ORIGINAL ARTICLE

Intrathecal fentanyl as an adjuvant to 0.75% isobaric ropivacaine for infraumbilical surgery under subarachnoid block: A prospective study

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ABSTRACT

Background: Subarachnoid blockade can be used in all surgical procedures carried out on the infraumbilical region. This study was aimed to evaluate the clinical efficacy and safety of intrathecal fentanyl as an adjuvant to 0.75% isobaric ropivacaine on onset, duration, intensity, and recovery time of sensory and motor blockade of subarachnoid block for infra umbilical surgery. **Methods:** One hundred sixty adult consented patients of either gender with American Society of Anesthesiologist ASA I and II scheduled for infraumbilical surgery were randomized into two groups of 80 patients each to receive either intrathecal study solution of 4 mL of 0.75% ropivacaine with 0.4 mL of 0.9% sodium chloride (Group I-Ropivacaine Control Group RC) or fentanyl (20 μg) (Group II-Ropivacaine with Fentanyl RF). The end points were hemodynamic variability, onset of analgesia at T 10, maximum sensory analgesic level, time to complete motor blockade, duration of sensory and motor blockade and adequacy of surgical anesthesia. The post-spinal nausea and vomiting, shivering, pruritus, respiratory depression or any other side-effects were also assessed. At the end of study, data were systematically complied and analyzed for statistically significance. **Result:** The intrathecal fentanyl has accelerated the onset time to achieve sensory blockade to T10 dermatome and motor blockade. Small dose of intrathecal fentanyl with ropivacaine has prolonged the duration of analgesia in the early post-operative period when compared with intrathecal ropivacaine alone. The intraoperative hemodynamic variability showed no statistically significant differences between groups. **Conclusion:** Intrathecal fentanyl as an adjuvant to 0.75% isobaric ropivacaine demonstrated better clinical profile as compared to ropivacaine alone.

Key words: *Fentanyl, ropivacaine, subarachnoid block*

INTRODUCTION

Subarachnoid blockade can be used in all surgical procedures carried out on the lower half of the body, which includes surgery on the lower limbs, pelvis, perineum, and urological procedures. It also has utility in obstetric practice to provide anesthesia for elective and emergency procedures. Dural puncture is performed and the small amount of local anesthetic drug is deposited into the cerebrospinal fluid to produce anesthesia, which works by inhibition of sodium ion channel. All local anesthetic drugs except ropivacaine are racemic mixtures with different potency and toxicity.[1]

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Ropivacaine, a long acting amide local anesthetic, shares many physiochemical properties with bupivacaine, but with less systemic toxicity and greater margin of safety due to its purity in S-enantiomer form. Recent clinical data have shown that ropivacaine is effective and safe for regional anesthetic techniques. The low lipid solubility of ropivacaine leads to greater sensory-motor differentiation by blocking sensory nerve fibers more readily than motor fibers. Early recovery of motor function is associated with decreased incidences of venous thrombo-embolism and shorter hospitalization.[2-4]

The factors which affect the distribution of local anesthetic in the subarachnoid space are baricity of local anesthetic

solution, position of the patient during and just after injection and dose of local anesthetic injected. Isobaric solution of ropivacaine is as dense as CSF with baricity equal to 1.0 and patient positioning does not affect the spread of ropivacaine.[5,6]

Local anesthetic and opioid combination techniques have been studied in the surgical population. The local anesthetic works at nerve axons while the opioid works at the receptacle site in the spinal cord. Fentanyl acts primarily as agonist at μ opioid receptors to enhance spinal analgesia.[7,8]

Considering above facts, this study was aimed to evaluate the anesthetic effects of intrathecal fentanyl as an adjuvant to 0.75% isobaric ropivacaine on onset, duration, intensity and recovery time of sensory and motor blockade of subarachnoid block for infra umbilical surgery.

METHODS

After approval from the Institutional Ethical Committee and a written informed consent, the present prospective double-blind randomized study was carried out on 160 ASA grade I and II patients aged 18-65 years of either sex, scheduled for elective infra umbilical surgeries of less than 120 min duration under subarachnoid block.

All patients were subjected to pre-anesthetic assessment prior to enrolment for the study. Patients with history of pre-existing cardiac or pulmonary diseases, neurologic or renal dysfunction, bleeding or coagulation disorder, deformity of the spinal column, known hypersensitivity to study drugs or using any drug that modifies pain perception, cutaneous infection and patient refusal to technique were excluded from the study. Before the commencement of subarachnoid block, all patients were instructed on the methods of sensory and motor assessments.

Patients were randomized, according to computer generated number, 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 drug was prepared by an anesthesiologist who was blinded to study protocol and was not involved in patient assessment.

After arrival into the operation theater, standard monitor was attached and base line vital parameters of heart rate, electrocardiogram, pulse oximetry, and non-invasive arterial blood pressure were recorded. An intravenous line was secured and patients were preloaded with ringer lactate solution 10 mL/kg, 15 min before initiation of subarachnoid block. Under all aseptic conditions, lumber puncture was performed with a 25 gauge Quincke spinal needle, using the midline approach at L2-3 or L3-4 intervertebral space, in a sitting position. After free flow of cerebrospinal fluid, one of the study drug solutions was injected over a period of 30 s and patient was laid supine on a horizontal table.

The sensory and motor blockade characteristics were assessed after the intrathecal injection at 2 min intervals until the surgical anesthesia was achieved. The segmental level of sensory block to pin prick was assessed bilaterally along the midclavicular line by using a short beveled 27 G hypodermic needle. The motor blockade of the lower extremities was evaluated bilaterally by modified Bromage scale (0-3): 0 = full movement and no power impairment, 1 = unable to raise extended leg at the hip but able to flex knee, 2 = unable to flex the knee but able to move ankle joint, 3 = no motor activity. The surgical anesthesia was considered effective when at least T 10 dermatome level was anesthetized. Post-operatively the sensory and motor block levels were assessed at 30 min intervals until normal sensation returned.

The onset time of sensory blockade at T 10 dermatome, level of maximum cephalad dermatome anesthetized, time taken to achieve maximum sensory block and time to total regression of sensory block was observed. Time taken to achieve complete motor blockade and time to complete recovery from motor blockade was also observed.

Hemodynamic parameter of systemic arterial blood pressure and heart rate were recorded at baseline and thereafter at every 3 min interval during the first 10 min, and then at 5 min interval during the intra-operative period. Oxygen was administered at a rate of 3 L/min via Hudson face mask. Any change in heart rate and blood pressure was defined as an increase or decrease of more than 20% from the baseline. The hypotension was treated with additional ringer lactate solution and bolus of mephentermine 6 mg. Bradycardia (heart rate <55 beats/min) was treated with intravenous atropine 0.25-0.5 mg. Nausea and vomiting was treated with ondansetron.

Post-operatively, all patients were evaluated for possible adverse effects of nausea, vomiting, sedation, pruritus, shivering, urinary retention or any transient neurologic deficit and managed symptomatically.

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 Analysis of Variance (ANOVA), student *t*-test, and Chi-square test as applicable. Block characteristics were compared using Mann Whitney U test. A '*P*' value <0.05 was considered statistically significant.

RESULTS

The study of intrathecal fentanyl as an adjuvant to 0.75% isobaric ropivacaine for infraumbilical surgery under subarachnoid block was successfully completed and all patients have co-operated fully with the subsequent assessments of block characteristics. The demographic data were similar between groups for age, sex, weight, height and ASA physical status [Table 1].

Hemodynamic characteristics

The baseline mean heart rate and systemic arterial blood pressure were comparable between the groups. The mean values of systolic blood pressure did not show statistically decline from the base values. Both groups have shown an initial moderate fall in mean arterial blood pressure of statistically significance. Only seven patients of Group I and 10 patients of Group II have suffered hypotension and were managed with an increased rate of intravenous ringer lactate and mephentermine 6 mg. Only two patients of Group I and six patients of Group II were treated with bolus of intravenous atropine [Figures 1 and 2].

Sensory and motor block characteristics

The mean onset time of adequate sensory analgesia at T10 dermatome was 3.2 ± 1 min in Group I and 3.5 ± 1 min in Group II. The mean time to reach the highest level of T6 for sensory blockade was 9.8 ± 3.2 min in Group I and 8.13 ± 1.92 min in Group II with no statistically significant difference. The mean total duration of sensory analgesia was 316.40 ± 41.53 min in Group I and 359.80 ± 66.96 min in Group II. The difference in total duration of sensory analgesia between groups was statistically highly significant.

The mean time taken for motor blockade up to Bromage scale 3 was 12.4 ± 2.6 min in Group I and 11.9 ± 2.5 min in Group II. Bromage scale 3 was observed in 96% of patients of both groups. The mean duration of motor blockade was 283.67 ± 40.77 min in Group I and 310.34 ± 52.81 in Group II. The difference in mean duration of motor blockade was statistically highly significant [Table 2].

The motor blockade was of shorter duration in both groups when compared to duration of sensory analgesia (283.67 ± 40.77 min vs. 316.40 ± 41.53 min in Group I and 310.34 ± 52.81 min vs. 359.80 ± 66.96 min in Group II).

The respiratory depression was not observed in any patient. Mild pruritus was observed in six patients and no medical treatment was required. Shivering was noticed in 7 (4.3%) patients, whereas nausea occurred in 10 (5.5%) patients and was managed by intravenous ondansetron. No patient complaint of any neurological symptoms [Table 3].

DISCUSSION

The present study has evaluated the clinical efficacy and safety of intrathecal fentanyl as an adjuvant to 0.75% isobaric ropivacaine for infraumbilical surgeries under subarachnoid block. The intrathecal fentanyl with 0.75%

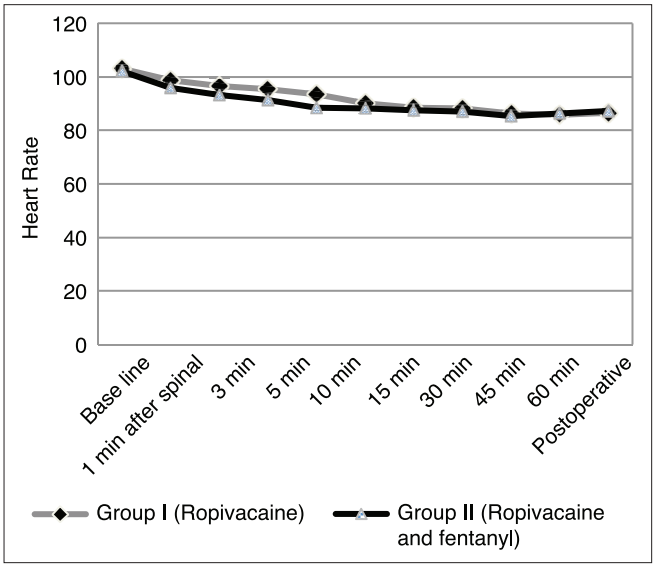

Figure 1: Comparison in heart rate between groups

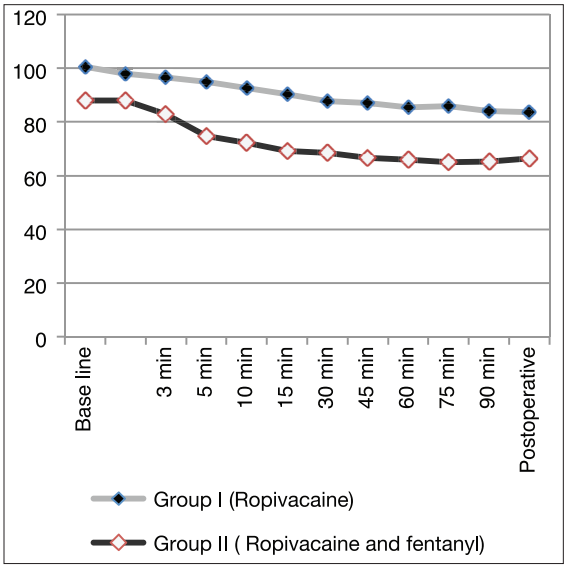

Figure 2: Comparison in mean arterial blood pressure

Table 1: Demographic profile of patients

Parameters	Group I-RC	Group II-RF	*P* value
Age (years)	36.84±13.19	38.42±14.32	0.25
Sex (male:female)	55:25	62:18	-
Weight (kg)	60.38±9.65	61.92±10.11	0.25
Height (cm)	165.81±6.97	166.88±5.88	0.15
ASA grade I/II	72:8	74:6	-

RC – Control Group; RF – Fentanyl Group; ASA – American Soiciety of Anesthesiologist Data expressed as mean and standard deviation

Table 2: Sensory and motor blockade characteristics

Parameters	Group I-RC	Group II-RF	*P* value
Onset time of sensory blockade at T 10 level (min)	3.2±1.5	3.5±1	0.08
Maximum cephalad dermatome	T 6 (T6-T10)	T 4 (T4-T10)	0.14
Time taken to achieve maximum sensory blockade (min)	9.8±3.2	8.13±1.92	0.06
Total regression of sensory block (S1 level)	316.40±41.53	359.80±66.96	0.0000017**
Time taken to achieve complete motor blockade (modified Bromage scale 3) (min)	12.4±2.6	11.9±2.5	0.05*
Duration of motor blockade (modified Bromage scale -0) (min)	283.67±40.77	310.34±52.81	0.00029**

RC – Control Group; RF – Fentanyl Group. Data expressed as Mean±SD. **P* value <0.05 statistically significant; ***P* value <0.05 statistically highly significant

Table 3: Intraoperative and post-operative adverse events

Adverse events	Group I-RC (%)	Group II-RF (%)
Hypotension	07 (8.75)	10 (12.5)
Bradycardia	02 (2.5)	06 (7.5)
Shivering	04 (5)	03 (3.75)
Headache	0	0
Nausea, vomiting	03 (3.75)	02 (2.5)
Pruritus	02 (2.5)	04 (5)
Respiratory depression	0	0
Urinary retention	0	0
TNS	0	0

TNS – Transient Neural Symptoms; RC – Control Group; RF – Fentanyl Group

ropivacaine was well-tolerated and provided clinically effective surgical anesthesia. The mean duration of sensory analgesia was increased when intrathecal fentanyl was added to ropivacaine. All patients showed motor blockade of shorter duration as compared to sensory blockade; hence, more rapid recovery was observed along with early ambulation and voiding. Intrathecal ropivacaine provided cardiovascular stability with only few episodes of hypotension, which were manageable with rapid intravenous infusion and vasopressors. No systemic and neurotoxic effects of intrathecal ropivacaine were observed in any patient during the study.

Ropivacaine has demonstrated improved safety profile during regional anesthesia techniques. It has been used for providing effective regional anesthesia for patients undergoing total hip replacement, transurethral resection of prostate and lower abdominal or limb surgery.[9-12] Intrathecal ropivacaine provided cardiovascular stability with low incidence of bradycardia. Nuray and Berrin in their study of intrathecal ropivacaine with fentanyl did not find any significant difference with respect to hemodynamic parameters.[13] The outcome in their study was comparable to our study.

Clinical efficacy and safety of two doses of 0.75% ropivacaine, 3.5 ml (26.25 mg) and 4.5 ml (33.75 mg) for spinal anesthesia were compared by Wong *et al*. in patients undergoing lower limb and lower abdominal surgery and concluded that both doses of 0.75% ropivacaine have the same efficacy and safety in these patients.[14] The duration of blockade profile is in accordance to present study.

By using small doses of local anesthetics, the distribution of spinal block can be limited, but low doses could not provide an adequate level of sensory block. Adjuvants like opioids can be used to enhance analgesia and successful spinal anesthesia due to their synergetic action. Fentanyl has been widely used as an adjuvant to local anesthetics for enhancement of analgesia without intensifying motor and sympathetic block of spinal anesthesia, thus resulting in lower incidence of hypotension, early recovery and mobilization.[7]

Various reports have shown that the addition of small dose intrathecal fentanyl (10-25 μg) to local anesthetics during spinal anesthesia has enhanced the duration of sensory analgesia without intensifying the motor block or prolonging recovery. The combination of 0.75% ropivacaine and fentanyl (20 μg) has accelerated the onset of sensory and motor blocks during the subarachnoid blockade as compared with ropivacaine alone in the present study.

The potency of intrathecal ropivacaine is altered by co-administration with opioids. Previous study by Yegin *et al*. 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.[15]

Parlow *et al*. established the fact that hypobaricity influenced the extent of subarachnoid block and explained high

cephalic levels of sensory block when fentanyl was added to isobaric local anesthetic solution.[16] In the present study, sensory level of T4 was observed in group RF but in group RC the extent of sensory block reached only up to T6 dermatome.

Although ropivacaine is safe and well-tolerated during subarachnoid block, a few adverse effects were observed in the present study. Besides hypotension and bradycardia, pruritus, shivering, and nausea were also encountered.

CONCLUSION

Intrathecal fentanyl as an adjuvant to 0.75% ropivacaine was safe and well-tolerated for infra umbilical surgeries under subarachnoid blockade with reduced systemic toxicity. Early mobilization and voiding accelerate post-operative recovery and earlier discharge. Its clinical profile gives reasonable choice due to rapid recovery of motor function.

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