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A Randomized Double Blind Comparative Study Of Fentanyl And Dexmedetomidine As Intrathecal Adjuvants To 0.75% Hyperbaric Ropivacaine In Lower Limb Orthopaedic Surgeries.

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ABSTRACT

Background: Ropivacaine, a long-acting amide local anesthetic agent, is a pure S enantiomer of bupivacaine. Intrathecal adjuvants have been used with local anesthetics for better hemodynamics and to provide postoperative analgesia. In this study we used Dexmedetomidine in comparison with Fentanyl, as an intrathecal adjuvant. The aim of this study is to evaluate the onset and duration of sensory and motor block, hemodynamic effect, and adverse effects of Dexmedetomidine or Fentanyl given intrathecally with hyperbaric 0.75% Ropivacaine.

Materials and Methods: In this randomized clinical trial, sixty patients belonging to American Society of Anesthesiologists class I and II scheduled for elective lower limb orthopaedic surgeries were studied. Patients were randomly allocated into two groups. Group RD received 3ml Hyperbaric Ropivacaine 0.75 % plus Dexmedetomidine 15 *microgram* and Group RF received 3ml of Hyperbaric Ropivacaine 0.75 % plus Fentanyl 25 *microgram*.

Results: The time of onset of sensory block with Dexmedetomidine group (RD) (1.563±0.3min) when compared to Fentanyl group (RF) (2.475±0.4 min), was significantly shorter (P<0.05). The time of onset of motor blockade was also significantly faster (P<0.05) with Group RD (1.86±0.35min) than that of Group RF (3.75±0.67min). Patients in Dexmedetomidine group (RD) had a significantly longer sensory and motor block time than patients in Fentanyl group (RF).

Conclusion: Dexmedetomidine as an intrathecal additive is associated with faster onset and prolonged duration of sensory and motor blockade, hemodynamic stability, and reduced demand for rescue analgesics in 24 hour post-operative period as compared to Fentanyl.

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 1, 2024

Keywords: Subarachnoid block, Hyperbaric Ropivacaine 0.75%, Dexmedetomidine, Fentanyl, lower limb orthopaedic surgeries.

INTRODUCTION

Subarachnoid block is a well-established anesthetic technique that is simple to perform and has a high success rate. It is a better and safer alternative to general anesthesia for a variety of infra-umbilical, perineal and lower limb surgeries [1].Orthopaedic surgeries are commonly performed under regional anesthesia, with subarachnoid block being preferred technique for lower limb surgeries. As patient will be awake, it helps in minimizing the problems associated with airway manipulation and need for supplemental intravenous analgesia.Bupivacaine is one of the first drugs approved for spinal anesthesia. Its side-effects such as bradycardia, hypotension, cardiac and central nervous system toxicity, have led to the search for better alternative drugs.

One of the recent alternatives to bupivacaine is Ropivacaine, a pure s-enantiomer, which is a long-acting amide with less lipid solubility and less toxicity. Low lipid solubility causes less motor blockade as it blocks A-alpha and C fibers, thereby carrying information related to muscle sense more slowly than bupivacaine does. [(2)]In this study, we used 0.75% hyperbaric Ropivacaine with Fentanyl 25 microgram (mcg) as additive in one group (RF) and 0.75% hyperbaric Ropivacaine with Dexmedetomidine 15mcg in another group (RD).Fentanyl is a synthetic opioid with central action. Intrathecal fentanyl improves the quality of intraoperative anaesthesia and early postoperative analgesia with lesser requirement of local anaesthetic dosage.[(3,4,5)]

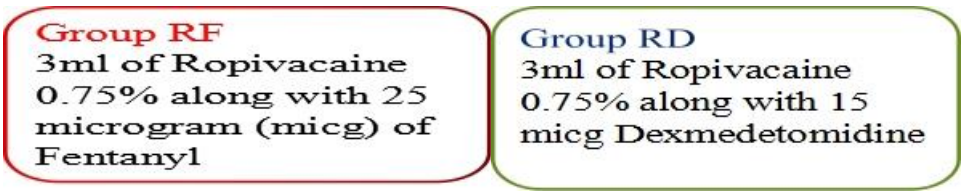
Dexmedetomidine is highly selective alpha-2 adrenergic agonist. It is antinociceptive (due to its agonistic property) for both somatic and visceral pain, and thus prolongs the duration of sensory blockade. It also has sedative, anti-anxiety, analgesic, neuroprotective, and anesthetic-sparing effects. [(5)]Post surgical pain is one of the most important problems that causes discomfort for the patient and prolongs hospital stay. Using analgesics alone cannot effectively control moderate to severe pain. Femur fractures in middle or old age cause severe pain after surgery and might lead to complications such as delayed movement, deep vein thromboembolism, and bed sores [(6,7,8)]Hence in this study we use adjuvants in subarachnoid block to control postoperative pain. [(9,10,11)]

METHODS AND METHODOLOGY

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 1, 2024

The study was conducted at Hassan Institute of Medical Sciences, A tertiary referral health care center, from October 2022 to December 2022. After approval of ethical committee of the institution, informed written consent was obtained from all the patients. Inclusion criteria was age 18–60 years, either sex, American Society of Anesthesiologists (ASA) physical status I or II, presenting for elective lower limb orthopaedic surgeries. Exclusion criteria was patient aged more than 60 and less than 18yrs, hypersensitivity to drug, infection at injection site, bleeding diathesis, posted for emergency surgeries, ASA 3 or 4, patient taking beta blockers.

All patients received tablet Alprazolam 0.25 mg and tablet ranitidine 150mg orally, the night before surgery. All the patients were kept for 8 hour fasting prior to surgery. The patients were co-loaded with Ringer's Lactate solution at 15 mL/kg. They were monitored with noninvasive blood pressure, heart rate, respiratory rate, pulse oximetry, and electrocardiogram. Patients were assigned into two groups by randomization based on allocation sequence by computer generated random number tables. The syringes were made to look identical, and both the patient and the investigators were blinded for the study. Using aseptic precautions, 25G Quincke Babcock's spinal needle was introduced through L3–L4 interspaces in sitting position.



Intrathecal injection was given over approximately 0.2ml/sec. 3ml 0.75% hyperbaric Ropivacaine plus Dexmedetomidine 15 *microgram* (group RD) or 3ml 0.75 % hyperbaric Ropivacaine plus Fentanyl 25 *microgram* (group RF) was used. Immediately after completion of the injection patients were made to lie supine.

` Oxygen (4 L/min) was administered via a mask if the pulse oximeter reading decreased below 90%. Hypotension, defined as a decrease of systolic blood pressure by more than 20% from baseline or a fall below 90 mmHg, was treated with incremental IV doses of mephentermine 6 mg and IV fluid as required. Bradycardia, defined as heart rate < 50 bpm, was treated with IV atropine 0.6 mg. Vitals including heart rate, blood pressure, respiratory rate and spO2 was recorded at regular intervals. Sensory block was assessed every 5 minutes till 20 mins, then every 10 mins till one hour of surgery, using the loss of sensation to pinprick, using 22-guage hypodermic needle. Assessment of motor block will be performed according to the Modified Bromage scale. Sedation was assessed by a Modified Ramsay sedation scale. The incidence of adverse effects, such as nausea, vomiting, shivering, pruritus, respiratory depression, sedation, bradycardia and hypotension if any, will be documented.

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 1, 2024

Assessment of motor block: Motor block in the lower limbs was graded according to the Modified Bromage scale [8]
Grade 0 = No motor block
Grade 1 = Inability to raise extended leg, able to move knees and feetGrade 2 = Inability to raise extended leg and move knee, able to move feetGrade 3 = Complete motor block of the lower limbs.

Assessment of sensory block: Sensory block was assessed every 5 minutes till the loss of sensation to pinprick, using 22-guage hypodermic needle.
3-points scale used:0 - Sharp pain,
1 - Dull pain (analgesia),2 - No pain (anesthesia).

Duration of analgesia was measured till the patient has VAS score >3 and Inj. Diclofenac 75mg IV slow was given as rescue analgesic.VAS score: 0-10 score: 0-No pain; 1,2-Mild pain; 3,4,5-Moderate pain; 6,7-Severe pain; 8,9-Very severe pain; 10-Worst possible pain

Modified Ramsay score for sedation:scoring from 1- 6 1 -Anxious, agitated, restless.2- Cooperative, oriented, tranquil.3- Responds to commands only.4- Brisk response to light glabellar tap or loud noise.5- Sluggish response to light glabellar tap or loud noise.6- Asleep or unarousable.

STATISTICAL ANALYSIS

Statistical analysis was done using the Statistical Package for Social Science (SPSS22.0 version). In this study 95% confidence limit, 1% error and 90% power was used. Sample size of 60 was considered to be adequate. The results were expressed as Mean ± standard deviation or percentage. Unpaired t-test is the test of significance for quantitative data. Chi square test is the test of significance for qualitative data. P-values of <0.05 were considered statistically significant.

RESULTS

Demographic data:

The groups were comparable with respect to age, height, gender, weight, and ASA physical status (*P*> 0.05). Mean age, height, weight in Group RD were 42.21 ± 3.8 years, 158±1.3cm, 65.13 ±13.4kg, and Group RF were 44.35 ±4.08 years, 156 ± 1.8 cm and 64.42 ± 9.6kg, respectively (Table 1).

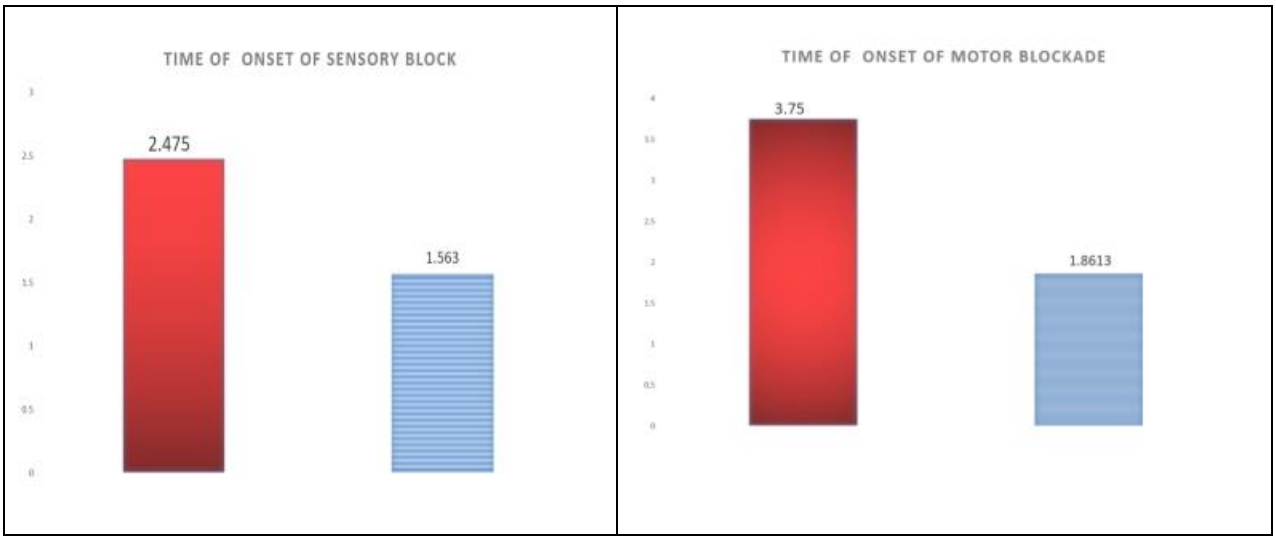
ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 1, 2024

	Group RD (N=30)	Group RF (N=30)	p value
Age (years)	42.21 ± 3.8	44.35±4.08	>0.05
Sex (M:F)	18:7	20:5	>0.05
Height (cm)	158±1.3	156±1.8	>0.05
Weight (kg)	65.13±13.4	64.42±9.6	>0.05
ASA I : II	21:9	22:8	>0.05

Table 1: Demographics

Onset and level of sensory and motor for Group RD and Group RF:

Onset time for sensory was significantly earlier in Group RD (1.563±0.3min) but delayed in Group RF (2.475±0.4 min). The time of onset of motor blockade was also faster with Group RD (1.86±0.35min) than that of Group RF (3.75±0.67min). In the comparison, time taken for the onset of sensory block and for the onset of motor block between the two groups, a significant difference ($p< 0.05$)was observed, with Group RD taking less time than that of Group RF (Fig 1).



ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 1, 2024

Fig. 1: Time of onset of sensory and motor blockade

Total Duration Of Sensory And Motor Block For Group RD And Group RF:

The time for regression of sensory block to L1 dermatome in group RD was (405.96± 18.17 mins) when compared to group RF (253.53 ± 34.9 minutes) and Bromage 0 motor block was significantly prolonged in Group RD (361.4±22.35 mins) compared to RF group (274.23 ± 36.05), was statistically significant $p<0.05$. (Fig. 2)

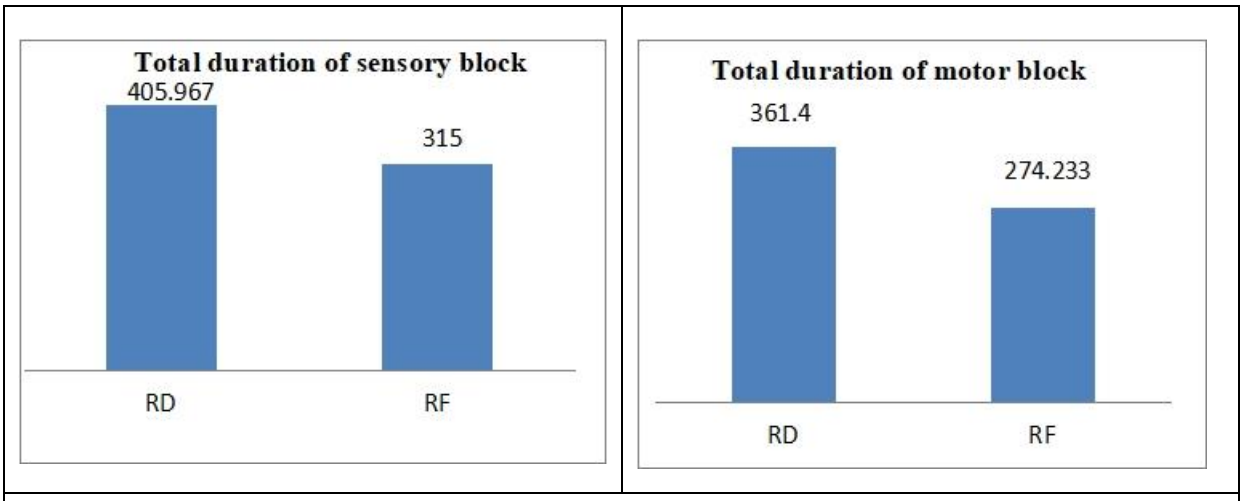


Fig. 2: Total duration of sensory and motor blockade

The total amount of fluid administered following subarachnoid block, amount of mephentermine or atropine, bradycardia and hypotension, need of additive analgesia intraoperatively or in post-anaesthesia care unit was comparable in the two groups ($P> 0.05$). Hemodynamic parameters like Heart rate, Systolic Blood pressure, Diastolic blood pressure, Mean arterial pressure, Respiratory rate, Sp02 were too comparable in both the groups intraoperatively as well as postoperatively. Systolic, diastolic arterial blood pressures, heart rate, and SpO_2 remained stable, and there was no significant difference between the groups. ($P> 0.05$). (Fig 3-8)

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 1, 2024

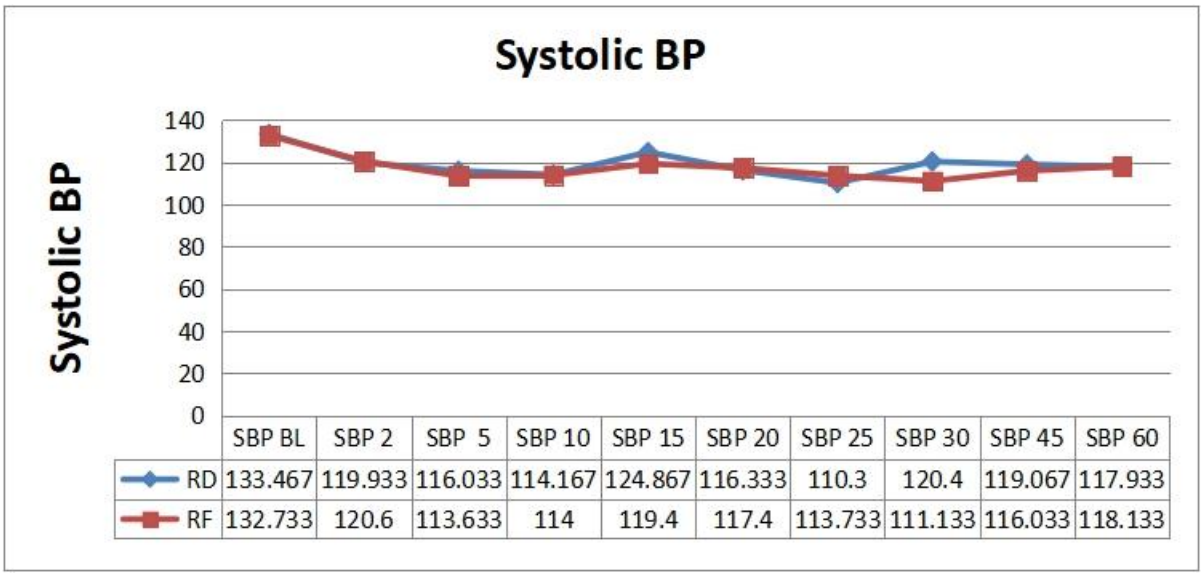


Fig. 3: Systolic BP

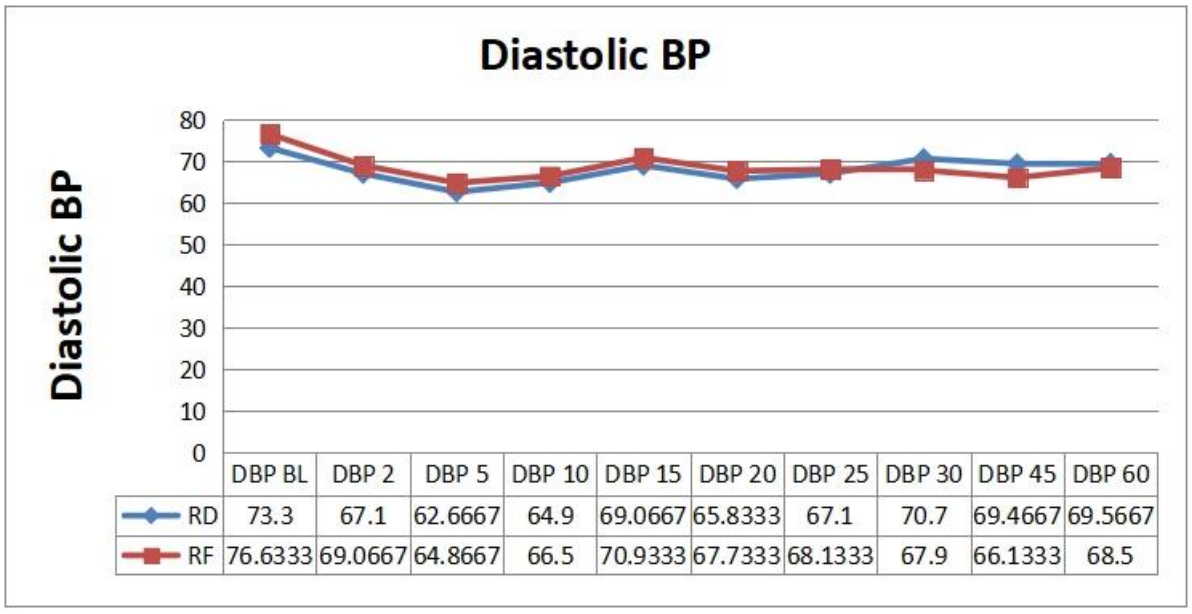
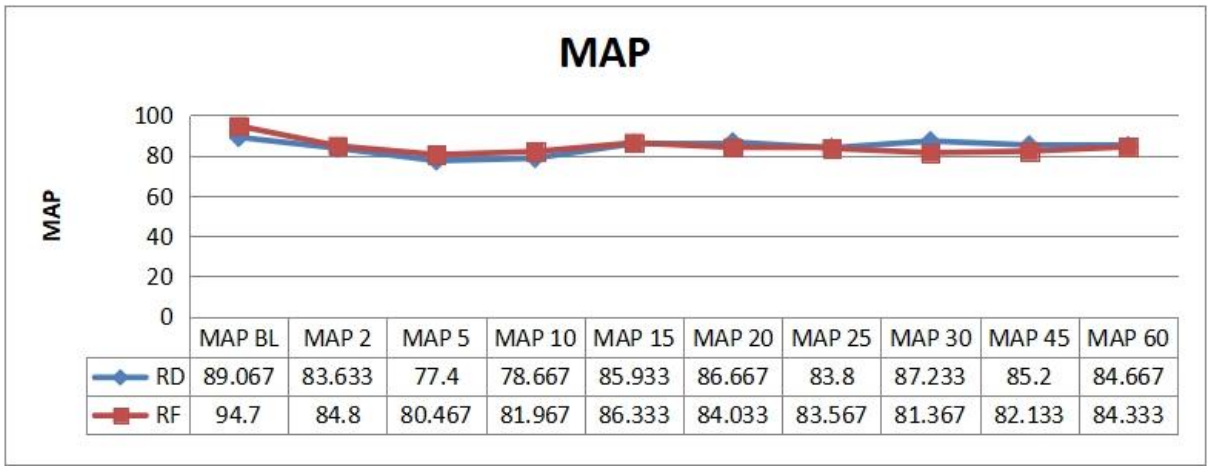


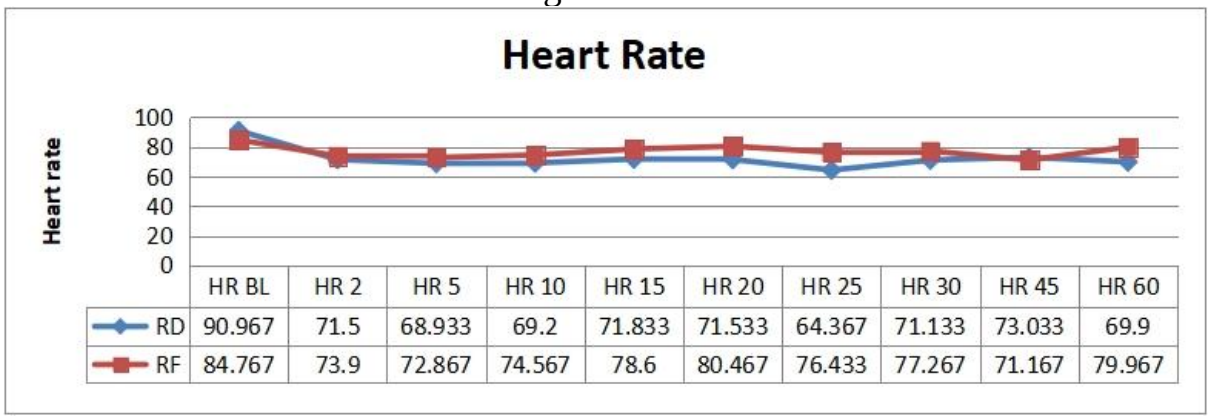
Fig. 4: Diastolic BP

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 1, 2024



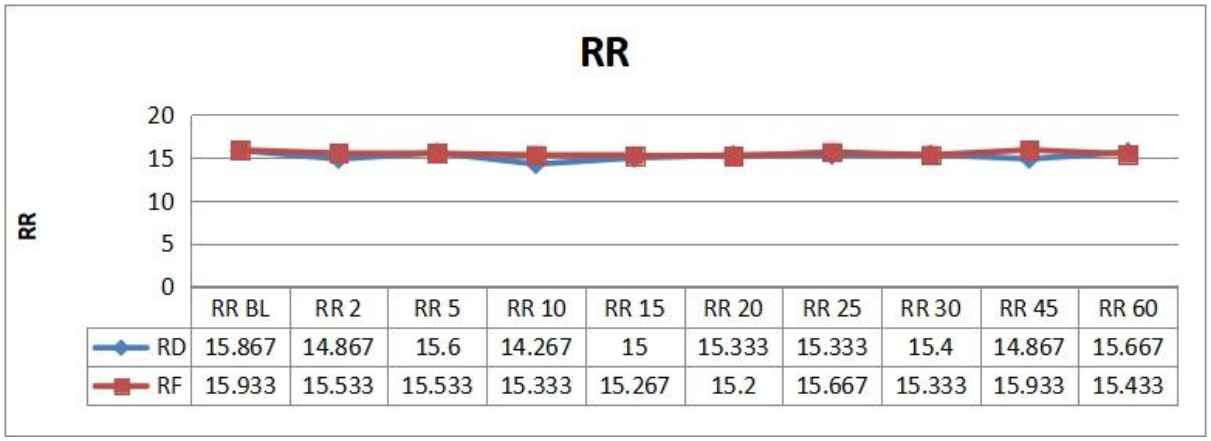
	MAP BL	MAP 2	MAP 5	MAP 10	MAP 15	MAP 20	MAP 25	MAP 30	MAP 45	MAP 60
RD	89.067	83.633	77.4	78.667	85.933	86.667	83.8	87.233	85.2	84.667
RF	94.7	84.8	80.467	81.967	86.333	84.033	83.567	81.367	82.133	84.333

Fig. 5: MAP



	HR BL	HR 2	HR 5	HR 10	HR 15	HR 20	HR 25	HR 30	HR 45	HR 60
RD	90.967	71.5	68.933	69.2	71.833	71.533	64.367	71.133	73.033	69.9
RF	84.767	73.9	72.867	74.567	78.6	80.467	76.433	77.267	71.167	79.967

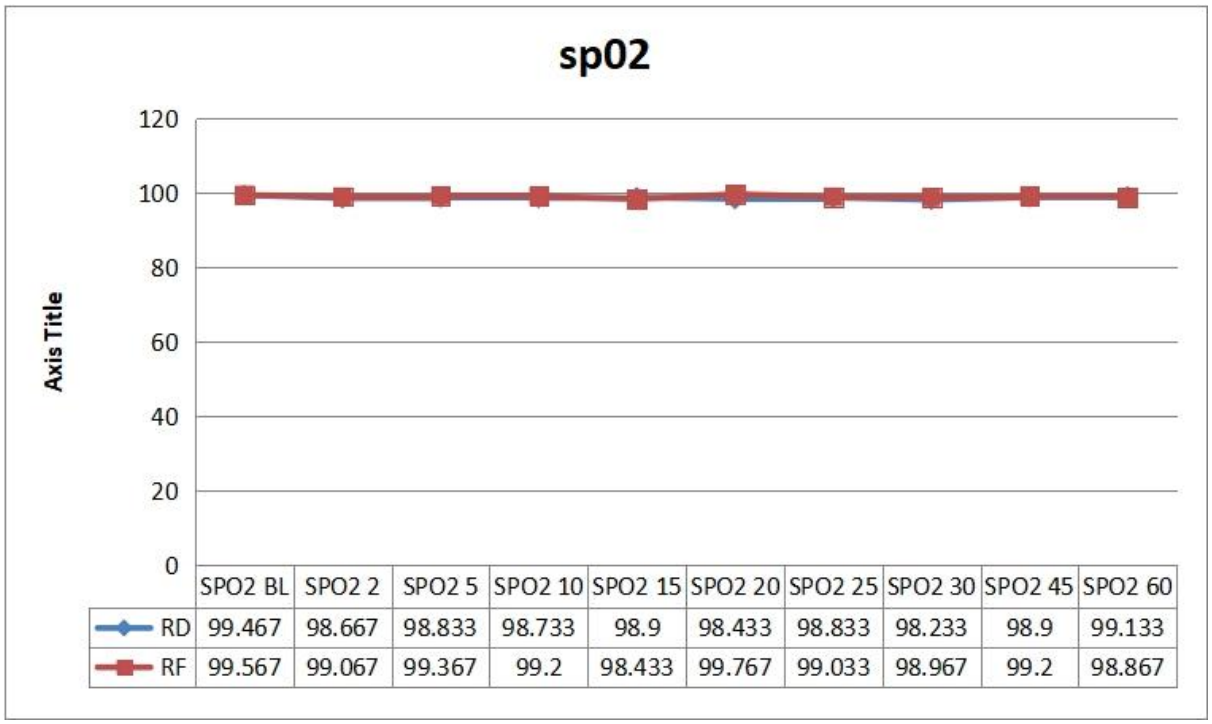
Fig. 6: Heart rate



	RR BL	RR 2	RR 5	RR 10	RR 15	RR 20	RR 25	RR 30	RR 45	RR 60
RD	15.867	14.867	15.6	14.267	15	15.333	15.333	15.4	14.867	15.667
RF	15.933	15.533	15.533	15.333	15.267	15.2	15.667	15.333	15.933	15.433

Fig. 7: Respiratory rate

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 1, 2024



	SPO2 BL	SPO2 2	SPO2 5	SPO2 10	SPO2 15	SPO2 20	SPO2 25	SPO2 30	SPO2 45	SPO2 60
RD	99.467	98.667	98.833	98.733	98.9	98.433	98.833	98.233	98.9	99.133
RF	99.567	99.067	99.367	99.2	98.433	99.767	99.033	98.967	99.2	98.867

Fig. 8: Spo2

DISCUSSION

In this study, we evaluated the efficacy of spinal anesthesia methods, between Ropivacaine with dexmedetomidine or fentanyl in lower limb orthopedic surgeries.

Time of sensory block onset with 0.75% Hyperbaric Ropivacaine with Dexmedetomidine, Group RD (1.563±0.3min) when compared to 0.75% Hyperbaric Ropivacaine with Fentanyl, Group RF(2.475±0.4 min) was significantly shorter- with p value <0.05 hence statistically significant. The time of onset of motor blockade was also faster with Group RD (1.86±0.35min) than that of Group RF (3.75±0.67min) -with p value <0.05 hence statistically significant.

Fettes P D et al.[4] has compared plain (0.5%) and hyperbaric solutions of ropivacaine for patients undergoing elective perineal surgery under spinal anaesthesia. They concluded that addition of glucose 50 mg ml (-1) to ropivacaine 5 mg ml (-1) increases the speed of onset, block reliability, duration of useful block for perineal surgery, and speed of recovery. Plain solutions are less reliable for surgery above a dermatomal level of L1.

Kallio[10] et al. compared hyperbaric and plain ropivacaine 15 mg in spinal anaesthesia for lower limb surgery. In this study also plain ropivacaine was made hyperbaric by adding 0.5 ml of 300mg dextrose. They concluded that in comparison with the plain solution,15 mg of intrathecal hyperbaric ropivacaine produced a

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 1, 2024

faster onset, greater success rate of analgesia at the level of T (10) dermatome, and faster recovery of the block. Study conducted by Ravipati P reported faster onset of motor block for dexmedetomidine compared to fentanyl group Highest sensory level achieved was T6 in both the groups. [(1)]

In our study, group RD had longer duration of sensory block (405.96± 18.17 mins) when compared to group RF (253.53 ± 34.9 minutes), with p value <0.05 hence statistically significant. [(12,13)] Group RD had longer duration of motor block (361.4±22.35 mins) compared to RF group (274.23 ± 36.05), with p value <0.05 hence statistically significant. None of the patients requested analgesic during the surgery. Bromage 3 occurred in all patients before operation. Complete regression of motor block (Bromage 0) was reached in all patients and with the highest duration in group RD.

Kalbande JV et al. [11] concluded that dexmedetomidine produced prolonged block compared with fentanyl. Gupta M et al.[(13)] concluded that increasing the dose of dexmedetomidine from 2.5 μg to 10 μg would show better and longer sensory and motor block, with longer duration of anesthesia. Gupta R et al[3]. conducted a study using dexmedetomidine and fentanyl, as adjuvants to bupivacaine in 60 patients undergoing lower abdominal surgeries. They concluded intrathecal dexmedetomidine is associated with increased motor and sensory block, hemodynamic stability, and decreased demand for rescue analgesics in 24 h as compared to fentanyl. Mahendra V et al[(14)]. concluded that dexmedetomedine to be better drug for lower limb orthopedic surgeries when compared to fentanyl, which is consistent with our study.

In our study three patients in group RD had bradycardia (HR<50/min) but it was successfully managed with atropine 0.6 mg IV. However there were no complications, such as nausea, vomiting, shivering, itching, pruritus, sedation, respiratory depression, and hypotension, in patients of either groups from our study.

As concluded by Gupta M et al., increasing the dose of dexmedetomidine from 2.5 μg to 10 μg would show better and longer sensory and motor block, with longer duration of anesthesia and comparable hemodynamic and side effects profile.[(13)] Study by Zhang Q et al. [1] aimed to find appropriate dosage of intrathecal Dexmedetomidine Combined With Ropivacaine in Caesarean Section. 5μg of dexmedetomidine as an adjuvant to ropivacaine relieved chills and no change in hemodynamic were observed, hence concluded that this dosage to be appropriate.The results of the aforementioned study are consistent with the results of the present study in this regard.

LIMITATIONS

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 1, 2024

Small sample size in this study, which is conducted in one center. It is suggested to perform this study in the future with more participants and multiple centers.It is conducted in a non-trauma center. For this reason, there was a wide age range for the patients. It is suggested to follow this method in other centers with younger patients.

CONCLUSION

We conclude that using Dexmedetomidine as an intrathecal adjuvant to 0.75% hyperbaric Ropivacaine in Orthopedic lower limb surgeries has faster onset and prolonged duration of sensory and motor blockade, as compared to Fentanyl. Reduced need for analgesics in the post-operation period, more stable hemodynamics, longer duration of sensory and motor block for dexmedetomidine suggest it being better drug than fenranyl.This study's hypothesis was that Dexmedetomidine was a better adjuvant to Ropivacaine when compared to Fentanyl for obtaining early onset and prolonged duration of motor and sensory block. The results of the present study confirmed the aforementioned hypothesis.

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