



TO STUDY THE EFFECT OF LEVOBUPIVACAINE WITH FENTANYL FOR KNEE ARTHROSCOPY

Anaesthesiology

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ABSTRACT

Background: In recent years levobupivacaine, the pure S (-) stereoisomer of bupivacaine has emerged as safer alternative to bupivacaine. Fentanyl has been used commonly with bupivacaine for enhancement of analgesia without intensifying motor and sympathetic block in intrathecal anesthesia. In our study we compare the clinical efficacy and adverse effects of levobupivacaine alone and in combination with fentanyl in knee arthroscopy under intrathecal anesthesia.

Materials and methods: In this prospective, randomized, double blind study, 60 patients undergoing knee arthroscopy under intrathecal anesthesia were randomized into two groups of 30 patients each. 2.8ml of 0.5% isobaric levobupivacaine (14mg) plus 0.2ml of normal saline in group a and 2.8ml of 0.5% isobaric levobupivacaine (14mg) plus 0.2ml fentanyl (10mcg) in group b were administered intrathecally. The efficacy was compared in terms of onset, duration and quality of sensory and motor block, hemodynamic changes and adverse effects.

Results: The duration of sensory block was significantly prolonged in levobupivacaine plus fentanyl group ($p < 0.05$). Levobupivacaine plus fentanyl group also had significantly better degree of motor block compared to plain levobupivacaine group ($p < 0.05$). Hemodynamic changes were similar in both the groups.

Conclusion: The study concludes that combination of fentanyl with levobupivacaine offered an advantage of improved degree of motor block and prolonged duration of sensory block with least side effects.

KEYWORDS

Standard Operating Protocols, Training, Compliance, Safe Surgery

INTRODUCTION

Spinal anesthesia also referred to as intrathecal anesthesia, or subarachnoid block. It creates an intense sensory and motor block that can be effectively achieved with a small amount of local anesthetic. Almost all local anesthetics have been used at some point in spinal anesthesia.^[1] First case of spinal anesthesia in humans was performed by August Bier in 1898 using cocaine.

Racemic bupivacaine is the most frequently used long acting agent for intrathecal anesthesia. But it also carries undesirable effects like prolonged post-operative motor blockade, cardio-toxicity and CNS toxicity. In recent years levobupivacaine, the pure S (-) stereoisomer of bupivacaine, emerged as a safer alternative for regional anesthesia than its racemic parent due to its low cardio toxicity and less undesired effects on the central nervous system than bupivacaine.^[2] Clinical studies comparing levobupivacaine and racemic bupivacaine in epidural and intrathecal analgesia show that both are equally effective.^[3] Because of its significantly reduced side effects, levobupivacaine seems to be a suitable alternative to bupivacaine. Neuraxial opioids are widely used in conjunction with local anesthetics as they permit the use of lower dose of local anesthetics, while providing adequate anaesthesia and analgesia.^[4] Neuraxial opioids also allow prolonged analgesia in the postoperative period and faster recovery from spinal anesthesia.^[5] Fentanyl a lipophilic opioid has been used commonly with bupivacaine, for enhancement of analgesia without intensifying motor and sympathetic block in intrathecal analgesia.^[6] Knee arthroscopy may be performed under local, regional or general anesthesia. In recent years intrathecal anesthesia using low dose of local anesthesia in combination with opioid has gained popularity due to high success rate, faster recovery and patient satisfaction with decreased resource utilization when compared to general anesthesia. Hence in our study we compare the clinical efficacy and adverse effects of levobupivacaine alone and in combination with fentanyl in knee arthroscopy under intrathecal anesthesia.

MATERIALS AND METHODS

After obtaining institutional ethics committee approval and informed consent, 60 patients belonging to ASA class I and II of either sex aged between 25 to 75 years scheduled for knee arthroscopic surgeries under intrathecal anesthesia were studied. This prospective randomized double blind study was conducted on patients who were admitted at Father Muller Medical College Hospital in orthopedics department.

Inclusion criteria:

1. Between the ages of 25-75 years.
2. Patient scheduled for knee arthroscopy.
3. ASA grade I or II.

Exclusion criteria:

1. Contraindication to intrathecal anesthesia.
2. History of renal, hepatic, respiratory, cardiac disease, diabetes mellitus and patients with preexisting neurological impairment.
3. Known hypersensitivity to any drugs.
4. BMI > 38kg/m².
5. Height < 150cms or > 185cms.

A detailed history and complete clinical examination of patients was done to rule out the exclusion criteria's. Routine investigations like blood grouping, hemoglobin, blood urea, serum creatinine, coagulation test and blood sugar were done. Electrocardiogram (ECG) whenever indicated was taken to rule out the presence of any cardiac disease. Pre-operative pulse rate, respiratory rate and blood pressure values were noted. Patients involved in the study were premedicated with tablet ranitidine 150mg and tablet diazepam 5mg night prior to the surgery. On arrival to the operating room all the patients were met by an anesthesiologist other than the one who was in charge of giving intrathecal anesthesia. Patients were randomly allocated by means of sealed envelope into either Group A or Group B.

Group A: Received 2.8ml of 0.5% isobaric levobupivacaine (14mg) plus 0.2ml normal saline

Group B: Received 2.8ml of 0.5% levobupivacaine (14mg) plus 0.2ml fentanyl (10mcg)

Standard monitors like pulse oximetry, noninvasive blood pressure (NIBP) and electrocardiogram (ECG) were connected to the patient. An average of three recordings was considered as baseline recording. Intravenous line was secured and patients were preloaded with Ringer's lactate solution 10ml kg⁻¹ over 20 minutes prior to surgery. The anesthesiologist, who performed the intrathecal injection and assessment of intrathecal block, was blinded to the group of study solution. The study solution was prepared by another anesthesiologist who was not involved in the clinical care of the patient. Under aseptic conditions the study solution was injected by inserting 25G Quincke Babcock spinal needle at L3-L4 level using midline or paramedian approach with patient in lateral decubitus position. On completion of intrathecal injection, patient was immediately turned back to supine

position. Oxygen (5L/min) was administered via face mask. During the procedure heart rate, blood pressure, pulse oximetry and ECG were monitored continuously. The following parameters were assessed.

The sensory block was evaluated by pinprick method using 22G hypodermic needle. Sensory block was assessed at 1min interval until block reached T12, and then repeated every 2mins until the level stabilized for four consecutive tests. This level was noted as the peak sensory block level. Onset of adequate sensory block was defined as the achievement of a sensory block level of T12 dermatome or higher which was required to initiate the surgery. After the surgery, sensory block level was evaluated every 30mins in recovery room until its regression to L5 level. Motor block was assessed using modified Bromage scale.

Intraoperative recordings included heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and oxygen saturation (SpO2). Recordings were done every 2 minutes for the first ten minutes, every 5 minutes for the next thirty minutes and every 10 minutes thereafter till the end of surgery. In postoperative ward sensory and motor block was assessed every 30mins. Two segment sensory regression time, time taken for sensory block to reach L5, which was taken as duration of analgesia and time taken for the patient to attain complete motor recovery (Bromage scale-0) which was taken as duration of motor block were noted.

Adverse effects like bradycardia, hypotension, respiratory depression, nausea, vomiting, shivering and pruritus was noted. Hypotension was defined as decrease in systolic blood pressure of more than 30% from the base line or < 100mmHg. This was treated with intravenous infusion of Ringer Lactate or intra venous boluses of mephentremine 6mg. Bradycardia was defined as heart rate of < 50 beats min⁻¹ and was treated with intra venous injection of atropine 0.01mg/kg. The addition of any sedative drugs if required was recorded.

STATISTICAL ANALYSIS

Statistical analysis of data are presented as mean and standard deviation. The qualitative data as frequency and percentage.

Hemodynamic parameters like HR, SBP, DBP and MAP was analyzed using ANOVA. Sensory and motor block characteristics were analyzed with t-test. Chi square test was used to analyze the peak sensory level attained adverse effects between the two groups.

- p < 0.01 statistically highly significant ([#]p < 0.01)
- p < 0.05 statistically significant (^{*}p < 0.05)
- p > 0.05 statistically not significant (p > 0.05)

The statistical software SPSS version 18.0 was used for the analysis of data. Microsoft word and Excel were used to generate graphs and tables.

RESULTS

Sixty subjects aged between 25 and 75 years belonging to ASA class I and II were randomly divided into 2 groups of 30 patients each (n=30):

- Group A** - Levobupivacaine 0.5%
- Group B** - Levobupivacaine 0.5% plus fentanyl

Table 1: Demographic data and duration of surgery

	Group A (n=30)	Group B (n=30)	p value
Age (yrs)	43.07 ± 12.18	41.6 ± 12.08	0.641
Weight (kgs)	65.87 ± 8.05	65.23 ± 7.695	0.757
Height (cms)	164.93 ± 7.11	166.13 ± 6.33	0.493
Male/Female ratio	20/10	20/10	1
Duration of surgery(mins)	83.53 ± 15.79	85 ± 12.73	0.694

Table 2: Characteristics of sensory block and its duration

	Group A (n=30)	Group B (n=30)	p value
Time to T ₁₂ (mins)	5.77 ± 1.79	4.93 ± 1.85	0.082
Time for maximum sensory level (mins)	12.7 ± 2.5	12.6 ± 3.25	0.894
Two segment sensory regression (mins)	106.17 ± 9.44	127.17 ± 9.34	< 0.001
Time to L ₅ (mins)	228 ± 25.31	262 ± 26.44	< 0.001

Figure 1: Maximum level of sensory block attained

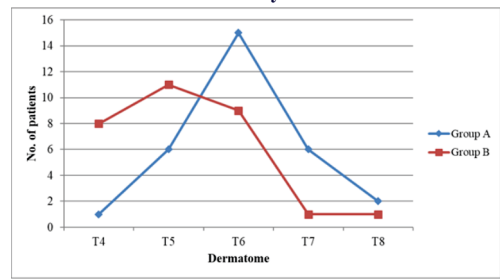


Table 3: Characteristics of motor block and its duration

Characteristics	Group A (n=30)	Group B (n=30)	p value
Maximum motor block (Bromage scale)	2.77 ± 0.43	2.97 ± 0.18	0.024 [*]
Time for maximum motor block (mins)	6.53 ± 1.79	4.5 ± 1.52	<0.01 [#]
Duration of motor block (mins)	201.5 ± 17.37	201.83 ± 15.17	0.937

Figure 2: Mean heart rate at different time intervals between the two groups

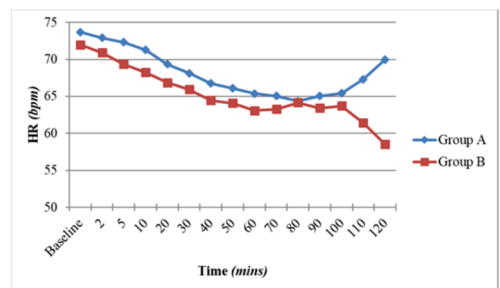


Figure 3: Mean systolic blood pressure at different time intervals between the two groups

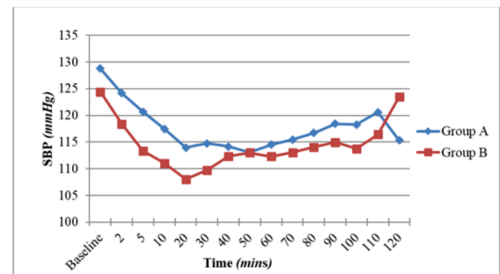


Figure 4: Mean diastolic blood pressure at different time intervals between the two groups

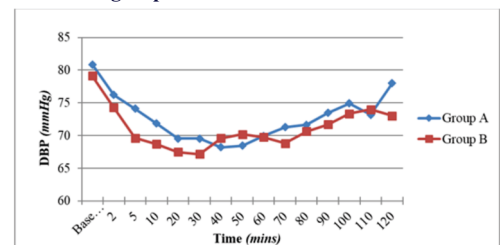


Figure 5: Mean arterial pressure at different time intervals between the two groups

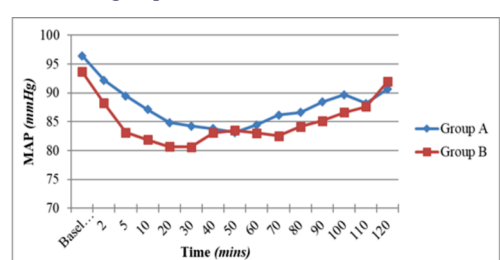


Table 4: Adverse effects

	Group A (n=30)	Group B (n=30)	p value
Hypotensive episode	1(3.33%)	2 (6.66%)	0.553
Shivering	3 (10%)	3 (10%)	1
Pruritus	-	3 (10%)	0.075

Values are number of patients in (%)

DISCUSSION

Spinal anesthesia is one of the most commonly used technique in anesthesia. It is economical, safe, easy to administer and needs less sophisticated anesthetic equipment's and hence preferred over general anesthesia. It is very popular because of its profound analgesia and good muscle relaxation. Regional techniques, such as spinal anesthesia, may offer advantages over general anesthesia including reduced stress response to surgery and improved postoperative pain relief.^[7]

Levobupivacaine is the pure S (-) enantiomer of racemic bupivacaine and has low cardio toxicity and less undesired effects on the central nervous system. Because of its significantly low side effects, levobupivacaine seems to be an attractive alternative to bupivacaine.^[8,9] Intrathecal local anesthetics work by inhibiting voltage-gated sodium channels in the spinal cord. This inhibition of voltage-gated sodium channels interferes with afferent, efferent sensory and motor impulses. The degree of sensory and motor block depends on the technique, agent, and dose administered.^[10]

Opioids work in the intrathecal space by activating opioid receptors in the dorsal gray matter of the spinal cord, which modulates the function of afferent pain fibers. Intrathecal opioids seem to modulate pain primarily at the spinal cord level rather than in the brain, as do intravenous opioids. A site of action in spinal cord provides analgesia with less sedation, confusion, and nausea, which are adverse effects often associated with intravenous opioids.

Numerous studies support the combination of local anesthetics with opioids to provide safe anesthesia and analgesia while reducing the required doses and adverse effects of each agent.^[8,11]

Nowadays for daycare surgeries highly lipid soluble synthetic opioid such as fentanyl is being increasingly used along with very low concentrations of local anesthetic agents as it produces a synergistic effect without increasing the sympathetic block or delaying discharge.^[11]

Arthroscopic knee surgery is one of the most commonly performed ambulatory orthopedic surgeries. The main goals of the anesthetic techniques used in ambulatory surgery are to reduce anesthetic complications, provide adequate postoperative analgesia and allow for early patient discharge.

There are many studies comparing intrathecal bupivacaine with fentanyl. Being a newer and safer alternative to bupivacaine and also lack of enough studies comparing levobupivacaine with fentanyl especially for knee arthroscopic surgeries, we decided to conduct this study.

This prospective, double-blinded and randomized study has shown that 2.8ml (14mg) of 0.5% isobaric levobupivacaine plus 10mcg fentanyl was an effective mixture for intrathecal anesthesia for knee arthroscopy that required a sensory block upto T₁₂ dermatome. The duration of sensory block and quality of motor block was significantly ($p < 0.05$) better in the levobupivacaine with fentanyl group, with similar hemodynamic effects and without significant ($p > 0.05$) adverse effects when compared to plain levobupivacaine group.

Cuvas *et al.*^[12] compared the characteristics of the spinal block produced by combining 12.5mg levobupivacaine and 11mg levobupivacaine with 15mcg fentanyl and it was found that there was no difference between time to reach maximum sensorial block, two-segment regression and motor block level. The duration of motor block was reduced for levobupivacaine with fentanyl. They used levobupivacaine in a lower dose but fentanyl in a higher dose than that in the present study.

Girgin *et al.*^[11] compared the effectiveness of 7.5mg levobupivacaine

alone and 5 mg levobupivacaine combined with 25mcg fentanyl in ambulatory inguinal herniorrhaphy. This study showed a rapid recovery of sensorial and motor block in the group levobupivacaine combined with fentanyl.

The values obtained with levobupivacaine plus fentanyl correlate well with that obtained by Santiago *et al.*^[13] (4mins). The onset time for levobupivacaine plus fentanyl was slightly different from Erdil *et al.*^[14] (7.8mins). This difference may be due to higher dermatomal level (T10) taken for reference.

The maximal level of sensory block achieved in majority of patients in the plain levobupivacaine 4group was T6 (50%) and in levobupivacaine with fentanyl group was T5 (36%) these levels are much higher when compared to the study done by Akan *et al.*^[15] and Borazan *et al.*^[16] The reason for a higher level of sensory block in our study might be due to the larger dose of levobupivacaine (14mg) was used. When compared to 7.5mg and 10mg of levobupivacaine were used by the study conducted by above authors respectively

Brahmbhatt *et al.*^[17] in their study evaluated the effects of fentanyl added to low dose levobupivacaine scheduled for lower abdominal & perianal surgeries concluded that fentanyl added to levobupivacaine provides good surgical anesthesia and early motor recovery which is well suited for outpatient anesthesia.

Whereas we found prolonged duration of sensory block and improved degree of or block when compared to study conducted by Lee *et al.*^[18] this prolonged duration may be due to the dose of levobupivacaine what we used is more (14mg) instead of 11.5mg what they used in their study.

Heart rate and blood pressure remained stable and comparable in both the groups intraoperatively. Akan *et al.*^[15] also concluded that there was no significant difference in the mean heart rate and blood pressure in plain levobupivacaine group and levobupivacaine plus fentanyl group. Similar results were reported by Cuvas *et al.*^[12] and Lee *et al.*^[18]

Hypotension is a very frequent side effect after spinal anesthesia. There was fall in blood pressure in both the groups. In our study a total of 3 patients had hypotensive episodes. Two in group levobupivacaine and one in levobupivacaine with fentanyl group had hypotension which was adequately managed with mephentramine boluses. Systemic hypotension and bradycardia being the most common side effects seen during spinal anesthesia and marked hypotension being harmful particularly in elderly, Erdil *et al.*^[14] in their study compared the block duration and hemodynamic effects with intrathecal levobupivacaine and bupivacaine both combined with fentanyl found that levobupivacaine with fentanyl had better hemodynamic stability and fewer side effects.

The most common side effect observed with intrathecal opioids is pruritus. It may be generalized, or localized to the face, neck and upper thorax. We noticed 3 (10%) of the patients in levobupivacaine with fentanyl group had pruritus when compared to none in plain levobupivacaine group, which is statistically not significant ($p > 0.05$). Pruritus which didn't require was also reported by many studies.^[33,39] whereas Erdil *et al.*^[14] have noticed pruritus in 75% of the patients. This may be due to higher dose of fentanyl i.e. 25mcg was used when compared to the present study, i.e. 10mcg. The side effects of intrathecal fentanyl are dose related. Another frequently seen side effect during spinal anesthesia is shivering. We noticed shivering in both the groups. Regarding shivering our results doesn't match with that of study conducted by Erdil *et al.*^[14] This may be due to the study conducted on elderly patients.

Limitation of this study might be the relative low sample size. Especially the frequency of the adverse effects could have altered if conducted on a large study group. In conclusion both the plain levobupivacaine and levobupivacaine with fentanyl were effective in providing surgical anesthesia and hemodynamic stability, but levobupivacaine with fentanyl group offered an advantage of improved degree of motor block and prolonged duration of sensory block, with least side effects.

CONCLUSION

Both regimes were effective in providing surgical anesthesia and hemodynamic stability, but levobupivacaine with fentanyl group

offered an advantage of improved degree of motor block and prolonged duration of sensory block, with least side effects.

CONFLICT OF INTEREST STATEMENT

The research was conducted without commercial or financial relationships with any organization that could be a conflict of interest.

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