Clinical Investigation

Comparison of intrathecal ropivacaine-fentanyl and bupivacaine-fentanyl for major lower limb orthopaedic surgery: A randomised double-blind study

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ABSTRACT

Background and Aims: Intrathecal bupivacaine results in complete anaesthetic block of longer duration than ropivacaine. Fentanyl as an adjuvant may improve the quality of spinal block of ropivacaine while maintaining its advantage of early motor recovery. In this study, we proposed to compare the efficacy and safety of intrathecal ropivacaine-fentanyl (RF) with bupivacaine-fentanyl (BF) for major lower limb orthopaedic surgeries. **Methods:** Sixty patients were randomly allocated to receive either intrathecal 15 mg 0.5% ropivacaine with 25 mcg fentanyl (Group RF) or 15 mg 0.5% bupivacaine with 25 mcg fentanyl (Group BF). The onset, duration, spread of sensory and motor block, haemodynamic parameters and side effects were recorded. Statistical Package for Social Sciences 20 software was used for statistical analysis. **Results:** Time to reach highest sensory level and complete motor block were comparable. Sensory regression to L1 dermatome was 226 ± 46.98 min in Group RF and 229.33 ± 50.51 min in Group BF, $P = 0.36$. The motor recovery to Bromage scale 1 was faster in Group RF (242.8 ± 47.06 min) than Group BF (268 ± 49.9 min) $P = 0.023$. Time for rescue analgesia was prolonged in Group BF (263.33 ± 63 min) when compared to Group RF (234.44 ± 58.76 min), $P = 0.021$. The haemodynamic stability was better in Group RF than Group BF. **Conclusion:** Intrathecal RF provided satisfactory anaesthesia with haemodynamic stability for major lower limb orthopaedic surgery. It provided similar sensory but shorter duration of motor block compared to BF which is a desirable feature for early ambulation, voiding and physiotherapy.

Key words: Bupivacaine, fentanyl, intrathecal, orthopaedic surgery, ropivacaine

INTRODUCTION

Spinal anaesthesia is the most convenient anaesthetic technique that offers many advantages over general anaesthesia, including reduced stress response and improved post-operative pain relief. Spinal lignocaine not only provides shorter duration of anaesthetic blockade but also can cause transient neurological symptoms, and hence has been withdrawn.[1] However, spinal bupivacaine induces profound motor block of longer duration and delays home discharge after ambulatory surgery.[2] Ropivacaine, an amide local anaesthetic, has been introduced recently and used successfully to provide epidural analgesia for labouring women, caesarean delivery and post-operative analgesia.[3] Intrathecally, it has been used for day care procedures as it provides adequate sensory block with early motor recovery.[4] Ropivacaine has an improved safety profile over bupivacaine with a reduced central nervous system and cardio toxic potential and hence is gaining favour.[1,5]

Intrathecal opioids are synergistic with local anaesthetics and intensify the sensory block without increasing the sympathetic block while achieving

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satisfactory quality of spinal anaesthesia at a much lower dose of local anaesthetic.[6,7]

Hence, we conducted a study to compare the effects of ropivacaine with fentanyl (RF) versus bupivacaine with fentanyl (BF) on spinal anaesthesia characteristics for major lower limb orthopaedic surgeries.

METHODS

After approval of Institutional Ethical Committee, a prospective, randomised, double-blind study was conducted on 60 patients undergoing major lower limb orthopaedic surgeries. Written informed consent was obtained from all patients. Inclusion criteria include - patients of American Society of Anaesthesiologists physical Status I or II of either sex, aged between 18 and 60 years, presenting for lower limb orthopaedic surgery. Exclusion criteria were - patients having contraindications to spinal anaesthesia, a resting heart rate of <60/min, allergy to amide local anaesthetic, a significant history of substance abuse and pregnant women. Visual analogue score (VAS) for pain was explained to the patients pre-operatively as a 10-point scale wherein '0' indicates no pain and '10' indicates worst imaginable pain.

The study was conducted in 60 patients over a period of 6 months. They were randomly divided into two groups of 30 patients each by using the computer randomization table. Patients were randomly allocated to receive either intrathecal 3.5 ml of 15 mg of 0.5% ropivacaine with 25 mcg fentanyl (Group RF) or 15 mg of 0.5% bupivacaine with 25 mcg of fentanyl (Group BF).

Following arrival into the operation theatre, intravenous access was established, multipara monitor (electrocardiogram, non-invasive blood pressure and pulse oximeter) was attached and baseline parameters were recorded. After ensuring sterile conditions, spinal anaesthesia was performed, and the patient received one of the two study drugs. The drug combinations were prepared by the first anaesthesiologist, however various observations were made by the second anaesthesiologist who was blinded to the type of drug combination administered.

Heart rate, blood pressure, respiratory rate and oxygen saturation were monitored throughout the study. A decrease of more than 25% from the baseline in the systolic blood pressure (SBP) was considered hypotension and decrease in the heart rate below 50 beats/min was considered bradycardia and treated with intravenous ephedrine and atropine respectively.

The level of sensory and motor block was evaluated at 2, 4, 6, 8, 10 and 15 min and thereafter at 15 min interval for 6 h. The sensory block level was evaluated with the pin prick test, and the motor block level was determined according to the Bromage Scale (0 – no motor block, 1 – inability to raise extended leg, able to bend knee, 2 – inability to bend the knee, can flex ankle; and 3 – no movement).

During the tracking of the sensory block in patients, maximum sensory block level, time to achieve maximum sensory block, and it's regression to L1 dermatome were recorded. While tracking the motor block, time to achieve maximum motor block and the duration were recorded.

In the post-operative period, the time to first analgesic demand was noted when VAS was more than 4 and intravenous diclofenac, 75 mg was administered. Patients were observed for any discomfort, nausea, vomiting, shivering, pruritus, bradycardia and any other side effects and the need for additional medications was recorded.

Statistical Package for Social Sciences 20 software was used for statistical calculation. Statistical evaluation was performed using paired and unpaired *t*-test and analysis of variance. Data are presented as mean ± standard deviation and $P < 0.05$ was considered significant. Categorical data were analysed using the Chi-square test.

Assuming an increase in duration of sensory block of atleast 20% with addition of fentanyl to ropivacaine and with the power of 80% and Type 1 error of 5%, the sample size required was calculated as 30 in each group.

RESULTS

The demographic data in both the groups were comparable in terms of age, gender, height, weight and duration of surgery [Table 1].

The highest sensory level achieved was comparable at T6 dermatome. Time required to reach highest sensory level (Group RF - 6.86 ± 3.73 min,

Group BF - 7.07 ± 2.99 min, P = 0.34), complete motor block (Group RF - 6.02 ± 2.1 min, Group BF - 6 ± 3.6 min, P = 0.31) and sensory regression to L1 dermatome (Group RF - 226 ± 46.98 min and Group BF - 229.33 ± 50.51 min, P = 0.36) were comparable [Table 2]. The motor recovery to Bromage grade 1 was faster in Group RF (242.8 ± 47.06 min) than Group BF (268 ± 49.9 min) P = 0.023 [Table 2]. In group RF, 70% patients recovered with Bromage grade 1 at 240 min and Bromage Grade 0 at 360 min [Figure 1]. In Group BF, 40% patients recovered with Bromage grade 1 at 240 min and only 10% recovered with Bromage grade 0 at 360 min [Figure 2].

No patients required supplemental analgesia intraoperatively.

Both intrathecal RF and BF produced an initial moderate fall in blood pressure in keeping with the expected sympathetic blockade produced by the spinal anaesthesia. Although the SBP stabilised after 30 min, there was a statistical significant difference in two groups from 120 to 210 min [Figure 3]. Hypotension is requiring treatment with ephedrine occurred in 1 (3.3%) patient in Group RF as compared to 3 (10%) patients in Group BF. One patient in each group also required 0.6 mg atropine for bradycardia. The most commonly occurring adverse effect was the pruritus, experienced in 3 (10%) patients in each group. One patient in Group RF had nausea/vomiting and shivering as compared to none in Group BF [Table 3].

Table 1: Demographic data

Parameters	Group (n=30)	
	RF	BF
Age (years)	41.54±15.58	39.63±15.19
Weight (kg)	60.03±15.52	59.27±9.84
Height (cm)	156.48±8.54	154.2±6.80
Gender (male/female)	20/10	19/11
Duration of surgery (min)	125.43±58.43	125±59

Values are in mean±SD both groups were comparable. P > 0.05 non-significant.
SD – Standard deviation; RF – Ropivacaine fentanyl; BF – Bupivacaine fentanyl

Table 2: Spinal block characteristics

Parameters	Group RF	Group BF	P value
Highest sensory level (range)	T6 (T5-T8)	T6 (T5-T8)	
Time to reach peak sensory level (min)	6.86±3.73	7.07±2.99	0.34
Time to reach peak motor block, Grade 3 (min)	6.02±2.1	6±3.6	0.31
Time to sensory regression to L1 (min)	226±46.98	229.33±50.51	0.36
Time to motor regression to Grade 1 (min)	242.8±47.06	268±49.9	0.023*
Duration of analgesia (min)	234.44±58.76	263.33±63	0.021*

Values are in mean±SD. P > 0.05 non-significant; *P < 0.05 significant.
SD – Standard deviation; RF – Ropivacaine fentanyl; BF – Bupivacaine fentanyl

DISCUSSION

Ropivacaine is a long acting, enantiomerically pure (S-enantiomer) amide local anaesthetic, with low lipid solubility, which blocks nerve fibres involved in pain transmission (Aδ and C fibers) to a greater degree than those controlling motor functions (Aβ fibers).[1]

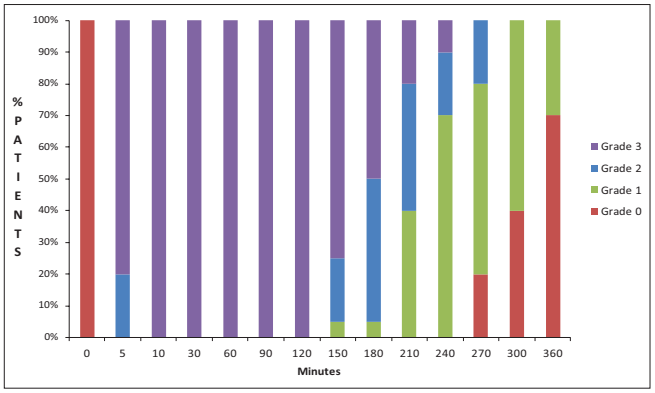

Figure 1: Motor block Grade 0 to Grade 3. Ropivacaine-fentanyl (Group RF)

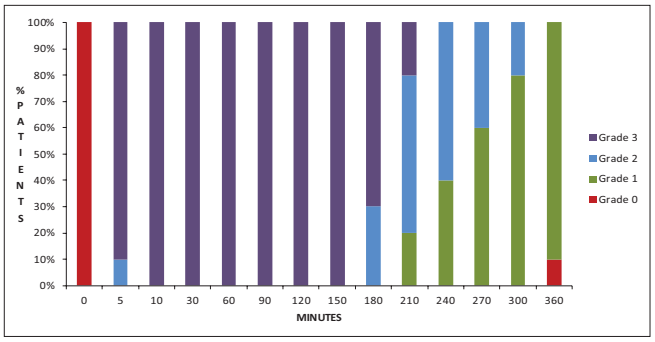

Figure 2: Motor block Grade 0 to Grade 3. Bupivacaine-fentanyl (Group BF)

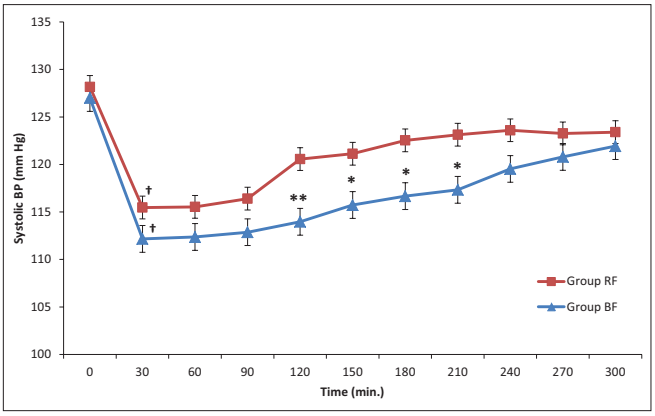

Figure 3: Systolic blood pressure over time in group ropivacaine-fentanyl and group bupivacaine-fentanyl. Paired t-test †P < 0.001. Unpaired t-test *P < 0.05, **P < 0.01

Table 3: Side effects

Parameters	Group RF (%)	Group BF (%)	*P* value
Hypotension	1 (3.3)	3 (10)	0.154
Bradycardia	1 (3.3)	1 (3.3)	0.5
Pruritis	3 (10)	3 (10)	0.5
Nausea/vomiting	1 (3.3)	0 (0)	0.160
Shivering	1 (3.3)	0 (0)	0.160

P > 0.05 non-significant. RF – Ropivacaine fentanyl; BF – Bupivacaine fentanyl

Intrathecal ropivacaine, in animal studies has shown to produce effective sensory block but shorter motor block than intrathecal bupivacaine and with no signs of neurological side effects.[8]

The present study demonstrated that both RF and BF as an adjuvant provided satisfactory anaesthetic conditions for lower limb surgeries. Most sub-arachnoid block features being comparable; there was significant early motor recovery with RF whereas BF provided prolonged post-operative analgesia.

McNamee *et al*. studied the efficacy and safety of two concentrations of intrathecal ropivacaine –7.5 mg/ml (18.75 mg) and 10 mg/ml (25 mg) for total hip arthroplasty where they found satisfactory anaesthetic conditions in terms of sensory and motor block.[9]

A dose response study done by Lee *et al*. provided a useful guide for clinicians to choose optimal dose of the spinal ropivacaine under different clinical situations. They observed that the ED50 and ED95 for the spinal ropivacaine in lower limb surgery of 50 min or less were 7.6 mg and 11.4 mg respectively.[10]

Malinovsky *et al*. compared intrathecal ropivacaine to bupivacaine in patients scheduled for trans-urethral resection of prostrate.[11] They found that 15 mg of intrathecal ropivacaine provided similar motor and haemodynamic effects but less potent anaesthesia than 10 mg bupivacaine for endoscopic urological surgery. 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.[12]

We proposed to study the efficacy of ropivacaine for major orthopaedic surgeries as an alternative to bupivacaine, using equimilligram dose (15 mg) as used by Luck *et al*.[12] While maintaining the advantage of low dose local anaesthetic, the use of analgesic adjuvants can improve the intra-operative quality of anaesthesia. Lipid soluble opioids such as sufentanil and fentanyl are the most commonly used adjuvants.[2,3] Studies have shown that intrathecal opioids can greatly enhance analgesia of sub-therapeutic doses of local anaesthetics.[13] Fentanyl added to local anaesthetic agent seems to be the most frequently used combination to enhance and increase the duration of sensory analgesia without intensifying the motor blockade or prolonging recovery from spinal anaesthesia.[14,15]

In obstetrics and non-obstetric patients, RF and BF in different concentrations and doses have been studied. Koltka *et al*. compared equipotent doses of the isobaric ropivacaine, 19.5 mg and bupivacaine, 13 mg, both with fentanyl, 20 mcg for the sub-arachnoid block in lower abdominal surgery, where they found that the RF is associated with lower level of sensory block and a shorter duration of motor block.[16] In another study by Lee *et al*., equal doses of intrathecal ropivacaine and bupivacaine (10 mg) with 15 mcg fentanyl were used for urology surgeries, and it was reported that ropivacaine provided similar sensory anaesthesia but shorter duration of motor block compared to bupivacaine.[17]

Our results are consistent with Lee *et al*. as we observed comparable levels of highest dermatome blocked, the time taken to reach the peak sensory and motor level and the duration of the sensory block up to L1 dermatome. The motor block was significantly shorter with Group RF (242.8 ± 47.06 min) although it outlasted the duration of orthopaedic surgery (125.43 ± 58.43 min). This feature is desirable as it encourages early ambulation, voiding and physiotherapy. Neurological side effects, if any, can also be detected early. The mean time for analgesia is significantly prolonged in Group BF as compared to Group RF. There was no demand for any intra-operative supplementary analgesics in either group.

After the initial fall in SBP in both the groups, Group RF recovered earlier than Group BF with a statistical significance between 120 min and 210 min ($P < 0.05$). This coincides with motor power recovery in Group RF that may explain the stabilizing of SBP during that period. The patients in Group RF were more stable haemodynamically, hypotension

was observed in 3.3% patients in the Group RF and 10% patients in the Group BF. This is in contrast to McNamee's study where he reported the hypotension in 24% patients with higher doses of the plain ropivacaine (17.5 mg, 25 mg) for total hip arthroplasy. Hypotension was also observed when he compared ropivacaine (17.5 mg) with bupivacaine (17.5 mg) in 12% and 26% patients respectively for the same surgery.[8,18] Pruritus is a well-known adverse effect of neuraxial narcotics. Three patients (10%) in each group experienced pruritus. This incidence is much lower compared to the incidence reported by Patra *et al*.(46%) and Khanna and Singh (20%) who also used fentanyl as adjuvant intrathecally.[19,20]

CONCLUSION

Intrathecal RF provides satisfactory anaesthesia with haemodynamic stability for major lower limb orthopaedic surgery. It provides similar sensory but shorter duration of motor block compared to BF which is a desirable feature for early ambulation, voiding, and physiotherapy.

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