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Research Article

A RANDOMIZED CONTROLLED STUDY TO COMPARE THE ANALGESIC AND HEMODYNAMIC EFFECTS OF INTRATHECAL ROPIVACAINE WITH OR WITHOUT NEOSTIGMINE AND DEXMEDETOMIDINE IN LOWER LIMB SURGERIES

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Abstract :

Objective: To compare the analgesic and hemodynamic effects of intrathecal ropivacaine with or without neostigmine and dexmedetomidine in lower limb surgeries.**Methods:** Patient aged 18-50 years belonging to ASA phycal status 1 or 2 planned for lower limb surgery were included in this study. Group 1: Patients received 3ml of ropivacaine 0.5% intrathecally; Group 2: Patient received 3ml of ropivacaine 0.5% plus 3mic.gm dexmedetomidine intrathecally; Group 3 Patient received 3ml of ropivacaine 0.5% plus 50mic.gm neostigmine intrathecally.**Results:** After spinal anesthesia, the mean HR decreased in all three groups and the decrease was evident highest in R+D group as compared to both Group R+N and especially Group R. The mean MAP in all three groups decreased up 20 min and then increase gradually in all three groups till end with highest being in Group R+N and lowest in Group R+D. The mean time to achieve T10 sensory block ($F=7.57$, $p=0.001$), Time to 2-segment regression ($F=235.84$, $p<0.001$) and Duration of regression to L4 ($F=199.39$, $p<0.001$) significantly different among the groups. The mean Maximum modified bromage scores of Group R+D ($p<0.001$) also lowered significantly as compared to Group R+N. **Conclusion:** Our study establishes dexmedetomidine as superior drug compared to neostigmine as an adjunct to intrathecal ropivacaine 0.5% for patients undergoing lower limb surgery as it provides faster onset of anesthesia, better intraoperative and postoperative analgesia and prolonged duration of motor and sensory blockade without significant increase in adverse effects.

Key words: Dexmedetomidine, Neostigmine, Intrathecal ropivacaine

INTRODUCTION

Neuraxial blockade (spinal or epidural) is the preferred mode of anesthesia for lower limb surgeries. Spinal block is still the first choice because of its rapid onset, superior blockade, low risk of infection as from catheter *in situ*, less failure rates and cost-effectiveness, but has the drawbacks of shorter duration of block and lack of postoperative analgesia. In recent years, use of intrathecal adjuvants has gained popularity with the aim of prolonging the duration of block, better success rate, patient satisfaction, decreased resource utilization compared with general anesthesia and faster recovery. Adequate pain management is essential to facilitate rehabilitation and accelerate functional recovery, enabling patients to return to their normal activity more quickly. The quality of the spinal anesthesia has been reported to be improved by the addition of opioids such as morphine, fentanyl and sufentanil[1,2].

Ropivacaine is a first single enantiomer-specific compound, which has a reduced risk of cardiotoxicity, neurotoxicity, and rapid recovery of motor function[3]. Postoperative pain relief is an important issue with ropivacaine. It has been used with many adjuvants for lower limb surgery, which has other side effects. So, our concern is of using a drug as an adjuvant with ropivacaine which provides better intraoperative hemodynamic condition as well as prolonged postoperative analgesia with minimal side effects.

Intrathecal neostigmine causes dose-dependent postoperative analgesia[4,5] by inhibiting the breakdown of acetylcholine in the dorsal horn[6].

Dexmedetomidine (DXM) is a new generation highly selective α2- adrenoreceptor agonist that dose-dependently reduces blood pressure (BP) and heart rate (HR) and has sedative effect. It might permit sedation and analgesia without the unwanted vascular effects from activation of α1 receptor. In addition, it has been shown to induce a centrally mediated reduction of sympathetic nervous system activity and decrease hemodynamic and plasma catecholamine response to stressful events. It has been used for premedication and as an adjunct to general anesthesia and reduces opioid and inhalational anesthetics requirements. Kanazi et al[7]found that 3μg DXM added to 12 mg spinal bupivacaine produced the significant short onset of sensory and motor block as well as significantly longer duration of sensory and motor block than bupivacaine and Al-Mustafa et al[8] reported that intrathecal DXM as an adjuvant to 12.5 mg bupivacaine in spinal anesthesia has a dose-dependent effect on the onset and regression of sensory and motor block. Intrathecal α2-receptor agonists are found to have antinociceptive action for both somatic and visceral pain.

The present study was designed to compare the analgesic and hemodynamic effects of intrathecal ropivacaine with or without neostigmine and dexmedetomidine in lower limb surgeries.

MATERIAL AND METHODS

Patient aged 18-50 years belonging to ASA phycal status 1 or 2 planned for lower limb surgery were included in this study. Twenty five patients per group were required to detect a significant difference of 25% or more in the requirement of rescue analgesia between the two groups (power of 85%, α=0.05).

Proper PAC of patient was done, IV line was established with 18G canula and ringer lactate solution 500ml was infused in 10 to 15 min. to preload IV compartment.

On the basis of computer generated random list, patient would be divided in to following groups:

Group 1 Patients received 3ml of ropivacaine 0.5% intrathecally.

Group 2 Patient received 3ml of ropivacaine 0.5% plus 3mic.gm dexmedetomidine intrathecally.

Group 3 Patient received 3ml of ropivacaine 0.5% plus 50mic.gm neostigmine intrathecally.

With all aseptic precautions, a midline spinal puncture was performed at ¾ interspace(at 2/3, if for an anatomical reason it was not possible at ¾) with 25G pencil point needle (Pancan,B.Braun, Melsungen, Germany) with patient in sitting position and anesthetic solution was injected without barbotage or aspiration at the beginning or at the end of injection.

All injections were made with hole in the spinal needle facing upward. The patient and the anaesthesiologist who delivered the drug were blinded to the study solution. The injection was given over a span of 15 seconds and the patients were returned to supine position immediately after the completion of the block,

Hypotention (defined as systolic blood pressure of <90 mm Hg) was treated with increments of 5mg ephedrine, bradycardia (defined as heart of <50 bpm) was treated with 0.3 mg of

atropine, and oxygen desaturation (defined as pulse oxymetry saturation <90% on room air) were treated with oxygen via Hudson's face mask. If a patient complained about discomfort or pain, midazolam 0.05 mg/kg and fentanyl 25 mic. gm IV was administered by the anaesthesiologist in incremental doses. In the event of inadequate spinal block (defined as pain severe enough to interfere with surgical procedure), general anaesthesia was induced and the patient was excluded from the study.

Adverse events (hypotention, bradycardia, sedation ,nausea and vomiting, shivering, pruritus etc) were recorded during operation and recovery.

Hemodynamic data, including systolic pressure, diastolic pressure, mean arteriar pressure , and heart rate were recorded every two min in the first 10 min after spinal anesthesia, then every 5minutes till 30 minutes until motor and sensory recovery.

RESULTS

The basic characteristics (age, sex, height, weight and ASA grade) of three groups of patients (Group R: Ropivacaine, Group R+D: Ropivacaine + Dexmedetomidine and Group R+N: Ropivacaine + Neostigmine) are summarized in Table 1. On comparing, the age, sex, height, weight and ASA grade of three groups were found similar i.e. did not differed significantly ($p>0.05$).

The mean HR in Group R and R+D increased just after the surgery while in Group R+D it remains almost similar to baseline. Further, after spinal anesthesia, the mean HR decreased in all three groups and the decrease was evident highest in R+D group as compared to both Group R+N and especially Group R. Comparing the mean HR of three groups, ANOVA revealed significant effect of both groups (drugs) ($F=107.19$, $p<0.001$) and time (period) ($F=40.83$, $p<0.001$) on HR. Further, the interaction (groups x time) effect of both on HR was also found to be significant ($F=6.88$, $p<0.001$) (Fig.1).

The mean MAP in Group R increased just after the spinal anesthesia while in Group R+N it decreased as compared to baseline. In contrast, the mean MAP in group R+D remained similar as compared to baseline. Hereafter (from 2min), the mean MAP in all three groups decreased up 20 min and then increase gradually in all three groups till end with highest being in Group R+N and lowest in Group R+D. Comparing the mean MAP of three groups, ANOVA revealed significant effect of both groups (drugs) ($F=19.87$, $p<0.001$) and time (period) ($F=115.71$, $p<0.001$) on MAP. Further, the interaction (groups x time) effect of both on MAP was also found to be significant ($F=4.28$, $p<0.001$) (Fig.2).

The mean time to achieve T10 sensory block ($F=7.57$, $p=0.001$), Time to 2-segment regression ($F=235.84$, $p<0.001$) and Duration of regression to L4 ($F=199.39$, $p<0.001$) significantly different among the groups. Further, Tukey test revealed that the mean Time to achieve T10 sensory block lowered significantly in both Group R+D ($p<0.001$) and Group R+N ($p<0.05$) groups as compared to Group R. In contrast, mean time to 2-segment regression delayed significantly in both groups R+D ($p<0.001$) and group R+N ($p<0.01$) as compared to group R. It also delayed significantly in group R+D ($p<0.001$) as compared to Group R+N. Like time to 2-segment regression, the duration of regression to L4 was also significantly delayed in both groups R+D ($p<0.001$) and group R+N ($p<0.01$) as compared to group R. Further, it was also found to be significantly ($p<0.001$) delayed in group R+D as compared to Group R+N. The mean Maximum modified bromage scores of Group R+D ($p<0.001$) also lowered significantly as compared to Group R+N. Similarly, mean Bromage score at 2 hr lowered significantly in both Group R+D ($p<0.001$) and Group R+N ($p<0.001$) as compared to Group R. The mean Bromage score at 2 hr of Group R+D ($p<0.001$) also lowered significantly as compared to Group R+N. The Total fentanyl and Total midazolam required only in Group R and Group R+N. Comparing the mean requirements of Total fentanyl and Total midazolam of two groups, t test revealed similar ($p>0.05$) requirements of

Total fentanyl (t=1.20, p=0.260) and total midazolam (t=0.13, p=0.900) between the two groups i.e. found to be statistically the same. The Surgeon's assessment of motor block lowered significantly in both Group R+D (p<0.001) and Group R+N (p<0.001) as compared to Group R. Similarly, the patient's assessment of intra-operative analgesic lowered significantly in both Group R+D (p<0.001) and Group R+N (p<0.001) as compared to Group R. Tukey test revealed that the mean highest intra-operative VAS (pain level) lowered significantly in R+D group (p<0.05) as compared to group R. Similarly, the maximum sedation was significantly higher in Group R+D as compared to both Group R (p<0.001) and Group R+N (p<0.001). ANOVA revealed significantly different time to 1st analgesic requirement (F=132.24, p<0.001) and the time to 1st analgesia requirement was significantly delayed in both Group R+D (p<0.001) and Group R+N (p<0.001) as compared to Group R. Further, the time to 1st analgesia requirement in Group R+D (p<0.05) was also found to be significantly delayed as compared to Group R+N. However, total dose of tramadol did not differ among the groups (Table-2).

Comparing the proportion (Y/N) of each observed adverse effect between the three groups, χ^2 test revealed significantly higher Nausea (χ^2=35.11, p<0.001) and Vomiting (χ^2=26.85, p<0.001) in Group R+N as compared to both Group R and Group R+D. However, rest of the adverse effects were similar (p>0.05) among the three groups i.e. not differed significantly (Table-3).

Table-1: Patient characteristics

Characteristics	**Group R (n=25)**	**Group R+D (n=25)**	**Group R+N (n=25)**	**p value**
Age (yrs)	36.20 ± 7.96 (24-48)	32.72 ± 8.39 (19-17)	36.40± 7.73 (24-49)	0.198
Sex: Males Females	14 (56.0%) 11 (44.0%)	19 (76.0%) 6 (24.0%)	20 (80.0%) 5 (20.0%)	0.136
Height (cm)	168.00 ± 9.70 (153-180)	166.64 ± 7.97 (151-177)	167.36 ± 9.94 (150-180)	0.874
Weight (kg)	62.76 ± 8.88 (47-78)	65.76 ± 5.95 (53-74)	62.88 ± 9.55 (47-80)	0.354
ASA physical status: 1 2	9 (36.0%) 16 (64.0%)	8 (32.0%) 17 (68.0%)	14 (56.0%) 11 (44.0%)	0.182
Duration of surgery (min)	171.60 ± 13.75 (150-180)	163.20 ± 17.49 (120-180)	171.60 ± 13.75 (150-180)	0.083

Numbers in parenthesis indicates the range (min-max)

Table-2: Comparison of secondary outcomes among the groups

Characteristics	Group R (n=25)	Group R+D (n=25)	Group R+N (n=25)
Sensory block characteristics			
Time to achieve T10 sensory block (min)	14.68 ± 3.47	5.96 ± 1.54*	12.84 ± 2.15•
Time to 2-segment regression (min)	89.44 ± 16.59	174.48 ± 12.52*	105.28 ± 14.79•†
Duration of regression to L4 (min)	176.00 ± 14.87	360.28 ± 37.29*	300.48 ± 41.38•†
Motor block characteristics			
Maximum modified bromage score	3.92 ± 0.81	1.52 ± 0.51*	2.48 ± 0.71•
Bromage score at 2 hrs	4.60 ± 0.58	2.56 ± 0.51*	3.44 ± 0.71•
Time to motor recovery (min)	165.52± 14.79	370.68 ± 29.22*	221.44 ± 20.56†•
Intraoperative drug requirement			
Total fentanyl requirement (µg)	29.17 ± 10.21	0.00 ± 0.00	37.50 ± 13.69
Total midazolam requirement (mg)	3.50 ± 1.22	0.00 ± 0.00	3.60 ± 1.34
Total dose of ephedrine (mg)	8.00 ± 2.74	10.00 ± 3.54	6.67 ± 2.89
Total dose of atropine (mg)	0.45 ± 0.21	0.68 ± 0.15	0.35 ± 0.12
Intraoperative VAS and Sedation score			
Highest intraoperative VAS	1.36 ± 0.99	0.56 ± 0.65*	0.92 ± 1.12
Maximum sedation	1.12 ± 0.33	2.76 ± 0.60*	1.44 ± 0.71†
Postoperative analgesia requirement			
Time to 1st analgesic requirement (min)	245.04 ± 36.66	390.68 ± 29.34*	366.88 ± 35.46
Total dose of tramadol (mg)	83.33 ± 25.00	75.00 ± 35.36	81.25 ± 25.88•
Surgeon's and patient's assessment of anesthesia			
Surgeon's assessment of motor block	3.48 ± 0.51	1.24 ± 0.52*	2.20 ± 0.41•
Patient's assessment of intraoperative analgesia	3.56 ± 1.04	1.12 ± 0.33*	2.16 ± 0.37•

*Group R vs RD; p value <0.05, • Group R vs RN; p value <0.05

Table-3: Frequency distribution of adverse effects in three groups

	Group R	Group R+D	Group R+N	χ^2value	P value
Bradycardia	1 (4.0%)	5 (20.0%)	4 (16.0%)	3.00	0.223
Hypotension	4 (16.0%)	7 (28.0%)	3 (12.0%)	2.28	0.319
Oxygen desaturation	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA	NA
PDPH	1 (4.0%)	0 (0.0%)	1 (4.0%)	1.03	0.598
Shivering	2 (8.0%)	1 (4.0%)	0 (0.0%)	2.08	0.353
Nausea	1 (4.0%)	2 (8.0%)	18 (72.0%)	35.11	p<0.001
Vomiting	1 (4.0%)	1 (4.0%)	14 (56.0%)	26.85	p<0.001
Itching	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA	NA

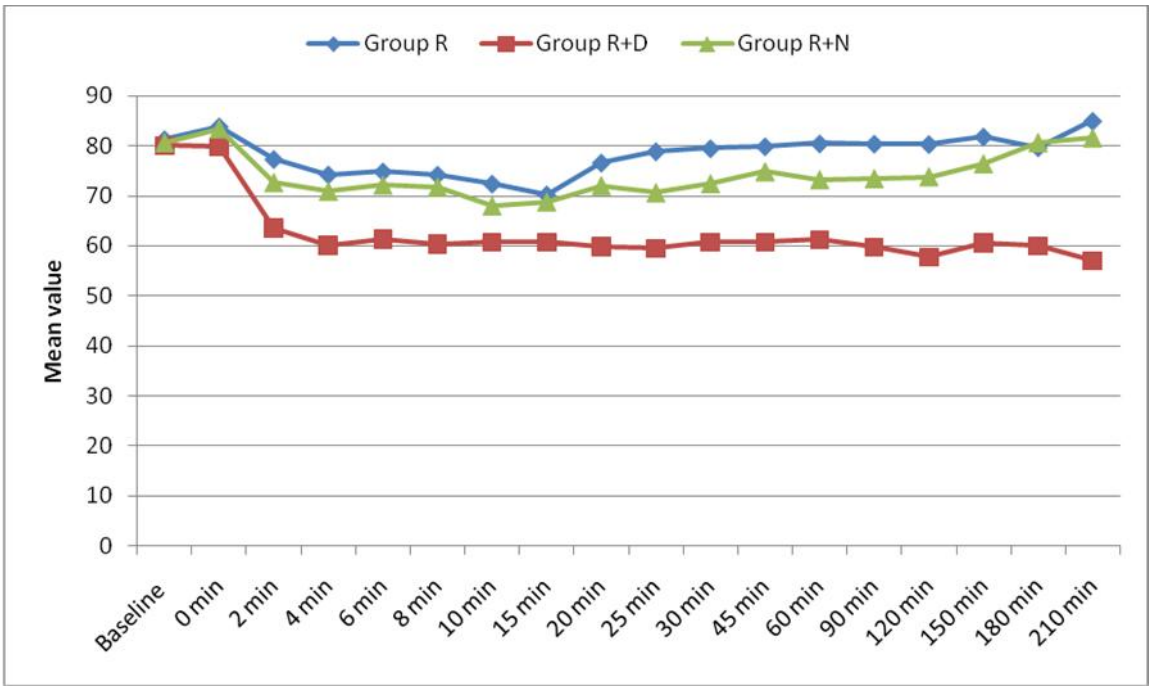

Fig.1: Heart Rate in three groups

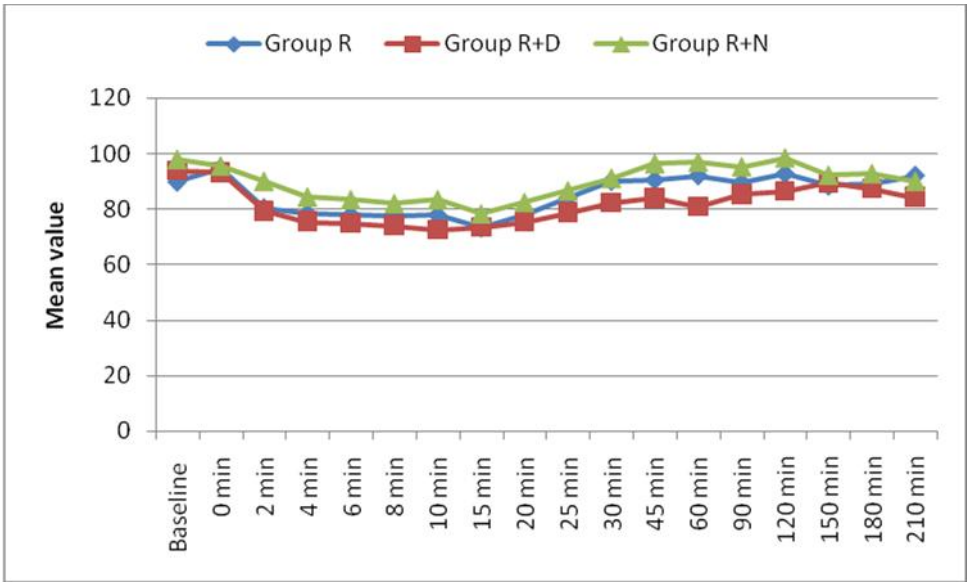

Fig.2: MAP in three groups

DISCUSSION

The basic characteristics (age, gender, height, weight , ASA grade and duration of surgery) of three groups (Group R, Group R+D, and Group R+N) were compared and the statistical analysis revealed similar age (p=0.198), proportion of genders (p=0.136), height (p=0.874), weight (p=0.354), ASA grade(p=0.182) and duration of surgery(p=0.083) among the three groups, respectively i.e. did not differed significantly (p>0.05). In other words, the subjects of three groups were matched in all demographic variables and thus comparable

Liu et al[9] studied dose-response effects of spinal neostigmine added to bupivacaine spinal anesthesia and found that Neostigmine at 50 mcg. dose had no effect on hemodynamic parameters. Kanazi et al[7] concluded in their study that addition of 3µg dexmedetomidine or 30 µg clonidine to 12 mg bupivacaine did not produce significant change in heart rate. Gupta R et al[10] showed in their study that Intrathecal dexmedetomidine is associated with hemodynamic stability during the period of anesthesia. In our study, the mean HR decreased in all three groups and the decrease was evident highest in R+D group as compared to both Group R+N and especially Group R. Tukey's test revealed significantly (p<0.001) different and lower HR of Group R+D from 2 min to till end (210 min) as compared to both Group R and Group R+D. However, mean HR remained similar between Group R and Group R+N at all periods i.e. did not differed significantly (p>0.05).

Liu et al[9] studied dose-response effects of spinal neostigmine added to bupivacaine spinal anesthesia and found thatthe addition of 50 microg neostigmine significantly increased the duration of sensory block. Tan et al[11] evaluated the efficacy and safety of intrathecal neostigmine and showed that intrathecal neostigmine at 50 pg or 100 microg enhanced the onset of tetracaine anaesthesia and provided analgesia lasting for 6-9 h. Kanazi et al[7] found that 3µg DXM added to 12 mg spinal bupivacaine produced the significant short onset of sensory blockade. Al-Mustafa et al[8] studied effect of adding dexmedetomidine to spinal bupivacaine for urological procedures and found the regression time to reach S1 dermatome was 338.9±44.8 minutes in group D10(10 mcg dexmedetomidine + bupivacaine), 277.1±23.2

minutes in D5(5mcg dexmedetomidine + bupivacaine), and 165.5±32.9 minutes in group N(bupivacaine only). In our study, mean Time to achieve T10 sensory block (F=7.57, p=0.001), Time to 2-segment regression (F=235.84, p<0.001) and Duration of regression to L4 (F=199.39, p<0.001) significantly different among the groups. Further, Tukey test revealed that the mean Time to achieve T10 sensory block lowered significantly in both Group R+D (p<0.001) and Group R+N (p<0.05) groups as compared to Group R. In contrast, mean time to 2-segment regression delayed significantly in both groups R+D (p<0.001) and group R+N (p<0.01) as compared to group R. It also delayed significantly in group R+D (p<0.001) as compared to Group R+N. Like time to 2-segment regression, the duration of regression to L4 was also significantly delayed in both groups R+D (p<0.001) and group R+N (p<0.01) as compared to group R. Further, it was also found to be significantly (p<0.001) delayed in group R+D as compared to Group R+N. Overall, dexmedetomidine and neostigmine both produces faster sensory blockade and daleyed sensory regression than the control group but the blockade is rather significantly prolonged by dexmedetomidine than neostigmine.

Liu et al[9] studied dose-response effects of spinal neostigmine added to bupivacaine spinal anesthesia and found thatthe addition of 50 microg neostigmine significantly increased the duration of motor block. Kanazi et al[7] stated in their study that patients in groups D (12 mg of bupivacaine supplemented with 3 µg of dexmedetomidine) and C (12 mg of bupivacaine supplemented with 30 µg of clonidine) had a significantly shorter onset time of motor block. Al-Mustafa et al[8] studied effect of adding dexmedetomidine to spinal bupivacaine (12.5 mg) for urological procedures. The mean time to reach Bromage 3 scale was 10.4±3.4 minutes in group D10 (10 mcg dexmedetomidine), 13.0±3.4 minutes in D5 (5 mcg dexmedetomidine), and 18.0±3.3 minutes in group N (normal saline). In our study Maximum modified Bromage score, Bromage score at 2 hrs and Time to motor recovery (min) were compared between the groups and statistical differences between the groups in all possible combinations (Group R vs R + D; p value <0.05, Group R + D vs R + N; p value <0.05**,** Group R vs R + N; p value <0.05) were significant regarding all variables mentioned above. Overall, neostigmine produces much profound and prolonged motor blockade in comparison to control group but less intense and shorter blockade when compared to dexmedetomidine.

In our study, The Surgeon's assessment of motor block lowered significantly in both Group R+D (1.24 ± 0.52, p<0.001) and Group R+N (2.20 ± 0.41, p<0.001) as compared to Group R (3.48 ± 0.51). Similarly, the patient's assessment of intra-operative analgesic lowered significantly in both Group R+D (1.12 ± 0.33,p<0.001) and Group R+N (2.16 ± 0.37, p<0.001) as compared to Group R(3.56 ± 1.04). But both the mean values of those variables are much less in R+D group than in R+N group. It signifies that though neostigmine is better than control group regarding surgeon's and patient's assessment of anesthesia, it is lesser in comparison to dexmedetomidine regarding the same.

Sabbe et al[12] concluded that dexmedetomidine produces a powerful antinociceptive effect, mediated at the spinal level, while systemic redistribution of the drug leads to a hypnotic state. The maximum sedation was significantly higher in Group R+D as compared to both Group R (p<0.001) and Group R+N (p<0.001). So, it is evident dexmedetomidine produces much more sedation than neostigmine and control when used with ropivacaine. Chung et al[13] evaluated the postoperative analgesic efficacy and safety of intrathecal (i.t.) neostigmine, i.t. morphine, and their combination in patients undergoing cesarean section under spinal anesthesiaand concluded that the combination of i.t. neostigmine 12.5 microg and i.t.

morphine 50 microg may produce better postoperative analgesia with fewer side effects than i.t. neostigmine 25 microg or i.t. morphine 100 microg alone.

Lauretti et al[14] evaluated the analgesic action of spinal neostigmine and found that the combination of 25 microg neostigmine with 25 microg fentanyl given intrathecally with 15 mg of hyperbaric bupivacaine delayed postoperative pain and lowered the number of rescue analgesics. Tan et al[11] compared the postoperative analgesic efficacy and safety of intrathecal (IT) neostigmine and IT morphine in patients undergoing total knee replacement under spinal anesthesia and concluded that IT neostigmine 50 microg produced postoperative analgesia lasting about seven hours with fewer side effects and better satisfaction ratings than IT morphine 300 microg. Ho et al[15] in this meta-analysis aimed to evaluate the effectiveness and side-effects of intrathecal neostigmine in the perioperative and peripartum settings and found that adding intrathecal neostigmine to other spinal medications improves perioperative and peripartum analgesia marginally when compared with placebo.

Gupta et al[10] showed that Intrathecal dexmedetomidine is associated with reduced demand for rescue analgesics in 24 h as compared to fentanyl. In our study, the highest intra-operative VAS (pain level) lowered significantly in R+D group ($p<0.05$) as compared to group R. ANOVA revealed significantly different time to 1st analgesic requirement ($F=132.24$, $p<0.001$) and the time to 1st analgesia requirement was significantly delayed in both Group R+D ($p<0.001$) and Group R+N ($p<0.001$) as compared to Group R. Further, the time to 1st analgesia requirement in Group R+D ($p<0.05$) was also found to be significantly delayed as compared to Group R+N. However, total dose of tramadol did not differ among the groups. Overall, we can say that dexmedetomidine produces better intra and post-operative analgesia than neostigmine when used with ropivacaine though the latter is beneficial than the control regarding the same variables.

Lauretti et al[14] in a multicenter, placebo-controlled trial investigated the effects of 25-75 microg intrathecal neostigmine and found that only the 75-microg dose of neostigmine increased the nausea score in the recovery room. The incidence of treatment for nausea was greater in patients receiving neostigmine (61%) than in those receiving saline placebo (29%) and was unaffected by neostigmine dose. Ho et al[15] in this meta-analysis aimed to evaluate the effectiveness and side-effects of intrathecal neostigmine in the perioperative and peripartum settings and found that it is associated with significant side-effects and the disadvantages outweigh the minor improvement in analgesia achieved.

In our study, comparing the proportion (Y/N) of each observed adverse effect between the three groups, χ^2 test revealed significantly higher Nausea ($\chi^2=35.11$, $p<0.001$) and Vomiting ($\chi^2=26.85$, $p<0.001$) in Group R+N as compared to both Group R and Group R+D. However, rest of the adverse effects were similar ($p>0.05$) among the three groups i.e. not differed significantly. Though our study also revealed that the mean Total dose of ephedrine requirement of Group R+D was significantly ($p<0.001$) higher as compared to Group R+N. Similarly, the mean Total dose of atropine requirement of Group R+D was found to be significantly ($p<0.001$) higher as compared to both Group R and group R+N. Overall, neostigmine is comparable to dexmedetomidine and control except its emetogenic potential and use of dexmedetomidine may require higher rate of administration of ephedrine and atropine.

CONCLUSION

Our study establishes dexmedetomidine as superior drug compared to neostigmine as an adjunct to intrathecal ropivacaine 0.5% for patients undergoing lower limb surgery as it provides faster onset of anesthesia, better intraoperative and postoperative analgesia and prolonged duration of motor and sensory blockade without significant increase in adverse effects.

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