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To Determine the Efficacy of Prophylactic use of Ephedrine and Mephentermine in Caesarean Section to Manage Hypotension under Subarachnoid Block

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Abstract

Introduction: Anaesthesia to a parturient is not only unique but also requires highest degree of care because the anesthesiologist has to look after two individuals, the mother and foetus. Hypotension during subarachnoid block for caesarean delivery can have detrimental effects on both mother and foetus.

Objectives: To determine the efficacy of Ephedrine and Mephentermine prophylactically in managing the hypotension for caesarean section under sub arachanoid block and their undesirable side effects.

Materials and Methods: Patients were divided randomly into 2 groups (E group and M group) of 30 each. Patients were premedicatated with inj. Pantaprazole 40mg and inj. Metoclopramide 10 mg and pre loaded with ringer's lactate at 10ml/kg infusion in the morning of the day of surgery. Baseline pulse rate, blood pressure, and SpO_2 were recorded. Subarachnoid block was performed in sitting position, under aseptic conditions with a hyperbaric Bupivacaine 0.5%, 2cc (10mg) using 25 gauge Quincke's needle. Group E received Ephedrine 3mg and Group M received Mephentramine 3mg prophylacticaly immediately after subarachnoid block.Blood pressure and pulse rate were measured every minute until the delivery, then every 5 minutes till the end of surgery. APGAR score were noted to assess the fetal outcome. Patient were monitored for 2 hours in the post operative recovery room soon after surgery for any untoward complications.

Results: Mephentermine significantly increases the systolic blood pressure, mean arterial pressure and reduces the heart rate compared to Ephedrine.

Conclusion: Maintenance of SBP between 'hypotension value' and baseline value by carefully titrating the vasopressor results in a satisfactory fetal outcome. Both ephedrine and mephentermine are equally efficacious for the management of maternal hypotension in terms of frequency of usage and result in a similar neonatal outcome. Our results suggest that Mephentermine increases the systolic blood pressure and decreases heart rate compared to Ephedrine and therefore more potent for management of hypotension before delivery of the baby during spinal anaesthesia in patients undergoing elective Caesarean section.

Keywords: Ephedrine; Mephentermine; Subarachnoid block; APGAR score; Caesarean section.

Introduction

Anesthesia to pregnant women is very unique and demands highest degree of care because it involves two lives, the mother and foetus. In elective caesarean section under subarachnoid block nearly 85% mothers will have hypotension recorded.[1] This recorded hypotension will have detrimental effect on both mother and foetus. This hypotension will cause decreased uteroplacental blood flow, impaired foetal oxygenation with asphyxia stress and acidosis. Mothers will develop symptoms of low cardiac output such as nausea, vomiting, dizziness and decreased consciousness.[2] In literature we have sufficient methods to prevent and manage hypotension during subarachnoid block. Initially careful positioning with left uterine displacement and volume preloading with crystalloids or colloids were used to prevent hypotension. Many times vassopressors are required to correct hypotension quickly during subarachnoid block.[3]

These are the two commonly used definitions for hypotension. Firstly hypotension defined as a decreased in arterial pressure greater than 20% from baseline systolic pressure. Secondly combination of two criteria i.e a drop of systolic bloods pressure to 100mm Hg or lower and a drop to 80% from baseline or lower.[4]

Vassopressors are group of drugs used to treat hypotension by contracting blood vessels and raise blood pressure.[5] Ephedrine, Mephentermine, Phenylepherine, Metaraminol and Methoxamine are commonly used vassopressors to treat hypotension in subarachnoid block.

In following study we have compared the efficacy of Ephedrine and Mephentermine prophylactically in managing hypotension for caesarean section under subarachnoid block and their undesirable side effects. This study is a double blinded prospective randomized control study to evaluate the efficacy of prophylactic use of Ephedrine and Mephentermine in caesarean section to manage hypotension under Subarachnoid block. The incidence of undesirable side effects and neonatal outcome in terms of Apgar score were also studied.

Aim of the study

To compare the efficacy of Ephedrine and Mephentermine in the management of hypotension during subarachnoid block for cesarean section based on the following parameters

1. Efficacy of vasopressors in managing hypotension
2. Incidence of undesirable side effects
3. Effects on neonatal outcome (APGAR score).

Materials and Methods

This double blind prospective randomized control study was designed to evaluate the efficacy of prophylactic use of Ephedrine and Mephentermine in managing hypotension during subarachnoid block for cesarean section done during the period of 2018 -2019 in our institute. After obtaining ethical committee clearance and written informed consent 60 cases were taken.

Inclusion criteria:

1. Full term elective singleton parturient,
2. weighing less than 90 kg,
3. height between 150 – 160cms (classified as American Society of Anesthesiologists status II).

Exclusion criteria:

1. Patients with severe pre-eclampsia, epilepsy, gestational diabetes, precious pregnancy
2. Emergency LSCS with fetal distress

Patients were divided randomly into 2 groups (E group and M group) of 30 each. Patients were pre medicatated with inj. Pantaprazole 40mg and inj. Metoclopramide 10 mg and pre loaded with ringer's lactate at 10ml/kg infusion before surgery. Baseline pulse rate, blood pressure, and SpO_2 were recorded. Subarachnoid block was performed in sitting position under aseptic conditions with a hyperbaric Bupivacaine 0.5%, 2cc (10mg) using 25 gauge Quincke's (BD, Becton Dickenson, Madrid, Spain) spinal needle in L3_4 intervertebral space.

Group E received Ephedrine 3mg and Group M received Mephentramine 3mg prophylacticaly immediately after subarachnoid block.

This study was done in a prospective double blind randomized manner. The investigator was blinded to the content of envelope and decoding was undertaken at the end of the surgery. After intrathecal injection, upper level of sensory block was assessed by loss of pinprick sensation. Assessment of the block height was made and recorded at the time of skin incision, 5min and 10min. The target level of sensory anesthesia (block height) was up to T-5 segment. The surgery was asked to commence after obtaining the said level.

Blood pressure and pulse rate were measured every minute until the delivery, then every 5 minutes till the end of surgery. APGAR scores

were noted to assess the fetal outcome. Patients were monitored for 2 hours in the post operative recovery room soon after surgery for any untoward complications.

Statistical analysis:

Analysis of the present study was made using the following parameters.

1. Percentages
2. The arithmetic mean (m or x)
3. The standard deviation (SD)
4. Student's test
5. Proportion test.

The results of continuous variables are presented as mean ± SD and proportion as percentage. The difference between the two groups was assessed by Student's test and Chisquare test. For all the tests, a $P \leq 0.05$ was considered statistically significant.

Results

60 pregnant patients were divided into two groups of 30 each in this study. (Table 1).

Table 1: The two groups were comparable with respect to age and BMI and were statistically insignificant.

Variable	Group E	Group M	P Value
Age	25.53±3.51	24.9±2.78	O.99
Bmi	28±1.7	29±1.17	0.46

Statistical analysis of changes in heart rate at different time intervals in both the study groups is presented (Chart 1 and Table 2).

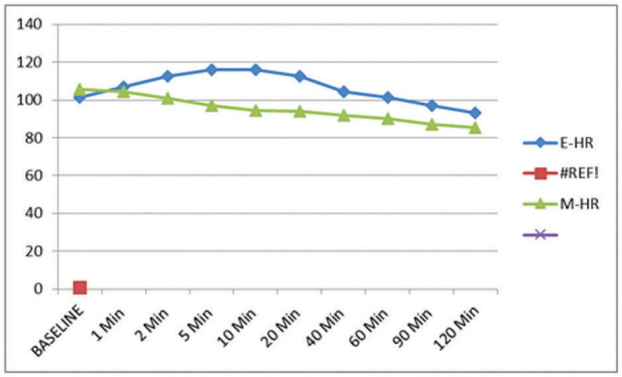

Chart 1: Analysis of heart rate (HR).

There was statistically significant increase in heart rate response after giving study drug in group E when compared to group M at time intervals of 2nd, 5th, 10th, 20th, 40th and 60th minute and it was statistically significant.

Statistical analysis of changes in systolic blood pressure at different time intervals in both the study groups is presented (Table 3).

No significant variations were noted in both the groups in SBP at baseline, 1st and 2nd minute after giving study drug.

But there was increase in SBP in group M at different at 5, 10, 20, 40 and 60 time intervals and it was statistically significant.

Table 2: Analysis of heart rate (HR).

HR	Baseline	1 min	2	5	10	20	40	60	90	120
Group E Mean ±SD	101.1±5.98	107.1±5.18	112.4±4.23	115.8±3.45	116±3.7	112.4±3.97	104.4±3.57	101.2±4.16	96.96±4.46	93.13±4.72
Group M Mean ±SD	105.4±5.74	104.4±5.45	101±6.16	97.13±6.3	94.6±6.39	94.13±5.58	92±5.45	90±5.18	87.3±5.26	85.33±4.46
P Value	0.006	0.06	1.45E–11	1.45E–20	9.52E–23	4.62E–21	6.09E–15	5.6E–13	2.18E–10	1.54E–08

Table 3: Analysis of systolic blood pressure (SBP).

SBP	Baseline	1 min	2	5	10	20	40	60	90	120
Group E Mean±SD	115.26±8.49	109±7.85	103.13±10.57	93.03±4.9	96.66±6.55	102±6.14	105.46±4.5	109.53±5.55	111±4.71	112.4±4.88
Group M Mean ±SD	116.53±9.86	110.2±10.75	104.86±10.91	95.16±12.4	105.53±9.16	108.7±6.77	110.66±6.68	112.06±5.9	113.1±6.39	113.33±7.26
P Value	0.596	0.64	0.53	0.38	6.43E–05 (<0.05)	0.0001	0.0008	0.092	0.15	0.56

Table 4: Analysis of diastolic blood pressure (DBP).

DBP	Baseline	1 min	2	5	10	20	40	60	90	120
Group E Mean±SD	67.33±4.67	62.4±4.59	56.5±6.32	50.86±3.04	54.4±4.91	57.06±5.4	56.6±3.59	59.2±4.5	63.13±6.06	65.6±5.529
Group M Mean ±SD	67.06±6.208	62.33±6.26	57±7.38	52.46±5.47	55.33±5.44	56.53±4.48	57.76±4.04	61.4±6.14	63.2±5.93	64.66±5.78
P Value	0.851	0.96	0.79	0.167	0.488	0.67	0.24	0.108	0.96	0.496

Table 5: Analysis of mean arterial pressure (MAP).

Map	Baseline	1 Min	2	5	10	20	40	60	90	120
Group E Mean ±SD	80.6±8.8	77.5±5.39	71.6±7.57	64.6±3.21	68.3±4.89	71.7±5.53	72.6±3.56	75.6±4.35	78.76±5.19	81.53±4.43
Group M Mean ±SD	82.4±8.14	78.13±7.8	72.6±8.47	66.16±7.7	73.03±8.24	73.5±4.76	75.3±5.602	77.9±5.33	79.43±5.41	80.93±5.47
P Value	0.43	0.73	0.63	0.329	0.009	0.166	0.0298	0.064	0.628	0.642

Statistical analysis of changes in diastolic blood pressure at different time intervals in both the study groups is presented (Table 4).

No significant variations in DBP between the two groups were noted.

Statistical analysis of changes in mean arterial pressure at different time intervals in both the study groups is presented (Table 5).

No significant variations were noted in MAP in both the groups at baseline, 1st to 5th minute.

There was slight increase in MAP in group M compared to group E from 10th to 40th minute and it was statistically significant.

Table 6: Analysis of APGAR score and efficacy of vasopressors

Variable	Group E	Group M	P value
APGAR score at 1 minute	8	8	
APGAR score at 5 minute	9	9	
Frequency of usage of vasopressor	1.066±0.5208	1.033±0.49	0.799

According to the above findings, APGAR score remains same in both the groups. (Table 6).

Similarly, both the vasopressors are equally efficacious in managing hypotension.

Discussion

In caesarean section under subarachnoid block hypotension can be minimized by the use of IV fluid preload, avoidance of aortocaval compression and use of vasopressor agents. It's been well documented that percentage decrease in placental perfusion is directly related to percentage reduction in maternal arterial pressure and not to the total reduction of pressure.[6]

Since many decades in India Mephentermine has been used to prevent hypotension during cesarean section under subarchanoid block. But there is lack of literature regarding its dose and relative potency compared with other vasopressors.

In 1978, Lauckner et al used Mephentermine 30 mg IV to treat hypotension in pregnant females,[7] whereas the drug information by Wyeth® India gives a dose of 30 to 45 mg intramuscularly for prevention and 30 to 45 mg IV infusion for treatment of post-spinal hypotension.[8] Other doses used are 6 mg boluses[9] and 5 mg bolus followed by an infusion.[10]

On other hand Ephedrine is a potent sympathomimetic drug that has both α-and β-adrenergic agonist actions and acts directly and indirectly at adrenergic nerve endings. Cardiac stimulation is a more prominent action, so that the blood pressure and cardiac output are increased.[11]

Ephedrine is the most commonly used drug to treat hypotension associated with subarachnoid block in obstetrics. According to a survey, Ephedrine is used as the sole vasopressor by 95% of consultant obstetric anesthetists in the UK.[12]

Recently, there have been reports of worsening fetal acidosis with the use of ephedrine,[13] and demonstrating better outcomes with other vasopressor drugs like angiotensin II,[14] phenylephrine[15] and metaraminol.[16]

The mechanism of action for ephedrine and Mephentermine is similar. Both drugs have α and β-adrenergic agonist action, direct and indirect effects at adrenergic nerve endings. But effect on β-receptors is more prominent.

Despite similar actions, the studies comparing efficacy and potency of these vasopressor drugs have yielded variable results. During early studies Mephentermine was reported to be as potent as Ephedrine with respect to its effect on total vascular and venous resistance in the perfused foreleg of the dog,[17] whereas it was found to be more potent than other agents including Ephedrine for restoring the contractility of depressed and hypodynamic isolated frog heart.[18]

Very few clinical studies have compared efficacy of Ephedrine and Mephentermine.

Sahu et al[9] compared 6mg bolus doses of Ephedrine and Mephentermine following onset of hypotension and observed similar requirements for both drugs for maintenance of arterial pressure. The apparently lower requirements of

Mephentermine due to longer half time period compared to Ephedrine. The half-life period of Ephedrine is three to six hours[19,20] whereas that of Mephentermine is 17 to 18 hours.[21]

The important complication of spinal anesthesia is hypotension hence prompt effective treatment is considered essential to prevent fetal acidaemia. The results of our study indicate that Mephentermine is as effective as ephedrine in maintaining maternal arterial pressure during spinal anesthesia and both drugs have similar effects on neonatal outcome. Similar results with regards to maternal haemodynamics and neonatal Apgar scores have been reported by Sahu et al.[9]

According to our study, Mephentermine significantly increases the systolic blood pressure and reduces the heart rate compared to Ephedrine due to reflex bradycardia.[22] In terms of efficacy i.e frequency of usage, both are equally efficacious in managing hypotension under subarachnoid block with good neonatal outcome and no side effects such as nausea, vomiting and decreased consciousness.

Conclusion

Maternal hypotension should be aggressively managed to reduce the risk of fetal acidosis. We have noted definite correlation maximum decrease in SBP as percentage of baseline and umbilical arterial pH. Hence maintenance of SBP between 'hypotension value' and baseline value by carefully titrating the vasopressor results in good fetal outcome.

Both Ephedrine and Mephentermine are equally effective for the management of maternal hypotension and has similar neonatal outcome. Our results suggest that Mephentermine increases the systolic blood pressure and decreases heart rate compared to Ephedrine and therefore more potent for management of hypotension before delivery of the baby during spinal anesthesia in patients undergoing elective Caesarean section.

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Conflict of Interest: There are no conflicts of interest.

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