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ORIGINAL ARTICLE

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Optimal intrathecal hyperbaric bupivacaine dose with opioids for cesarean delivery: a prospective double-blinded randomized trial

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ABSTRACT
Background: Single-shot spinal anesthesia is commonly used for cesarean delivery. Achieving adequate anesthesia throughout surgery needs to be balanced with associated complications. We investigated the optimal dose of intrathecal hyperbaric bupivacaine, co-administered with opioids, for anesthesia for cesarean delivery.
Methods: This prospective, randomized, double-blinded, dose-ranging trial included parturients scheduled to undergo cesarean delivery under spinal anesthesia. An epidural catheter was first inserted at the T11–12 vertebral interspace, followed by spinal anesthesia at the L2–3 or L3–4 vertebral interspace. Subjects were randomly assigned to one of seven doses of intrathecal hyperbaric bupivacaine 0.5% (6, 7, 8, 9, 10, 11 or 12 mg), with added 15 μg fentanyl and 75 μg morphine. Successful induction of anesthesia ($success_{ind}$) was defined as achievement of bilateral sensory loss to cold at the T6 dermatome or higher, within 10 minutes. Successful maintenance of anesthesia ($success_{main}$) was defined by no epidural supplementation within 60 minutes of intrathecal injection. The effective doses for 50% (ED_{50}) and 95% (ED_{95}) of patients were estimated using logistic regression analysis.
Results: The ED_{50} and ED_{95} for $success_{main}$ were 6.0 mg (95% CI: 4.5 to 7.5 mg) and 12.6 mg (95% CI: 7.9 to 17.2 mg), respectively. The incidence of respiratory discomfort and maternal satisfaction scores did not differ significantly between dose groups. Phenylephrine dose and nausea/vomiting incidence increased with increasing doses of bupivacaine.
Conclusion: Under study conditions, our results suggest that 12.6 mg of intrathecal bupivacaine, administered with fentanyl and morphine, is required to achieve adequate intraoperative analgesia without the need for epidural supplemention.

Keywords: Cesarean delivery; Hyperbaric bupivacaine; Spinal anesthesia

Introduction

Spinal anesthesia is commonly used for cesarean delivery. For single-shot techniques, important considerations include the risks of inadequate anesthesia and adverse events such as hypotension. The incidence and severity of hypotension is influenced by the dose of intrathecal local anesthetic administered.[1–3] Several studies have examined the use of low-dose intrathecal bupivacaine.[4–7] However, low-dose bupivacaine may be associated with an inadequate level of anesthesia, so epidural catheterization is often used in conjunction.

Many factors may influence the choice of dose of intrathecal local anesthetic and this may vary across institutions because of variations in patient demographics, surgical duration and use of adjuvant medications. The standard protocol in our hospital for single-shot spinal anesthesia for elective cesarean delivery is to administer 8 mg of intrathecal hyperbaric bupivacaine with 15 μg fentanyl and 75 μg morphine. Ginosar et al.[8] examined the dose of intrathecal hyperbaric bupivacaine with fentanyl and morphine that was effective in 50% (ED_{50}) and 95% (ED_{95}) of patients. They found that the ED_{95} of bupivacaine was approximately 11 mg, which is substantially greater than our usual dose. Yet despite our usual dose being close to the ED_{50} reported by Ginosar et al. we have not observed a high incidence of anesthetic failures. This may be explained in part by differences between our populations with respect to

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demographics, surgical times and patient positioning during administration of anesthesia. In addition, there are also important methodological differences. In the study by Ginosar et al.[8] an epidural catheter was inserted after spinal drug administration, which required the patients to remain sitting for a relatively long period of time. This may have reduced the upper dermatome level of the block and resulted in a relatively high estimate of ED_{95}.

Accordingly, we designed a study with similar methodology, except that the epidural catheter was inserted and fixed prior to intrathecal injection. This allowed immediate placement of patients in the position required for surgery. This study design more closely represents the situation during single-shot spinal anesthesia. Further, we confirmed the level of spinal injection by radiographic examination after surgery.

Methods

This prospective, randomized, double-blinded, dose-ranging trial is reported according to the Consolidated Standards of Reporting Trials (CONSORT) statement and was registered with the University Hospital Medical Information Network Clinical Trial Registry (UMIN-CTR: 000023692). The Tohoku Kosai Hospital Institutional Review Board reviewed and approved the study protocol. All subjects provided written informed consent to participate and all study conduct adhered to the tenets of the Declaration of Helsinki. All study procedures were conducted at Tohoku Kosai Hospital (Miyagi, Japan).

Healthy, term parturients who were scheduled for elective cesarean delivery were enrolled. Inclusion criteria were: American Society of Anesthesiologists physical status class <3, age >20 years, height 140–180 cm, singleton pregnancy, gestational age ≥37 weeks. Exclusion criteria were: active labor, ruptured membranes, ≥3 previous cesarean deliveries, gestational diabetes, pregnancy-induced hypertension, intrauterine growth retardation, placenta previa or a body mass index (BMI) >35 kg/m^2.

Patients were randomized, according to a computer-generated randomization list using sealed opaque envelopes, into seven groups. The patient and assessing investigator were blinded to group allocation. On the day of surgery the envelope was handed to an anesthesiologist not involved in the study who prepared the study medications. The study medication was given to the blinded anesthesiologist having charge of perioperative anesthetic management before induction of anesthesia.

All patients received intravenous 500 mL lactated Ringer's solution after entering the operating room. Patients received one of seven doses of hyperbaric bupivacaine: 0.5%: 6, 7, 8, 9, 10, 11 or 12 mg. Morphine (75 μg in 0.15 mL), fentanyl (15 μg in 0.3 mL) and dextrose 10% (0–1.2 mL) were added to each dose, for a total injection volume of 2.85 mL.

Patients were placed in the right lateral position and received 3 L/min of oxygen via a nasal cannula. An epidural needle was inserted at the T11–12 vertebral interspace using a loss-of-resistance-to-saline technique and a single-orifice epidural catheter (Arrow® FlexTip Plus® epidural catheter, Teleflex, Morrisville, NC, USA) was threaded 5–10 cm into the epidural space. An epidural test dose was not given. After taping the catheter in place, spinal anesthesia was administered at the L2–3 or L3–4 target vertebral level using a 25-gauge Quincke needle (UNIEVER® disposable spinal anesthesia needle, UNISIS Corp, Tokyo, Japan). Correct needle tip placement was confirmed by observation of free flowing cerebrospinal fluid. The anesthetic drug was diluted with cerebrospinal fluid to a final volume of 3 mL and this fluid was then injected over 15–20 seconds. An electrocardiogram electrode was used to mark the needle puncture site so that the injection site could be confirmed by a postoperative X-ray examination. The patient was helped back into the supine position within two minutes of intrathecal drug injection. We did not use left uterine displacement or tilt the bed, as this would affect anesthetic height.

Success of anesthesia induction ($success_{ind}$) was defined as a bilateral level of sensory loss to ice at the T6 dermatome or higher, within 10 minutes of intrathecal drug administration. Success of anesthesia maintenance ($success_{main}$) was defined as no requirement for epidural supplementation within 60 minutes of intrathecal drug administration. The need for supplementation was determined by a subject's request for more anesthetic or by a visual analogue scale (VAS) pain score >20 (where 0=no pain and 100=worst pain imaginable). In cases of failure, 5 mL lidocaine 2% was administered epidurally as required. Neonatal weight and Apgar scores were recorded after delivery.

Baseline systolic blood pressure (SBP) was measured non-invasively and the average of three measurements used as a reference. The SBP was measured every minute after drug injection until the time of delivery and every 2.5 minutes thereafter until the end of surgery. Hypotension was defined as SBP <85 mmHg or a 30% decline from baseline value. Phenylephrine was administered when hypotension occurred or when a patient complained of nausea that was thought to be caused by hypotension. The total dose of phenylephrine administered during surgery was recorded.

The level of anesthesia was tested bilaterally using an ice pack 2, 4, 6, 8, and 10 minutes after intrathecal injection and at the end of surgery. Pain scores were measured at the beginning of surgery and during delivery, uterine manipulation, peritoneal suturing and skin closure. Maternal satisfaction was quantified using a VAS score (0=no satisfaction and 100=full satisfaction) at