead>
<tr>
<th>GROUP</th>
<th>DOSE OF EPH (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.12</td>
</tr>
<tr>
<td>2</td>
<td>0.72</td>
</tr>
<tr>
<td>3</td>
<td>1.32</td>
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Table 2: Comparison of the dose of Rescue Ephedrine (in mg)
They found that only 8% patients in the ephedrine group developed hypotension with systolic blood pressure values <90 mm Hg, whereas 42% patients in the saline group experienced hypotension of this severity. The total amount of rescue ephedrine administered did not differ between groups.

This study establishes the prophylactic efficacy of low dose ephedrine even though they did not mention about reactive hypertension, and contradicts the study by Warwick D., Ngan Kee, Kim S. Khaw, and Tony Gin where hypotension occurred in 35% of patients who received a higher dose of 30 mg of ephedrine. This study also proves that patient characteristics, tilt of the table, left lateral position, fluid preload, the dose of anaesthetic agent alone or in combination, etc, may modify the effect of a given dose of prophylactic ephedrine and no intervention reliably prevents hypotension during spinal anaesthesia for caesarean section and a combination of methods are necessary for achieving this.

It is difficult to draw any conclusions regarding the effects of the given prophylactic doses with the small number of study groups.

There was no incidence of reactive hypertension in this study and no patients developed bradycardia requiring atropine.

This study supports the statement given by Jackson R., Reid J.A., Thorburn J. that, volume preloading is not essential to prevent spinal induced hypotension at caesarean section as preloaded patients also developed hypotension and that the incidence was less in the ephedrine groups, proving that preload alone is not effective and a combination of preload and a prophylactic vasopressor may often becomes necessary for the prevention of hypotension.

Neonatal status was assessed by Apgar scoring and all the neonates showed good Apgar scores. None of the groups showed Apgar score < 7, despite a difference in the incidence of hypotension among the groups. These findings are supported by a systematic review conducted by Anna Lee, Warwick, Ngan Kee analyzing Randomized, controlled trials obtained through MEDLINE, EMBASE, the Cochrane Controlled Trials Registry, and contact with leading experts, and a reference list of published articles.

In the present study the minimum effective doses of ephedrine were used and all the neonates had good Apgar scores suggesting that within these range of doses the potential vasoconstrictive effects of ephedrine may have a less detrimental effect on uteroplacental blood flow than the effects of hypotension, which is the cause for fetal acidosis in the control group.

The adverse effect of ephedrine on the mother include maternal arrhythmias, reactive hypertension, palpitation, tremor, anxiety etc and these are rare, dose dependent and may not manifest with the low doses studied here.

The incidence of maternal tachycardia was similar among group II and III due to β-stimulation by ephedrine. Other factors like anxiety, use of oxytocin, use of sedatives etc are also involved in the causation. The results are comparable to the trials included in a quantitative systematic review by Anna Lee and Warwick D.

Significant difference was noted in the maternal heart rates between the 3 groups, group I showing heart rates on the lower side compared to groups II and III. Other studies included in the quantitative review by Anna Lee and Warwick D could not give an account on bradycardia with low dose ephedrine and the incidence was the same in both test and control groups.

After analyzing the results it was observed that although preblock crystalloid administration is generally a safe procedure, its effectiveness is questionable. In this study, prophylactic intravenous ephedrine bolus followed by a low dose ephedrine infusion was found to be more effective than crystalloid administration in preventing hypotension in this patient population.

There was no incidence of reactive hypertension but the maternal heart rates in group II and III remained on the higher side as compared to group I. Ephedrine does not improve neonatal outcome but decreases the incidence of nausea and vomiting by preventing hypotension.

Conclusion:
In conclusion, it was found that, although preblock crystalloid administration is generally a safe procedure, its efficacy in preventing hypotension is questionable. Crystalloid preloading does not prevent the incidence of hypotension. Rescue ephedrine bolus had to be used in the crystalloid group to prevent hypotension. Ephedrine infusion alone is more effective than crystalloid preloading in preventing hypotension. Low dose ephedrine infusion does not cause tachycardia or hypertension. The overall benefits of prophylactic intravenous ephedrine is small. Hence a combination of the beneficial interventions is recommended for the prevention of hypotension, i.e. colloid or crystalloid preloading followed by prophylactic intravenous ephedrine in minimum effective doses and left lateral uterine displacement with leg compression using bandages, stockings or inflatable boots, or using two vasopressors, in combination.

References


12. Marcel P. Vercauteren, Hilde C. Coppejans, Vincent H. Hoffmann - refer - 27