ORIGINAL RESEARCH

A Study to Compare the Adjuvant Effects of Clonidine and Dexmedetomidine Given Intrathecally Along with Isobaric Ropivacaine in Lower Limb Surgeries

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ABSTRACT

Introduction: Spinal anesthesia has been the choice of anesthesia for infraumblical surgeries. Aim: to evaluate the efficacy of adding clonidine (30µg) or dexmedetomidine (5µg) to 0.75% isobaric ropivacaine for administration of subarachnoid lumbar block in lower limb surgical procedures.

Methods: The Hospital based comparative, randomized, double blind, study was done on 120 patients (ASA grade 1-2) undergoing lower limb surgeries at S.M.S. Medical College and attached group of hospitals, Jaipur, after taking permission from the institutional ethical committee and review board. 120 patients were randomized into three groups of 40 each by sealed envelope method as follow: GROUP RS (0.75% Ropivacaine + 0.5 ml Isotonic saline), GROUP RC (0.75% Ropivacaine + 30µg Clonidine), GROUP RD (0.75% Ropivacaine + 5µg Dexmedetomidine).

Results: The mean time taken to achieve maximum sensory level was 18.40 minutes, 11.70mins and 18.80mins in groups RS, RC and RD, respectively ($p<0.05$). Mean time taken for sensory block to regress to L1 sensory level was 227.50minutes, 202.30minutes and 159.40minutes in groups RC, RD and RS, respectively($p<0.05$). The time between the administration of subarachnoid block and request for rescue analgesic was 193.10 minutes, 347.60 minutes and 381.30 minutes in groups RS, RC and RD, respectively ($p<0.05$).

Conclusion: We conclude that both drugs, Clonidine and dexmedetomidine can be safely added as adjuvant to intrathecal Ropivacaine for lower limb surgeries, in view of similar sensory and motor block characteristics.

Keywords: Clonidine, Dexmedetomidine, Ropivacaine, Spinal Anesthesia.

INTRODUCTION

Spinal anesthesia has been the choice of anesthesia for infraumblical surgeries since the inception of spinal anesthesia due to its inherent advantages like intense motor and sensory

blockade, good relaxation, reliability, lack of side effects due to multiple drugs used in general anesthesia, no postoperative respiratory depression, nausea, vomiting, drowsiness etc. It also has good patient and surgeon acceptability and is safe enough for early discharge from the hospital. Bupivacaine has been the preferred local anesthetic agent for intrathecal use due to its longer duration of action in comparison to lignocaine, but it is also associated with potential cardiac toxicity. Ropivacaine is a long-acting local anesthetic agent structurally related to bupivacaine with improved motor and sensory block profile and lowers cardiovascular and neurotoxic effect hence better tolerance and efficacy. In comparison, potency of ropivacaine to bupivacaine is two-third with regard to sensory block and half with regard to motor block[6]. The sensory or motor dissociation property of ropivacaine has suggested faster recovery of motor function, as compared to bupivacaine[7,8]. Co-administration of ephedrine and opioids and alpha agonists like clonidine, dexmedetomidine are assuming greater importance as anesthetic adjuvants to local anesthetic. Alpha agonists provide neuraxial analgesia via alpha –adrenergic receptors and by opioid independent mechanisms[9]. Intrathecal alpha-2 receptor agonists are found to have ant-nociceptive action for both somatic and visceral pain[10].

With this background we planned the present study to evaluate the efficacy of adding clonidine (30µg) or dexmedetomidine (5µg) to 0.75% isobaric ropivacaine for administration of subarachnoid lumbar block in lower limb surgical procedures, on onset, duration and level of sensory and motor block, duration of analgesia and observation of any side effects.

MATERIALS AND METHODS

The Hospital based comparative, randomized, double blind, study was done on 120 patients (ASA grade 1-2) undergoing lower limb surgeries at S.M.S. Medical College and attached group of hospitals, Jaipur. After taking permission from the institutional ethical committee and review board. Patients having age between 18 – 65years of age of either sex. Patients having Sepsis, bacteremia, skin infection at site severe hypovolemia, anemia, compromised renal, cardiac or respiratory status known history of allergic reaction to local anesthetic, spinal deformities, chronic history of headache and backache and surgeries exceed 2 ½ hours were excluded from the study.

Sample size - was calculated as 36 subjects for each of three groups at alpha error 0.05 & power 80% assuming difference in means to be detached 14.6±19.86 (as per seed article) so far the study purpose 40 subjects were taken for each of three groups i.e.: group Ropivacaine with Isotonic saline (RS), group Ropivacaine with Clonidine (RC) and group Ropivacaine with Dexmedetomidine (RD).

After taking written informed consent, 120 patients were randomized into three groups of 40 each by sealed envelope method as follow:

1. GROUP RS (Ropivacaine + Isotonic saline)
   They were administered 3.0 ml of 0.75% isobaric Ropivacaine +0.5ml of isotonic Saline (total volume of injective 3.5ml)
2. GROUP RC (Ropivacaine + Clonidine)
   They were administered 3.0 ml of 0.75% isobaric Ropivacaine + 30µg of clonidine. (0.2ml inj. Clonidine diluted to 0.5 ml in isotonic saline, total volume of injective 3.5ml)
3. GROUP RD (Ropivacaine + Dexmedetomidine)
   They were administered 3.0 ml of 0.75% isobaric Ropivacaine + 5µg of Dexmedetomidine (0.05ml of Dexmedetomidine diluted to 0.5ml in isotonic saline, total volume of injective 3.5ml)

Each patient was assessed thoroughly in pre anesthetic clinic one day prior to surgery. Patients were instructed to undergo overnight fasting after midnight and they were

premeditated with tab. Alprazolam 0.5mg and tab. Ranitidine 150mg orally the night before and also on the morning of surgery at 06: 00 AM with 1-2 sips of water. After arrival in the operating room, routine monitoring including heart rate (HR) non-invasive blood pressure (NIBP) (systolic, diastolic and mean blood pressure), Electrocardiogram (ECG) and oxygen saturation ($SpO_{2)}$ was initiated, and baseline parameters were recorded. Venous access was secured using an 18G intravenous (i.v.) cannula and ringer lactate solution @15ml/kg was administered as preload within 30 minutes. Thereafter ringer lactate infusion was continued during the intraoperative period till the end of surgery, as per requirement.

Vitals just before lumbar puncture were noted. Under strict aseptic conditions, spinal anesthesia was performed at L3-L4 intervertebral space with the patient in sitting position by using a 25 Gauge Quincke needle. After ensuring free flow of cerebrospinal fluid (CSF), the study drug was injected. The patient was placed supine immediately after the procedure, with OT table placed horizontally. The time of intrathecal injection was recorded in all the cases. The patient was given 5 L/min of oxygen by venti-mask. Vital parameters i.e. NIBP and HR were monitored every 2 minutes for the first 10 minutes and thereafter, every 5 minutes till the end of the surgery. If the systolic blood pressure decreased to ≤ 80mm of Hg or 20% below the baseline value (hypotension), Inj. Ephedrine 5mg i.v. was administered. If the heart rate decreased to ≤ 50 beats/minute (bradycardia)associated with a fall in SBP ≤ 80mmHg, Inj. Atropine Sulphate 0.6mg was given i.v.

The level of sensory block was assessed by loss of sharp sensation to prick by testing with a tooth-pick along the mid-clavicular line bilaterally every 2 minutes till the T10 dermatome level was achieved and thereafter every 5 minutes till the highest dermatome level was reached.

Motor block was assessed by the Modified Bromage Score. Similar to the sensory block assessment, motor block was assessed every 5 minutes till the maximum degree of motor block was achieved.

THE FOLLOWING VARIABLES WERE RECORDED

- Time to onset of sensory block to T10dermatomal level (time between injection and no sensation to prick at T10 level)
- Maximum upper dermatomal level of sensory block and time taken to achieve it.
- Time to regression of sensory block to L-1 dermatomal level
- Duration of sensory block (time between injection and regression to L-1 dermatome level
- Total duration of analgesia (time between injection and first request for analgesic drug).
- Time to onset of maximum degree of motor block (complete motor block)
- Maximum degree of motor block.
- Total duration of motor block (from initial onset until complete recovery)
- Heart rate, Blood pressure (SBP, DBP, MBP)

After completion of surgery, the patient was shifted to the ward. They were assessed for motor block by Modified Bromage Score till there was complete recovery from motor block. Assessment of sensory block was also carried out till the block regressed to L1 dermatomal level.

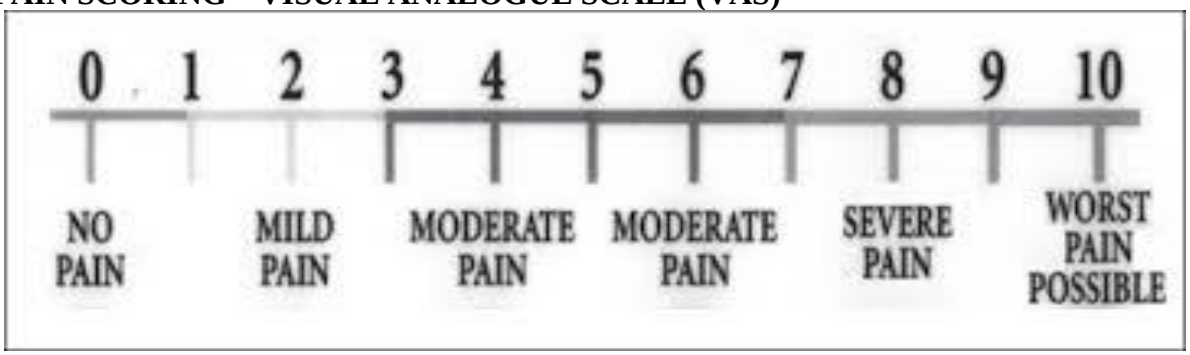
Time of request for the first dose of analgesic was noted. Those complaining of pain were administered inj. diclofenac 75mg intramuscular (i.m.)

Post-operative pain was assessed by Visual Analogue Scale (0-10) at rest and on passive movements at 0, 1 and 2 hours.

GRADING OF MOTOR BLOCK
MODIFIED BROMAGE SCORE

Score	Criteria
1	Complete motor block (unable to move feet or knees)
2	Almost complete block (able to move feet only)
3	Partial block (just able to move knees)
4	Detectable weakness of hip flexion while supine (full flexion of knees)
5	No detectable weakness of hip flexion while supine.
6	Able to perform partial knee bend.

PAIN SCORING – VISUAL ANALOGUE SCALE (VAS)



Score0	No pain
Score 1,2,3	Mild Pain
Score 4,5,6	Moderate Pain
Score 7,8,9	Severe Pain
Score 10	Worst Imaginable pain

RESULTS

In the present study, the demographic profile was found to be comparable between the three groups. Considering the hemodynamic parameters (HR, SBP, DBP and MBP),the 3 groups did not differ. None of the patients in either of the groups required treatment for intra-operative bradycardia and hypotension. The characteristics of sensory block are summarised in table 1.

Table shows that time taken to achieve sensory block up to T10 dermatomal level was statistically significant between the three groups. T4 was the highest sensory level achieved in groups RC and RD; highest sensory level achieved in group RS was T5. Maximum number of patients in groups RS, RC and RD achieved T10, T6 and T5 sensory levels, respectively. The mean time taken to achieve maximum sensory level was 18.40 minutes, 11.70mins and 18.80mins in groups RS, RC and RD, respectively. Meantime taken for sensory block to regress to L1 sensory level was 227.50minutes, 202.30minutes and 159.40minutes in groups RC, RD and RS, respectively; this was found to be statistically significant among the three groups. Total duration of sensory block was maximum in group RC and minimum in group RS. This was found to be statistically significant among groups RC and RD; and between groups RC and RS.

Table 2 shows total duration of analgesia i.e. the time between the administration of subarachnoid block and request for rescue analgesic was 193.10 minutes, 347.60 minutes and 381.30 minutes in groups RS, RC and RD, respectively; this was observed to be statistically significant among the three groups.

Maximum degree of motor block attained in the three groups was not found to be statistically significant. Time for attainment of maximum degree of motor block was 12.60 minutes, 11.28 minutes and 8.90 minutes in groups RS, RD and RC respectively. Total duration of motor block was 176.23 minutes, 230.35 minutes and 246.75 minutes in groups RS, RD and RC respectively. It was statistically significant between the three groups.

The quality of intraoperative analgesia was not found to be statistically significant among the three groups.

The VAS score was significantly higher at rest and on movement at 1 hour and 2 hours after the surgery in groups RS. However, VAS score was comparable between groups RC and RD at rest and on movement at every points of assessment.

There was no complication in RD group, nausea/ vomiting (1 patient each in the RC and RS groups), transient backache (1 patient in group RS) and delayed voiding of urine (1patient in group RC) were the only complications reported by patients in the post-operative period.

Table 1: Characteristic of Sensory Block

Characteristic	RC	RD	RS	P value	RC Vs RD	RC Vs RS	RD Vs RS
Onset of sensory block to T10 dermatomal level	4.3 ±1.8	7.5 ±6.0	13.6±5.1	< 0.001	< 0.001	<0.001	0.001
Time to max upper level(min)	11.7 ±3.4	18.8 ±4.6	18.4 ±5.2	0.001	<0.001	< 0.001	0.75 (NS)
Time for regression to L1 (min)	227.5 ± 34.6	202.3 ± 38.9	159.4 ± 16.3	<0.001	<0.001	<0.001	< 0.001
Total duration of block(min)	238.8 ± 34.8	220.8 ± 39.7	178.7 ± 15.9	<0.001	<0.001	< 0.001	<0.001

Table 2: Total Duration of Analgesia

	RC	RD	RS	P value	RC vs RD	RC Vs RS	RD Vs RS
Total duration of analgesia(minutes)	347.6 ± 47.4	381.3 ±30.9	193.1 ±23.1	< 0.001	0.001	< 0.001	<0.001

Table 3: Characteristics of motor block

Characteristic	RC	RD	RS	P value	RC vs RD	RC Vs RS	RD Vs RS
Time for max degree(minutes)	8.90 ± 3.24	11.28 ±4.35	12.60 ±5.49	<0.001	<0.001	<0.001	0.23 (NS)
Total duration of block(minutes)	246.75±42.17	230.35± 42.76	176.23 ±23.49	<0.001	0.10(NS)	<0.001	<0.001

DISCUSSION

This study compared isobaric ropivacaine (0.75%) with the addition of adjuvants – clonidine and dexmedetomidine, administered intrathecally, in adult patients undergoing lower limb surgeries. Al- Ghanem et al 2009, in their study concluded that 5 µg dexmedetomidine

seemed to be an ideal adjuvant to spinal bupivacaine for surgical procedures, especially of long duration and provided excellent quality of analgesia with minimal side effects[11].

In our study, 120 patients scheduled for lower limb surgery were randomly allocated in 3 equal groups of 40 patients each. Patients in Group RS received 3ml of 0.75% isobaric Ropivacaine + 0.5ml isotonic saline. Patients in Group RC received 3ml of 0.75% isobaric Ropivacaine +30µg (0.5ml) Clonidine. Patients in Group RD received 3ml of 0.75% isobaric Ropivacaine +5µg (0.5ml) Dexmedetomidine. Total volume of injectate in all the 3 groups was 3.5 ml. Time to onset of sensory block to T10dermatome level, maximum upper dermatome level of sensory block and time taken to achieve it, time to regression of sensory block to L-1 dermatome level, duration of sensory block, total maximum degree of motor block and total duration of motor block were recorded in all groups.

Considering the hemodynamic parameters (HR, SBP, DBP and MBP), the 3 groups did not differ. None of the patients in either of the groups required treatment for intra-operative bradycardia and hypotension.

Similar to our study, Kallio et al 2004, in their study, compared hyperbaric and isobaric ropivacaine (15mg), in spinal anesthesia for lower limb surgery, found that none of the patient required sympathomimetic for hypotension[6].

Wahedi et al 1996, conducted a study comparing 3ml of 0.5% isobaric ropivacaine with 3ml of 0.75% isobaric ropivacaine in spinal anesthesia. They observed bradycardia in 55% of their patients and fall in SBP of >20% in 5% of patients, with 3ml of 0.75% isobaric ropivacaine. In their study, they did not mention the peri-operative hydration regimen of their patients, which could have possibly contributed to bradycardia and hypotension, as observed in their subjects[12]. However, in our study, we pre-loaded the patients with 15ml/kg Ringer's lactate solution over 30mins and did not observe any episode of hypotension in our subjects.

Gupta et al 2001, compared intrathecal 3ml of 0.75% isobaric ropivacaine+0.5ml normal saline with 3ml of 0.75% isobaric Ropivacaine +5µgDexmedetomidine in 0.5ml normal saline. They had observed that intraoperative ephedrine requirements were more in the Dexmedetomidine group[13]. Furthermore, they had administered subarachnoid block in the sitting position and injected the drug rapidly over 10-15 seconds compared to 25 seconds in our study. This could have resulted in rapid cephalad ascent of the drug resulting in both bradycardia and hypotension.

In the present study, meantime to achieve maximum dermatome level was 18.40 ± 5.20 mins in group RS, 11.70 ± 3.40 mins in group RC and 18.80 ± 4.60 mins in group RD. Wahedi et al 1996, in their study[12], observed that time taken for maximum cranial spread with 3ml of 0.75% isobaric ropivacaine was more (32mins) than that observed in our study, But, in another study conducted by Singh et al 2012 , the time for attainment for maximum sensory block was much less (9.8 ± 3.10mins) compared to our study which could possibly be due to the higher dose of ropivacaine (3.2ml of 0.75%) used by them as well as the altered physiological status of patients (pregnant patients) in their study[14] .

Ogun et al 2007, in their study, observed the prolongation in the duration of analgesia with addition of clonidine to plain isobaric ropivacaine, which is consistent with the findings of our study[15].

In our study, the number of patients who attained complete motor block was not significantly different among the groups. In the study conducted by Wahedi et al 1996, only 70% of patients achieved complete motor block with 3ml of 0.75% ropivacaine, which is much less as compared to our study[12]. In another study by Sagiroglu et al 2009, maximum motor block recorded with clonidine was 1.06 ± 0.40 (Modified Bromage Scale), which is consistent with the findings in our study[16].

In the present study, the time taken to achieve maximum degree of motor block was 12.60 ± 5.50mins, 8.90 ± 3.20mins and 11.30 ± 4.30mins in groups RS, RC and RD, respectively.

This difference was statistically significant (p value – 0.001). In the study by Sagiroglu et al 2009, time taken to achieve maximum motor block was more in comparison to our study both with isobaric ropivacaine and clonidine (11.36 ± 4.64 mins compared to 8.90 ± 3.20mins in our study) added as an adjuvant which could be explained by the lesser dose of ropivacaine used by them[16].

In our study, nausea/ vomiting (1 patient each in the RC and RS groups), transient backache (1 patient in group RS) and delayed voiding of urine (1patient in group RC) were the only complications reported by patients in the post-operative period. In agreement with our study, Gupta et al 2001, observed no serious complications in their study with either dexmedetomidine or plain ropivacaine[13]. De kock et al 2001, reported significant delay in voiding urine with intrathecal clonidine (45 µg and 75 µg). In our study, a lower dose of clonidine(30µg) used could possibly explain the difference in observation with their study[17].

In the present study, we found that sensory block was superior with intrathecal clonidine added as an adjuvant to isobaric ropivacaine in terms of onset and time to attain the maximum level. Time to onset of maximum motor block and duration of sensory and motor block were comparable when clonidine or dexmedetomidine were added as adjuvant to intrathecal ropivacaine. The quality of motor block was comparable in the three groups. Also, patients receiving dexmedetomidine as an intrathecal adjuvant to isobaric ropivacaine had a longer duration of analgesia post-operatively. Intraoperative haemodynamic parameters were comparable among the three groups. No serious complication was reported in any patient in any of the three groups.

CONCLUSION

Thus, based on the observations of the present study we conclude that both drugs, Clonidine and Dexmedetomidine can be safely added as adjuvant to intrathecal Ropivacaine for lower limb surgeries, in view of similar sensory and motor block characteristics. However, the duration of analgesia was observed to be longer with intrathecal Dexmedetomidine used as an adjuvant to Ropivacaine. Both Clonidine and Dexmedetomidine have been demonstrated to have a safety profile as is evident from the present study.

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