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FETAL EFFECTS OF PHENYLEPHRINE AND EPHEDRINE DURING SPINAL ANAESTHESIA FOR CAESAREAN SECTION.

Anaesthesiology

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ABSTRACT

Introduction: Spinal anaesthesia is the choice of anaesthesia for caesarean section because of its faster onset, good analgesia, lesser airway manipulations, avoidance of polypharmacy. But it is also associated with side effects, hypotension being the most common which occurs in 80% of the patients. Hypotension has deleterious effects on both the mother and the foetus. To prevent this, using vasopressors like Ephedrine and phenylephrine is an effective method. But studies were done comparing the efficacies of both the drugs and their side effects on the mother and foetus. This is a study on comparision of ephedrine and phenylephrine, when administered prophylactically to prevent spinal induced hypotension and its effect on the foetus.

Methods: A total of 60 patients belonging to ASA I were randomised into two groups receiving bolus of phenylephrine (100 mcg) and ephedrine (5 mg) prophylactically after the administration of spinal anaesthesia. Maternal systolic blood pressure was maintained at near baseline values by administration of boluses during the episodes of hypotension (SBP <80% of the baseline SBP). At delivery, APGAR scores and umbilical arterial and venous blood gases and lactate levels were measured.

Results: The study concluded that both phenylephrine and ephedrine had similar effect on the acid base status of the foetus.

Conclusion: Both phenylephrine and ephedrine can be used in treatment of maternal hypotension in spinal anaesthesia without causing adverse effect on the foetus.

KEYWORDS:

INTRODUCTION

Spinal Anaesthesia was experimented by James Leonard Corning, but was not conducted in surgeries. Later it was introduced into clinical practice by Karl August Bier in 1898 which proved to be an effective method to relieve pain during the surgery. But at that time it was associated with lot of complications like headache, nausea, hypotension and even death. After a thorough research on these aspects, various modifications were done inorder to reduce the complications. After rigorous cycles of audits to monitor the safety and efficacy of spinal anaesthesia, the 3rd National Audit Project of The Royal College of Anaesthetists (January 2009) reaffirmed that central neuraxial blocks (including spinal anaesthetics, epidurals and combined spinal epidurals) are beneficial and carry an acceptably low incidence of major complications. Now it is one of the most popular techniques used in lower abdominal and lower limb surgeries. It is commonly used for caesarean section because it avoids the risks of general anesthesia related to difficult intubation and aspiration of gastric contents. The reason why spinal anaesthesia is preferred because of its simplicity, rapid onset, adequate relaxation, no airway involvement, low failure rate. But it is also frequently associated with hypotension, which can have detrimental effects on the mother and the neonate, including nausea, vomiting and dizziness in the mother, as well as decreased utero placental blood flow resulting in impaired foetal oxygenation and foetal acidosis.

Various preventive methods are currently used to prevent or minimize hypotension like: displacing the gravid uterus to avoid the aortocaval compression, crystalloids or colloid preloading, utilizing compression stocking onto the lower extremities, using vasopressors like ephedrine, phenylephrine. Administration of colloids is associated with adverse effects like anaphylaxis, coagulopathy, renal failure. But none of these methods were effective in controlling the maternal blood pressure. A meta analysis was done on the effectiveness of each of these techniques in preventing spinal induced hypotension. Despite these conservative measures, a vasopressor drug is often required. An ideal vasoconstrictor agent should have a short latency period and effect, favourably affect the foetal heart rate, economic and easily available. The drug usually recommended in this context is ephedrine, which is effective in restoring maternal arterial pressure after hypotension. Despite the wide acceptance of ephedrine as the vasopressor of choice for obstetric anaesthesia, its superiority over other vasopressors has not been clearly defined.

Recent studies have shown that prophylactic ephedrine is associated with foetal acidosis and tachyphylaxis. Due to its catecholamine releasing effect, it can increase myocardial oxygen demand and arrhythmias. It can also increase the metabolism in the foetus, thus leading to foetal acidosis. Recent studies show that phenylephrine is a safer alternative for both mother and foetus. It was found that mothers treated prophylactically with phenylephrine had higher umbilical arterial pH values than with ephedrine. The side effects like dizziness, nausea, vomiting which are the effects of maternal hypotension were less in patients treated with phenylephrine. The blood gas analyses showed lesser incidences of foetal acidosis. Other vasoconstrictor agents like ethylephrine, metaraminol, methoxamine, angiotensin II can be used but the evidence of safety and effectiveness are few.

In this study, we compared the effect of phenylephrine and ephedrine administered prophylactically for prevention of spinal induced hypotension and its effect on the foetus measured in terms of umbilical cord blood analysis and apgar scores.

Materials and methods:

After obtaining institutional ethics committee approval and informed consent, 60 healthy parturients, belonging to ASA I scheduled for elective caesarean section were studied. This prospective, randomised, double blind study was conducted on parturients admitted in obstetrics and gynaecology department of Father Muller Medical College hospital, Mangalore.

Inclusion criteria:

- Women posted for elective LSCS with singleton pregnancy of 39-41 weeks of gestation.
- Age between 20-40 yrs.
- Weight between 45-70 kgs.

- Height between 145-160 cms.
- Women belonging to ASA I category.

Exclusion criteria:

- Parturients with obstetric complications like pregnancy induced hypertension (PIH), obesity, pre-existing hypertension, cardiovascular diseases, cerebrovascular diseases and gestational diabetes.
- Evidence of foetal anomalies.
- Patients who were contraindicated for spinal anaesthesia.

A detailed history and complete clinical examination of patients was done to rule out the exclusion criterias. Routine investigations like Blood grouping, Haemoglobin, Blood Urea and Serum Creatinine, Coagulation tests and blood Sugar levels were done. ECG whenever indicated were taken. Pre operative pulse rate, respiratory rate, blood pressure values noted. Written and informed consent were taken prior to the scheduled operation. Patients were explained about the procedure of intrathecal anaesthesia. All the patients were kept nil per oral for 6-8 hours. Patients involved in the study were premedicated with tablet ranitidine 150mg on the night prior to the surgery.

On arrival to the operating room, all the patients were met by an anaesthesiologist other than the one who is in charge of giving spinal anaesthesia. Patients were randomly allocated by means of sealed envelope into either Group E or Group P. In order to maintain the blinding, the vasopressor solutions were prepared in identical syringes by an anaesthetist or investigator who was not involved in subsequent patient care. The solutions contained:

- Group E: ephedrine 5 mg/ml.
- Group P: phenylephrine 100 mcg/ml.

Intravenous access was obtained by an 18 G IV cannula. Standard monitors like pulse oximetry, non invasive blood pressure and electrocardiography were connected to the patient. An average of three recordings at time intervals of 2 minutes will be considered as baseline recording. Patients were preloaded with Ringer's lactate solution 10ml/kg over 20 mins prior to the caesarean section.

With the patients in the left lateral position, under strict aseptic precautions, lumbar puncture was performed with 25G Quincke's needle at L3-L4 intervertebral space using midline or paramedian approach. Once free flow of cerebrospinal fluid was obtained, 12 mg of 0.5% Bupivacaine (heavy) was administered over 10-15 seconds. Time of injection of drug was noted and the patient was turned supine immediately, and a wedge was placed under her right buttock to facilitate left uterine displacement. Oxygen was given at 5L/min by facemask until clamping of the umbilical cord. The level of block was assessed by pinprick test using 22 G hypodermic needle every minute after the puncture, until it reached the dermatome level of T5. Surgery was started when the sensory level of block reached T5 dermatome. The time from blockade to skin incision, uterine incision and extraction of foetus were recorded. Immediately after induction of spinal anaesthesia, systolic blood pressure, diastolic blood pressure and heart rate were recorded. Immediately after intrathecal injection, bolus 1 ml of the study drugs were administered. Additional boluses of 1 ml of the vasopressor solution was administered whenever the SBP fell below 80% of the baseline systolic blood pressure.

Intraoperative monitoring includes systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate. These were recorded every 2 minutes for the first 10 minutes and then every 5 minutes for the next 20 minutes and thereafter every 10 minutes till the end of the surgery. Whenever the systolic blood pressure decreased to less than 80 mm Hg or below 80% from the baseline, it was considered as hypotension, and a bolus dose of the study vasopressor was administered.

Bradycardia was considered when heart rate was lower than 50 beats per minute and when accompanied with hypotension, it was treated with atropine 0.6 mg. Tachycardia was considered at a heart rate greater than 100 beats/ min. Episodes of hypotension, reactive hypertension (SBP >30% of the baseline value), tachycardia, bradycardia, need for rescue doses of vasopressors , Atropine administration and episodes of nausea and vomiting were recorded until the end of caesarean section and if nausea and vomiting occurred, they were treated with Ondansetron 4 mg IV.

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. An umbilical pH of less than 7.2 was considered foetal acidosis. Newborns were evaluated for APGAR scores at 1st and 5th minutes of birth, and a low APGAR was considered when the values assigned were less than 7.

Results:

The study involved 60 healthy parturients belonging to ASA I posted for caesarean section under spinal anaesthesia. They were randomly allocated in to either Group E (Ephedrine group) or Group P (Phenylephrine group).

Table 1 Demographic data and operative details

	Group E *(n=30)*	Group P *(n=30)*	P value
Age *(yrs)*	25.63±4.03	25.07± 3.939	0.584
Weight *(kg)*	58.6 ±6.79	58.03± 5.391	0.722
Height *(cm)*	156.67 ± 4.859	156.23 ± 4.732	0.728
SI-UI *(min)*	4.93 ± 1.998	4.62 ±0.906	0.462
UI-D *(min)*	3.2 ± 0.973	3.13 ± 0.628	0.790
Block height *(dermatome)*	T4 (T4-T5)	T4-T5	0.605

Values are in mean ± SD or median (range).
SI- skin incision; UI- uterine incision; D- delivery.

There was no significant difference between the groups in age, weight and height of the patients in both the groups. There was no significant difference in the time intervals between skin incision (SI) and uterine incision (UI) and uterine incision (UI) to delivery of the baby (D) between both the groups. The average upper level of the block was same in both the groups (T4-T5) (table 1).

Table 2 neonatal outcome:

		Group E (n=30)	Group P (n=30)	P value
APGAR Score (*min*)	**1**	8	8	
	5	9	9	
Umbilical arterial blood	**pH**	7.219± 0.0563	7.24 ± 0.0376	0.057
	pO_2	11 ± 4.503	10.5 ± 3.531	0.634
	pCO_2	49.2 ±9.042	48.17 ± 8.433	0.649
	Base Excess	-10.5 ± 2.6	-9.2 ± 4.2	0.0065
Umbilical venous blood	**pH**	7.314 ± 0.031	7.318± 0.0301	0.687
	pO_2	21.97 ± 6.682	21.63 ±6.739	0.848
	pCO_2	44.9 ±9.338	47.97 ± 6.189	0.139
	Base Excess	-7.2± 3.5	-7.9 ± 4.4	0.0087

Values are in mean ± standard deviation.
*P<0.05 is considered significant.
P<0.01 is considered highly significant.

The APGAR score at 1 min and 5 min were good in both the groups (table 2). There were no significant differences in the umbilical arterial blood pH, pO_2, pCO_2 and base excess between the two groups. But the pH of group E was slightly lower than group P, but this was not significant. There were no significant differences in the venous blood pH, pO_2, pCO_2 and base excess (figure 1 and 2).

Figure 1 Umbilical cord blood analysis of pH.

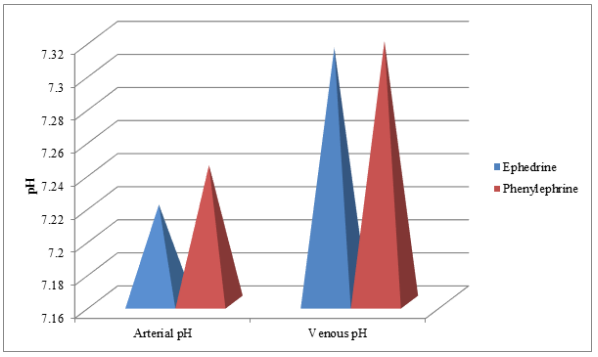
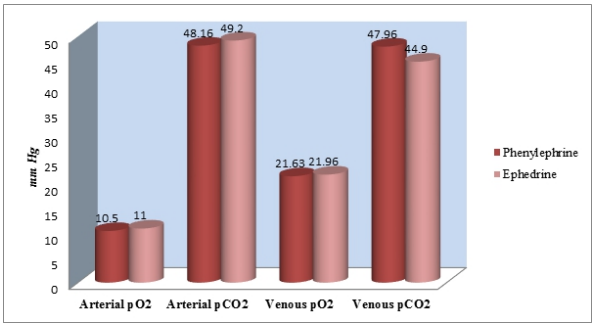


Figure 2 Umbilical cord blood analysis of Arterial and Venous pO_2 and pCO_2.



Conclusion:

This study concludes that both the vasopressors- phenylephrine and ephedrine can be safely used in the treatment of hypotension in caesarean section with minimal affection of the foetus.

Discussion:

After years of research and advancements in the field of regional anaesthesia, it is now the preferred choice by anaesthesiologists for most of the upper limb, lower limb and some intra abdominal surgeries. After it was found to be safe and effective in pregnant women, it is the choice of anaesthesia for lower segment caesarean section. General anaesthesia is preferred only in few cases where spinal anaesthesia is contraindicated. The risks associated with general anaesthesia like management of difficult airway, aspiration of gastric contents, oral, pharyngeal and laryngeal trauma, post operative nausea and vomiting, retarded lactation and sedation of the neonate can be avoided with the use of regional anaesthesia. There comes a role of emotional component when regional anaesthesia is used. It is now the preferred technique of choice because of its simplicity, low dose of drug being used, adequate muscle relaxation. The need of post operative analgesia is fulfilled by the use of spinal anaesthesia.[1]

But spinal anaesthesia has got its own side effects. The most common side effect is hypotension which occurs in 50-80% of the patients. Sub arachnoid block causes sympathetic blockade after its administration. Sympathectomy reduces the peripheral vascular resistance, venous return and cardiac output. Aortocaval compression due to the weight of the gravid uterus, sympathetic hyperactivity seen during pregnancy also contributes to the hypotension. Maternal side effects due to hypotension are nausea, vomiting, dizziness. These are a result of reduced cerebral perfusion. Untreated maternal hypotension leads to loss of consciousness, aspiration of gastric contents, cardiorespiratory arrest. Hypotension can reduce the uteroplacental perfusion and lead to foetal hypoxia and acidosis. Persistent hypoxia may lead to neurological compromise and foetal death.[2]

Various methods have been studied in order to prevent this adverse effect. Prehydration of the patients with crystalloids, colloids, keeping the patient in 15^0 left lateral tilt, compressive leg devices, slow injection of the local anaesthetic, treatment with a vasopressor are the common methods employed. But the most effective method among these is the treatment with a vasopressor. The vasopressors used are Ephedrine, phenylephrine, metaraminol, mephentermine and ethylephrine. A large number of studies have been done to determine the most effective method of prevention and treatment of hypotension.

Desalu *et al.* found prophylactic Ephedrine infusion to be effective in preventing hypotension compared to colloid prehydration.3 Lee *et al.* conducted a metanalysis of Ephedrine in 14 trials, found Ephedrine to be effective in treating hypotension.[4]

But controversies arose on the safety of Ephedrine regarding its effect on foetus. Many studies found that Ephedrine causes foetal acidosis(ngan kee, maghalhaes). Hence an alternative vasopressor, phenylephrine was studied. Although, its action on α_1 receptors reduces the uteroplacental blood flow and causes foetal acidosis (saravnan), A meta analysis by Fu-Qing Lin *et al.* proved that the parturients treated with phenylephrine had neonates with higher umbilical pH value than those treated with Ephedrine.[5] Aragao *et al.* in their study of comparision of phenylephrine and Ephedrine infusions in preventing spinal induced hypotension, found that the unwanted side effects of hypotension like nausea, vomiting, foetal acidosis was higher with Ephedrine.

Neonatal outcome was good in both the groups as assessed by APGAR scoring. Study by Armstrong *et al.* recommended umbilical cord blood gas analysis as gold standard to assess the newborn status.[41] Hence both APGAR scores and umbilical cord blood gas analysis were used to assess the status of the neonate. On analysing the data from umbilical cord blood, the umbilical blood gas tensions and acid-base status were similar in both the groups. This is similar to the study done by Warwick *et al.*[6] Although uteroplacental flow was not measured in this study, the results of this study suggest that within the range of doses used in this study, the effect of Ephedrine on the uteroplacental flow has less detrimental effect. A study done by Maghalhaes *et al.*[7] found that its effect on the foetus was transitory as indicated by the normal umbilical arterial pH values.

Thus, in this study, it was found that both the vasopressors were effective in preventing spinal induced hypotension when administered prophylactically. The neonatal outcomes were similar in both the groups which suggest that both the drugs can be safely used in prevention of hypotension.

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