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Comparison of 0.75%Isobaric Ropivacaine Alone And 0.75%Isobaric Ropivacaine with Fentanyl as Adjuvant in Spinal Anesthesia for Orthopaedic Lower Limb Surgeries

Authors
Mudita Bhatia[1], Alaka Purohit[2], Mohit Pareek[3], Pradeep Charan[4]
[1]MBBS, MD, Senior Resident, Department of Anesthesia, Pt.B.D.Sharma PGIMS
[2]MBBS, MD, Professor, Department of Anesthesia, SMS Medical College
[3]MBBS, 3RD Year Resident, Department of Otolaryngology, Pt.B.D.Sharma PGIMS
[4]MBBS, MD, Assistant Professor, Department of Anesthesia, SMS Medical College

ABSTRACT

Background: *Fentanyl, a potent, short acting, synthetic opioid analgesic has been commonly used as an adjuvant with local anesthetics for post operative analgesia because of its superior intraoperative conditions, hemodynamic stability and minimal side-effects.*

The aim of this study was to evaluate the efficacy and safety of addition of Intrathecal Fentanyl to 0.75% Isobaric Ropivacaine in spinal anesthesia in orthopaedic lower limb surgeries.

Subjects and Methods: *Hundred patients belonging to American Society of Anesthesiologists physical status I and II scheduled for orthopedic lower limb surgery under spinal anesthesia were included. The study was a prospective double blinded randomized controlled trial where patients were randomly allocated into two groups of fifty patients each to receive either 2.6 ml of 0.75% (19.5 mg) isobaric ropivacaine with 0.4ml (20 µg) fentanyl (Group B) or 2.6 ml of 0.75% (19.5 mg) isobaric ropivacaine with 0.4 ml of 0.9% saline (Group A) intrathecally. The points studied were hemodynamic parameters, onset of sensory and motor blockade, duration of sensory and motor blockade, duration of analgesia, degree of sedation and side-effects were also assessed. At the end of study, data were systematically compiled and analyzed for statistical significance.*

Results: *No significant difference was found in hemodynamics, onset of sensory block and incidence of side effects with the addition of fentanyl to ropivacaine. The intrathecal fentanyl has accelerated the onset time to achieve motor blockade. There was a significant prolongation of the duration of sensory block and postoperative analgesia in Group B.*

Conclusion: *Intrathecal 20µg fentanyl is associated with prolonged sensory block, provides excellent quality of intraoperative and postoperative analgesia allowing early and pain free ambulation as compared to plain ropivacaine. It is haemodynamically stable in intraoperative and postoperative periods with insignificant side effects.*

Keywords: *Ropivacaine, Bupivacaine, Fentanyl, Spinal anesthesia.*

INTRODUCTION

The main aim of anesthesia during surgery is pain relief that should be extended into postoperative period. Severe post operative pain is the most common and most distressing complication of surgery. Options available for the treatment of

post-operative pain include systemic (i.e., opioid and non opioid) analgesics; and regional techniques. Neuraxial techniques can provide superior analgesia compared to systemic drugs.

Ropivacaine is a long acting amide local anesthetic with less systemic toxicity and greater margin of safety as compared to bupivacaine. Ropivacaine is associated with greater sensory-motor differentiation by blocking sensory nerve fibers more readily than motor fibers due to its lower lipid solubility. Early recovery of motor function is associated with lower incidences of venous thrombo-embolism and shorter hospitalization[1-3].

A number of adjuvants have been studied to prolong the effect of spinal anesthesia. For many years, there has been interest in the efficacy and safety of use of intrathecal opioids to relieve post-operative pain. Fentanyl is a potent, short acting, highly lipophilic, synthetic opioid analgesic. It acts primarily as agonist at μ opioid receptors to enhance spinal analgesia.[4, 5] It is advantageous over morphine because of its rapid onset of action[6], superior intraoperative conditions and lesser side-effects. The duration of post operative analgesia is prolonged with fentanyl than with spinal local anesthetics alone[7]. Fentanyl also allows use of smaller doses of local anesthetics with better hemodynamic stability.

This study was aimed to evaluate the anesthetic effects of intrathecal fentanyl as an adjuvant to 0.75% isobaric ropivacaine in terms of onset, duration, intensity and recovery time of sensory and motor blockade and duration of analgesia of subarachnoid block for orthopaedic lower limb surgeries.

SUBJECTS AND METHOD

The study was conducted in the Department of Anesthesiology, S.M.S Medical College, Jaipur. Due permission from the institutional ethical committee and review board and written informed consent of patient had been obtained. This study included 100 Patients (age 20-50 years) undergoing elective surgery of lower limb who fulfilled the following inclusion criteria : patients aged 20- 50 years, height ≥ 150 cms ,weight 50-80 Kg, ASA grade I-II, undergoing orthopaedic procedures of lower limb and duration of surgery about 2 hrs. Patients with contraindications to spinal anesthesia, allergy to local anesthetics, ASA grade III or above and patients not willing to participate in the study were excluded. This study was conducted in the form of a prospective, comparative, randomized, double blind hospital based interventional study.

The patients were randomised by chit in box method into following two groups : group A (n=50, ropivacaine group) received 2.6ml (19.5gm) of 0.75% isobaric ropivacaine + 0.4ml normal saline and group B (n=50, fentanyl group) received 2.6ml(19.5gm) of 0.75% isobaric ropivacaine + 0.4ml fentanyl (20 μg) intrathecally.

Preanaesthetic assessment for all patients was done a day before the surgery. Informed written consent was obtained from the patient and first blood relative for performance of block after complete explanation about the study protocol and the procedure. Patients were kept nil per oral from midnight and were premedicated with tablet alprazolam 5 mg PO and tablet ranitidine 150 mg PO at night and 2 h before surgery.

In the operating room, patients were taken on the operation table. Standard monitors including noninvasive blood pressure (NIBP), electrocardiography and pulse oximeter were connected and baseline vitals like NIBP , heart rate (HR) , oxygen saturation were recorded. After securing an 18G IV cannula, 500ml Ringer lactate solution was administered as bolus dose to all patients before performing subarachnoid block.

Vitals just before lumbar puncture were noted. Following strict aseptic precautions with the patient in sitting position, spinal anesthesia was performed at L3-L4 interspace (L4-L5 in case of failure) by using a 25 Gauge Quincke spinal needle. After confirming a free flow of cerebrospinal fluid, the anesthetic solution was

administered over 15 seconds at the rate of 0.2ml/second. The intrathecal drug's composition was given according to the group to which patient belonged. The direction of the needle aperture was cranial during the injection. Perioperative monitoring was done using continuous pulse oximetry, non-invasive blood pressure and continuous electrocardiography (lead II & V5) and patients were given 4.0 L/min of oxygen by venti-mask. Intraoperatively, fluids were administered according to the blood loss and hemodynamic parameters.

Perioperatively, following parameters were monitored in both the groups: heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) for every 2min for the first 10min, every 5min till 60min and then every 10min till completion of surgery. The level of sensory block was tested by pin prick bilaterally at mid-clavicular line which was done every minute till the maximum sensory level was achieved and then after one hour at half an hour interval. Onset of sensory block was taken as the time taken to attain sensory level of T10 dermatome. Modified Bromage scale was used to assess the time of onset of motor block. Time of onset of motor block was taken as the time taken to achieve modified Bromage score 1 from the time of subarachnoid injection.

Side effects during the surgery like hypotension, bradycardia, pruritis, nausea, vomiting, respiratory depression, shivering were noted and managed immediately. Immediately after surgery patients were shifted to the recovery room. Vital parameters including SBP, DBP, HR were recorded at regular interval of 30 minutes for first 2hours and for 24 hours every 2hourly. Analgesia duration was observed and recorded following pain scoring system – Visual analogue score (VAS). VAS score was serially assessed at half an hour interval starting from 60 minutes to 300 minutes or till the patient complained of pain (VAS >3). Duration of effective analgesia was measured as the time from intrathecal drug administration to the patient's VAS score > 3 either in the recovery room or the ward, and was recorded in minutes. Patient's VAS > 3 and administration of rescue analgesia constituted the end point of the study. Diclofenac (75mg) IV was given as rescue analgesic. Duration of sensory block was defined as the time from onset of sensory block to the time taken for the sensory block to regress upto S1 dermatome. Duration of motor block was defined as the time between onset of motor block to complete return of motor power (modified Bromage score 6).

STATISTICAL ANALYSIS

The sample size was based in order to detect a 30 min difference in mean duration of sensory and motor blockade between the group for type 1 error of 0.01 and power of 90%. The data were recorded in tabulated manner and was analyzed using Microsoft Excel and SPSS software for windows. Statistical analysis was done using student *t*-test and Chi-square test as applicable. A '*P*' value <0.05 was considered statistically significant.

RESULTS

Patients in both the groups were comparable in terms of age, weight, height, sex and ASA grade. There was no significant difference between the two groups in their duration of surgery (Table 1). There was no statistically significant difference in the mean time of sensory onset at T10 dermatome and mean time taken to achieve maximum sensory blockade which was 3.6±1.2min and 8.3±1.9min (Group A) and 3.4±1.3min and 8.0±1.5min (Group B) respectively. Also there was no significant difference in the peak level of block attained between the two groups with the median upper sensory level T6 in Group A and T4 in Group B. The difference in mean onset of motor block was statistically significant being 5.5±1.5min in group A and 4.9±1.4min in group B. A complete motor block of modified Bromage score 1 was attained by all patients in both the groups. The difference in mean duration of sensory block was statistically highly significant

(277.4 ± 27.0 minutes in Group A and 325.1 ± 36.8minutes in Group B). The difference in mean duration of motor block was also statistically significant (225.8 ± 21.6 minutes in Group A and 240.8 ± 31.4 minutes in Group B) but clinically it was considered insignificant. The mean time of rescue analgesia in Group A was 310.4 ±39.8 min and in Group B was 343.7 ± 88.2 min.The p value was <0.05 between the groups and found to be statistically highly significant (Table 2).

There was no significant difference in the hemodynamic parameters between the two groups intraoperatively as well as postoperatively. Vital parameters like SBP, DBP, MBP (Graph 1) and HR (Graph 2) were comparable in both the groups. The incidence of adverse effects was same among both the groups. Hypotension occurred only in four patients in Group B (8%) as compared to three patients in Group A (6%) and was treated with injection ephedrine 6 mg IV boluses. This was found to be statistically insignificant. Episodes of bradycardia also occurred in 3 patients (6%) in Group B and 2 patients (4%) in Group A which was also insignificant and managed with injection atropine 0.5mg IV bolus. Pruritus after intrathecal fentanyl is known but it was not significant in our study. Nausea and vomiting were observed in 4% and 2% patients in Groups A and B respectively. This suggested that the incidence of nausea and vomiting was not changed significantly among different groups. No patient had residual neurological deficit, postdural puncture headache or transient neurological symptom (Graph 3). There were slightly higher sedation score in group B at 2 hours post spinal anesthesia but the difference between the two groups was not statistically significant (Graph 4).

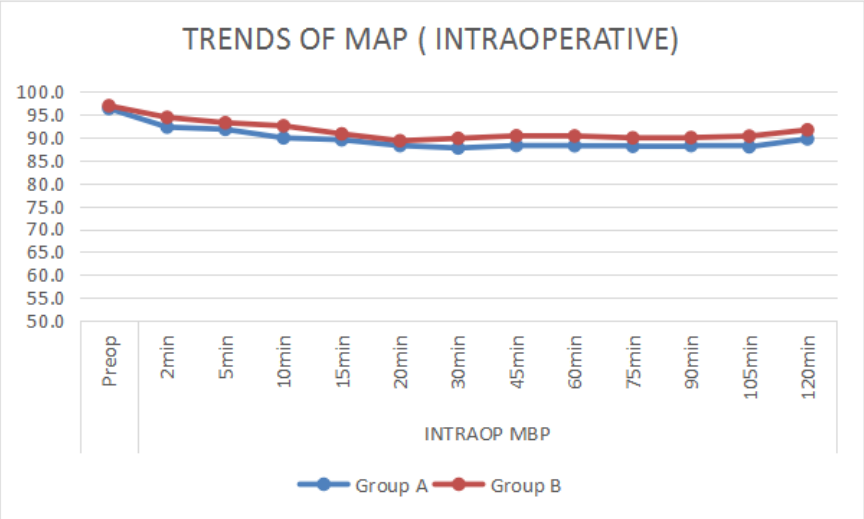
Table 1 Demographic Variables (Mean ± SD)

Variables	Group A	Group B	P Value	Significance
Age (yrs)	31.7 ± 9.7	31.9 ± 10.2	0.8963	N.S
Weight (kg)	69.7± 8.3	69.8± 6.8	0.9686	N.S
Height (cm)	165.7± 5.2	166.3 ± 3.6	0.5342	N.S
ASA Grade I/II	45/5	45/5	1.0	N.S
Duration of Surgery (minutes)	98.91±29.081	102.38±32.166	0.701	N.S

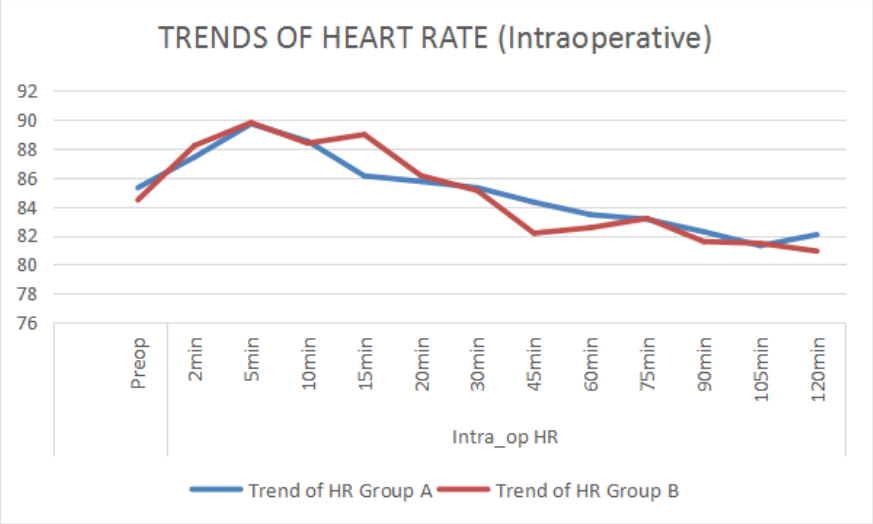
Table 2 Sensory and Motor Block Characteristics

Variables	Group A	Group B	P Value	Significance
Sensory Onset at T10 (min)	3.6± 1.2	3.4± 1.3	0.4830	N.S
Time to achieve max sensory blockade (min)	8.3± 1.9	8.0± 1.5	0.5165	N.S
Duration of sensory block (min)	277.4 ± 27.0	325.1±36.8	<0.0001	Significant
Motor onset (min)	5.5± 1.5	4.9± 1.4	0.0340	Significant
Duration of motor block (min)	225.8± 21.6	240.8 ± 31.4	0.0067	Significant
Time of Rescue analgesia (min)	310.4 ±39.8	343.7 ± 88.2	0.0177	Significant

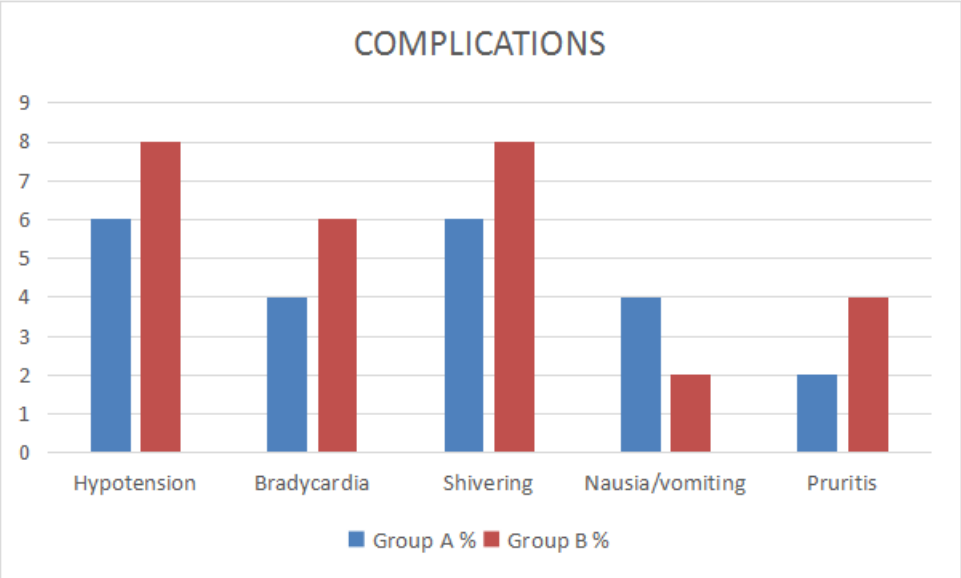
Graph 1



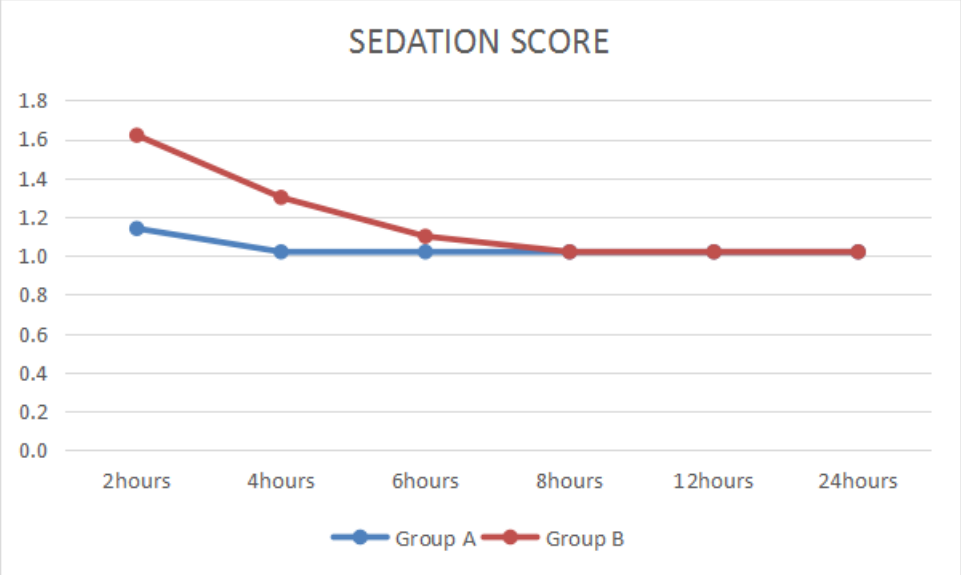
Graph 2



Graph 3



Graph 4



DISCUSSION

Subarachnoid block is the most widely used anaesthesia technique for lower extremity surgery[8]. Spinal anaesthesia offers many advantages over general anaesthesia which includes reduced stress response and improved post-operative pain relief.

Spinal lignocaine provides shorter duration of anaesthetic blockade but as it can also lead to the occurrence of transient neurological symptoms, its use is becoming obsolete[9]. Among the numerous drugs that have been used for spinal anesthesia, bupivacaine is the most popular. Bupivacaine, the first long‑acting amino amide local anesthetic is widely used because of its prolonged duration of action, however certain features of bupivacaine like prolonged motor blockade, cardiotoxic and neurotoxic effects have made ropivacaine a safer choice[10,11]. Also, spinal bupivacaine induces profound motor block of longer duration and delays home discharge after ambulatory surgery[12].

Ropivacaine, a long acting amide local anesthetic, has been used for day care procedures as it provides adequate sensory block with early motor recovery[11]. It has an improved safety profile over bupivacaine with a reduced central nervous system and cardiotoxic potential and hence is gaining favour[9,13].

Neuraxial opioids are widely being used as adjuvants with local anesthetics (LAs) as they allow dose reduction of local anesthetics, ensuring adequate anesthesia and analgesia at the same time[14,15]. With the use of neuraxial opioids, faster recovery from spinal anesthesia and also prolonged analgesia in the postoperative period has been observed[16,17]. The quality of intraoperative anesthesia is improved and onset of surgical block is shorter with neuraxial opioids[10]. Side effects like paralysis and hypotension are not seen with them as the antinociception is devoid of motor, sensory and autonomic blockade[18]. Apart from intraoperative pain relief, the postoperative recovery of orthopaedic patients depends largely on effective postoperative analgesia as it encourages early mobilization, recovery and rehabilitation.

Fentanyl is a synthetic lipophilic opioid with a rapid onset of action and unlike morphine, has fewer tendencies to cause delayed respiratory depression[19]. It is commonly used as an adjunct to intrathecal regional anesthesia.

With this background a comparative study was conducted to find out the effectiveness of intrathecal fentanyl as an adjuvant to isobaric ropivacaine in patients undergoing lower limb orthopaedic surgeries in terms of onset time and duration of sensory and motor block.

Haemodynamic parameters and rescue analgesic requirement in first 24 hours were also studied.

The patient age, weight and height were found to be comparable in both the groups. Also, there was no significant difference among the two groups in terms of ASA physical status and duration and type of surgery. Other parameters including hemodynamic variables, sensory and motor block characteristics, duration of analgesia (time to first rescue analgesic) and incidence of adverse effects were also studied and compared between the two groups.

Luck *et al*. used equal doses of hyperbaric ropivacaine, bupivacaine and levobupivacaine (15 mg) intrathecally for elective surgery and found that ropivacaine provided reliable spinal anaesthesia of shorter duration than bupivacaine and levobupivacaine and concluded that the recovery profile of ropivacaine may be useful where prompt mobilisation is required[20].

In 2005, Yegin A et al evaluated the effects of intrathecal fentanyl 25µg added to 18mg of 6mg/ml hyperbaric ropivacaine and observed that there was no significant difference between the groups in achieving the highest level of sensory block and in times taken to reach the maximum sensory block[21]. In 2015, a study was conducted by Seetharam KR et al in which patients were randomly assigned into two groups: Group RF (n = 50, fentanyl group) received 2.5 ml (18.75 mg) of 0.75% isobaric ropivacaine + 25 µg fentanyl (0.5 ml) and Group R (n = 50, saline group) received 2.5 ml (18.75 mg) of 0.75% isobaric ropivacaine + 0.5 ml normal saline intrathecally. There was no significant difference in the mean onset time for T10 level of blockade between the two groups (Group R vs. Group RF, 4.82 ± 0.748 min vs. 4.76 ± 0.797 min)[22]. The results of both the studies mentioned above correspond with our study in which the mean time of onset of sensory block at T10 dermatome and mean time taken to achieve maximum sensory blockade was 3.6±1.2min and 8.3±1.9min (Group A) and 3.4±1.3min and 8.0±1.5min (Group B) respectively.

In 2014, in a study conducted by Gupta K et al[23] patients were randomized into two treatment group of 80 patients each. Group I(RC) patients received intrathecal study solution of 4 mL 0.75% isobaric ropivacaine with 0.4 mL of 0.9% sodium chloride and Group II (RF) patients received 4 mL 0.75% isobaric ropivacaine with 0.4 mL fentanyl (20 µg). The mean total duration of sensory block was 316.40 ± 41.53 min in Group I and 359.80 ± 66.96 min in Group II. The difference in the total duration of sensory block between the two groups was statistically highly significant (p value – 0.0000017) similar to our study in which the mean duration of sensory block was 277.4 ± 27.0 minutes in Group A and 325.1 ± 36.8minutes in Group B (p-value < 0.0001) . Our study has shown that addition of fentanyl has significantly prolonged the duration of sensory block compared to the control group. Also, the mean duration of motor block was 225.8 ± 21.6 minutes in Group A and 240.8 ± 31.4 minutes in Group B. The motor blockade was of shorter duration in both groups when compared to duration of sensory blockade.

In our study, mean duration of analgesia (time to rescue analgesia) was 310.4±88.2 minutes in Group A and 343.7±39.8 minutes in Group B. Our study has shown that the addition of 20μg fentanyl to 0.75% isobaric ropivacaine significantly prolongs the duration of analgesia as compared to control group (p<0.0001).

Chung et al(2002)[24] also showed that adding 10 µg fentanyl to 18 mg hyperbaric ropivacaine improved intra-operative spinal anaesthesia for Caesarean sections and increased the analgesia in the early postoperative period. Goel *et al(2003)*[25] showed that adding fentanyl improved the quality and duration of analgesia when they compared fentanyl plus bupivacaine with bupivacaine alone for spinal anaesthesia in minor urological procedures. Yegin et al (2005)[21] showed that when intrathecal fentanyl was added to ropivacaine for transurethral resection of prostrate, the regression of block was delayed and time to first request of analgesia was longer.

Akanmu ON et al (2013)[26] compared the effect of addition of 25µg of fentanyl to 10 mg of 0.5% hyperbaric bupivacaine intrathecally on sixty consecutive ASA I and II patients scheduled to undergo elective open reduction and internal fixation of lower limb fractures. Time of complete analgesia (the time from injection of intrathecal drugs to the time of first complaint of pain by the patient) in fentanyl group was significantly longer than the control group with a p-value of <0.001.

The incidence of adverse effects was same among both the groups. Hypotension occurred only in four patients in Group B (8%) as compared to three patients in Group A (6%) and was treated with injection ephedrine 6 mg IV boluses. This was found to be statistically insignificant. Episodes of bradycardia also occurred in 3 patients (6%) in Group B and 2 patients(4%) in Group A which was also insignificant. Pruritis after intrathecal fentanyl is known but it was not significant in our study. Nausea and vomiting were observed in 4% and 2% patients in Groups A and B respectively. This suggested that the incidence of nausea and vomiting was not changed significantly among different groups. None of the patients experienced any residual neurological deficit, postdural puncture headache or transient neurological symptoms. There were slightly higher sedation score in group B at 2 hour and 4 hours post spinal anesthesia (i.e. 0 min and 2 hours postoperative) but the difference between the two groups was not statistically significant.

We conclude that intrathecal 20μg fentanyl seems to be an attractive alternative as an adjuvant to 0.75% isobaric ropivacaine in spinal anesthesia in lower limb surgeries. It is associated with prolonged sensory block, provides excellent quality of intraoperative analgesia and excellent quality of postoperative analgesia with early regression of motor block allowing early and pain free ambulation as compared to plain ropivacaine. It is haemodynamically stable in intraoperative and postoperative periods with insignificant side effects.

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