

## Final baricity of ropivacaine or bupivacaine combined with fentanyl for intrathecal administration

Berrin GÜNAYDIN<sup>1</sup>, İrfan GÜNGÖR<sup>1</sup>, Seval İZDEŞ<sup>2</sup>

**Abstract:** We determined the baricity of fentanyl-added bupivacaine or ropivacaine with or without dextrose by analyzing the specific gravity for a better understanding of the final baricity of the intrathecal drug combinations that are supposed to be used for surgery.

**Key words:** Physics, specific gravity, baricity, anesthetic technique, intrathecal, local anesthetics, bupivacaine, ropivacaine

### Introduction

The spread of intrathecal local anesthetics is determined principally by the baricity of the injection solution (1,2). Therefore, the choice of local anesthetic type and its glucose content, which determines its baricity, are important factors for achieving an adequate and satisfactory block for a specific operation. A comparison of the intrathecal administration of hyperbaric versus plain local anesthetic drugs revealed that hyperbaric bupivacaine 0.5% combined with sufentanil resulted in a greater cephalad spread of spinal block than bupivacaine 0.5% used alone (3). Additionally, a higher maximum block height and more rapid onset of pinprick analgesia at a certain level, such as T10, was provided with more hyperbaric local anesthetic solutions (4-6).

Establishing baricity, which is a measure of the relative density of the local anesthetic solution to the cerebrospinal fluid (CSF), requires the determination of density and specific gravity (SG). Density is determined from the measured weight and volume and SG is calculated using the density of water at the

same temperature. The SG of normal human CSF ranges between 1.0063 and 1.0075 and the mean CSF density of pregnant women was found to be  $1.00033 \pm 0.00010$  g/mL (6-8).

In terms of spinal anesthesia, all opioids except meperidine are hypobaric (8) and all concentrations of plain bupivacaine and ropivacaine behave hypobarically at 37 °C (9). For that reason, the addition of fentanyl, which is also hypobaric, to a local anesthetic renders the subsequent mixture even more hypobaric (9). Moreover, normal saline and 0.5% plain bupivacaine in saline were found to be hypobaric (10,11). To the best of our knowledge, however, the density and/or baricity of each local anesthetic, opioid, or even saline used for intrathecal route has only been investigated individually in all of these laboratory studies. We aimed to determine the final baricity of fentanyl-added bupivacaine or ropivacaine with or without dextrose in a single in vitro laboratory set up by analyzing SG in order to understand the final baricity of the intrathecal drug combinations that are supposed to be used for surgery.

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<sup>1</sup> Department of Anesthesiology & Reanimation, Faculty of Medicine, Gazi University, Ankara - TURKEY

<sup>2</sup> Department of Anesthesiology, Faculty of Medicine, Yıldırım Beyazıt University, Ankara - TURKEY

**Correspondence:** Berrin GÜNAYDIN, Department of Anesthesiology & Reanimation, Faculty of Medicine, Gazi University, Ankara - TURKEY  
E-mail: gunaydin@gazi.edu.tr

## Materials and methods

Four drug solutions (local anesthetic + fentanyl + saline) were prepared at room temperature (23 °C), as presented in Table 1. Then these solution samples were kept in a warm water bath until reaching 37 °C, the point at which the temperature mimics body temperature (37 °C).

Four solutions for intrathecal use were prepared, as presented in Table 1. The solutions and their contents were as follows: Bh, which included hyperbaric bupivacaine (Marcaine® Spinal heavy, 0.5%, 4 mL ampule, AstraZeneca); Bp, which included plain bupivacaine (Marcaine® 0.5%, 20 mL flacon, AstraZeneca); Rh, which was prepared combining plain ropivacaine (Naropin® 7.5 mg/mL, 10 mL injection, AstraZeneca) with 0.5 mL 30% dextrose; and Rp, which included plain ropivacaine (Naropin® 7.5 mg/mL, 10 mL injection, AstraZeneca).

Bupivacaine 10 mg (2 mL) and ropivacaine 15 mg (2 mL) were selected based on the published studies about the equipotency ratio of 2/3 between bupivacaine and ropivacaine for intrathecal use co-administered with fentanyl 20 µg (12-15). Fentanyl 20 µg was added to 10 mg of commercially available 0.5% (2 mL) hyperbaric and plain bupivacaine solutions and to 15 mg of 0.75% (2 mL) plain ropivacaine solution in the Bh, Bp, and Rp, respectively. Since there is no commercially available hyperbaric ropivacaine, 15 mg (0.75%) of plain ropivacaine was initially combined with glucose

30% to create hyperbaric ropivacaine before 20 µg of fentanyl was added to Rh. Finally, saline was added to give a final total volume of 3 mL in each group. The resulting hyperbaric ropivacaine solution in Rh had a glucose concentration of 5% (50 mg mL<sup>-1</sup>), while the commercially available hyperbaric bupivacaine ampule contained 8% glucose (80 mg mL<sup>-1</sup>) and the final glucose concentration in the Bh was approximately 5.3%.

Afterwards, the SG of each solution was measured (Combi-screen®, Biotechnologies AG). Written informed consent was obtained from a parturient scheduled for a cesarean section (C/S) under spinal anesthesia in order to collect 3 mL of CSF; this was used for in vitro laboratory analysis to determine the SG for the further calculation of baricity. To determine baricity, the SG of each solution was divided by the SG of CSF, which was determined to be 1.005 by Combi-screen®, Biotechnologies AG.

## Results

The results of laboratory analysis of the SG and the baricities of these solutions are presented in Table 2. Solutions containing the commercially available hyperbaric bupivacaine and the prepared hyperbaric ropivacaine were confirmed to be hyperbaric. The solution containing plain bupivacaine was found to be isobaric and the plain ropivacaine solution was less isobaric than the solution including plain bupivacaine (Table 2).

Table 1. Information on the 4 local anesthetic solutions created for intrathecal use.

Solution	Local anesthetic	Dextrose	Fentanyl	Saline
Bh	2 mL 0.5% Heavy Marcaine including 8% dextrose (10 mg bupivacaine)	-	0.4 mL fentanyl (20 µg)	0.6 mL
Bp	2 mL 0.5% Marcaine (10 mg bupivacaine)	-	0.4 mL fentanyl (20 µg)	0.6 mL
Rh	2 mL 7.5 mg/mL Naropin (15 mg ropivacaine)	0.5 mL 30% dextrose	0.4 mL fentanyl (20 µg)	0.1 mL
Rp	2 mL 7.5 mg/mL Naropin (15 mg ropivacaine)	-	0.4 mL fentanyl (20 µg)	0.6 mL

Table 2. Results of the laboratory analysis of specific gravity and the calculation of baricity.

	Bh	Bp	Rh	Rp
SG at 23 °C	1.024	1.005	1.024	1.007
SG at 37 °C	1.023	1.005	1.024	1.006
Baricity (SG of local anesthetic/SG of CSF)	1.0179	1.0000	1.0189	1.0009

Specific gravity: SG, SG of CSF = 1.005

## Discussion

We have determined the final baricities of the 4 solutions including a local anesthetic (bupivacaine or ropivacaine) and fentanyl combined with saline to get a final volume of 3 mL where the 2 additives, fentanyl and saline, were known to be hypobaric. We demonstrated that the final baricity of the solution containing plain bupivacaine + fentanyl + saline was isobaric (1.0000), whereas plain ropivacaine + fentanyl + saline was less isobaric (1.0009).

When the intrathecal administrations of hyperbaric and plain drugs were compared for C/S, hyperbaric bupivacaine 0.5% combined with sufentanil resulted in a greater cephalad spread of spinal block than the plain bupivacaine 0.5%. For this reason, hyperbaric solutions have been considered more suitable as opposed to their plain equivalents for C/S (3). Hyperbaric bupivacaine 0.5% including 8% glucose caused a higher sensory block with a more rapid onset of pinprick analgesia at T10 than hyperbaric ropivacaine 0.5% including glucose 5% in patients undergoing lower abdominal, perineal, or limb surgery (4). Additionally, a higher median block height and more rapid onset of pinprick analgesia at T10 have been shown with intrathecal ropivacaine 0.5% containing greater glucose concentrations (50 mg mL<sup>-1</sup> vs. 10 mg mL<sup>-1</sup>) in the same type of operation (5).

With regard to spinal anesthesia for cesarean delivery, though hyperbaric bupivacaine is widely accepted to provide satisfactorily effective anesthesia (16), a comparably effective spinal block with a shorter duration of motor block was provided with hyperbaric ropivacaine (10,17). Currently, hyperbaric

bupivacaine (Bh) and hyperbaric ropivacaine (Rh) without fentanyl and saline include 80 mg/mL and 50 mg/mL dextrose, respectively. However, the final glucose concentrations of Bh and Rh with fentanyl and saline added were 5% and 5.3%, respectively, resulting in comparably consistent baricities of 1.0179 and 1.0189.

Based on the laboratory investigation of the density of intrathecal local anesthetics with or without dextrose, the density of local anesthetics is inversely proportional to temperature, whereas it is directly proportional to the addition of dextrose (9). In accordance with these results, the SG of the Bh and Rp solutions at 37 °C was lower than the measurements taken at 23 °C; the Bp and Rh solutions did not change with increased temperature in the present investigation, however. Interestingly, the final baricity of the Bp solution containing fentanyl and saline was isobaric although plain bupivacaine alone is considered to be hypobaric at body temperature.

In conclusion, we determined the baricity of fentanyl-added bupivacaine or ropivacaine with or without dextrose by analyzing the SG in order to gain a better understanding of the final baricity of the intrathecal drug combinations that are supposed to be used for surgery. Although direct clinical advice cannot be drawn from a single in vitro laboratory investigation, determination of the SG and baricity might be useful before embarking on clinical studies including spinal anesthesia.

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