COMPARISON OF BOLUS INTRAVENOUS EPHEDRINE AND PHENYLEPHRINE FOR MAINTENANCE OF ARTERIAL BLOOD PRESSURE IN CAESAREAN SECTION DURING SPINAL ANAESTHESIA

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ABSTRACT

CONTEXT (BACKGROUND)

Hypotension following spinal anaesthesia is a common problem. Preloading with IV Fluids alone is not sufficient, because inadequately treated hypotension during Caesarian section causes undue effects on both mother and fetus. So concomitant use of vasopressor drugs to treat spinal hypotension proved useful and well established.

AIM

To compare the efficacy of intravenous phenylephrine versus intravenous ephedrine for correction of intra operative hypotension following spinal anaesthesia for elective as well as emergency caesarean sections.

DESIGN

A randomized controlled study of patients undergoing surgery under spinal anaesthesia for elective and emergency caesarean section.

METHODS & MATERIALS

The present study includes 100 patients divided into two groups each of 50 patients. Group P (Phenylephrine group), Group E (Ephedrine group.) The baseline heart rate, systolic, diastolic and mean blood pressures were measured. Whenever Hypotension (fall in BP >20% of baseline or less than 90 mm of Hg)occurred, Group P received Phenylephrine 40 mcg and Group E received 6 mg Ephedrine as intravenous bolus.

STATISTICAL ANALYSIS

Was done using Student's t test and Mann-Whitney test. 'p' value of less than 0.05 was considered to be statistically significant

RESULTS & CONCLUSION

Phenylephrine in a dose of 40 microgram is more efficacious in comparison to Ephedrine 6 milligrams in maintaining arterial blood pressure following hypotension after spinal anaesthesia in Caesarean section. Phenylephrine has a quicker peak effect (within 2 minutes of IV bolus) as compared to Ephedrine (within 10 minutes of IV bolus) APGAR Score at 1 and 5 minutes is comparable in both Group P and Group E.

KEYWORDS

Ephedrine, Phenylephrine, Spinal Hypotension, Caesarean Section.

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INTRODUCTION: Pregnancy is generally expected to end with a healthy and happy experience of another delivering a healthy infant. However, a variety of either maternal or foetal conditions can change the outcome in certain situations. A high degree of care for the mother and the foetus is essential if desired result is to be achieved.

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The obstetric patient for Caesarean section usually presents more challenges to the anaesthesiologist than other patients. Spinal anaesthesia is perhaps the most accepted approach to these challenges. It offers a fast, profound, definite and higher quality of sensory and motor blockade for Caesarean delivery.

Spinal anaesthesia is associated with some complications, the commonest of these being hypotension of a reported incidence of greater than 80% despite fluid preload and lateral uterine displacement.[1] Maternal hypotension is associated with distressing symptoms like dizziness, nausea, vomiting and can also cause foetal bradycardia[2] and acidosis.[3]

It is very important to recognize hypotension timely with appropriate treatment of maternal hypotension. For last few decades left uterine displacement and volume preloading before subarachnoid block has been the cornerstone in prevention of hypotension. Rapid administration of crystalloids may restore uterine blood flow immediately but has a short half-life but infusion of large volume of crystalloids can exacerbate the dilutional anaemia and can increase the risk of pulmonary oedema in the term parturient.

Several other methods have been tried for prevention of hypotension during

Caesarean section, which includes left uterine displacement,[4] leg compression and

Elevation,[5] prophylactic administration of vasopressors including Ephedrine, Mephentermine, Phenylephrine.[6] Prophylactic infusion of Angiotensin II[7] and Atrial Natriuretic peptide[8] have also been tried.

Presently the mainstay in management of hypotension is the use of Vasopressor agents, but those currently available are not ideal and there has been an ongoing search for ideal vasopressor.

Ephedrine is supposed to be most widely used agent for this purpose, but causes maternal tachycardia due to its non-selective action on both alpha and beta-adrenergic receptors.

It is difficult to titrate and also exhibits the phenomena of tachyphylaxis due to its indirectly acting nature. Hence there is a need to find an alternative drug for the treatment of hypotension, which lacks the fore mentioned maternal side effects and also does not cause any detrimental effect on the foetus.

Phenylephrine is one such drug, which is a directly acting sympathomimetic agent with selective alpha1 adrenergic activity. It is easy to titrate and maintain maternal blood pressure without producing undue tachycardia. Moreover, the administration of phenylephrine is reported to be associated with lower incidence of foetal acidosis than is Ephedrine. Numerous studies have been carried out to evaluate the various doses of Phenylephrine, from 20 to 100 micrograms and a dose of 20mcg has been found to be ineffective but dose as high as 100mcg has caused maternal bradycardia.

Hence, an attempt has been made to compare the efficacy of intravenous phenylephrine 40 micrograms and Ephedrine 6 milligram as a vasopressor therapy in case of hypotension associated with spinal anaesthesia in patients undergoing caesarean section. A good control of maternal blood pressure is one of the main stay requirements for ensuring safety during spinal anaesthesia in Caesarean section.[9]

AIM AND OBJECTIVES:

AIM: To compare the efficacy of intravenous phenylephrine versus intravenous ephedrine for correction of intra operative hypotension following spinal anaesthesia for elective as well as emergency caesarean sections.

OBJECTIVES: The objectives of this study are:

1. To compare the efficacy of intravenous bolus dose of Phenylephrine (40mcg) with Ephedrine (6mg) to maintain arterial blood pressure during spinal anaesthesia for Caesarean section.
2. To compare the dose of drug effective in maintaining arterial blood pressure in both the groups.
3. To compare the effect of two drugs on heart rate.
4. To compare the neonatal APGAR scores in both the groups.

MATERIALS AND METHODS: The present study was conducted in the Department of Anaesthesiology, MediCiti Institute of Medical Sciences, Ghanpur village, Medchal Mandal, Ranga Reddy District, Telangana state during the period of Dec 2012–June 2014.

STUDY DESIGN: A randomized controlled study of patients undergoing surgery under spinal anaesthesia for elective and emergency caesarean section.

Sample Size: A total sample size of 100 cases.

Inclusion Criteria:

- Uncomplicated pregnancy.
- Weight not more than 70kg's.
- Aged between 24 to 30 years.
- ASA class I & II.
- Baseline systolic blood pressure between 100 to 140mm Hg.
- Baseline diastolic blood pressure between 70 to 89mm Hg and developed hypotension during the surgery.

Hypotension is defined as fall in systolic pressure greater than 20% from baseline value or value less than 90 mm Hg.

Exclusion Criteria:

- Patient refusal.
- Patient with medical complications like Diabetes mellitus, cardiovascular diseases, severe anaemia.
- Patient with obstetrical complications like Ante Partum Haemorrhage, Pregnancy induced hypertension.

Contraindications to spinal anaesthesia.

METHODOLOGY: Approval from institutional ethical committee was obtained prior to study. After explaining the anaesthetic procedure, written informed consent for Participation in the study was obtained from the patient. 100 patients were randomly divided into two groups of 50 each, Group P (Phenylephrine group) and Group E (Ephedrine group) using computer generated randomization table. Study drugs were prepared and dispensed in syringes labelled "Study Vasopressor" by an anaesthesiologist not involved in the study. In the operating room Spo2, ECG, NIBP, HR monitored. The baseline heart rate, systolic, diastolic and mean blood pressures were measured. Intravenous preloading was done with 10ml/kg of Ringer lactate solution. Preloading was given over 15 minutes. Following this, all patients received intrathecal 2ml of 0.5%

hyperbaric Bupivacaine through 23G Quincke needle at L3-L4 subarachnoid space in left lateral position. Immediately following the injection, patient was turned to supine position and received oxygen at the rate of 5Litre/min by face mask. Level of sensory block was assessed by pinprick method from below upwards 5 minutes after SAB. Heart rate, systolic diastolic and mean arterial pressures were recorded every 2 minutes for 20 minutes and thereafter every 5 minutes for 1 hour or till the end of the surgery.

Whenever Hypotension (fall in BP >20% of baseline or less than 90mm of Hg) occurred, Group P received Phenylephrine 40mcg and Group E received 6mg

Ephedrine as intravenous bolus. Time taken to develop hypotension and the number of boluses administered were noted.

APGAR score of every neonate at 1 min and 5 mins after delivery.

STATISTICAL ANALYSIS: Statistical analysis was done using Student's t test and Mann-Whitney test. 'p' value of less than 0.05 was considered to be statistically significant.

OBSERVATIONS AND RESULTS: The objective of the present study is to compare the efficacy of intravenous bolus dose of Phenylephrine (40mcg) and Ephedrine (6mg) to treat hypotension following spinal anaesthesia for Caesarean section.

A total of 100 patients were grouped into two groups, Group P (Phenylephrine group, n=50) and Group E (Ephedrine group, n=50) by a computer generated randomization table.

After collecting data in both the groups the observations and analysis of the data are presented in tabular form.

DEMOGRAPHIC PROFILE:

	Group P	Group E
Age (Yrs)	26.80±1.68	26.88±1.73
Weight (Kgs)	55.40±5.55	55.20±5.33
Height (Cms)	151.34±1.72	151.24±1.78
Parity	1.60±0.72	1.68±0.71

Table 1: Showing age, weight, height, parity of both the groups

The age, weight, height and parity are comparable in both the groups

The baseline parameters recorded in the study groups were maternal heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure.

	Group P	Group E
Maternal HR	89.52±11.89	92.20±11.56
Maternal SBP	123.52±7.84	123.14±8.98
Maternal DBP	80.94±8.10	81.18±9.12
Maternal MAP	95.00±7.20	95.00±8.26

Table 2: Shows the baseline parameters in both the groups

Thus, the two study groups are comparable with the Baseline parameters.

Time (In minutes)	Group P	Group E	P value
SAB to Hypotension	3.36±0.81	3.52±0.81	0.3265
Duration of Surgery	68.28±8.46	69.40±8.18	0.5027

Table 3: Shows SAB to hypotension time and duration of surgery

The data of subarachnoid block to hypotension time and duration of surgery were compared. There was no statistically significant difference found in the two groups (p >0.05).

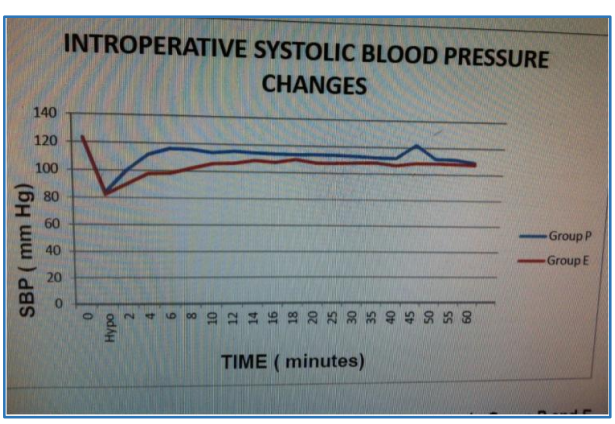
	Mean number of bolus	Standard deviation	Mean dose
Group P	1.2	0.45	48mcg
Group E	1.4	0.64	8.4mg

Table 4: Shows number of bolus and mean drug dose required in each group

- Group P required average of 1.20 boluses whereas Group E required 1.40 as boluses.
- Mean dose of 48 mcg was required in Group P and 8.4 mg was required in Group E.

Systolic Blood Pressure in Both the Groups:

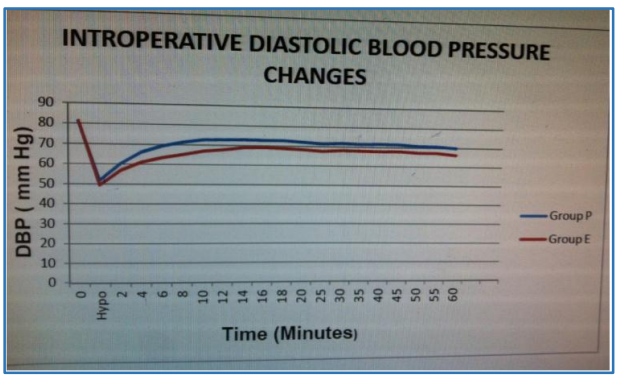
- It was observed that Basal SBP in Phenylephrine group was 123.52±7.84 and that of Ephedrine group was 123.14±8.98.
- Similarly, SBP during hypotension was 83.58±7.88 in Group P and 82.06±12.81 in Group E, which was found to be statistically comparable.



Graph 1

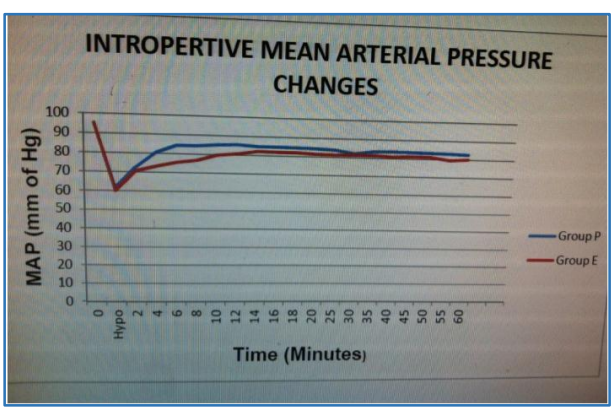
- Systolic blood pressure in Group P at 2 minutes after IV bolus was 100.18 mm of Hg while in Group E was 89.82 mm of Hg. This shows a very strong statistical significance as indicated by p value of less than 0.001 (p<0.001).

- Systolic blood pressure values showed a strong statistical significance until 25minutes indicated by p value of less than 0.001.
- Systolic blood pressure in Group P remains high until 50 minutes compared to Group E.



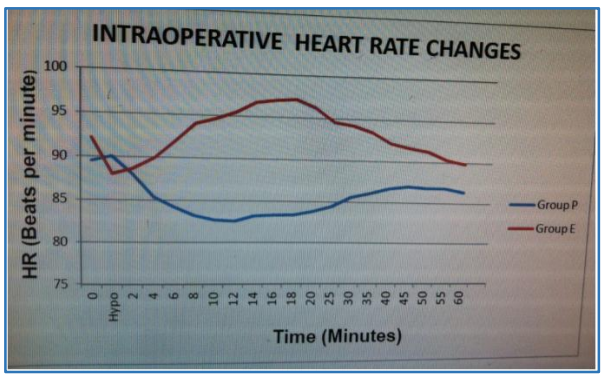
Graph 2

- Basal DBP and DBP during hypotension was statistically comparable in both the groups.
- Diastolic blood pressure in Group P at 2 minutes after bolus dose was 60.24±6.91mm of Hg, whereas, in Group E was 56.82±7.33mm of Hg. This difference is statistically significant. (p<0.01).
- Diastolic blood pressure in Group P was strongly significantly when compared with Group E until 10 minutes as indicated by p value of less than 0.001.
- P value is less than 0.05 till 50 minutes which indicates the difference is significant between the two groups, Group P & Group E.



Graph 3

- It was observed that Basal MAP in Phenylephrine group was 95.1±7.27 and that of Ephedrine group was 95.12±8.28.
- Similarly, MAP during hypotension was 61.48±5.41 in Group P and in Group E60±7.19, which was found to be statistically comparable.
- Mean Arterial pressure in Group P at 2 minutes after IV bolus was 78.62±8.42mm of Hg while in Group E was 72.54±9.757mm of Hg. This shows a very strong statistical significance as indicated by p value of less than 0.001 (p<0.001).
- Mean Arterial pressure showed a strong statistical significance until 10 minutes, indicated by p value of less than 0.001, between the two groups.



Graph 4

- Basal HR in Group P was 89.52±11.89 and Group E was 92.20±11.56.
- Mean HR during hypotension in Group P was 90.04±11.71 while in Group E was 88.02±15.45bpm. Both were found to be statistically comparable.
- Phenylephrine group shows a significant fall in HR while in Ephedrine group there is a significant rise in the HR.
- Heart rate values showed a strong statistical significance until 35 minutes indicated by p value of less than 0.001.
- Heart rate between the two Groups showed statistical significance until 50minutes as indicated by p value of less than 0.05.

	Group P	Group E	P value
APGAR 1 min	9.66±0.478	9.58±0.49	0.41
APGAR 5 min	9.78±0.418	9.78±0.41	0.99

Table 5: Comparison of APGAR Scores in both the Groups

- The APGAR 1 min Score difference between the two groups is not statistically significant as indicated by p value of greater than 0.05.
- The APGAR 5 min Score difference between the two groups is not statistically significant as indicated by p value of greater than 0.05.

DISCUSSION: The most common side effect following spinal anaesthesia is hypotension.[1]

Prevention and treatment of hypotension remains a frequent problem with no consensus in the optimal mode of management.

Fluid preloading with intravenous crystalloid or colloid solutions is a standard practice for prevention of hypotension but it has been found to be not satisfactory in preventing hypotension if used alone, without concomitant use of vasopressor drugs.

Inadequately treated hypotension occurring during Caesarean section can cause undue effects on both mother and foetus. There have been several attempts to find the optimal therapy for hypotension occurring during Caesarean

section without jeopardizing the physiology of mother and outcome of foetus.

Since sympathetic blockade resulting in vasodilatation is the primary cause of fall in arterial pressure, use of vasopressors in conjunction with fluid preloading appears to be a more logical approach to correct it. It has been shown that the percentage decrease in placental circulation is related to percent of reduction in maternal arterial pressure but not absolute reduction in pressure.

Incidence of hypotension clearly depends on its definition. Hypotension in most of the studies has been defined as values ranging from 20 to 30 percent reduction from baseline systolic arterial pressure.[10] In the present study hypotension was defined as decrease in systolic arterial pressure 20 percent from the baseline systolic pressure.

Bradycardia was defined as fall in heart rate of 20 percent or more from then baseline value.

The role of intravenous vasopressors has been well established in case of post spinal hypotension during Caesarean section. Ephedrine acts directly as well as indirectly on alpha and beta adrenergic receptors. Phenylephrine has selective alpha adrenergic activity due to which it was considered to cause reduction in uterine blood flow, but it has been mentioned that Phenylephrine causes less foetal acidosis than Ephedrine in a review by N gan et al.[11]

The present study is compared only with the studies in which Phenylephrine and Ephedrine was given as iv bolus to treat hypotension following spinal anaesthesia in caesarean section and the studies that have used prophylactic im and iv doses of the drug as well as those studies which have given the drug as infusions are not taken into consideration**.** Dinesh Sahu[12] et al studied 60 patients undergoing elective as well as emergency caesarean section under spinal anaesthesia who developed hypotension after subarachnoid block. They were randomly allocated to one of three groups to receive an IV bolus of the following Group P Phenylephrine 100mg (n=20), Group E Ephedrine 6mg (n=20) or Group M Mephentermine 6mg (n=20). Hypotension was defined as a decrease in systolic arterial pressure >20% of baseline values or < 90mm Hg, whichever was greater. They concluded that elevation of systolic arterial pressure in Phenylephrine group was significantly high for first 6min of bolus dose as compared to Ephedrine & Mephentermine groups. There was significant reduction in heart rate in Phenylephrine group. Neonatal Apgar score were >7 in all three groups.

Bhattarai et al,[13] study compares three vasopressors-Phenylephrine, Ephedrine, Mephentermine. Study included 90 patients undergoing elective and emergency caesarean section who developed hypotension following sub-arachnoid block. They were randomly divided into 3 groups, each group of 30 each. Group P received bolus of Phenylephrine 25mcg, Group E 5mg of Ephedrine, Group M 6mg of Mephentermine. It was found that rise of BP was significantly higher in case of Phenylephrine group in first 6 minutes, after the bolus, there was significant reduction in heart rate in Phenylephrine group, but there was tachycardia following administration of bolus Ephedrine and Mephentermine. Neonatal APGAR scores were similar in all the groups.

To Summarize:

- Systolic blood pressure values showed a strong statistical significance until 25minutes indicated by p value of less than 0.001.
- A mean dose of 48 mcg and 8.4 mg was used for Phenylephrine and Ephedrine respectively.
- There was a reduction in heart rate with Phenylephrine.
- Number of boluses required and neonatal APGAR scores were comparable in both Phenylephrine and Ephedrine.

The results of the present study is in accordance with the studies of Sahu et al and Bhattarai et al.

SUMMARY: The present study "Comparison of bolus intravenous Ephedrine and Phenylephrine for maintenance of arterial blood pressure in caesarean section during spinal anaesthesia" was carried out in the Department of Anaesthesiology, MediCiti Institute of Medical Sciences, Ghanpur village, Medchal Mandal, Ranga Reddy District, Telangana state during the period of Dec 2012 – June 2014. A randomized controlled study included 100 patients undergoing elective as well as emergency Caesarean section under spinal anaesthesia who developed hypotension after subarachnoid block. They were randomly allocated to one of the groups to receive an IV bolus of following

- Group P–Phenylephrine 40 mcg each IV bolus.
- Group E–Ephedrine 6 mg each IV bolus.

The study vasopressor drug was given whenever hypotension occurred following subarachnoid block. Hypotension was defined as fall in SBP >20 percent from baseline value or SBP <90mm of Hg. The present study revealed that SBP was significantly high in Phenylephrine group within 2min of administration of a bolus dose as compared to Ephedrine. A mean dose of 48mcg and 8.4mg of Phenylephrine and Ephedrine respectively was required to maintain the blood pressure. There was a reduction in heart rate with Phenylephrine whereas Ephedrine caused increase in heart rate. Number of boluses required and neonatal APGAR scores were comparable in both Phenylephrine and Ephedrine groups.

CONCLUSIONS:

- Phenylephrine in a dose of 40 microgram is more efficacious in comparison to Ephedrine 6 milligrams in maintaining arterial blood pressure following hypotension after spinal anaesthesia in Caesarean section.
- Phenylephrine has a quicker peak effect (within 2 minutes of IV bolus) as compared to Ephedrine (within 10 minutes of IV bolus).

- A dose of 48 mcg of Phenylephrine and 8.4 mg Ephedrine was found to be effective in maintaining arterial blood pressure within normal range.
- Phenylephrine caused a reduction in heart rate as compared to Ephedrine, which caused tachycardia.
- APGAR score at 1 and 5 minutes is comparable in both Group P and Group E.

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