

A Randomized Double Blind Controlled Interventional Study of Intrathecal Ropivacaine (0.75%) Alone or Ropivacaine (0.75%) with Fentanyl as Adjuvant in Lower Limb Surgeries under Spinal Anaesthesia

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Abstract: ***Background and Aim:** Postoperative pain is a well known morbidity and causes distress to the patients. Aim of this study was to assess the clinical efficacy of 3 ml of 0.75% ropivacaine alone versus ropivacaine with 25mcg fentanyl in spinal anesthesia for lower limb surgeries in terms of duration of analgesia, sensory and motor block characteristics, haemodynamic profile and complications. **Methods:** This study was conducted in a randomized double blind fashion on 80 ASA physical status I-II patients scheduled for lower limb surgeries. They were randomized into two groups of 40 patients in each group using sealed envelope technique. **Group A:** Patients received 3 ml 0.75% Isobaric Ropivacaine hydrochloride **Group B:** Patients received 3ml 0.75% Isobaric Ropivacaine with 25µg Fentanyl hydrochloride. We evaluated whether addition of fentanyl to intrathecal ropivacaine could make a significant effect on onset and duration of analgesia, sensory and motor block. **Results:** Isobaric Ropivacaine 3 ml 0.75% alone and with fentanyl (25mcg) in spinal anesthesia produced effective sensory-motor blockade of sufficient duration with stable hemodynamic profile to accomplish lower limb surgeries. Addition of fentanyl to Isobaric 0.75% Ropivacaine prolonged the duration of analgesia and sensory block, without affecting sympathetic or motor block characteristics. **Conclusion:** Addition of fentanyl to ropivacaine prolongs the duration of sensory block with stable hemodynamics and minimal side effects.*

Keywords: Lower limb surgeries, Isobaric Ropivacaine, Fentanyl, Spinal Anesthesia

1. Introduction

Pain is a distressing feeling often caused by intense or damaging stimuli. Because it is a complex, subjective phenomenon, defining pain has been a challenge. International Association for the Study of Pain (IASP) widely used definition states "Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage".^[1] Pain is frequently the result of nociception, an activity in the nervous system that results from stimulation of nociceptors.^[2] The first planned spinal anaesthesia for surgery in man was administered by August Bier on 16 August 1898.^[3] Subarachnoid block has a wide range of clinical applications for surgery (lower abdominal, lower limbs, pelvis, perineum and urological procedures). It is a convenient, early and effective method of anaesthesia. It has got inherent advantages like intense motor and sensory blockade, good relaxation, reliability, avoids side effects of multiple drugs used in general anaesthesia etc.^[4] However, it also produces a fixed duration of anaesthesia, postdural puncture headache, hypotension and lesser control of block height. LA when used alone is associated with short duration of action. Thus early analgesic intervention is needed in postoperative period. Various adjuvants have been used intrathecally to improve the quality and duration of spinal anaesthesia with better postoperative analgesia like epinephrine, neostigmine, midazolam, ketamine, fentanyl, buprenorphine, clonidine and dexmedetomidine.^[4] Local

anesthetics commonly used for spinal anaesthesia are lignocaine, bupivacaine, levobupivacaine and ropivacaine^[5]. Nowadays, Ropivacaine is gaining increasing popularity because of reduced risk of central nervous system and cardiac toxicity, early ambulation and good quality of postoperative analgesia^[5]. It is a long acting amide LA and has low lipid solubility; hence it blocks nerve fibres involved in pain transmission to a greater degree than those controlling motor functions. Fentanyl is an opioid which works at the receptacle site in the spinal cord. It acts primarily as agonist at mu opioid receptors to enhance spinal analgesia.^[6] With this background, this study was designed to compare intrathecal ropivacaine (0.75%) alone or ropivacaine (0.75%) with fentanyl as adjuvant in lower limb surgeries under spinal anaesthesia in terms of onset & duration of sensory & motor block, duration of analgesia & to evaluate the side effects, if any.

2. Material and Methods

After approval from the institutional ethics committee, this prospective, randomized, double blind, comparative study was conducted in Department of Anaesthesia and Department of Orthopaedics, S.M.S. Medical College and attached Group of Hospitals (Raj.) and informed consent was taken from each patient for participation in the study. Present study was conducted on 80 ASA physical status I-II patients, 40 in each group posted for lower limb surgeries. The patients having age between 25-60 year, weight 40-70

kg and height >140cm, were included. Exclusion criterias were patient refusal, any contraindication to regional anaesthesia, history of significant coexisting diseases like renal, cardiac or respiratory diseases etc., presence of anemia, fused spine, coagulation disorder, psychiatric illness patient on any medication for systemic disease and allergy to amide local anaesthetics and opioids. **GROUP A:** Patients received 3 ml 0.75% Isobaric Ropivacaine. **GROUP B:** Patients received 3ml 0.75% Isobaric Ropivacaine with 25µg Fentanyl. After taking written informed consent and confirming overnight fasting, patient was taken on the operation table. Routine monitors were attached and baseline vitals like BP, pulse rate, ECG and spo₂ were recorded. An 18G intravenous cannula had been inserted in the forearm, lactated Ringer's solution was started at 10ml/kg before subarachnoid block to all patients. Vitals were noted just before lumbar puncture. Spinal anaesthesia was performed at L₃-L₄ interspace with the patient in sitting position by using a 25G Quincke needle under strict aseptic conditions. Free flow of cerebrospinal fluid was verified before injection of the anesthetic solution 3.5ml volume, which was administered over 30 seconds. All patients were immediately placed in supine position. Monitoring was done using continuous electrocardiography, heart rate, non-invasive blood pressure and continuous pulse oximetry and patients were given 4.0L/min of oxygen by venti-mask. Vitals were checked every 5 minutes for first 30minutes then every 10minutes till surgery and then every 30 min for 4 hours and hourly upto the time when motor and sensory block recover completely, postoperatively. When adequate spinal block was achieved, the time from the end of intrathecal injection to readiness for surgery was recorded. Then the patient was positioned for planned surgery. **Hypotension** was defined as systolic arterial blood pressure (SABP) <90mmHg or a decrease in SABP by 25% or more from baseline values and was treated by incremental doses of mephentermine 5mg IV and IV fluid as required. **Bradycardia** was defined as fall in heart rate below 60beats per minute and was treated with incremental doses of atropine 0.3mg-0.6mg IV. **Respiratory depression** was defined as respiratory rate less than 8 breaths per minute and/or oxygen saturation less than 90% on room air. The sensory and motor blockade characteristics were assessed after the intrathecal injection at 2 min intervals until the surgical anaesthesia achieved. Sensory block was assessed by loss of sensation to pin-prick in the midline using short bevelled 27G hypodermic needle. **Surgical anaesthesia** was considered effective when at least T₁₀ dermatome level was anaesthetized: **Time 0** - the time of end of intrathecal injection was taken as time 0. **Onset of sensory blockade** when patient did not feel pin prick at T₁₀ level. **Duration of sensory block** time to regression of sensory block to S₁. **Duration of analgesia** time of first complaint of pain in the post operative period when patient demanded first dose of rescue analgesia. **Rescue analgesia** Injection diclofenac 75 mg i.m. was given when VAS score is more than 3. **Motor Blockade:** Motor block was assessed by Modified Bromage Score. **Onset of motor block:** was defined as the time taken from intrathecal injection of the study drug to the time taken to achieve complete motor block (grade-3) by using M. Bromage score. **Duration of motor block:** was assessed by recording the time elapsed from the maximum to the lowest M. Bromage score (3-0)

Modified Bromage Score

Grade	Criteria	Degree of block
0	Free movement of legs & feet	NIL (0%)
1	Just able to flex knees with free movement of feet	Partial (33%)
2	Unable to flex knees but with free movement of feet	Almost complete (66%)
3	Unable to move legs	Complete (100%)

Total duration of analgesia: Time taken from intrathecal drug administration to patient's first demand of rescue analgesia (VAS ≥ 3). **Visual analog score-** Postoperatively, the pain was assessed by using visual analog pain scale (VAS) between 0 and 10(0- no pain, 10- most severe pain), It was assessed every 30minutes.

Visual analog pain scale (VAS)

Score	Criteria
0	No pain
1,2,3	Mild pain
4,5,6	Moderate pain
7,8,9	Severe pain
10	Worst imaginable pain

Patients were allowed to receive rescue analgesics on VAS score of 3. I.M. Diclofenac 75mg was given as rescue analgesic. The time from intrathecal injection to first administration of rescue analgesic (total duration of analgesia) was noted. **Postoperative** sensory and motor block levels were assessed at 30 min intervals until normal sensation return. **Side effects** The incidence of adverse effects such as nausea, vomiting, shivering, respiratory depression, urinary retention, pruritus, sedation and hypotension were recorded. **End point of study-** Complete recovery of motor and sensory block. Volume and type of solution used, duration of surgery, surgeon complaint regarding operative condition if any were noted.

3. Statistical Analysis

All the statistical analysis of data was done with statistical programming software – SPSS (Statistical Package for the Social Science) version 21.0.0 (SPSS Inc., Chicago, Illinois, USA). The continuous variables (quantitative data) like age, weight, blood pressure, pulse rate, time were presented as mean and standard deviation and analyzed by applying t-test. The categorical variables (qualitative data) like ASA grade were presented in frequency and percentage and were analyzed with Chi-Square test (for nominal data). p value of <0.05 was considered statistically significant in all the analysis. For significance cut off values were as follows: p>0.05 = not significant
P<0.05 = significant

4. Observations and Results

Both groups were statistically comparable regarding mean age, weight of patients and duration of surgery (60-120 min).

Sensory and Motor block characteristics, Duration of Analgesia

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Onset time of Sensory Block (mins)	3.45	0.78	3.13	0.40	0.022 (S)
Duration of Sensory Block (mins)	289.50	10.61	307.00	15.06	P<0.001
Onset Time of Motor Block (mins)	7.03	1.10	7.33	1.16	0.239 (NS)
Duration of Motor Block (min)	274.25	10.35	277.88	15.31	0.218 (NS)
Duration of Analgesia (mins)	252.00	12.65	279.50	15.52	P<0.001 (S)

The haemodynamic parameters (PR, SBP, DBP, MAP & SPO₂) intra-operative and post-operative were similar in the two groups with no statistical significant difference. The mean onset of sensory block was statistically significant (P=0.022) between the two groups. The mean onset of motor block was not statistically significant (P=0.239) between the two groups. The mean duration of sensory block was statistically significant (P<0.001) between the two groups. The mean duration of motor block was not statistically significant (P=0.218) between the two groups. The duration of analgesia (requirement of first analgesic dose) was greater in Group B in comparison of Group A. It was statistically significant between the two groups. (P<0.001) There was no significant incidence of any side effects (nausea, vomiting, hypotension & bradycardia) in the two groups.

5. Discussion

Spinal anaesthesia is the most common anaesthesia technique used for lower extremity surgery.^[15] Ropivacaine is levo-isomer of bupivacaine which is less toxic than bupivacaine. Ropivacaine has an improved safety profile over bupivacaine with a reduced central nervous system and cardiotoxic potential and hence is gaining favour.^[16,17] Fentanyl is a synthetic lipophilic opioid with a rapid onset of action and unlike morphine, has fewer tendency to migrate rostrally to the fourth ventricle in sufficient concentration to cause delayed respiratory depression.^[18] It is commonly used as an adjunct to intrathecal regional anaesthesia and reduces visceral and somatic pain.^[19] Gupta K et al (2013)^[20] conducted a study to evaluate the anaesthetic efficacy of intrathecal 0.75% isobaric ropivacaine alone or with fentanyl in elderly patients undergoing transurethral resection of prostate. They concluded that intrathecal 0.75% isobaric ropivacaine alone or with fentanyl provided effective surgical anaesthesia for transurethral resection of prostate in elderly patients. Our study clearly demonstrates that addition of fentanyl to Ropivacaine results in significant shortening of onset time of sensory block. It is a well known fact that opioids act synergistically to intrathecal opioids and potentiate the block. Opioids work in intrathecal space by agonist interaction with opioid mu receptors in dorsal gray horn of spinal cord which modulates the function of afferent pain fibres.^[7] Results of present study clearly show that addition of fentanyl to ropivacaine prolongs the duration of sensory block with stable hemodynamics and minimal side effects.

Sensory Block Characteristics

Results of our study showed that addition of fentanyl to Ropivacaine led to significant shortening of sensory onset time, because fentanyl has synergistic effect with local anaesthetic and addition of fentanyl also makes the intrathecal solution hypobaric facilitating its cephalic spread. Another contributing factor was change in baricity of Ropivacaine solution by adding Fentanyl, therefore intrathecal solution became little hypobaric in Group B (Ropivacaine with fentanyl) as compared to Group A (Ropivacaine alone) and resulted in faster onset of sensory block in Group B in present study. Fentanyl acts on μ receptor in the spinal cord and exerts its action by opening K⁺ channels and reducing Ca⁺⁺ influx resulting in inhibition of transmitter release^[21]. This is the reason that patients in whom fentanyl was given along with ropivacaine in spinal anaesthesia had significantly longer duration of the sensory block as compared to patients receiving ropivacaine alone. In terms of sensory block duration our results are similar to study by Yegin A et al (2005)^[22] who compared addition of fentanyl to ropivacaine versus ropivacaine alone in TURP surgeries and concluded that addition of fentanyl improved the quality and prolonged the duration of analgesia. Result of our study match with study done by Fauzia A Khan et al^[23] in which the addition of 30mcg buprenorphine to bupivacaine increased the duration of sensory block significantly.

Motor Block Characteristics

The result of our study demonstrated that addition of fentanyl to ropivacaine in spinal anaesthesia accelerated the sensory onset but has no effect on motor onset time. The synergistic interaction between spinal opioids and local anaesthetics is characterized by enhanced somatic analgesia without effect on the degree or level of the local anaesthetic induced sympathetic or motor blockade.^[24,25] The result of our study was comparable with study done by Kumkum G et al^[26] which was aimed to evaluate the anaesthetic effects of intrathecal fentanyl as an adjuvant to 0.75% ropivacaine on onset, duration, intensity and recovery time of sensory and motor blockade of subarachnoid block for infra-umbilical surgery. In terms of motor block duration our results validates the findings of Gupta K et al (2013)^[20] who conducted a study to evaluate the anaesthetic efficacy of intrathecal 0.75% isobaric ropivacaine alone or with fentanyl in elderly patients undergoing transurethral resection of prostate. They found no statistically significant difference in motor block duration between the group R (218.5 ± 45.7) and group RF (235.13 ± 26.8) (P=0.14).

Duration of Analgesia

In our study time of first complaint of pain in postoperative period was considered as duration of analgesia, which was significantly longer in Group B (ropivacaine with fentanyl) (279.50±15.52 min) as compared to Group A (ropivacaine alone) (252.00±12.65 min) (P<0.001). Similar to our study, Seetharam et al (2015)^[27] conducted a study to evaluate the effects of the isobaric ropivacaine in combination with fentanyl versus isobaric ropivacaine alone in 100 hundred patients in spinal anaesthesia for lower abdominal and lower limb surgeries. They reported that duration of analgesia was significantly longer in Group RF (442.2±25.3 min) as compared to group R (314.3±15.6 min) (p< 0.01). Fentanyl

has an analgesic effect as it modulates pain mainly at the spinal cord rather than in the brain. A site of action in the spinal cord may provide analgesia with less sedation, confusion and nausea, which are adverse effects often associated with intravenous narcotics.

Hemodynamic Parameters

In our study, HR, SBP, DBP, and SpO₂ showed no significant change from baseline during intraoperative period in both groups. Both groups were statistically comparable regarding vital parameters like heart rate, systolic blood pressure, diastolic blood pressure and SpO₂ during intra-operative period ($p > 0.05$). Similarly Gupta K et al (2014)^[26] conducted a study to evaluate the clinical efficacy and safety of intrathecal fentanyl as an adjuvant to 0.75% isobaric ropivacaine in subarachnoid block for infra umbilical surgery in 160 patients. They reported that there was no statistically significant difference in hemodynamic data including SBP, DBP, MBP, HR, SpO₂ ($p > 0.05$), between two groups. This showed that isobaric Ropivacaine alone and with fentanyl in spinal anaesthesia produces effective sensory motor blockade without affecting hemodynamic variables significantly.

Side Effects

In our study, we looked for side effects such as nausea, vomiting, hypotension and bradycardia after spinal anesthesia. We did not encounter any significant intraoperative and post operative side effects. No other adverse effects were observed in study. There were no significant difference regarding side effects between two groups ($p > 0.05$).

6. Conclusion

We concluded that

- Addition of fentanyl to ropivacaine results in significant shortening of sensory onset time, significant prolongation of duration of analgesia and duration of sensory block.
- Isobaric Ropivacaine (22.5 mg) in spinal anesthesia produces effective sensory-motor block of sufficient duration with stable hemodynamic profile to accomplish lower limb surgeries.
- The motor block duration was shorter as compared to sensory block duration in various studies using ropivacaine in spinal anesthesia including ours that imparts the benefits of early mobilisation and voiding. Being less cardio-neuro toxic Ropivacaine seems to be reasonable alternative to most commonly used agent isobaric ropivacaine in spinal anesthesia for lower limb surgery without significant side effects.

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