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COMPARATIVE EVALUATION OF PHENYLEPHRINE, EPHEDRINE, AND MEPHENTERMINE FOR MANAGEMENT OF SPINAL ANAESTHESIA-INDUCED HYPOTENSION IN CAESAREAN SECTION: A RANDOMIZED DOUBLE-BLIND STUDY

Anaesthesiology

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ABSTRACT

Background: Spinal anaesthesia is widely preferred for caesarean section because of its rapid onset, reliability, and minimal fetal drug exposure, but maternal hypotension remains its most frequent complication and may impair uteroplacental perfusion and neonatal acid-base status (Corke et al., 1982; Rout & Rocke, 1994).**Aim:** To compare phenylephrine, ephedrine, and mephentermine in the management of spinal anaesthesia-induced hypotension during caesarean section. **Methods:** Ninety-nine ASA II parturients aged 18–35 years who developed hypotension after spinal anaesthesia were randomized into three groups (n=33 each) to receive ephedrine 6 mg, mephentermine 6 mg, or phenylephrine 100 µg intravenously as bolus doses. Hypotension was defined as systolic blood pressure with a fall of at least 20% from baseline. Primary outcome was the number of hypotensive episodes. Secondary outcomes included number of vasopressor boluses, maternal heart rate changes, side effects, Apgar scores, and umbilical arterial pH. **Results:** Mean hypotensive episodes were significantly higher in the mephentermine group than in the phenylephrine and ephedrine groups (p=0.03). Phenylephrine required more repeat boluses (p=0.008). Umbilical arterial pH was significantly higher with phenylephrine than with mephentermine and ephedrine (p=0.001), while Apgar scores and maternal side effects were comparable among groups. **Conclusion:** All three drugs were effective, but phenylephrine provided better haemodynamic control and superior neonatal acid-base status, supporting its use as the preferred vasopressor during caesarean section under spinal anaesthesia (Cooper et al., 2002; Ngan Kee, 2010).

KEYWORDS

Spinal anaesthesia, caesarean section, hypotension, phenylephrine, ephedrine, mephentermine

INTRODUCTION

Spinal anaesthesia is the technique of choice for caesarean section because it provides rapid, dense surgical block while allowing the mother to remain conscious and minimizing neonatal exposure to systemic anaesthetic agents (Pernoll & Mandell, 1995; McCrae & Wildsmith, 1993). Despite these benefits, spinal anaesthesia-induced hypotension remains common, with reported incidence as high as 70–85% when preventive measures are not used (Rout & Rocke, 1994; Riley et al., 1995).

The main mechanism of hypotension is sympathetic blockade, which causes vasodilatation, venous pooling, reduced venous return, and decreased cardiac output (Wright & Shnider, 1993). In pregnancy, this is worsened by aortocaval compression from the gravid uterus. Because uteroplacental circulation lacks autoregulation, even brief maternal hypotension may reduce fetal oxygen delivery and cause fetal acidosis (Corke et al., 1982; Eloner et al., 1960).

Fluid loading alone is often insufficient to prevent hypotension, so vasopressors remain the cornerstone of treatment (Jackson et al., 1995; Karinen et al., 1995). Ephedrine has long been used in obstetric anaesthesia, but increasing evidence links it with lower umbilical arterial pH because of placental transfer and fetal metabolic stimulation (Lee et al., 2002; Cooper et al., 2002). Phenylephrine has emerged as a preferred alternative because it maintains blood pressure effectively and is associated with better neonatal acid-base status (Ngan Kee et al., 2004; Ngan Kee, 2010). Mephentermine is still widely used in India because of its availability and low cost, although direct comparative data remain limited (Kansal et al., 2005; Mahajan et al., 2009).

The present study was conducted to compare phenylephrine, ephedrine, and mephentermine in the treatment of spinal anaesthesia-induced hypotension during caesarean section.

MATERIALS AND METHODS

This prospective randomized double-blind comparative study was conducted in a tertiary care teaching hospital after ethics committee approval and informed consent. Ninety-nine parturients aged 18–35 years, ASA II, with singleton term pregnancy undergoing caesarean section under spinal anaesthesia were included if they developed hypotension after subarachnoid block.

Patients with pre-eclampsia, chronic hypertension, diabetes mellitus, cardiovascular disease, coagulopathy, infection at puncture site, spinal deformity, or failed spinal block were excluded. Sample size was calculated to provide adequate statistical power, and 33 patients were allocated to each group by computer-generated randomization.

Group E received ephedrine 6 mg IV, Group M mephentermine 6 mg IV, and Group P phenylephrine 100 µg IV as bolus doses when hypotension occurred. The study drug was prepared in identical syringes by an anaesthesiologist not involved in data collection, ensuring blinding.

All patients were monitored with ECG, non-invasive blood pressure, and pulse oximetry. Spinal anaesthesia was administered with hyperbaric 0.5% bupivacaine at the L3–L4 or L4–L5 interspace, and patients were positioned supine with left uterine displacement. Hypotension was defined as systolic blood pressure with a fall of at least 20% from baseline.

The primary outcome was the number of hypotensive episodes. Secondary outcomes included number of vasopressor boluses, maternal heart rate response, side effects such as nausea, vomiting, bradycardia, tachycardia, and hypertension, and neonatal outcome measured by Apgar scores and umbilical arterial pH. Data were analysed using one-way ANOVA and Chi-square test, with $p<0.05$ considered statistically significant.

RESULTS

The three groups were comparable in age, weight, gestational age, ASA status, and baseline haemodynamic variables, indicating adequate randomization.

The mean number of hypotensive episodes was significantly higher in Group M than in Group E and Group P (2.1±0.9 vs 1.4±1.1 and 1.2±1.0 respectively; p=0.03). This suggests that mephentermine produced less stable blood pressure control than ephedrine or phenylephrine.

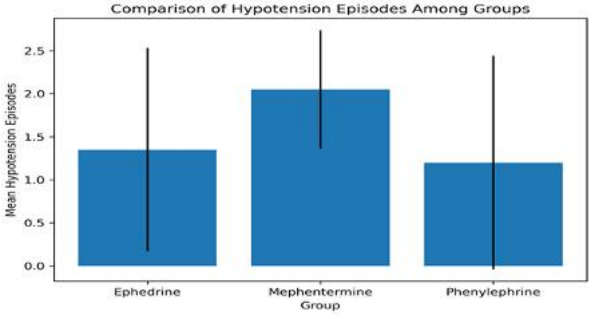

Fig. Hypotension bar graph

The mean number of vasopressor boluses required was significantly higher in the phenylephrine group (1.9±0.6) compared with

mephentermine (1.6±0.8) and ephedrine (1.1±0.4), with p=0.008. This likely reflects the shorter duration of action of phenylephrine, necessitating more frequent titration.

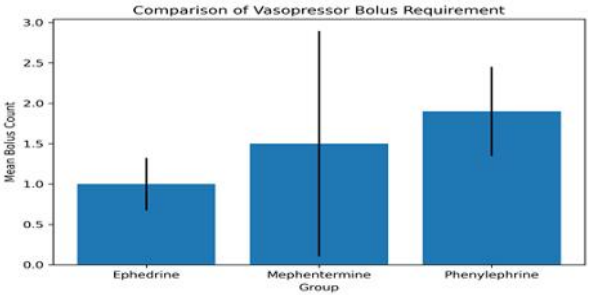

Fig- Comparison of Vasopressor Bolus requirement

Heart rate was lower in the phenylephrine group and higher in the ephedrine group, consistent with their pharmacological actions. However, clinically significant bradycardia, tachycardia, nausea, vomiting, and hypertension were not significantly different between groups.

Apgar scores at 1 and 5 minutes were similar among all groups. Umbilical arterial pH, however, was significantly higher with phenylephrine (7.31±0.02) than with mephentermine (7.27±0.04) and ephedrine (7.24±0.02), with p=0.001. This indicates superior neonatal acid-base status with phenylephrine and is consistent with previous studies comparing phenylephrine and ephedrine.

DISCUSSION

The present study shows that all three vasopressors effectively treated spinal anaesthesia-induced hypotension during caesarean section, but phenylephrine provided better blood pressure stability and improved neonatal acid-base status. Mephentermine was associated with more recurrent hypotension, while phenylephrine required more frequent repeat boluses because of its shorter action.

Ephedrine has historically been preferred because it increases blood pressure mainly by raising cardiac output, and earlier work suggested that this might better preserve uterine blood flow (Ralston et al., 1974). However, more recent clinical evidence has consistently shown that ephedrine is associated with lower umbilical arterial pH than phenylephrine (Lee et al., 2002; Cooper et al., 2002). The present findings support that observation.

Phenylephrine, a selective alpha-1 agonist, increases vascular tone and restores maternal blood pressure without significant placental transfer, which may explain the better neonatal acid-base profile seen in this and other studies (Ngan Kee et al., 2004; Ngan Kee, 2010). Although reflex bradycardia may occur, it was not clinically important in this study.

Mephentermine remains important in Indian anaesthetic practice because of its low cost and widespread availability, but the present study suggests that it may provide less consistent haemodynamic control than phenylephrine and ephedrine. Still, maternal and neonatal outcomes remained acceptable across groups.

The strengths of this study include randomized double-blind design, equal group allocation, and inclusion of umbilical arterial pH as an objective neonatal outcome. Limitations include single-centre design, modest sample size, and use of intermittent bolus dosing rather than infusion techniques.

CONCLUSION

Phenylephrine, ephedrine, and mephentermine are all effective for managing spinal anaesthesia-induced hypotension during caesarean section. However, phenylephrine offers better haemodynamic control and significantly higher umbilical arterial pH without increased maternal adverse effects, making it the preferred vasopressor in this setting (Cooper et al., 2002; Ngan Kee, 2010).

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