A comparative study between the effect of intrathecal hyperbaric bupivacaine with fentanyl and hyperbaric levobupivacaine with fentanyl for knee arthroscopy

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Background The use of levobupivacaine as a pure S (–) enantiomer of bupivacaine was progressively increased due to lower cardiotoxicity and neurotoxicity and shorter motor block duration. The aim of this work was to compare the effectiveness of lower-dose local anesthetics' use together with higher opioid dose to decrease the side effects of drugs. We compared sensorial, motor block levels and side effects of equal doses of hyperbaric bupivacaine and levobupivacaine with intrathecal fentanyl addition in knee arthroscopy.

Patients and methods After hospital ethics committee approval and getting written informed consent from patients, 100 patients with American Society of Anesthesiologists grade I–II, aged 18–40 years were included in the study. They were randomized to either group A receiving 7.5 mg (1.5 ml) hyperbaric levobupivacaine with 25 μg (0.5 ml) fentanyl, or group B receiving 7.5 mg (1.5 ml) hyperbaric bupivacaine with 25 μg (0.5 ml) fentanyl.

Results Hemodynamic parameters such as the 45th minute mean arterial pressure of group B was found to be lower ($P<0.05$). In group A, maximum sensorial block level and postoperative visual analog scale scores were higher ($P<0.05$). Onset of motor block time, time to maximum motor block, time to sensorial block, reversal of two dermatome and first analgesic need were similar in both groups.

Conclusion Intrathecal hyperbaric levobupivacaine–fentanyl combination is a better and good alternative to bupivacaine–fentanyl combination in knee arthroscopy, as it maintains hemodynamic stability.

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Keywords: fentanyl, hyperbaric bupivacaine, hyperbaric levobupivacaine, knee arthroscopy, motor block, sensory block, spinal anesthesia

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Introduction

For the local anesthetic selection, it is known that the agent onset and duration of action, sensorial block level to motor block level and cardiac toxicity should be considered. An overall 0.5% heavy bupivacaine is more commonly used for spinal anesthesia for knee arthroscopy [1]. Levobupivacaine, being the S enantiomer of bupivacaine, is less cardiotoxic and less neurotoxic in cases of accidental intravascular injection and has a shorter duration of motor block than racemic bupivacaine; its use has increased progressively [2,3]. There is the clinical profile of potency for motor block for the pipecolylxlidines when administered spinally: low, intermediate, and high for ropivacaine, levobupivacaine, and bupivacaine, respectively [4,5].

The use of low doses of anesthetics and opioids in spinal anesthesia was reported to have advantages such as faster onset of action, better efficacy with minimum toxic effect and selective sensorial block [6]. Fentanyl can be combined with local anesthetics for spinal anesthesia, and, when used in this way, it prolongs the duration of action and spread of sensory block as well [7]. Fentanyl has been combined with bupivacaine for lower limb surgery and also for inguinal herniorrhaphy and cesarean section [6–9]. We planned to compare the onset and duration of action, sensorial and motor block levels, and side effects of equal doses of hyperbaric bupivacaine and levobupivacaine with intrathecal fentanyl addition in spinal technique in knee arthroscopy.

Aim of work

The aim of this work was to compare the effectiveness of low-dose levobupivacaine and bupivacaine with fentanyl in unilateral block for knee arthroscopy.

Patients and methods

This study across sectional comparative study was carried out after approval of the hospital ethical committee in Al-Azhar University Hospitals and informed consent was obtained in all patients; this study was carried out during the period spanning from 20/10/2017 to 20/10/2018.

One hundred patients aged between 18 and 40 years, classified as American Society of Anesthesiologists

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grades I–II of both sexes undergoing knee arthroscopy surgery were included in the study. Patients with a history of allergy to any drug of the study and with any contraindication to regional anesthesia were excluded. Patients were divided equally into the two groups by a randomized table created by a computer software program using sealed envelopes:

Group A received 7.5 mg (1.5 ml) hyperbaric levobupivacaine and 25 μg (0.5 ml) fentanyl. Group B received 7.5 mg (1.5 ml) hyperbaric bupivacaine and 25 μg (0.5 ml) fentanyl.

The primary outcomes

The primary outcome of the study was the intensity of block as regards the onset and duration of sensory and motor blockade.

The secondary outcomes

The secondary outcomes of the study were the hemodynamic changes, postoperative analgesia, and incidence of complications.

All patients were evaluated by medical history and a complete physical examination. No premedication was administered. Hemodynamic parameters were recorded with ECG, systolic and diastolic blood pressure, heart rate and oxygen saturation (SpO_2). Intravenous prehydration with 500 ml of 0.9% isotonic NaCl infusion was administered. Hypotension, defined as a decrease of systolic blood pressure more than 20% from baseline or a fall below 90 mmHg, was treated with incremental intravenous doses of 3 mg of ephedrine and intravenous fluid as required, and bradycardia, defined as a heart rate below 50 beats/min, was treated with 0.3–0.6 mg of intravenous atropine.

Patients were placed on the operation table in the sitting position and were administered 3 ml (60 mg) 2% lidocaine infiltration anesthesia through L3–4 after sterilization with antiseptic solution (povidone iodine). The intrathecal space was reached with a 27 G spinal needle (Standard Quincke Babcock, Cutting Sharp Bevel). After intrathecal injection of anesthetic drugs, patients were placed in the lateral position for 10 min to achieve unilateral block and then returned to the supine position.

The ice cubes were used for sensorial block evaluation (onset, offset) and sensorial block reversal time. The time of the first analgesic need was recorded as first analgesia time.

Bromage scale was used for assessment of the intensity of motor block. In the Bromage scale, the intensity of motor block is assessed by the patient's ability to move their lower extremities as follows: 0=free movement of legs and feet; 1=just able to flex knees with free movement of feet; 2=unable to flex knees, but with free movement of feet; and 3=unable to move legs or feet.

'Onset of motor block' is recorded as when Bromage scale is '1' after administration of local anesthetics, and 'onset of highest motor block' is recorded as time to reach the highest scale of motor block. 'Operation duration' is recorded as time until end of operation after administration of local anesthetics.

Pain intensity was recorded during skin incision, 2 and 4 h postoperatively by visual analog scale (VAS). Before operation, VAS was explained to patients as '0' no pain and '10' intolerable pain. During operation, in cases where analgesia was insufficient (VAS: 3–4), patients were excluded from the study in both groups.

The hemodynamic parameters [systolic, diastolic blood pressure, heart rate and oxygen saturation (SpO_2)] were recorded at 0, third, and fifth minutes and every 5 min after injection of local anesthesia. Sensorial and motor block was recorded at the first, third, and fifth minutes, and it was recorded every 15 min until reversal of motor block.

Side effects such as pruritus, nausea, vomiting, anxiety, and respiratory depressions were followed-up 24 h postoperatively (Fig. 1).

Statistical analysis

Statistical analysis was performed by statistical package for the social sciences for Windows 17.0 program Version 22.0 (SPSS Inc., Chicago, Illinois, USA). All data were expressed as means, SD, and frequency. Statistical significance was accepted as P value less than 0.05. The comparison between groups was tested using the independent t test. The comparisons within groups were tested using Fisher's exact test and χ^2 test.

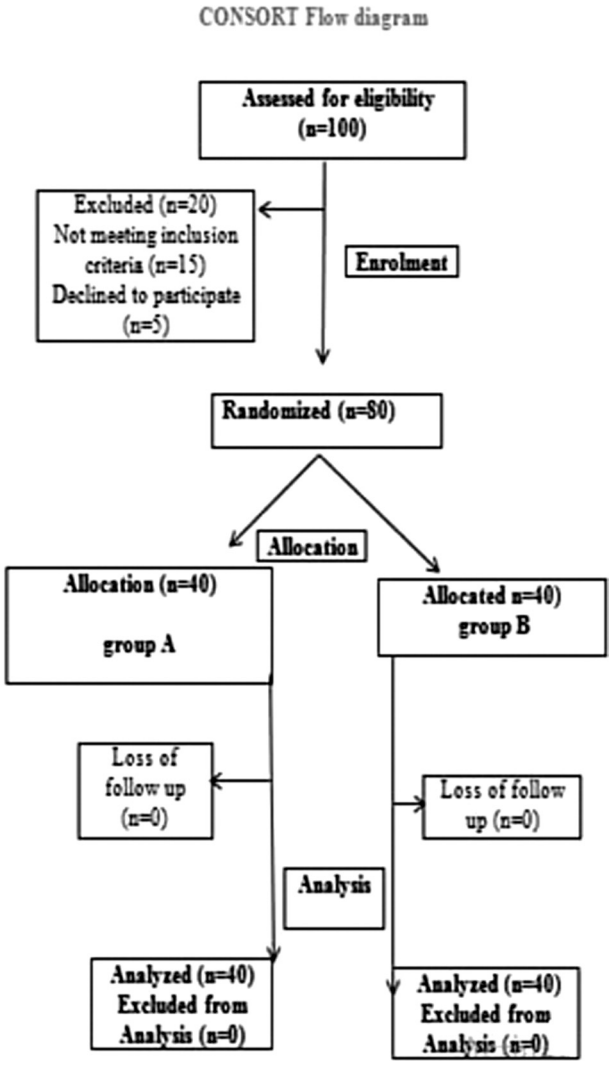
Results

Demographic data of study

A total of 100 patients were included in the study. However, in 20 patients, due to insufficient regional anesthesia, additional local anesthetics were given, and the patients were excluded from the study, as the doses were changed.

Statistically nonsignificant differences were detected among the groups with respect to age, weight, and height (Table 1).

Figure 1



Consort flow chart.

Table 1 Demographic data of the study population

Parameters	Groups (mean±SD)		*P* value
	Group A	Group B	
Age (year)	28.75±4.41	29.21±3.98	0.735
Height (cm)	160.90±6.66	160.16±4.42	0.686
Weight (kg)	76.40±11.09	74.74±9.98	0.626
Sex (male : female)	55 : 45	58 : 42	0.75
Duration (min)	67.20±12.87	69±14.39	0.89

Group A: 7.5 mg (1.5 ml) hyperbaric levobupivacaine and 25 μg (0.5 ml) fentanyl, group B: 7.5 mg (1.5 ml) hyperbaric bupivacaine and 25 μg (0.5 ml) fentanyl.

Anesthesia determination parameters

There was statistically no significant difference between groups at the first minute motor block level; however, the third and fifth minute motor block levels were significantly different between groups (Table 2). The Bromage score at the third minute in group A was '1', and it was '2' in group B. The Bromage score at the fifth minute was '2' in group A and '3' in group B.

Maximum motor block level and time to end of motor block were found to be higher in the bupivacaine group B ($P<0.05$).

The onset of motor block time, time to maximum motor block, time to sensorial block, reversal of two dermatome, and first analgesic need were similar in both groups (Table 3). Reversal of motor block was statistically significantly different between groups, and the mean value of group B was statistically significantly higher than that of group A.

Hemodynamic parameters

The basal heart rate of group A was 93.10±14.14 beats/min and 89.21±12.78 beats/min in group B. There was a statistically significant difference between the heart rate of groups (Table 4).

Preoperative mean arterial pressure (MAP) of group A was 94.20±14.33 mmHg, and MAP of group B was 91.68±09.27 mmHg. There was a statistically significant difference between MAP of groups at the 40th minute ($P<0.05$); the MAP of group A (86.30±8.80 mmHg) was statistically significantly higher than that of group B (79.32±08.90 mmHg). At other time measurements, there was a statistically nonsignificant difference between the MAP of groups (Table 5).

Visual analog scale

Postoperative VAS was found to be higher in the levobupivacaine group (group A) ($P<0.05$). There was a significantly nonsignificant difference between VAS scores of both groups at skin incision. However, postoperative 30th and 60th minute VAS distribution of groups was statistically significantly different (Fig. 2).

Side effects of groups

There was a statistically significant difference in the incidence of side effects between groups (Table 6) ($P<0.05$).

Discussion

There was increased popularity of regional anesthesia among anesthetists in knee arthroscopy. Regional anesthesia has some risks; deaths are primarily related to excessive high regional blocks and toxicity

Table 2 Motor block level of groups

Time	Bromage score	Group A [*n* (%)]	Group B [*n* (%)]	*P* value
1st min	0	22 (55)	12 (32)	0.178
	1	14 (35)	14 (36)	
	2	4 (10)	12 (32)	
3rd min	0	6 (15)	0 (0)	0.015*
	1	20 (50)	6 (15)	
	2	10 (25)	20 (53)	
	3	4 (10)	12 (32)	
5th min	1	6 (15)	0 (0)	0.015*
	2	22 (55)	10 (26)	
	3	12 (30)	28 (74)	

*$P<0.05$ using analysis of variance test among groups. Significance between groups.

Table 3 Anesthesia determination parameters of groups

Parameters	Groups		*P* value
	Group A (mean±SD)	Group B (mean±SD)	
Onset of sensorial block (s)	345.0±134.69	304.26±110.99	0.279
Onset of motor block (s)	135.0±75.70	97.89±42.82	0.069
Maximum motor block (s)	288.0±68.41	250.26±85.59	0.136
Two dermatome regression (min)	89.85±16.29	82.74±07.13	0.089
First analgesic need (min)	162.55±37.30	173.05±10.74	0.245

Group A: 7.5 mg (1.5 ml) hyperbaric levobupivacaine and 25 μg (0.5 ml) fentanyl, group B: 7.5 mg (1.5 ml) hyperbaric bupivacaine and 25 μg (0.5 ml) fentanyl.

Table 4 Intraoperative heart rate of both groups (beats/min)

Parameters	Groups (mean±SD)		*t* test
	Group A	Group B	*P* value
0 min	93.10±14.14	89.21±12.78	0.295
5 min	89.00±7.89	80.25±4.25	0.044*
10 min	88.75±61.29	70.75±2.93	<0.001*
20 min	83.00±7.75	58.50±4.73	<0.001*
30 min	78.25±5.96	67.00±6.99	<0.001*
40 min	81.25±7.87	68.75±4.72	0.003*
50 min	82.75±6.97	71.75±2.22	0.040*
60 min	82.75±6.88	69.50±1.70	0.042*

*$P<0.05$ using analysis of variance test among groups. Significance between groups.

Table 5 Mean arterial pressure measurements of the groups

Parameters	Groups (mean±SD)		*t* test
	Group A	Group B	*P* value
0 min	94.20±14.33	91.68±09.27	0.075
5 min	92.25±2.04	90.00±4.41	0.04*
10 min	91.75±3.72	82.20±3.43	<0.001*
20 min	90.50±4.13	65.75±4.61	<0.001*
30 min	88.00±3.07	71.75±5.16	<0.001*
40 min	86.30±8.80	79.32±8.80	0.024*
50 min	85.50±3.40	83.00±4.03	0.062
60 min	86.00±4.11	84.75±4.83	0.078
80 min	85.50±3.11	83.50±4.95	0.060

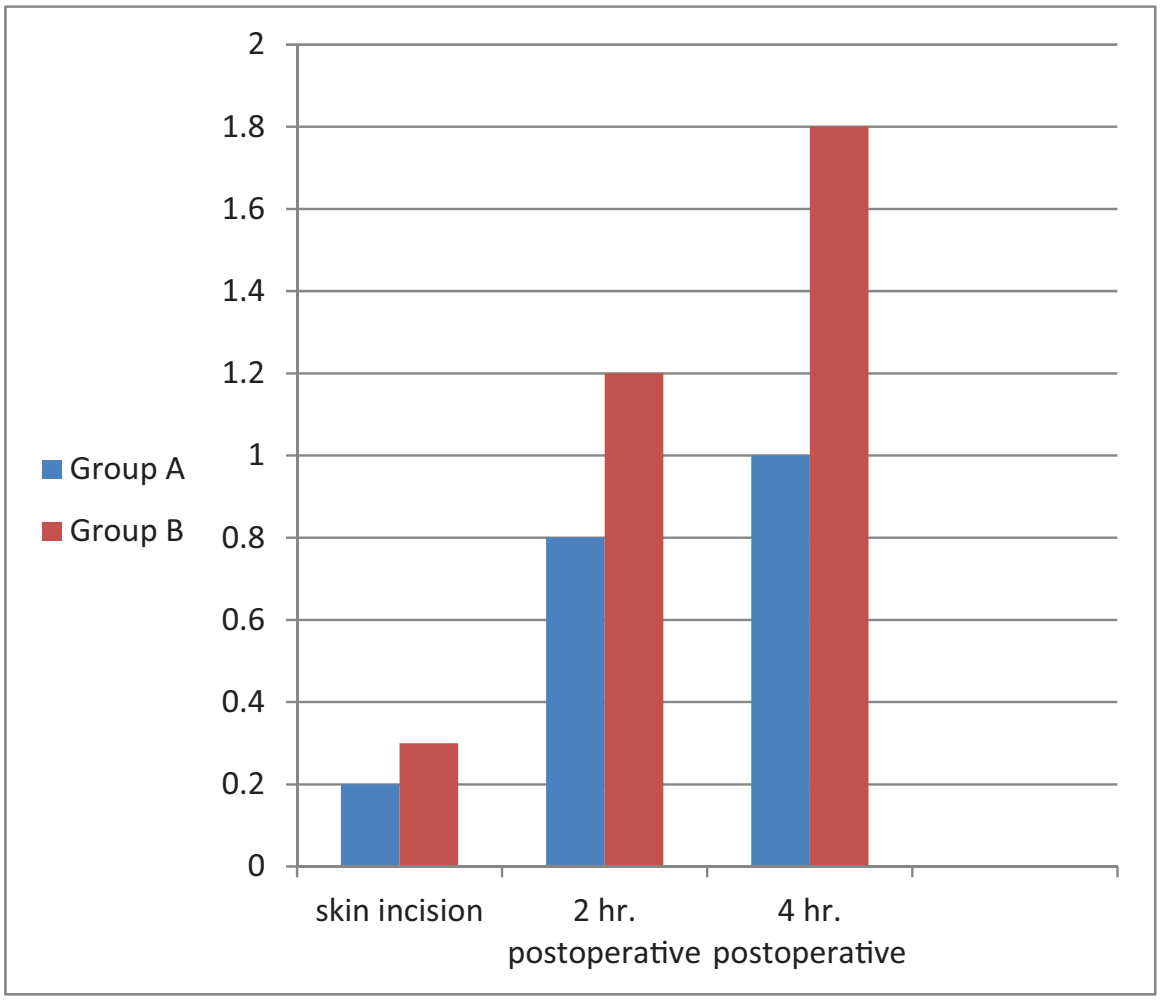
SpO_2 measurements were statistically nonsignificantly different between groups.

of local anesthetics. Reduction in doses and improvement in technique to avoid higher block levels and heightened awareness of the toxicity of local anesthetics have contributed to the reduction of complications related to regional anesthesia [10].

Over the last decade, spinal anesthesia has been refined with the addition of opioids to local anesthetic solutions. It was reported that use of only local anesthetics in knee arthroscopy operation under spinal anesthesia is not sufficient in the prevention of pain during manipulation, has a short duration of action, and has disadvantages such as the early need for analgesia [10–12]. The addition of morphine significantly prolongs postoperative analgesia to 18–24 h, whereas the more lipophilic opioids such as sufentanil and fentanyl improve and prolong intraoperative analgesia and reduce the amount of local anesthetics required to perform sufficient block intensity necessary for knee arthroscopy. By adding opioids to spinal anesthesia, a reduction in local anesthetic dose is possible. This reduction in local anesthetic requirements reduces the intensity and duration of motor blockade and allows patients to ambulate faster. Initial reports on low-dose spinal anesthesia suggest that this may also reduce hypotension [13].

Heavy bupivacaine 0.5% is most commonly used for spinal anesthesia for knee arthroscopy. Many studies have claimed successful anesthesia with very low doses of intrathecal bupivacaine (5–9 mg) when coadministered with opioids [7]. Kim and Moneta

Figure 2



Visual Analogue Scale scores of the groups.

Table 6 Incidence of side effects between groups

Parameters	Groups [*n* (%)]		*P* value
	Group A	Group B	
Hypotension	24 (60)	20 (53)	<0.05
Nausea	22 (55)	10 (26)	<0.05
Vomiting	14 (35)	4 (11)	<0.05
Ephedrine need	14 (35)	18 (47)	<0.05
Bradycardia	14 (35)	6 (16)	<0.05
Pruritus	26 (65)	18 (47)	<0.05

[13] advocated the use of 7.5 mg bupivacaine for knee arthroscopy, as this dose was associated with a decreased incidence of hypotension, but, again, a large number of patients rated the analgesic quality as poor. Ginosar *et al.* [14], reported ED_{50} and ED_{95} of hyperbaric bupivacaine in cesarean section with combined spinal epidural technique were 7.6 and 11.2 mg, respectively. In our study, anesthesia was successful with 25 µg fentanyl added to 7.5 mg hyperbaric bupivacaine. Only in 20 patients, it was not sufficient, and local anesthetics were administered.

Because of the lower cardiovascular side effect and central nervous system toxicity, the use of levobupivacaine as the pure S (–) enantiomer of bupivacaine has progressively increased [3,15]. Epidural levobupivacaine has the advantage of decreased cardiotoxicity in cases of accidental intravascular injection [16]. Parpaglioni *et al.* [17] reported the minimum intrathecal levobupivacaine dose to be 10.58 mg. Alley *et al.* [18] evaluated three intrathecal doses of levobupivacaine and bupivacaine (4, 6, and 8 mg) in healthy volunteers and found no differences in the clinical profile of sensory and motor blocks and recovery from spinal anesthesia. In some studies, levobupivacaine and racemic bupivacaine showed an undistinguishable clinical profile in spinal anesthesia [19,20].

In the selection of local anesthetics, it is desired that the agent's onset of action is short, the duration of action is longer and sensorial block level to motor block level is higher. Camorcia *et al.* [21] reported that intrathecal 0.5% levobupivacaine had weaker motor block potency than 0.5% bupivacaine in CSE anesthesia technique.

In our study, levobupivacaine had lesser motor potency. Bromage score at the third and fifth minutes was one to two in levobupivacaine and two to three in bupivacaine. In contrast, maximum sensorial block level was found to be higher in the levobupivacaine group.In our study, preoperative VAS scores were similar in both groups, whereas postoperative 2 and 4 h VAS scores were lower in the bupivacaine group than in the other group.

Intrathecal opioid administration has side effects in both groups, such as nausea, vomiting, pruritus, respiratory depression, and urinary retention [22]. Highly lipid soluble opioids cause temporary pruritus, whereas intrathecal morphine causes long-acting and intensive pruritus [22].

In the study by Bremerich and colleagues, fixed doses of intrathecal hypertonic levobupivacaine 0.5% (10 mg) and bupivacaine 0.5% (10 mg) combined with either intrathecal fentanyl (10 and 20 μg) or sufentanil (5 μg) were compared in terms of sensory and motor block characteristics. However, we compared the lesser 7.5 mg hyperbaric levobupivacaine and 7.5 mg bupivacaine combined with higher fentanyl dose (25 μg) than that used in the study by Bremerich *et al.* [23]. Moreover, in the study of Gautier *et al.* [20], different doses than that of our study were used.

Intrathecal 7.5 mg hyperbaric levobupivacaine and 25 μg fentanyl combination is a good alternative to 7.5 mg bupivacaine 25 μg fentanyl combination in knee arthroscopy, as it maintains hemodynamic stability at higher sensorial block levels.

Conclusion

Intrathecal hyperbaric low-dose levobupivacaine–fentanyl combination is a better and good alternative to bupivacaine–fentanyl combination in knee arthroscopy, as it maintains hemodynamic stability.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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