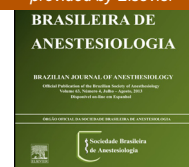




# REVISTA BRASILEIRA DE ANESTESIOLOGIA

Official Publication of the Brazilian Society of Anesthesiology  
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## SCIENTIFIC ARTICLE

# Low-dose levobupivacaine plus fentanyl combination for spinal anesthesia in anorectal surgery

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Received 19 November 2013; accepted 15 January 2014

Available online 20 February 2014

### KEYWORDS

Hyperbaric  
levobupivacaine;  
Fentanyl;  
Spinal;  
Anorectal surgery

### Abstract

**Background:** the aim of this study was to investigate the effects of spinal anesthesia using two different doses of fentanyl combined with low-dose levobupivacaine in anorectal surgery.

**Methods:** in this prospective, double-blind study, 52 American Society of Anaesthesiologists I–II patients scheduled for elective anorectal surgery were randomized into two groups. The patients in group I received intrathecal 2.5 mg hyperbaric levobupivacaine plus 12.5 µg fentanyl and in group II received intrathecal 2.5 mg hyperbaric levobupivacaine plus 25 µg fentanyl. All the patients remained in the seated position for 5 min after completion of the spinal anesthesia. Sensory block was evaluated with pin-prick test and motor block was evaluated with a modified Bromage scale.

**Results:** motor block was not observed in both of the groups. The sensory block was limited to the S2 level in group I, and S1 level in group II. None of the patients required additional analgesics during the operation. Time to two-segment regression was shorter in group I compared with group II ( $p < 0.01$ ). One patient in group I and 5 patients in group II had pruritus. Hemodynamic parameters were stable during the operation in both of the groups.

**Conclusion:** spinal saddle block using hyperbaric levobupivacaine with both 12.5 µg and 25 µg fentanyl provided good quality of anesthesia without motor block for anorectal surgery in the prone position.

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**PALAVRAS-CHAVE**

Levobupivacaína;  
Fentanil;  
Raquianestesia;  
Cirurgia colorretal

**Combinação de levobupivacaína em dose baixa e fentanil para raquianestesia em cirurgia anorretal****Resumo**

*Justificativa:* O objetivo deste estudo foi investigar os efeitos da raquianestesia com o uso de duas doses diferentes de fentanil em combinação com dose baixa de levobupivacaína em cirurgia anorretal.

*Métodos:* Neste estudo prospectivo e duplo-cego, 52 pacientes com estado físico ASA I-II, programados para cirurgia eletiva anorretal, foram randomicamente alocados em dois grupos. Os pacientes do Grupo I receberam 2,5 mg de levobupivacaína hiperbárica mais 12,5 µg de fentanil por via intratecal e os do Grupo II receberam 2,5 mg de levobupivacaína hiperbárica mais 25 µg de fentanil por via intratecal. Todos permaneceram em posição sentada por cinco minutos após o término da raquianestesia. O bloqueio sensorial foi avaliado com o teste da picada de agulha e o bloqueio motor com a escala modificada de Bromage.

*Resultados:* O bloqueio motor não foi observado em ambos os grupos. O bloqueio sensorial limitou-se ao nível S2 no Grupo I e S1 no Grupo II. Nenhum dos pacientes precisou de analgésico suplementar durante a operação. O tempo de regressão de dois seguimentos foi menor no Grupo I em comparação com o Grupo II ( $p < 0,01$ ). Um paciente do Grupo I e cinco do Grupo II apresentaram prurido. Os parâmetros hemodinâmicos permaneceram estáveis durante a cirurgia em ambos os grupos.

*Conclusão:* O bloqueio espinhal em sela com o uso de levobupivacaína hiperbárica, tanto com 12,5 µg quanto com 25 µg de fentanil, proporciona boa qualidade de anestesia sem bloqueio motor para cirurgia anorretal em decúbito ventral.

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**Introduction**

Spinal anesthesia for anorectal surgery is a popular and commonly used method characterized by rapid onset and offset, easy mobilization and short hospital stay.<sup>1</sup>

Levobupivacaine hydrochloride is the pure S(-)-enantiomer of racemic bupivacaine with less effects to cardiovascular and central nervous system than bupivacaine.<sup>2</sup> Both hyperbaric levobupivacaine and isobaric levobupivacaine have been used in anorectal surgery.<sup>3-5</sup> However there are not enough data yet, whether one form is superior to the other. Hyperbaric local anesthetics used in spinal saddle block in the prone position have some disadvantages. Patients are recommended to stay in the sitting position for several minutes after intrathecal administration to prevent the occurrence of hypotension. Also hyperbaric local anesthetic solutions might cause high levels of spinal anesthesia.<sup>6,7</sup> The side effects can be reduced with using low doses of local anesthetics. Adjuvants such as fentanyl and sufentanil potentiate the afferent sensory blockade and facilitate reductions in the dose of local anesthetics.<sup>8</sup> The aim of this prospective, double-blind, randomized trial was to compare the differences in sensory and motor blockade, patient and surgeon satisfaction and complications of intrathecal 2.5 mg hyperbaric levobupivacaine plus 12.5 µg fentanyl with intrathecal 2.5 mg hyperbaric levobupivacaine plus 25 µg fentanyl.

**Materials and methods**

After approval from the Hospitals Ethics Committee and obtaining patients' written informed consent, 52 patients, aged >18 years, with American Society of Anaesthesiologists

(ASA) physical status I and II scheduled for ambulatory anorectal surgery, were included in this study.

Patients were randomized into two groups using a computer-generated randomization sequence with sealed envelopes. Patients with abnormal coagulation profiles, severe cardiopulmonary disease, diabetes, peripheral neuropathy, infection at the injection site, marked scoliosis, and patients receiving chronic analgesic therapy were excluded from the study. None of the patients received premedication. Patients were monitored with electrocardiogram, noninvasive arterial blood pressure and pulse oximetry in the operating room. A 20-G cannula was inserted at the dorsum of the left hand and 8 mL/kg/h of 0.9% sodium chloride infusion was established 1 h before initiation of the regional block. Group I ( $n = 26$ ) received 2.5 mg hyperbaric levobupivacaine 0.5% (5 mg/mL, Chirocaine, Abbott Laboratories, North Chicago, IL, USA) plus 12.5 µg fentanyl whereas Group II received ( $n = 26$ ) 2.5 mg hyperbaric levobupivacaine 0.5% (5 mg/mL, Chirocaine, Abbott Laboratories, North Chicago, IL, USA) plus 25 µg fentanyl. Both of the solutions were aseptically prepared by an anesthesiologist blinded to the study. All solutions were completed to a total volume of 2 mL with 10% dextrose solution. The specific gravity of the solutions was determined with a refractometer (T2-NE, Atago Co. Ltd, Japan), measured at 37 °C. The specific gravity of the mixture used in group I was 1025 g mL<sup>-1</sup> and was 1020 g mL<sup>-1</sup> in group II. Due to the specific gravity of cerebrospinal fluid is 1003–1008 g mL<sup>-1</sup> at 37 °C, these mixtures were accepted as hyperbaric. Spinal anesthesia was performed at the L4-5 or L5-S1 intervertebral space using a 25 G Quincke type of spinal needle in the seated position. The test solution was injected slowly in 2 min and the patients were kept in the sitting position for 5 min to achieve sufficient block. Sen-

sory block was evaluated by the pin-prick method at every 2 min until the sufficient block reached the S4 level and testing was conducted at every 5 min until the end of the operation. After sitting for 5 min patients were placed in the prone position. Motor block was evaluated according to a modified Bromage scale (0: no motor block, 1: inability to raise extended legs, 2: inability to flex knees, able to move feet, 3: inability to flex ankle points). Onset time of S4 level sensory block (time to readiness for surgery), maximum level of sensory block, time to 2 segment regression, time to urination and time to first analgesic requirement were evaluated by an observer blinded to the study groups and recorded. Postoperative side effects like nausea, vomiting, headache and pruritus were recorded by nursing staff. Diclofenac sodium 75 mg intramuscular (IM) was used for rescue analgesia and first analgesia requirement time was recorded. Hypotension was defined as a decrease in systolic arterial blood pressure >20% of baseline and was treated with intravenous (IV) 5–10 mg bolus doses of ephedrine. Bradycardia was defined as heart rate <60 beat per minute and was treated with 0.01 mg/kg bolus doses of atropine. After completion of the surgery, patients were asked to rate the quality of their anesthesia using a 4 point scale (1: Perfect, 2: Satisfactory, comfortable but some feelings of pressure or traction, 3: Poor, discomfort because of feeling intense pressure or traction, 4: Worst: Major discomfort because of pain).

The statistical analysis was performed using SPSS for Windows version 10.0.1. The sample size was calculated, based on 80% power, to be able to detect a 25 min (min) difference in mean time to sensory block recovery. Pre-study power analysis using our population mean and standard deviation suggested that 24 patients in each group would be sufficient to detect a difference of 25 min assuming a type I error of 5%. Data were presented as mean  $\pm$  standard deviation, median (minimum–maximum) or frequencies as appropriate. Student's *t*-test was performed for analysis of the parametric data and Mann–Whitney *U* test was performed for analysis of the non-parametric data. Results were considered statistically significant if  $p < 0.05$ .

## Results

Fifty-two patients were enrolled in the study. No significant difference was observed between the groups with respect to gender, age, height, weight, ASA physical status, and duration of the operation (Table 1). The maximum sensory block level reached to S1 dermatome in both of the groups. The median upper limit of the sensory block was S2 in Group II and S1 in Group I preoperatively. Time to reach S4 dermatome was similar between the groups. Pre-operative and postoperative maximum blocked dermatomes in both of the groups are given in Table 2. Mean times to

**Table 1** Patient characteristics, operation time, type of surgical procedure.

	Group I (n = 26)	Group II (n = 26)	<i>p</i>
Age (years)	24 $\pm$ 8	30 $\pm$ 10	0.061
Height (cm)	173 $\pm$ 8	175 $\pm$ 8	0.94
Weight (kg)	81 $\pm$ 17	82 $\pm$ 14	0.346
Gender (female/male)	3/23	4/22	0.687
Duration of surgery (min)	21 $\pm$ 7	36 $\pm$ 12	0.233
Surgical procedure (n)			
Pilonidal sinus excision	22	21	0.021
Hemorrhoidectomy	2	3	
Anal fissure	2	2	

Data are expressed as mean values  $\pm$  SD.

**Table 2** Spinal block characteristics, time to first voiding of urine, analgesic requirement and patient satisfaction.

	Group I (n = 26) Median (range)	Group II (n = 26) Median (range)	<i>p</i> value
Time to reach S4 blockade (min)	3 (2–5)	3 (3–5)	0.821
Preoperative maximum blocked dermatome	S2 (S1–S3)	S1 (S1–S3)	0.014
Postoperative maximum blocked dermatome	S2 (S1–S3)	S1 (S1–S2)	0.408
2-Segment regression time (min)	25 (20–40)	35 (30–75)	$p < 0.001$
Time to first analgesic requirement (min)	180 (60–240)	250 (15–340)	$p < 0.001$
Time to first void (min)	192 (120–292)	240 (105–420)	0.085
Patient satisfaction, n (%)			
1 = perfect	20 (76.9)	22 (84.6)	
2 = satisfactory	6 (23.1)	4 (15.4)	
3 = poor	0	0	
4 = worst	0	0	

Data are expressed as median (range).

two-segment regression were shorter in group I than group II ( $p < 0.001$ ). All patients in both of the groups were able to position themselves with Bromage scores 0. Time to voiding was similar in both of the groups ( $p = 0.085$ ), and none of the patients needed catheterization. First analgesic requirement time was shorter in group I compared with group II ( $p < 0.001$ ). None of the patients needed supplemental analgesic during the operation. Patients satisfaction were similar in both of the groups, and 76.9% of the patients in group I and 84% of the patients in group II assessed the anesthetic quality as 'perfect' (Table 2). The adverse effects during the intraoperative and postoperative period; nausea vomiting and pruritus were similar in both of the groups. One patient in group I and five patients in group II received treatment for the pruritus ( $p = 0.086$ ). There were no significant differences between the groups regarding mean arterial blood pressure and heart rate values, before and during the surgery.

## Discussion

Levobupivacaine, the pure S(-)-enantiomer of bupivacaine, was demonstrated less affinity and strength of depressant effects onto myocardial and central nervous system compared with bupivacaine. Additionally, producing differential neuraxial block preserving motor function at low concentrations provides an advantage to levobupivacaine.<sup>9</sup> Adjuvants such as fentanyl and sufentanyl reduce the dose of local anesthetics and prolong the sensory block without delaying time to void. The recommended intrathecal doses of fentanyl as adjuvant to local anesthetics is 10–25  $\mu\text{g}$ .<sup>10,11</sup> Also these adjuvants improve tolerance to visceral sensations like bladder distension and peritoneal stretch. However adjuvants such as fentanyl to local anesthetics does not prolong the duration of motor blockade.<sup>10,11</sup> So, two different doses of fentanyl combined with low-dose levobupivacaine were used in this study. Both of the anesthetic combinations provided good quality of spinal anesthesia without motor block.

Cuvas et al.<sup>5</sup> compared 5 mg 0.5% plain bupivacaine in 1 mL volume with 5 mg 0.5% plain levobupivacaine in 1 mL volume for pilonidal cyst/sinus surgery in the prone position. They found similar results with regard to sensory and motor blockade in both of the groups. The median maximum level of sensory block reached to T10 dermatome in the levobupivacaine group. All the patients in the levobupivacaine group had motor blockade equivalent to Bromage score 1 or 2. Patient satisfaction was 92% in the levobupivacaine group. In the present study, we used 2.5 mg dose of hyperbaric levobupivacaine with two different doses of fentanyl. We also found similar results for the time of onset of the sensory block in the two groups and motor block was not observed in any of the patients. We used small dose of levobupivacaine than Cuvas et al. used in their study and maximum sensory block was limited to the S1 dermatome in both of the groups. The sensory block level was sufficient for anorectal surgery and all the patients expressed their anesthetic satisfaction as good or very good.

Erbay et al.<sup>12</sup> compared the effects of spinal anesthesia provided by 7.5 mg hyperbaric bupivacaine plus 25  $\mu\text{g}$  fentanyl with 7.5 mg hyperbaric levobupivacaine plus 25  $\mu\text{g}$  fentanyl for transurethral surgery. They found that

hyperbaric levobupivacaine plus 25  $\mu\text{g}$  fentanyl provided a shorter motor block time and a longer sensory block time than 7.5 mg hyperbaric bupivacaine plus 25  $\mu\text{g}$  fentanyl. In another study, Girgin et al.<sup>13</sup> suggested that intrathecal administration of 25  $\mu\text{g}$  fentanyl added to 5 mg levobupivacaine 0.5% for inguinal herniorrhaphy increased the quality of spinal anesthesia and allowed to use a sub-anesthetic levobupivacaine dose. In the present study, levobupivacaine in combination with 25  $\mu\text{g}$  fentanyl provided a sensory block with longer duration than the hyperbaric levobupivacaine in combination with 12.5  $\mu\text{g}$  fentanyl. Also first analgesic requirement time was significantly longer in the spinal anesthesia group provided by hyperbaric levobupivacaine plus 25  $\mu\text{g}$  fentanyl. As similar to other studies, combining fentanyl with levobupivacaine prolonged sensory block without affecting motor recovery or time to void.<sup>10,11</sup>

Hyperbaric local anesthetic solutions have a higher density compared with CSF. For this reason, hyperbaric local anesthetic solutions tend to move in a cephalad direction and may produce motor blockade in the anterior roots of the thoracic region in the prone position.<sup>6,7</sup> It has been shown that using small doses of local anesthetics with adequate basicity and appropriate patient positioning, only the nerve roots supplying a specific area is affected.<sup>6,7</sup> Also administration of local anesthetics with a high speed affects its distribution of levobupivacaine to the vertex position in the thecal cavity and causes hemodynamic changes.<sup>14</sup> In this study we used hyperbaric solutions of levobupivacaine and measured the densities of the solutions at 37 °C. Local anesthetics were administered at a rate of 1 mL/60 s in order to minimize the distribution of hyperbaric levobupivacaine depending on the conversion of patient posture from sitting position to prone position. Motor blockade was not observed in both of the study groups. No clinically significant hemodynamic changes such as bradycardia or treatment requiring hypotension occurred in any of the patients.

The minimal recommended dose of spinal hyperbaric bupivacaine is 4–5 mg for anorectal surgery.<sup>15</sup> Gurbet et al.<sup>3</sup> compared 5 mg 0.5% spinal hyperbaric bupivacaine and 2.5 mg 0.5% hyperbaric bupivacaine plus 25  $\mu\text{g}$  fentanyl in outpatient anorectal surgery. They found that addition of 25  $\mu\text{g}$  fentanyl to 2.5 mg 0.5% bupivacaine prolonged the duration of sensory blockade and reduced postoperative analgesic requirement. Upper limit of the sensory block reached to T9 (T4-L1) dermatome and median maximum motor blockade score was 2<sup>1-3</sup> in hyperbaric bupivacaine plus fentanyl group. We used 2.5 mg of hyperbaric levobupivacaine 0.5% with two different fentanyl combinations for spinal anesthesia in anorectal surgery. The median upper limit of the sensory block was S1 in the spinal anesthesia group provided by hyperbaric levobupivacaine plus 25  $\mu\text{g}$  fentanyl. Median time to S4 sensory blockade was 3 min and motor blockade was not observed in the any of the patients. Bradycardia or hypotension was not observed during the surgery. We suggest that 2.5 mg hyperbaric levobupivacaine with 25  $\mu\text{g}$  fentanyl can be preferred for spinal anesthesia in anorectal surgery with high risk patients because of better hemodynamic stability and without delay in initiation of the surgery.

Wassef et al.<sup>16</sup> investigated the efficacy of 1.5 mg bupivacaine in short perianal procedures with the dose of 6 mg which was regularly used in spinal saddle block. They

concluded that spinal perianal block produced by 1.5 mg bupivacaine provided a significantly restricted sensory block levels (median maximum = S4), and motor block was not observed in any of the patient in this group compared with the group which was 6 mg bupivacaine used. Also time to ambulation and voiding were shorter in the low dose bupivacaine group. They concluded that, maintaining the seated position is essential for restriction of blockade to the most caudal spinal nerve roots which supply the perianal area.<sup>15</sup> In another study, Kazak et al. compared the efficacy of spinal 1.5 mg hyperbaric levobupivacaine with 6 mg hyperbaric levobupivacaine for anal surgery. Sensory block was limited to S4 dermatome in the perianal block group provided by 1.5 mg hyperbaric levobupivacaine. They stated that 1.5 mg dose of intrathecal hyperbaric levobupivacaine provided shorter duration and faster regression of sensory block compared with 6 mg hyperbaric levobupivacaine.<sup>4</sup> Kazak et al. kept the patients in the sitting position at least 20 min in order to confine the small bolus of levobupivacaine to the lower end of the dural sac. As different from the study performed by Kazak et al., in the present study, the patients were kept in the sitting position for 5 min. The S4 sensory blockade was achieved in 3 min and maximum blocked sensory level reached to S1 level, so it can be said that there was no delay in readiness for surgery.

In conclusion, we found that the two regimens provided good quality spinal anesthesia in anorectal surgery without affecting the motor functions and hemodynamic stability. However the addition of 25 µg fentanyl increased duration of sensory analgesia with longer first analgesic requirement time without prolonging time to void or intensifying the motor blockade.

## Conflicts of interest

The authors declare no conflicts of interest.

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