ORIGINAL RESEARCH PAPER

Anaesthesiology

COMPARISON OF SAFETY AND EFFICACY OF INTRAVENOUS PHENYLEPHRINE OR INTRAVENOUS EPHEDRINE FOR CONTROL OF HYPOTENSION FOLLOWING SPINAL ANAESTHESIA GIVEN FOR ELECTIVE CAESAREAN SECTION

KEY WORDS:

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ABSTRACT

Background : Central neuraxial anesthesia remains the preferred choice for Lower segment Caesarean sections. Hypotension is an important side effect of spinal anesthesia and should be treated promptly and aggressively to minimize and avoid futher complications like ischmeic injury to vital organs like kidney, cardiac ischemia and brain injury. Vasopressors are of inestimable value in preventing and correcting hypotension caused by subarachnoid block. Also it has been found that the two vasopressors phenylephrine and ephedrine in intravenous bolus form, are effective in maintenance of arterial pressure within 20% limit of baseline. Hence the current study was undertaken to compare the vasopressors like ephedrine and phenylephrine for maintenance of blood pressure during spinal anaesthesia **Material and Methods:** Prospective Observational Comparative Clinical study was undertaken at tertiary care centre aster taking the Ethecis committee approval. Total of 100 parturient women between 18-36years ASA Grade I and II undergoing elective cesarean sections under spinal anaesthesia were included.. They were divided into two groups; Group P received Injection Phenylephrine 100 g OR group E who received Injection Ephedrine 6 mg after hypotension following spinal anaesthesia. Vital parameters were monitored at baseline and then every 2 mins for first 10 mins and every 5 mins after that till 30 mins and then every 15 mins till 60min. **Results and Analysis** : There was no statistically significant difference in both groups in pulse rate from 0 min to 6 min whereas from 8 min to 20min, pulse rate with ephedrine was significantly higher than phenylephrine ($p<0.05$). From 25min to 60min, there was no difference in two groups. There was no significant difference in SBP in two groups from 0min to 20min ($P>0.05$). However, at 25min , 45 min and 60 min mean SBP was significantly higher in Ephedrine group than Phenylephrine group ($P<0.05$). There was no significant difference in in DBP in both the groups. At 45 minutes, mean MAP in Ephedrine group was significantly higher than in Phenylephrine group. RR was slightly less in group-E compared with group-P i.e. ($P<0.05$). In 9 (18%) patients second dose of ephedrine was repeated but no patient required repeat dose of phenylephrine. Incidence of adverse events was similar in both groups. A total of 6(12%) and 3(6%) babies required NICU admission in Ephedrine and Phenylephrine group respectively.There was no significant difference in the time required for delivery of babies in both groups ($P>0.05$) **Conclusion:** Intravenous bolus administration of both Phenylephrine and Ephedrine is effective for controlling hypotension in females receiving spinal anaesthesia for caesarean section. More patients in Ephedrine group required repeat dosing. Incidence of adverse event was similar in both groups, but NICU admission rate was more in Ephedrine group

INTRODCTION

Elective delivery of a baby by abdominal route to a fully awake and a conscious mother is a most rewarding and exiciting experience in medicine With increasing incidence of LSCS the anaesthetist is trapped in a delicate web of decision making regarding the type of anaesthesia to be employed for the safety of the mother and the baby. In the recent decade there has been a shift in obstetrics anaesthesia in favour of regional anaesthesia as against GA with SA being the most popular among them. Central neuraxial anesthesia remains the preferred choice for Caesarean deliveries across the world as it offers a fast, profound and high quality sensory and motor block[1] The simplicity of the technique, reliable effect and lack of all those complications that are associated with GA has made it a safe alternative to general anaesthesia[2] It has been reported that the fatality rate directly attributed to anaesthesia was approximately 17-fold more frequent with general anaesthesia as compared to regional anaesthesia.[3]In elective caesarean section under spinal anaesthesia hypotension has been reported in as many as 85% of patients [4]. Hypotension during spinal anesthesia for caesarean delivery can have detrimental effects like decreased utero placental blood flow, impaired foetal oxygenation with asphyxial stress and foetal acidosis and maternal symptoms of low cardiac output such as nausea, vomiting, dizziness and decreased consciousness, cardiac ischemia ,injury to vital organs like kidney. This can lead to dizziness and vomiting .[5-8] Therefore there has been much attention in the literature to methods of preventing and treating hypotension in obstetric anaesthesia.The hypotension following spinal block is primarily due to preganglionic sympathetic blockade resulting in vasodilation and pooling of blood which reduces the cardiac preload and hence the cardiac output. To add to this supine hypotension syndrome due to aortocaval compression caused by gravid uterus could deteriorate the hemodynamic effect of SA[9-10] .Patient leg elevation, head down tilt and use of pressure stockings augment venous return and increase cardiac output and may be sufficient to restore blood pressure to an acceptable level.[11] Manual uterine displacement and pelvic tilt have been used in maternal hypotension during spinal anaesthesia for LSCS .Volume expansion can be done with crystalloids but 75% of it diffuses into the interstitial spaces so its effect is only transient. Some of these problems may be decreased by the use of smaller volumes of colloid solutions.[14] but their administration is fraught with its own risks and disadvantages. Albumin 5% is probably the most effective colloid solution but it is expensive and not universally available.[15] Other colloids have been shown to be less effective than albumin and also carry a risk of significant anaphylactic reaction.[16]

The higher molecular weight dextrans and hydroxyethyl starch (HES) solutions cause an increase in plasma viscosity, red cell aggregation, coagulopathy which is thought to be associated with increased blood loss after surgery.[17] Thus most of the strategies for decreasing the incidence of hypotension during spinal anaesthesia have proved far from being satisfactory or reliable. This has shifted the focus to various vasopressor agents for the prevention as well as treatment of spinal block induced hypotension. Also it was found that the two vasopressors phenylephrine, ephedrine in intravenous bolus form, are effective in maintenance of arterial pressure within 20% limit of baseline although phenylephrine has quicker peak effect in comparison to ephedrine.[23] Thus it is clear that the absolute supremacy of one vasopressor over the others has not yet been established

unequivocally, though arguments have been extended in favour of each vasopressor from time to time. Hence this prospective clinical observational study was conducted to evaluate the efficacy of Ephedrine and Phenylephrine in treating hypotension during spinal anaesthesia for cesarean section.

Aims And Objectives Primary-

1. To compare the **Efficacy** of Phenylephrine and Ephedrine in management of spinal anaesthesia induced hypotension in elective LSCS
2. To compare the **Safety** of Phenylephrine and Ephedrine in spinal anaesthesia induced hypotension in LSCS

Secondary:

To compare the APGAR SCORES and NICU Admission if required in both the groups

MATERIAL AND METHODS

The Prospective observational comparative clinical study was performed at a Tertiary care centre during the period of 2018 to 2020 after institutional Ethics committee approval . Informed consent was obtained from 100 ANC patients with ASA I/II status, scheduled for elective LSCS under spinal anesthesia *50 patients in Group E and 50 patients in Group P* .Each patient was assigned to one of the two study groups. The Group E received 1 ml ephedrine, 30 mg diluted to 5ml with normal saline I.e 6mg/ml if hypotension is present. The Group P was given 1 ml phenylephrine, 1 mg diluted to 10 ml, with normal saline I.e 100 mcg/ml if hypotension is detected. *Blood pressure, oxygen saturation, pulse rate, and respiratory rate was monitored every 2 min for the first 10 min, every 5 min from 10 to 30 min and every 15 min from 30 to 60 min. Time of baby extraction, vasopressor administration and duration of surgery was recorded. Neonatal monitoring was performed by attending neonatologist at 1 and 5 min using APGAR score & the number of babies requiring NICU was recorded.* In the post operative period each patient was monitored in the recovery room for 2 hours Prior to surgery each patient was examined and a thorough medical history taken with emphasis on respiratory and cardiovascular systems.

Inclusion Crieteria :

- All uncomplicated pregnancies aged 18 to 40 requiring elective LSCS for foetal indications/ maternal issues like Cephalopelvic disproportion, or history of previous one or 2 LSCS. Patient under ASA 1 and ASA2 and willing to give the consent

Exclusion Crieteria

Patients with ASA 3 or more,Patients with significant coagulopathies and other contra-indications for spinal anaesthesia ,Patient on any opioid or sedative medication and other medical complicaations like Hypertension & Pre-eclampsia or Pulmonary tuberculosis

RESULTS AND ANALYSIS

Measurement data for the pulse rate, blood pressure systolic ,diastolic and Mean arterial pressure respiratory rate and SPO2 was expressed as means with standard deviation (SD).Similarly, change from the baseline is computed for all measurement variables and expressed as means with standard deviation (SD). Differences between the two groups (Phenylephrine and Ephedrine) are computed for each variable at each time point and presented as means with 95% confidence intervals (C.I.).Categorical data and discrete data are expressed as numbers with percentages proportions).

The demographic profile of the patients in the study group was as follows :There was no statistically significant difference in the age of patients in both groups P>0.05.(Application independent T test or Unpaired T Test)

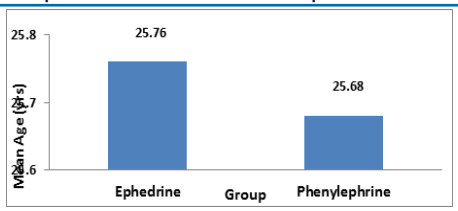

Figure 1: Comparison of age in Ephedrine and Phenylephrine group

Ephedrine group and Phenylephrine group.

There was no statistically significantt difference in both groups from 0 min to 6 min whereas from 8 min to 20min there was some variation i.e. statistically significant at 5% level i.e., P<0.05. During this time, pulse rate with ephedrine was significantly higher than phenylephrine. However, these changes were not clinically significant. Later on, from 25min to 60min, there was no difference in two groups. (Application independent T test or Unpaired T Test)

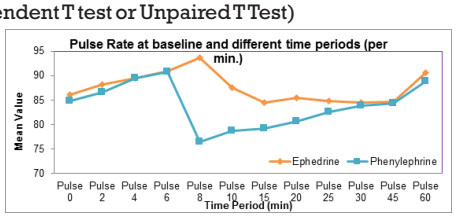

Figure 2: Comparison of pulse rate between Ephedrine and Phenylephrine groups

Figure 4 shows DBP of patients in both groups from 0min to 60min. There was no difference in two groups. i.e.,P>0.05. (Independent T test or Unpaired T Test)

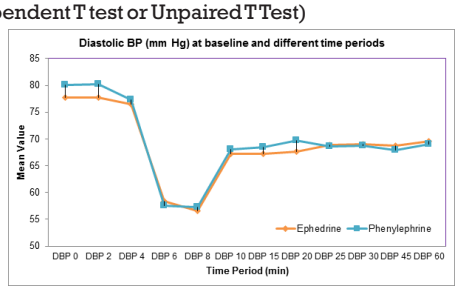

Figure 4: Comparison of DBP (Timing from 0 min to 60 min) between Ephedrine and Phenylephrine group

Figure 5 shows MAP patients in both groups at all time periods from 0min to 60min. There was no significant difference in both the groups at all time points except at 45 min (P>0.05; independent T test or Unpaired T Test). At 45 minutes, mean MAP in Ephedrine group was significantly higher than in Phenylephrine group

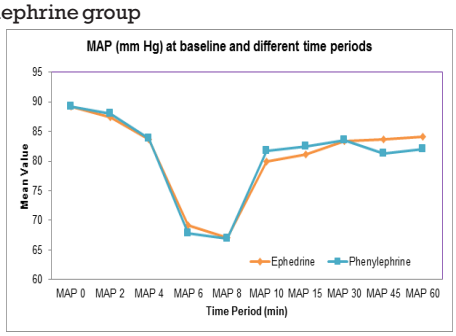

Figure 5: Comparison of MAP (Timing from 0 min to 60 min) between Ephedrine and Phenylephrine group

Figure 6 shows comparison of time for vasopressor requirement. There was no significant difference between two groups (P>0.05). *For comparison between qualitative or countable parameters between two groups non-parametric test Mann-Whitney U test {Wilcoxon rank sum test} was used.*

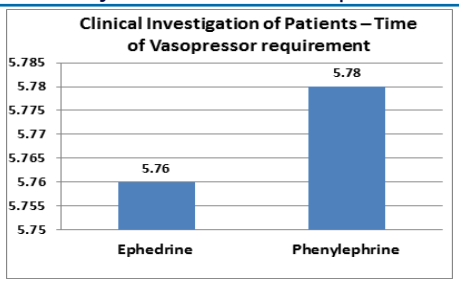

Figure 7 : Showing time of Vasopressor Administration

Figure 8 shows number and percentage of patients who required second dose of vasopressor. In 9 (18%) patients second dose of ephedrine was repeated but no patient required repeat dose of phenylephrine.

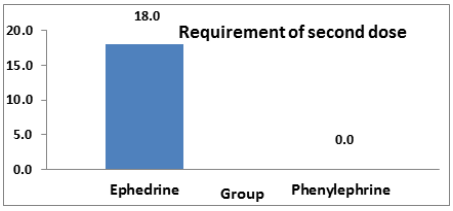

Figure 8: Requirement of second dose of vasopressor

Figure 9 shows adverse evens in two groups. In group-E , only 1 (2.0%) patient had nausea. Combined nausea & vomiting was seen in 4(8%) whereas shivering was observed in 5(10%) patients. In Phenylephrine group, combined nausea& vomiting was seen in 2(4%) patients. Headache was reported by 5(10%) patients. Headache with shivering was observed in 1(2%) patient.Two 2(4%) patients reported sweating

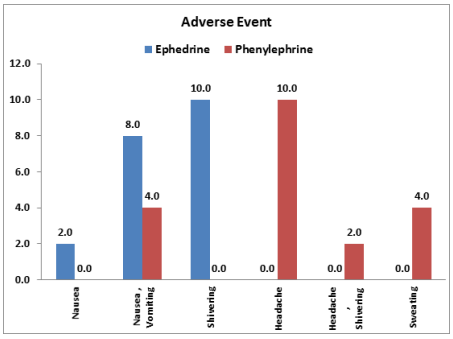

Figure 9 : Comparison of adverse events between Ephedrine and Phenylephrine group

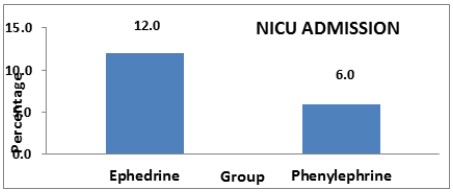

Figure 10: Comparison of NICU Admission in two groups

The incidence of undesirable side effects and neonatal outcome in terms of Apgar score,which is the surrogate clinical marker for foetal acidosis were also studied

DISCUSSION

Spinal anesthesia is widely used as the procedure of choice for cesarean delivery. In comparison to epidural anesthesia it is faster, easier to perform, patients are more comfortable, complication rates are lower, and it is more cost effective. Spinal anesthesia is routinely used in elective cesarean sections. However, hypotension resulting from sympathectomy is a common problem especially in pregnant women.Spinal block causes peripheral vasodilation and venous pooling which may result in maternal hypotension .Incidence of maternal hypotension after spinal anesthesia for cesarean delivery without prophylactic measures is very high almost 80%-100%.

Even though highly investigated, spinal induced hypotension remains a major concern and it has been referred to as the "Holy Grail" of obstetric anesthesia.The detrimental effects of the spinal induced hypotension are both maternal and fetal. Maternal effects are nausea, vomiting and dizziness Fetal detrimental effects are due to reduced uterine and intervillous blood flow with potential fetal hypoxia and acidosis.

Ephedrine was the first agent to be used successfully to treat hypotension induced by spinal anaesthesia.[18] However, the prophylactic administration of ephedrine in central neuraxial blockade is no longer advocated due to its variable absorption when used intramuscularly or subcutaneously and potential for causing reactive hypertension.[19] The role of ephedrine has been challenged because of potential complications like supraventricular tachycardia, tachyphylaxis and fetal acidosis.[20]. Intravenous bolus of 0.07 mg/kg of ephedrine is slightly more potent in restoring the mean arterial pressure MAP and the diastolic arterial pressure DAP. In other study it was concluded that phenylephrine infusion is associated with a lower incidence of fetal acidosis and maternal nausea and vomiting than ephedrine infusion.[21] but has been associated with bradycardia.[22]

Vasopressors are prefered drugs used to treat fall in BP.t where phenylephrine has become the drug os choice . Due to the absence of definitive evidence showing absolute clinical benefit of one over the other, especially in emergency and high-risk Caesarean sections choice of phenylephrine over the other vasopressors like ephedrine is guided by indirect evidence on fetal acid-base status. Routinely, vasopressors such as ephedrine and phenylephrine have been given prophylactically and preoperatively to combat maternal hypotension. Until recently, ephedrine has been the vasopressor used most often as it reliably prevents maternal hypotension[1]. Conversely, ephedrine has been implicated in lower umbilical pH levels, especially when used in high doses to treat hypotension [24-25]. Recent studies have indicated a decrease in side effects related to vasopressors, such as nausea and vomiting, and increased uteroplacental blood flow with the use of phenylephrine [26-29] Peak was reached earlier with Phenylephrine in comparison to Ephedrine and Mephentermine but it resulted in decreased heart rate which may be useful in patients with tachycardia Atropine is widely used to treat bradycardia , atropine given intravenously 1 min after SA shows a dose-dependent increase in heart rate[30]. All the three vasopressor had no significant adverse effects on neonatal outcome.[31]

Summary

Spinal anaesthesia is a popular technique for caesarean section. It however has the greatest disadvantage of causing rapid onset of maternal hypotension which may have detrimental maternal and neonatal effects. Thus, several strategies for treating hypotension have been investigated. Careful positioning and volume preloading with crystalloid or colloids have been used to prevent it, but these are not complete measures and vasopressor is required to correct hypotension quickly for better neonatal outcome.

We undertook a study to compare the efficacy of administration of IV bolus of two vasopressors i.e. Phenylephrine and Ephedrine for management of maternal hypotension during spinal anaesthesia in caesarean section. This prospective clinical observational comparative study was conducted on 100 parturient women undergoing caesarean sections under spinal anaesthesia.

Overall Ephedrine resulted in higher pulse rate at some points of time than Phenylephrine.The SBP and DBP were well maintained in both the groups. Requirement of repeat dose of

Ephedrine was more. No patient in Phenylephrine group received repeat dose. Incidence of adverse events in mothers receiving Phenylephrine and Ephedrine were almost similar. NICU admission requirement was more in patients receiving Ephedrine.

In summary, we found that the intravenous bolus of Ephedrine 6 mg and Phenylephrine 100 mcg were equally effective when given for hypotension following spinal anaesthesia without significant adverse effects on both mother and fetus. Phenylephrine may cause bradycardia which is amenable to treatment with Atropine.

The following can be summarized

- Intravenous bolus doses of Phenylephrine 100 mcg and Ephedrine 6 mg adequately corrected maternal hypotension following spinal anaesthesia in elective caesarean section.
- Phenylephrine administration may result in lower heart rate than Ephedrine, which can be corrected with injection atropine
- Repeat doses of Ephedrine were required in more patients
- No patient required repeat doses of phenylephrine
- More number of babies in Ephedrine required NICU care
- Both the drugs had similar incidence of adverse effects in the mother following spinal anesthesia for caesarean section.

CONCLUSION

Both the drugs:Phenylephrine and Ephedrine are efficient and equally safe in spinal anaesthesia induced hypotension in LSCS without adverse effects on Apgar Scores and NICU in management of spinal anaesthesia induced hypotension in elective LSCS

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