Which Local Anesthetic at what Dose is Recommended for Parturients Undergoing Cesarean Delivery Under Spinal Anesthesia?

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Abstract

Spinal anesthesia is the most popular regional anesthesia technique for cesarean delivery as it is easily performed and provides rapid onset of block followed by dense surgical anesthesia. Although bupivacaine seems to be widely and routinely used long acting amide type local anesthetic drug for spinal anesthesia, ropivacaine and levobupivacaine may occasionally be chosen. However, it is difficult to make decision of the best local anesthetic for intrathecal use with optimal dose selection. Therefore, either hyperbaric or isobaric long-acting local anesthetic (bupivacaine, ropivacaine and levobupivacaine) option associated with pharmacological or clinical dose recommendations are reviewed.

Keywords: Spinal anesthesia; Cesarean delivery; Local anesthetics; Dose response

Short Communication

Anesthesia choices for cesarean delivery include general, epidural, spinal or combined spinal epidural (CSE) anesthesia. According to ASA practice guidelines for obstetric anesthesia, induction to delivery times for general anesthesia are lower when compared to epidural or spinal anesthesia and rate of maternal hypotension due to epidural or spinal techniques are greater than general anesthesia. Results of meta-analysis demonstrate that Apgar scores at 1 and 5 minutes are lower with general anesthesia when compared to epidural and spinal anesthesia. As expected, time to skin incision with general anesthesia is shorter than either epidural or spinal anesthesia. But general anesthesia has increased risk of maternal complications associated with difficult airway and/or aspiration. When spinal and epidural anesthesia are compared, induction to delivery times are shorter for spinal anesthesia. However, epidural anesthesia does not result in increased risk of maternal complications like general anesthesia does [1]. Currently, single shot spinal anesthesia using local anesthetics with or without opioids has been the world wide preferred anesthetic technique for most of the elective cesarean section (CS) operations.

Bupivacaine is mostly a routine option for cesarean deliveries under spinal anesthesia. When hyperbaric and isobaric forms of bupivacaine were compared, rate of conversion to general anesthesia was significantly less and time to achieve sensory block at T4 was significantly faster with hyperbaric bupivacaine than that of isobaric bupivacaine [2]. Different dose selections are made based on either dose response studies (ED95 or ED50) or clinical experiences. Of note, rational dose for intrathecal use of local anesthetics are ED95 or ED50. ED50 is called as median effective dose and regarded as minimum local anesthetic dose (MLAD). ED95 dose is recommended to achieve surgical anesthesia with a 5 % failure rate for surgical anesthesia [3,4]. According to dose response studies, ED95 of intrathecal dose of

hyperbaric and isobaric bupivacaine when used with fentanyl (10 µg) and morphine (200 µg) to provide successful surgical anesthesia for cesarean delivery was found to be 11.2 mg and 13 mg, respectively [4,5]. There are two other amide type long-acting local anesthetics in addition to racemic bupivacaine which has 50% dextrorotatory and levorotatory molecules. These three local anesthetics have slightly different anesthetic potency as racemic bupivacaine>levobupivacaine>ropivacaine. Levobupivacaine and ropivacaine are levorotatory isomers and they have chiral center that provides bonding of carbon atom to 4 different molecules. The importance of being levorotatory isomer is to carry less potential for systemic toxicity in case of using catheter based regional anesthetic techniques [6]. Regarding dose response trials on ropivacaine, ED95 doses of hyperbaric and isobaric ropivacaine were 15,39 and 26.8 mg, respectively [7,8]. However, intrathecal use of ropivacaine is not approved by FDA. As for dose response studies with levobupivacaine, ED50 or MLAD was found to be 9.3 mg and 11.1 mg for hyberbaric and isobaric levobupivacaine, respectively [9,10].

We have retrospectively documented our anesthesia choices for CSs over seven years. Our audit demonstrated that rate of regional anesthesia progressively increased from 58% to 97% [11]. We performed mostly CSE and single shot spinal anesthesia for elective CS using either hyperbaric or isobaric bupivacaine or ropivacaine with fentanyl and/or morphine [11-13]. When we compared the effects of intrathecal fentanyl 25 µg with either intrathecal isobaric bupivacaine of 10 mg (Marcaine® 0.5%, 20 mL flacon, AstraZeneca) or isobaric ropivacaine of 15 mg (Naropin® 7.5 mg/mL Amp. 20 mL, AstraZeneca), maximum sensory block was achieved significantly faster with bupivacaine than ropivacaine (8.1 ± 4.1 min *vs.* 11.6 ± 5.6 min) with comparably same upper sensory block level at T3 (T6-T1). Sensory block regression to T10 and L1 dermatomes were significantly shorter with bupivacaine than that of ropivacaine and duration of motor block was significantly longer with bupivacaine than that of ropivacaine. Intrathecal isobaric ropivacaine was found to be superior in terms of providing longer sensory block with shorter motor block duration for

elective CSs [13]. We have also used same trademarks of hyperbaric or isobaric solutions of bupivacaine (10 mg) and ropivacaine (15 mg) with fentanyl (20 µg) intrathecally as part of CSE to compare their maternal and neonatal effects [12]. We demonstrated that time to observe maximum sensory block (which was around T3) with hyperbaric ropivacaine was significantly longer than both isobaric and hyperbaric bupivacaine solutions (20 ± 6.8 min *vs.* 13.2 ± 4.9 and 13.7 ± 4.7 min). Significantly lower ephedrine consumption was observed with both ropivacaine solutions when compared with both of the bupivacaine solutions. Fastest motor block recovery was obtained with hyperbaric ropivacaine [12].

As it has been well known, spread of intrathecal local anesthetics is established principally by baricity, which is a measure of relative density of local anesthetic solution to the cerebrospinal fluid (CSF) [14,15]. Density is determined by dividing weight to volume and specific gravity (SG) is calculated using density of water at the same temperature. Accordingly, final baricities of each of the local anesthetic solution (bupivacaine and ropivacaine) mixed with fentanyl and saline *in vitro* were presented in Table 1 [16]. The four solutions were identically prepared to have a final volume of 3 mL as they were in our previous study [12]. Since there is no commercially available hyperbaric ropivacaine (Rh) in the market, we prepared Rh by adding 0.5 mL of 30% dextrose to 2 mL of naropin 0.75% to have an approximately 8% dextrose like commercially available hyperbaric marcaine (Bh). Then, the resulting 3 mL of Bh and Rh solutions had comparable dextrose content as 5.3% and 5%, respectively [16]. In accordance with the information on the baricity of intrathecal drugs, all opioids except meperidine and normal saline are hypobaric and all concentrations of plain bupivacaine and ropivacaine solutions behave hypobaric at 37°C (regarded as body temperature) [17-19]. Because of the concern of the isobaricity of plain bupivacaine (marcaine 0.5%) at body temperature, we checked whether our 3 mL solution including 10 mg bupivacaine+fentanyl 20 µg+saline prepared for intrathecal use is isobaric or hypobaric under *in vitro* conditions. Although fentanyl and saline are considered as hypobaric, when they were mixed with plain bupivacaine the resulting final barcity of the solution was 1.0000 which was exactly isobaric [16]. As a result of our laboratory investigation, SG of the solutions did not significantly differ between room (23°C) and body temperatures (37°C). Depending on these *in vitro* findings, we could have comparatively studied the maternal and neonatal effects of true isobaric bupivacaine in vivo [12,16].

Solution	Fentanyl	Saline	Specific Gravity		Final Baricity
			23°C	37°C	
Bh: 10 mg (2 mL) 0.5% heavy marcaine including 8% dextrose	0.4 mL (20 µg)	0.6 mL	1.024	1.023	1.0179
Bp: 10 mg (2 mL) 0.5% marcaine	0.4 mL (20 µg)	0.6 mL	1.005	1.005	1
Rh: 15 mg (2 mL) 7.5 mg/mL Naropin + addition of 0.5 mL 30% dextrose	0.4 mL (20 µg)	0.1 mL	1.024	1.024	1.0189
Rp: 15 mg (2 mL) 7.5 mg/mL Naropin	0.4 mL (20 µg)	0.6 mL	1.007	1.006	1.0009
Bh: Hyperbaric Bupivacaine; Bp: Plain Bupivacaine; Rh: Hyperbaric Ropivacaine; Bp: Plain Ropivacaine					

Table 1: Baricity characteristics of local anesthetics mixed with fentanyl and saline.

On the other hand low dose spinal anesthesia as part of CSE for CS is recommended because of the favorable maternal effects on hemodynamics [20]. When the authors randomly administer either 9.5 mg (high dose group) or 6.5 mg (low dose group) of hyperbaric bupivacaine combined with 2.5 µg sufentanil intrathecally for CSE, the incidence of hypotension was significantly higher with the high dose group (68%) than the low dose group (16%). It has been concluded that low -dose spinal anesthesia (6.5 mg hyperbaric bupivacaine combined with sufentanil) preserved maternal hemodynamic stability with equally effective anesthesia better than high dose group [20]. Since the duration of anesthesia is more likely to be shorter with any low dose technique, catheter based techniques should be selected particularly for operations expected to be longer such as; CS followed by tubal ligation.

Regarding the addition of one of intrathecal lipid soluble opioid adjuvant (either fentanyl or sufentanil) to a local anesthetic, they both have pros and cons. Although lipid solubility of sufentanil is roughly two fold than that of fentanyl (1727 *vs.* 816), the main reason why we did not compare using intrathecal sufentanil as an adjuvan for spinal anesthesia during CS is its limited availability in our institution. Despite fentanyl is not approved by the FDA for intrathecal use, it has been a very well accepted choice in North America depending on its widespread use and safety written in the obstetric anesthesia textbooks since from the 1st edition to the latest one [21].

According to the latest guidelines related to anesthetic care for cesarean delivery, because of many equivocal reports, it has been strongly agreed that the decision to use a particular anesthetic technique for cesarean delivery should be individualized, based on anesthetic, obstetric, or fetal risk factors (e.g., elective *vs.* emergency), the preferences of the patient, and the judgment of the anesthesiologist; uterine displacement (usually left displacement) should be maintained until delivery regardless of the anesthetic technique used; consider selecting neuraxial techniques in preference to general anesthesia for most cesarean deliveries; if spinal anesthesia is chosen, use pencil-point spinal needles instead of cutting-bevel spinal needles; for urgent cesarean delivery, an indwelling epidural catheter may be used as an alternative to initiation of spinal anesthesia; and general anesthesia may be the most appropriate choice in some circumstances (e.g., profound fetal bradycardia, ruptured uterus, severe hemorrhage, severe placental abruption, umbilical cord prolapse, and preterm footling breech) [22].

In conclusion spinal anesthesia remains a fundamental part of modern obstetric anesthesia practice for cesarean delivery. Local anesthetic options are bupivacaine, ropivacaine or levobupivacaine. If baricity is taken into account, hyperbaric bupivacaine seems to be the

superior for intrathecal use according to systematic reviews [2]. Although hyperbaric bupivacaine which is commercially available is the widely used intrathecal local anesthetic, prepared hyperbaric ropivacaine when used intrathecally as part of CSE technique might be suitable for cesarean delivery [7,12]. It is much more reasonable to prefer ED95 dose for single shot spinal anesthesia to provide a 95% successful surgical anesthesia, whereas low dose spinal anesthetic as part of CSE is recommended either in operations with short duration or in parturients vulnerable to hemodynamic instability.

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