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ORIGINAL ARTICLE

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The effects of prophylactic bolus phenylephrine on hypotension during low-dose spinal anesthesia for cesarean section

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ABSTRACT

Background: Continuously infused phenylephrine is frequently used to reduce the incidence of hypotension in women undergoing cesarean section under spinal anesthesia, but less is known about the prophylactic bolus method. We evaluated three prophylactic bolus doses of phenylephrine during low-dose spinal anesthesia for cesarean section.

Methods: One-hundred-and-eighty-four patients were randomized to receive 0.9% saline 2 mL (Control Group) or phenylephrine 1.0 μg/kg (PHE1 Group), 1.5 μg/kg (PHE1.5 Group), or 2.0 μg/kg (PHE2 Group) immediately after induction of combined spinal-epidural anesthesia. Maternal blood pressure and heart rate were recorded at 1-min intervals until delivery. Hypotension, defined as systolic blood pressure <80% of baseline, was treated with rescue doses of phenylephrine 100 μg at 1-min intervals until hypotension resolved. The incidence of nausea, vomiting, bradycardia, and hypertension, as well as Apgar scores and umbilical blood gases, were recorded.

Results: The incidence of hypotension was 71.7% (33/46) in the Control Group, 68.9% (31/45) in the PHE1 Group, 37.0% (17/46) in the PHE1.5 Group and 45.7% (21/46) in the PHE2 Group (P=0.001). The total rescue dose of phenylephrine was greater in the Control Group than those in the PHE1.5 Group (P <0.05) and PHE2 Group (P <0.05). The incidence of hypertension increased as the dose of prophylactic phenylephrine increased (P <0.001) and was highest in the PHE2 group (37%). Other variables did not differ among the four groups.

Conclusions: Under the conditions of this study, prophylactic bolus injection of phenylephrine 1.5 μg/kg was a suitable alternative method for reducing the incidence of hypotension during low-dose spinal anesthesia for cesarean section.

Keywords: Cesarean section; Phenylephrine; Spinal hypotension

Introduction

Spinal anesthesia for cesarean section can avoid the serious maternal complications associated with general anesthesia.[1] However, hypotension after spinal anesthesia is frequent and may have deleterious effects on maternal and fetal outcomes.[2] Phenylephrine may be used to prevent hypotension:[3,4] it improves fetal acid-base balance, increasing fetal pH and reducing PCO_2 when compared with ephedrine.[5–8]

The optimal administration method of phenylephrine, which has a short duration of action, has not been established. Continuous infusions are commonly used and are associated with a very low incidence of hypotension and a reduction in the incidence of nausea and vomiting, even when high-dose spinal anesthetics are used.[9–11] Prophylactic infusion with rescue phenylephrine boluses is effective in maintaining maternal hemodynamic stability, and can also reduce physician interventions compared with rescue boluses alone.[12] However, although continuous infusion is effective and convenient, it requires an infusion pump and appropriately trained personnel. Doherty et al.[13] compared bolus and infusion phenylephrine regimens, and reported that blood pressure was better maintained with boluses, especially in the initial 6 min after spinal anesthesia. Thus, bolus regimens may be effective for early hypotension after spinal anesthesia.

Recently, das Neves et al.[14] reported that the incidence of hypotension after spinal anesthesia was 32.5% in patients who received a prophylactic bolus of

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phenylephrine 50 μg compared with 85% in a group that received phenylephrine as a therapeutic dose only after hypotension occurred. However, a prophylactic bolus of phenylephrine 50 μg is less than the ED95 of 122 μg reported by Tanaka et al.[15]

We hypothesized that an appropriate prophylactic bolus of phenylephrine may reduce the incidence of hypotension during spinal anesthesia for cesarean section. We evaluated the effects of three prophylactic doses of phenylephrine on hypotension, and also assessed hemodynamic adverse effects and neonatal status.

Methods

This prospective, randomized, clinical study included women who were American Society of Anesthesiologists physical status I and II with term singleton pregnancies scheduled for elective cesarean section under combined spinal-epidural anesthesia from September 2012 to January 2013 at the Asan Medical Center. The trial was registered with the Clinical Research Information Service (code number KCT 0001087) and received ethics approval by the Asan Medical Center Institutional Review Board. All patients provided written informed consent. Women were excluded if they had pre-existing or pregnancy-induced hypertension, cardiac or respiratory disease, cerebrovascular disease, fetal anomalies or contraindications to spinal anesthesia.

Patients were randomized to one of four groups by computer-generated random allocation (http://www.randomization.com/). An anesthesiologist not involved in patient care prepared 2 mL solutions in identical syringes, with the contents based on the random allocation. Patients in the Control Group received 0.9% saline 2 mL, whereas patients in the PHE1, PHE1.5, and PHE2 groups received phenylephrine 1.0, 1.5, and 2.0 μg/kg, respectively, diluted to 2 mL with saline.

Premedication of sodium citrate 30 mL and ranitidine 150 mg was given orally on the morning of surgery. Before the induction of anesthesia, an 18-gauge intravenous cannula was inserted without local anesthesia. Standard monitoring (Intellivue MP70; Philips Medizin Systeme, Boeblingen, Germany) was attached, including non-invasive blood pressure, electrocardiogram, and pulse oximetry. With patients in the supine position with left lateral tilt, blood pressure and heart rate were measured three times at 1-min intervals with the average of these three measurements recorded as baseline. Lactated Ringer's solution was infused with a fully opened clamp to a maximum of 2 L from induction to delivery.

Patients were placed in the left lateral decubitus position for the combined spinal-epidural procedure. After skin decontamination and injection of cutaneous local anesthetic, an 18-gauge Tuohy needle was inserted at the L3–4 or L4–5 interspace using a loss-of-resistance technique. The dura mater was punctured with a 27-gauge Whitacre spinal needle using a needle-through-needle technique (Portex®, Smiths Medical International Ltd, Hythe, Kent, UK). After verifying free flow of cerebrospinal fluid, a mixture of 0.5% hyperbaric bupivacaine 7 mg and fentanyl 15 μg was administered over 10 s. After withdrawal of the spinal needle, a 20-gauge multi-orifice epidural catheter was inserted 4–5 cm into the epidural space and the Tuohy needle was removed. The epidural catheter was firmly fixed and patients were immediately positioned supine. If the epidural catheter insertion was considered difficult, without further delay, patients were positioned supine. At the end of intrathecal injection (time 0 min) an anesthesiologist blinded to group allocation administered the intravenous study dose.

Block height was assessed bilaterally using loss of cold sensitivity to alcohol at 5-min intervals for 15 min. If the block height did not reach the T6 dermatome, spinal anesthesia was considered to have failed and epidural top-ups of 2% lidocaine 5 mL were administered to a maximum of 20 mL as required.

Blood pressure and heart rate were recorded at 1-min intervals until delivery. The primary outcome was the incidence of hypotension, defined as systolic blood pressure (SBP) <80% of baseline. Hypotension was treated with rescue doses of phenylephrine 100 μg every 1 min until hypotension resolved. The total rescue dose of phenylephrine administered to each patient was recorded.

Before induction of anesthesia, patients were asked to report any symptoms of nausea or vomiting. To evaluate adverse effects of prophylactic boluses of phenylephrine, the incidence of nausea, vomiting, bradycardia (heart rate <50 beats/min), and hypertension (SBP >120% of baseline) were recorded. Patients who experienced bradycardia concomitant with hypotension were given atropine 0.5 mg. Apgar scores at 1 and 5 min, estimated blood loss, and fluid administration until delivery were recorded. Umbilical cord blood gas analysis was performed to evaluate the possible effects of phenylephrine on the newborn.

Statistical analysis

In a pilot study, the incidence of hypotension during spinal anesthesia in women undergoing cesarean section was approximately 70%. Assuming that prophylactic administration of phenylephrine could reduce the incidence by 50%, power analysis indicated that a minimum of 42 subjects per group would be adequate to detect a difference in the incidence of hypotension, with power of 0.8 and an α error of 0.0083 (0.05/6). The final sample size was increased to 184 patients to accommodate an attrition rate of 10%. Intergroup comparisons of patient characteristics, obstetric data, and additional phenylephrine dose were analyzed using one-way ANOVA or