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ORIGINAL ARTICLE

Randomized double-blind comparison of ephedrine and phenylephrine for management of post-spinal hypotension in potential fetal compromise

M. Mohta,[a] M. Aggarwal,[a] A.K. Sethi,[a] P. Harisinghani,[a] K. Guleria[b]
[a]*Department of Anaesthesiology and Critical Care, University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi, India*
[b]*Department of Obstetrics and Gynaecology, University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi, India*

ABSTRACT
Background: Most studies comparing phenylephrine and ephedrine have been conducted during elective caesarean sections in healthy mothers with no fetal compromise. The effect of vasopressors on fetal outcome may differ between healthy and compromised fetuses. There has been little research into the effect of phenylephrine and ephedrine, when used for management of post-spinal hypotension in the presence of potential fetal compromise.
Methods: Healthy women with a singleton pregnancy undergoing emergency caesarean section for fetal compromise under spinal anaesthesia were studied. One-hundred-and-six consecutive subjects, who developed hypotension after spinal anaesthesia, were randomly allocated to two groups of 53 each, to receive either phenylephrine (Group P) or ephedrine (Group E). For every systolic blood pressure reading <100 mmHg patients received phenylephrine 100 μg or ephedrine 8 mg depending on group allocation. Umbilical blood gas parameters and Apgar scores were recorded.
Results: There was no statistically significant difference in umbilical arterial pH (P=0.79), umbilical venous pH (P=0.98), other blood gas parameters, incidence of fetal acidosis (P=1.00) and Apgar scores. The number of hypotensive episodes, vasopressor doses for treatment of the first hypotensive episode and the total number of doses used during the study period were comparable. The median [IQR] total number of doses of phenylephrine and ephedrine used before delivery were 2 [1–2] and 2 [1–2], respectively (P=0.67). More patients receiving ephedrine (24.5%) developed tachycardia than those receiving phenylephrine (3.8%) (P=0.004). Bradycardia was more common with phenylephrine, with 39.6% of patients in Group P as compared to only 1.9% of patients in Group E developing a heart rate <60 beats/min after vasopressor administration (P=0.001).
Conclusions: Both phenylephrine 100 μg and ephedrine 8 mg boluses are equally efficacious when treating post-spinal hypotension in the presence of potential fetal compromise. However, phenylephrine may be a better choice in the presence of maternal tachycardia.

Keywords: Ephedrine; Phenylephrine; Spinal anaesthesia; Caesarean section; Fetal compromise

Introduction

For many years, the nonspecific adrenergic agonist ephedrine was the vasopressor of choice for treating post-spinal hypotension in obstetric patients,[1] due to evidence of preservation of uteroplacental circulation.[2] However, ephedrine increases maternal heart rate, myocardial contractility and myocardial oxygen demand and may cause arrhythmias.[3] It can also lead to increased lactate concentration and decreased fetal pH.[4] Previously, animal studies have demonstrated a decrease in uteroplacental perfusion with α-agonists.[2] However, more recent studies have shown that phenylephrine, a pure α-agonist, is safe for managing post-spinal hypotension during caesarean section.[5] Phenylephrine is associated with a higher fetal pH and less incidence of fetal acidosis than ephedrine and is now considered by many as the vasopressor of choice in pregnant patients.[6] However, the use of phenylephrine often is associated with bradycardia[7] and a possible fall in cardiac output.[8]

There are many studies comparing phenylephrine and ephedrine in obstetric patients. However, most have been conducted in elective caesarean sections in healthy patients without fetal compromise.[9] There has been little

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Correspondence to: Dr Medha Mohta, 28-B, Pocket-C, SFS Flats, Mayur Vihar Phase-III, Delhi – 110096, India.
E-mail address: medhamohta@hotmail.com

research comparing phenylephrine and ephedrine for the management of post-spinal hypotension in the presence of actual or potential fetal compromise. In view of the limited available evidence, the present study was conducted to compare phenylephrine and ephedrine for treating maternal hypotension in the presence of fetal compromise in women undergoing emergency caesarean section under spinal anaesthesia.

Methods

This prospective, randomized, double-blind study was approved by the Institutional Ethics Committee – Human Research (IEC-HR), University College of Medical Sciences, University of Delhi. The trial was prospectively registered at http://ctri.nic.in (CTRI/2012/11/003150). Written informed consent was obtained from patients as soon as the decision to perform a caesarean section was made.

American Society of Anesthesiologists grade I or II women with a singleton pregnancy undergoing emergency caesarean section for potential fetal compromise under spinal anaesthesia were studied. Those having a non-reassuring fetal heart rate (FHR) status i.e. FHR >170 or <100 beats/min; FHR deceleration failing to recover after completion of uterine contraction (type-2 dips); meconium-stained liquor with FHR abnormality or thick meconium; cord prolapse; intrauterine growth restriction (IUGR); oligohydramnios; dystocia; placental abruption, placenta praevia; post- and prematurity were included in the study. Patients with maternal complications such as preeclampsia; cardiovascular disease; cerebrovascular disease; multiple gestation; known fetal abnormality; patients with absolute or relative contraindications for spinal anaesthesia; and maternal baseline systolic blood pressure (SBP) <100 mmHg were excluded from the study. Cases with a severely compromised fetus, where immediate administration of general anaesthesia was considered appropriate, were not studied.

Women undergoing caesarean section under spinal anaesthesia for potential fetal compromise were randomized. Of these, 106 patients who developed hypotension after spinal anaesthesia were studied. Patients were randomly divided into two groups of 53 to receive either phenylephrine (Group P) or ephedrine (Group E), using a draw-of-lots technique, according to the vasopressor to be used for treatment of hypotension. Patients in Group P received phenylephrine 100 μg and those in Group E received ephedrine 8 mg, in a volume of 1 mL. The potency ratio of phenylephrine and ephedrine has been calculated as approximately 80:1 so that phenylephrine 100 μg is equivalent to ephedrine 8 mg.[10]

For randomisation and blinding, 106 slips labelled with either phenylephrine or ephedrine (53 for each group) were sealed with adhesive and placed in a container. For each case a slip was taken and the study drug prepared by a person not involved in the study. If the spinal block failed or the patient did not develop hypotension, the study drug was not used and the patient excluded from analysis. Another slip for the same group was sealed and placed in the container by the person who had prepared the study drug. Phenylephrine 100 μg/mL or ephedrine 8 mg/mL were prepared in a 10 mL syringe. One millilitre of the vasopressor solution was injected to treat every SBP value <100 mmHg.

Immediately after the decision to perform a caesarean section, patients received intravenous ranitidine 50 mg and metoclopramide 10 mg. In the operating room, baseline values for maternal heart rate (HR) and SBP were recorded with the patient supine with left uterine displacement. Rapid infusion of Ringer lactate 15 mL/kg was used for coloading beginning at the time of spinal injection. Following this, the rate of intravenous infusion was reduced to keep the vein open. Spinal anaesthesia was performed in the lateral position using a midline approach at L2–3 or L3–4 with a 25-gauge Quincke spinal needle and 0.5% hyperbaric bupivacaine 2.0 or 2.2 mL was injected.

Heart rate and SBP were recorded every minute after spinal injection until delivery of the baby. Post-spinal hypotension was defined as SBP <100 mmHg. Therefore, each SBP value <100 mmHg was treated with either phenylephrine 100 μg or ephedrine 8 mg. The period from onset of hypotension until its correction was considered as one hypotensive episode. Recurrence of hypotension after one or more normal SBP values was considered as the next hypotensive episode. The number of hypotensive episodes, vasopressor doses used to treat the first hypotensive episode and the total number of doses required during the study period were recorded. The number of patients developing a HR <60 beats/min was noted. Significant bradycardia was defined as a HR <50 beats/min. Intravenous glycopyrrolate 0.2 mg was administered if a HR <50 beats/min was associated with hypotension, or the HR was <45 beats/min irrespective of SBP. Tachycardia was defined as a HR >130 beats/min.

The times of uterine incision and delivery of the baby were recorded. Umbilical cord arterial and venous blood samples were drawn for blood gas analysis from a double clamped umbilical cord segment. Apgar scores at 1 and 5 min were also recorded. The study period continued from the time of spinal injection until delivery of the baby. Any complications observed during the spinal anaesthetic technique were recorded and managed appropriately.

The admission of neonates to the neonatal intensive care unit (NICU) for observation and further management was at the discretion of the attending paediatrician. Indications for NICU admission included