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A prospective randomized double blind study to evaluate the analgesic efficacy of low dose of intrathecal neostigmine in combination with fentanyl and bupivacaine for lower abdominal and lower limb surgery

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Abstract---More than 80% of patients undergoing surgical procedures under spinal anesthesia experience acute post-operative pain. The aim of the study was to compare the analgesic efficacy and side effects of addition of neostigmine to fentanyl and bupivacaine. 50 patients scheduled for elective lower abdominal and lower limb surgeries likely to finish within 3 hours, were put into two groups. 25 patients in each group aged between 18 to 60 years of either sex belonging to the ASA grade I & II. Group A was given Intrathecal Bupivacaine 12.5 mg (2.5 ml) + Fentanyl 20 µg (0.4 ml)+0.1 ml Normal Saline (Total 3 ml) and Group B was given Intrathecal Bupivacaine 12.5 mg (2.5 ml) + Fentanyl 20 µg (0.4 ml) + Neostigmine 1µg (0.1 ml) (Total 3 ml). Subjects were monitored for occurrence of any adverse events after spinal injection. We observed statistically significant difference between the two groups in the onset of sensory blockade and recovery of sensory blockade. Onset of sensory blockade was earlier in Group B and recovery time was prolonged in Group B. No difference was seen in maximal sensory blockade. Intrathecal neostigmine precipitated the onset of sensory and motor blockade and prolonged the sensory and motor block significantly when used with fentanyl and bupivacaine in

spinal anesthesia in a low dose. The duration of analgesia was significantly prolonged among the neostigmine added groups as indicated by the time of first rescue analgesia.

Keywords---spinal anesthesia, intrathecal, fentanyl, neostigmine.

Introduction

Intrathecal (IT) neostigmine may be used as an adjunct to spinal anesthesia (SA) for the prevention of acute perioperative pain¹. It potentiates opioid analgesia while reducing undesirable side effects.²The multimodal pain therapy approach including spinal neostigmine and spinal opioids is efficacious but significant systemic side effects of IT neostigmine, especially nausea and vomiting, have been reported with doses higher than 6.25 mcg.² Thus analgesic effect and safety of low dose of intrathecal neostigmine in combination with fentanyl and bupivacaine for spinal anaesthesia was being evaluated in our study.

Material and Methods

Study Design

Prospective, randomized, double blind study.

Study Population

Approval from institutional ethical committee was taken. The study was conducted in the Department of Anaesthesia and Critical Care, Christian Medical College and Hospital, Ludhiana after informed consent, 50 patients who are divided into two groups , 25 patients in each group aged between 18 to 60 years of either sex belonging to the ASA grade I & II, scheduled for elective lower abdominal and lower limb surgeries, which are likely to be finished within three hours were included in this study from 15th Oct 2015 to 14th Oct 2016. Patients with history of allergy to neostigmine/fentanyl/ bupivacaine, intracranial pressure/convulsions, patient with bleeding diathesis, pregnant women ,any dysarrhythmias on ECG, any contraindication for spinal anaesthesia which includes infection at the site of injection, patient's refusal, pre-existing neurological disorders and surgery lasting for more than 3 hours were excluded from the study.

A detailed history and complete physical examination and relevant investigations was done for all patients prior to surgery. All patients included in this study were advised fasting for six hours. All patients were given Tab Diazepam 10 mg during the previous night. Informed consent was taken from all patients. Patients were familiarized with visual analogue scale (VAS) and its use for measuring the post-operative pain. In the operation theatre, electrocardiogram, pulse oximetry, and non-invasive blood pressure monitors were attached and baseline parameters were monitored and recorded. Intravenous access was secured and all patients were pre-loaded with ringer lactate solution (10 ml/kg). Patients were divided into two groups of 25 each by block randomization in Block of 2,4,6 in 1:1 allocation.

The study solution was prepared in a 5 ml syringe by an anaesthesiologist who then handed over to the attending anaesthesiologist blinded to the nature of drug given to him/her.

- GROUP A: Intrathecal Bupivacaine 12.5 mg (2.5 ml) + Fentanyl 20 µg (0.4 ml)+0.1 ml Normal Saline (Total 3 ml)
- GROUP B: Intrathecal Bupivacaine 12.5 mg (2.5 ml) + Fentanyl 20 µg (0.4 ml) + Neostigmine 1µg (0.1 ml) (Total 3 ml)

Subarachnoid block was administered at the L₂₋₃ or L₃₋₄ vertebral level using 25 gauge Quincke spinal needle under all aseptic precautions. Patients were made supine following the block. The anaesthesiologist performing the block recorded the intra-operative data. Age, gender, weight, height, BMI, duration of surgery, pre op heart rate, systolic BP, diastolic BP, and oxygen saturation of every patient was recorded. Pulse rate, blood pressure and oxygen saturation was recorded every two minutes till the first ten minutes, then every ten minutes till one hour, followed by every fifteen minutes till the end of surgery. Any decrease in heart rate below 50 beats per minute was noted and treated with incremental doses of injection atropine 0.3 mg intravenously. Episodes of hypotension (fall in systolic blood pressure > 20% of baseline value), was treated with ephedrine 6 mg intravenously.

Sensory blockade was assessed using pin-prick test in the mid axillary line. Motor block was assessed using Modified Bromage Score. Sensory and Motor blockade was assessed every two minutes for the first ten minutes and thereafter post-operatively. The highest sensory block level and its onset time was noted. Recovery time for sensory and motor block was recorded. Recovery time for sensory blockade was taken as two dermatome regression of anaesthesia from the maximum level. Patients were assessed for pain score by performing the Visual Analogue Self rating method. Patients with a VAS of three or more received injection Diclofenac 1 mg/kg intravenously for rescue analgesia. The time for the first request for rescue analgesia and the total doses of diclofenac required for supplemental analgesia was recorded. Duration of effective analgesia was measured as the time from onset of analgesia to the patient's first request for supplemental analgesic administration and recorded in minutes. Subjects was monitored for occurrence of adverse events after spinal injection like nausea, vomiting, desaturation, hypotension, bradycardia, and others, if any.

Statistical analysis

The data collected was entered using Microsoft Excel Spreadsheet. Data analysis was done using student t-test, paired t-test and chi square test using SPSS Version 21. P<0.05 was considered statistically significant.

Results and Observations

The mean age of patients in our study was 32.98 ± 12.86 years. The age and gender distribution were comparable in both the groups. Patient sex is an independent factor influencing both responsiveness to general anaesthesia and recovery after anaesthesia, mechanism being pharmacodynamic in nature. Other

demographic characteristics like Height, weight and BMI were also comparable in both the groups. The pre-op baseline clinical characteristics studied were systolic and diastolic blood pressure (mm Hg), heart rate per minute, oxygen saturation, and all were comparable in both the groups. Hemodynamic stability was comparable in both the groups till the end of follow up postoperatively. Shakya ML³ et al, compared intrathecal neostigmine with intrathecal fentanyl for postoperative pain relief. No significant difference in the mean of heart rate was found between the groups as seen in our study.

Tekin et al⁴ his study, found no significant difference in the mean arterial pressures at baseline and at 24 hours between all the groups as seen in our study. Shakya ML³ et al, also found no significant difference in the mean arterial pressure between the groups. Even Jain A et al¹ study showed that the intraoperative hemodynamic characteristics were comparable. The mean oxygen saturation in group A and group B at all follow ups were comparable except at 4 minutes, 6 minutes and 120 minutes. Tekin et al⁴ in his study, found no significant difference in the oxygen saturation at baseline and at 24 hours between all the groups. Shakya ML³ et al, also found no significant difference in the oxygen saturation between the groups. Even Jain A et al¹ study showed that the intraoperative hemodynamic characteristics were comparable.

Sensory blockade

Onset of Sensory blockade

In group A, the mean time of onset of sensory block was 7.3 minutes with a standard deviation of 0.98 whereas in group B, the mean time of onset of sensory block was 3.28 minute with a standard deviation of 0.66. On statistical analysis, there was significant difference between both the groups. The onset of sensory block was significantly earlier in group B (p value<.0001) Table 1. Neostigmine helped in the early onset of sensory blockade. Shakya ML¹ et al, in their study results showed that the mean onset of sensory block in Groups Neostigmine and bupivacaine was 246.57±95.56 s and in group fentanyl and bupivacaine was 263.97±50.92 s, respectively. This onset of sensory block was comparable in Groups 1 and 2. It did not corroborate with our study. In a study by Raghavan R K et al⁵, the onset of sensory block was 3.97 min with 25 mcg of neostigmine and 3.87 min with 50 mcg of neostigmine which was comparable with our study. Neostigmine inhibits the breakdown of acetyl choline and thereby induce analgesia. It also prolongs and intensifies the analgesic effect through release of nitric oxide in the spinal cord.

Maximum sensory blockade

In group A out of 25 patients, 12 patients (48%) attained maximum sensory level up to T8, 13 patients (52%) attained maximum sensory level up to T10. In group B out of 25 patients, 8 patients (32%) attained maximum sensory level up to T10, 15 patients (60%) attained maximum sensory level up to T8, and 2 patients (8%) attained level till T6. On statistical analysis, there was no statistical significance between both the groups (p value>.05). Table 2 So both the groups were comparable regarding maximum sensory level. No additional effect of neostigmine was seen on maximum sensory level achieved in our study. Jain A et al¹, in his

study also found no statistical significance between two groups (p value $>.05$). Maximal sensory block level in both the groups was T7.

Recovery of Sensory Blockade

In group A, the mean recovery time of sensory block was 132.72 minutes with a standard deviation of 17.77, whereas in group B, the mean recovery time of sensory block was 163.2 minutes with a standard deviation of 9.78 (Fig 1). On statistical analysis, there was significant difference between both the groups. The recovery time of sensory block was significantly earlier in group A. (p value $<.0001$). It was inferred that addition of Neostigmine prolonged the duration of Sensory block. Jain A et al ¹, in his study also found statistical significance between two groups (p value $>.05$). He found increase in the duration of analgesia. Tekin et al ⁴ in his study, found significant difference between the two groups.

Onset of Motor Blockade

In group A, the mean time of onset of motor block was 12.48 minutes with a standard deviation of 1.87, whereas in group B, the mean time of onset of motor block was 6.74 minute with a standard deviation of 1.63. On statistical analysis, there was significant difference between both the groups. The onset of motor block was significantly earlier in group B. (p value $<.0001$). Table 3 Neostigmine helped in the early onset of motor blockade. In a study by Fareed A et al ⁶ the time for the onset of motor block was 8.44 ± 1.05 minutes, and 8.46 ± 0.71 minutes. There was no statistically significant difference among the study groups ($p > 0.05$). Our study result did not corroborate with them or other studies by Harbhej Singh et al ⁷, Diana F Gabinsky et. al ⁸ and U Srivastava et al ⁹.

In a study by Sharma R et al ¹⁰ the onset of motor block was 12.4 mins and it was also significantly less than the control as seen in our study. Raghavan R K et al⁵, conducted a study with the aim to assess the effects of intrathecal neostigmine added to hyperbaric bupivacaine on the onset and duration of spinal anaesthesia and in prolonging postoperative analgesia. The onset of motor block was 4.43 min with 25 mcg of Neostigmine and 4.6 min with 50 mcg of Neostigmine, but no statistical difference between them and against the control. But in our study 1 mcg of Neostigmine produced earlier onset of motor blockade. Intrathecal Neostigmine causes motor block by an Acetyl choline mediated reduction in motor neuron outflow with no reduction in spinal cord blood flow or histopathological changes. In addition, increased spinal levels of acetylcholine may augment motor blockade of spinal bupivacaine. ⁵

Recovery of motor blockade

In group A, the mean recovery time of motor block was 264.28 minutes with a standard deviation of 19.4, whereas in group B, the mean recovery time of motor block was 325.4 minutes with a standard deviation of 19.94 (Fig 2). On statistical analysis, there was significant difference between both the groups. The recovery time of motor block was significantly earlier in group A. (p value $<.0001$). It was inferred that addition of Neostigmine prolonged the duration of Motor block. Jain A et al¹, in his study also found statistical significance between two groups (p

value>.05). Our study findings did not match the study by Fareed A et al⁶, in which the duration of motor block was 121±13.52 minutes, and 126±6.1 minutes. There was no statistically significant difference among the groups ($p>0.05$). Similar non significant results were seen by Harbhej Singh et al⁷ and Diana F Gabinsky et. al.⁸. Raghavan R K et al⁵, in his study found that the mean duration of motor analgesia was 181.5 minutes with 25 mcg of Neostigmine and 199.5 min with 50 mcg of Neostigmine, statistical difference was found between 50 mcg Neostigmine and control as seen in our study. This prolongation of motor blockade can be an undesirable side effect, especially for short duration surgeries and day-care procedures.

Analgesia Rescue analgesia

In group A, the mean time to rescue analgesia was 248.24 minutes with a standard deviation of 23.51. The maximum time to rescue analgesia was 320 minutes and minimum time was 210 minutes. In group B, the mean time to rescue analgesia was 321.8 minutes with a standard deviation of 17.31. The maximum time to rescue analgesia was 360 minutes and minimum time was 290 minutes. (Fig 4). On statistical analysis, there was significant difference between both the groups. The time for first request of rescue analgesia was significantly earlier in group A. (p value<.0001). Bhavsar M et al¹¹, showed that mean time to rescue analgesia in the Neostigmine, fentanyl and bupivacaine group was 476.7 min. There is a potential synergism between fentanyl and neostigmine along with bupivacaine as reported in an animal study by Wang et al. Pandey V et al¹², studied the efficacy and safety of intrathecal neostigmine at dose of 50 µg and 150 µg as an adjuvant to bupivacaine for postoperative analgesia under spinal anesthesia. The total duration of analgesia was 224.40 ± 23.28 min in Group I Control with bupivacaine , 367.60 ± 42.15 min in Group II with 50 mcg Neostigmine, and 625.60 ± 87.70 min in Group III with 150 mcg of Neostigmine. The requirement of rescue analgesia in form of injection diclofenac sodium 75 mg intramuscularly was significantly lower in both test groups ($P < 0.05$) as seen in our study.

Lauretti et al has also used IT fentanyl and neostigmine as an individual drug. They have demonstrated that duration of rescue analgesia for individual drug was lower as compare to combination of both these drugs. It indicates synergism of combined use of both drugs.¹³ Jain A et al showed that the addition of a low dose of neostigmine increased the duration of complete analgesia and effective analgesia by 75% and 78%¹. Akinwale MO et al¹⁴ conducted study with the objective to determine the analgesic and adverse effects of intrathecal neostigmine combined with hyperbaric bupivacaine and fentanyl. The mean duration of effective analgesia was 485.6 +/- 37.6 minutes in neostigmine group compared with saline group, 316.0 +/- 49.15 minutes ($p < 0.001$) as was seen in our study.

Visual analogue scale score

The VAS score was 0 in both groups upto 90 minutes. At 120 minutes VAS score was lower in group B as compared to group A but was not statistically significant (p value=.327). VAS score at 150 minutes and 180 minutes was significantly

higher in group A as compared to group B (p value <0.05), indicating better postoperative analgesia in group B. The VAS score was lower in group B because the duration of Sensory and motor block was increased in Group B. (Fig 3). Overall VAS scores were found to decrease with Neostigmine in other studies of Jain A et al ¹ and Tekin et al ⁴. In a study by Bhavsar M et al¹¹, Pain score immediately after and in first 24 hours in group Fentanyl and neostigmine were significantly better in comparison with control group as seen in our study. It was mainly because of combine use of both the drugs that synergise their effects which led to prolong duration of rescue analgesia.

Adverse effects

In group A, 5 patients (20%) reported hypotension, 2 patients (8%) reported bradycardia, no patient reported nausea and under any other, 1 patient (4%) reported shivering and 1 patient (4%) reported urinary. In group B, 3 patients (12%) reported nausea, 1 patient (4%) reported hypotension, no patient reported bradycardia and any other adverse effect. (Fig 5) No patient reported vomiting, and desaturation in both the groups. There was no statistical significance in adverse effect between two groups (p value >0.05). The reason of hypotension was blockade of the sympathetic nervous system during subarachnoid block, and subsequent decreases in systemic vascular resistance and cardiac output. The addition of neostigmine to bupivacaine intrathecally did not reduce hypotension. In contrast, some studies had observed that intrathecal neostigmine can counteract the hypotension induced by intrathecal local anesthetics by directly stimulating preganglionic sympathetic neurons in spinal cord.¹²

Jain A et al in his study showed that no increase in the incidence of nausea and vomiting was noted with addition of 1 mcg neostigmine IT to fentanyl–bupivacaine as was seen in our study.¹ Lauretti et al showed a dose-independent reduction of postoperative analgesia requirement, but a dose dependent increase in the incidence of postoperative nausea and vomiting following addition of various doses of IT neostigmine and fentanyl (ranging from 10 to 25 mcg) to 15 mg of hyperbaric bupivacaine 0.5%. So higher dose of Neostigmine was associated with more side effects than low dose Neostigmine. ¹³ In a study by Akinwale MO ¹⁴, the incidence of adverse effects such as hypotension, bradycardia, nausea and vomiting were not statistically significant in both groups ($p > 0.05$). Study showed that spinal neostigmine 25 mcg added to hyperbaric bupivacaine and fentanyl provided a significantly longer surgical analgesia and insignificant adverse effects in male adults who had lower abdominal surgery under spinal anaesthesia.

Pandey V et al ¹², in a study showed that the incidence of nausea and vomiting was more with 150 µg neostigmine group compared to 50 µg neostigmine. It was concluded that administration of intrathecal neostigmine in dose of 50 µg as an adjuvant to bupivacaine produces hemodynamically stable analgesia with minimal side effects as compared to high dose. In our study also minimal dose of 1 mcg of Neostigmine was used which was seen to have no significant difference in side effects from the group without Neostigmine. As in our study, only 1 mcg of Neostigmine was used, no significant increase in the side effects was seen. Intrathecal Neostigmine produces nausea in a dose dependent manner. This high incidence of nausea and vomiting could possibly be due to cephalad migration of

Neostigmine to the brain stem. At brain stem, Neostigmine causes accumulation of acetyl choline to act on the chemoreceptor trigger zone which induces vomiting. High incidence of nausea and vomiting may limit its clinical utility. So to reduce this, antiemetic prophylaxis with Inj.Ondansetron 4mg. IV prior to subarachnoid block is a good alternative.

Discussion

In our study, the onset of sensory and motor block was earlier by the addition of neostigmine. The recovery time of sensory and motor block was also prolonged by addition of neostigmine. Thus overall, time for first request of rescue analgesia was significantly prolonged with addition of Neostigmine to Bupivacaine and Fentanyl. Similar results with Neostigmine have been seen in other studies. Neostigmine has been proposed to enhance the effects by enhancing the mechanism of Opioids. As Opioid increase the concentration of norepinephrine in lumbar cerebrospinal fluid which in turn produces analgesia in part by activating spinal cholinergic neurons to release acetylcholine,⁴ and Neostigmine further accentuates the action by inhibiting Cholinesterase.⁵ The inhibition of spinal cholinesterase by neostigmine results in an increase of endogenous acetylcholine, which is most likely released from intrinsic cholinergic neurons within the dorsal horn of the spinal cord. These cholinergic neurons terminate in the vicinity of primary afferent express muscarinic receptors. The endogenous acetylcholine produces analgesic effect through muscarinic presynaptic inhibition of glutamatergic afferents, similar to how it has been described in the neostriatum. Muscarinic receptor antagonists have been shown to reverse the analgesic effects of IT neostigmine. A tonic cholinergic activity is an important prerequisite for the effectiveness of neostigmine. The enhanced analgesic efficacy of IT neostigmine results from greater release of spinal acetylcholine from the more intense and prolonged discomfort of postoperative pain, and consequent action at muscarinic M1 and M3 and presynaptic nicotinic receptors present in the cholinergic interneurons at the lamina III and V of the dorsal horn. An action at nicotinic receptors at the dorsal horn ganglion and at the spinal meninges has also been suggested.

The maximum sensory level attained was T10 in both the groups in our study. The time to reach maximum level of sensory block and the peak level attained was also not influenced by the use of IT neostigmine in other studies. It might be due to the difference in the onset of action of IT neostigmine and IT bupivacaine. The VAS score was 0 in both groups upto 90 minutes in our study. At 120 minutes VAS score was lower in group B as compared to group A but was not statistically significant. The VAS scores were significantly lower in the Neostigmine group at 3 hours postoperatively, indicating better postoperative analgesia. Similar results with Neostigmine have been seen in other studies. It thus helps in reducing the analgesic consumption postoperatively.

Adverse effect monitoring was done for both group A and group B. In group A, known side effects like hypotension, bradycardia, were seen. No patient reported nausea or vomiting. In group B, nausea and hypotension were seen. No patient reported bradycardia and any other adverse effect. No patient reported vomiting, and desaturation in either group in our study. Although many drugs like

morphine, epinephrine, have been used in addition to LA, but the increased side effects and relative ineffectiveness resulted in reluctance to them. In a study by Singh H *et al*,⁷ episodes of hypotension were more frequent in the fentanyl-treated group than in the control group. In our study, the side effects were less in the Neostigmine group but no significant difference was found between both the groups. Use of low-dose IT neostigmine in an attempt to reduce the incidence of untoward side effects, mainly nausea and vomiting, while retaining its analgesic efficacy has been tried by many investigators. In patients undergoing below knee surgery, Lauretti *et al*,¹³ showed a dose-independent reduction of postoperative analgesia requirement, but a dose-dependent increase in the incidence of PONV following addition of various doses of IT neostigmine (ranging from 25 to 100 mcg) to 15 mg of hyperbaric bupivacaine 0.5%. Even the dose as low as 6.25 mcg has been associated with high incidence of PONV. Almeida *et al*, demonstrated a trend toward more nausea with doses higher than 1 mcg in patients undergoing major gynecological surgeries.

In our study, there was no incidence of vomiting with the addition of Neostigmine to IT bupivacaine and IT fentanyl and thus lesser need for antiemetic (not significant). As significantly Lower VAS scores were seen in the Neostigmine group, it may be a reason for less postoperative pain, discomfort and vomiting. The main strengths of this study is the completeness of the investigations in terms of baseline and timely followup. ASA was taken into account. Detailed follow up of heart rate, oxygen saturation and BP was done minute by minutes and any disturbance in the same was noted and managed efficiently. This study did analyse the efficacy and side effects of addition of low dose Intrathecal Neostigmine to IT Bupivacaine and Fentanyl, thus contributing to the very limited data available on the same in other studies. In conclusion, low dose IT Neostigmine can be considered as a safe drug to increase the efficacy of anaesthesia intra operatively and post operatively when added to IT bupivacaine and IT Fentanyl thereby reducing the need of additional analgesics.

Conclusion

Hence, from our study we conclude that:

- Intrathecal neostigmine precipitated the onset of sensory and motor blockade and prolonged the sensory and motor block significantly when used with fentanyl and bupivacaine in spinal anesthesia in a low dose.
- There was no significant hemodynamic instability in our patients. The maximal upper level of sensory block achieved was not higher on addition of intrathecal neostigmine.
- The duration of analgesia was significantly prolonged among the neostigmine added groups as indicated by the time of first rescue analgesia.
- Although the addition of neostigmine produced side effects like nausea and hypo tension, they were not statistically significant and were cautiously managed.

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Tables and figures

Table 1
Onset time of sensory block(in minutes)

ONSET TIME OF SENSORY BLOCK(IN MINUTES)	Group A (n=25)	Group B (n=25)	P value
Mean $\pm$ Stdev	7.3 $\pm$ 0.98	3.28 $\pm$ 0.66	<.0001
Median	7	3	
Min-Max	6-9	2-5	

Table 2
Maximum sensory level

MAXIMUM LEVEL OF SENSORY BLOCK	Group A(n=25)	Group B(n=25)	Total	P value
T6	0 (0.00%)	2 (8.00%)	2 (4.00%)	0.172
T8	12 (48.00%)	15 (60.00%)	27 (54.00%)	
T10	13 (52.00%)	8 (32.00%)	21 (42.00%)	
TOTAL	25 (100.00%)	25 (100.00%)	50 (100.00%)	

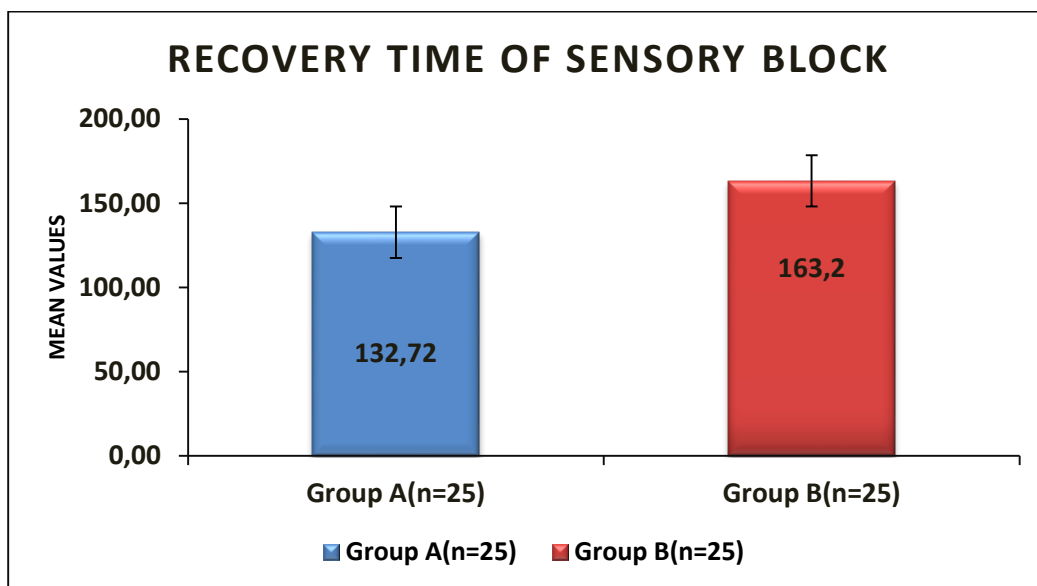


Figure 1. Recovery time of sensory block

GROUP A: Intrathecal Bupivacaine 12.5 mg (2.5 ml) + Fentanyl 20 µg (0.4 ml)+0.1 ml Normal Saline GROUP B: Intrathecal Bupivacaine 12.5 mg (2.5 ml) + Fentanyl 20 µg (0.4 ml) + Neostigmine 1µg (0.1 ml)

Table 3
Onset time of motor block(in minutes)

ONSET TIME OF MOTOR BLOCK(IN MINUTES)	Group A(n=25)	Group B(n=25)	P value
Mean ± Stdev	12.48 ± 1.87	6.74 ± 1.63	<.0001
Median	13	7	
Min-Max	9-15	4-10	

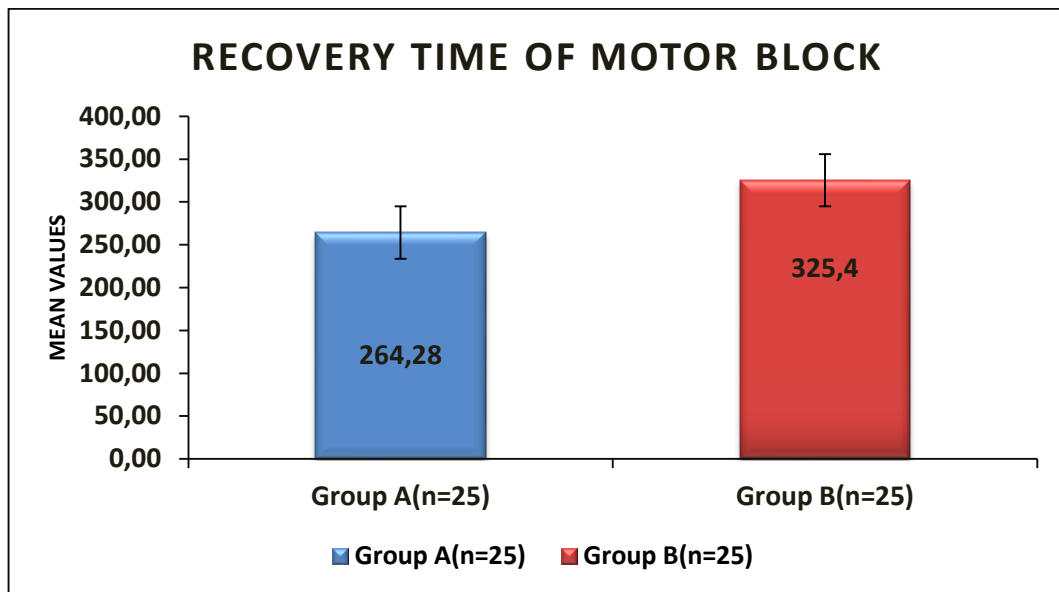


Figure 2. Recovery time of motor block

GROUP A: Intrathecal Bupivacaine 12.5 mg (2.5 ml) + Fentanyl 20 µg (0.4 ml)+0.1 ml Normal Saline GROUP B: Intrathecal Bupivacaine 12.5 mg (2.5 ml) + Fentanyl 20 µg (0.4 ml) + Neostigmine 1µg (0.1 ml)

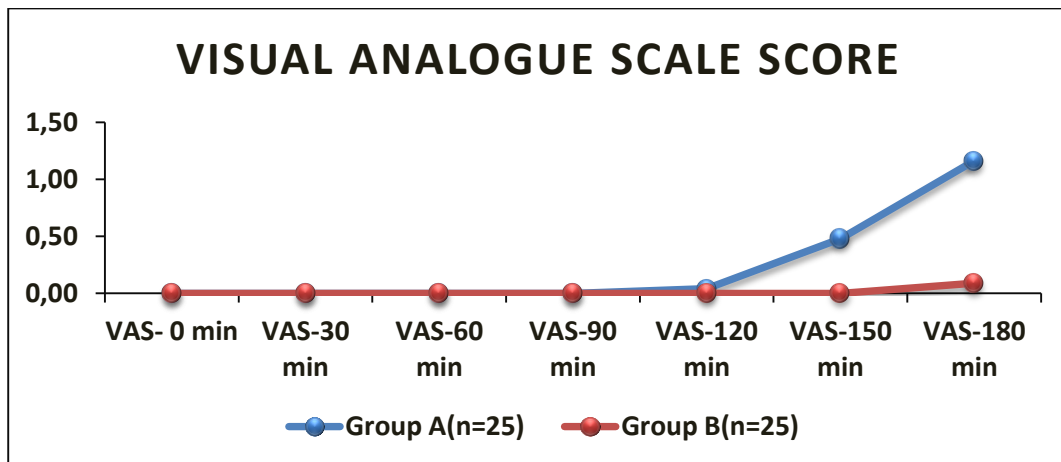


Figure 3. Visual analogue scale score

GROUP A: Intrathecal Bupivacaine 12.5 mg (2.5 ml) + Fentanyl 20 µg (0.4 ml)+0.1 ml Normal Saline GROUP B: Intrathecal Bupivacaine 12.5 mg (2.5 ml) + Fentanyl 20 µg (0.4 ml) + Neostigmine 1µg (0.1 ml)

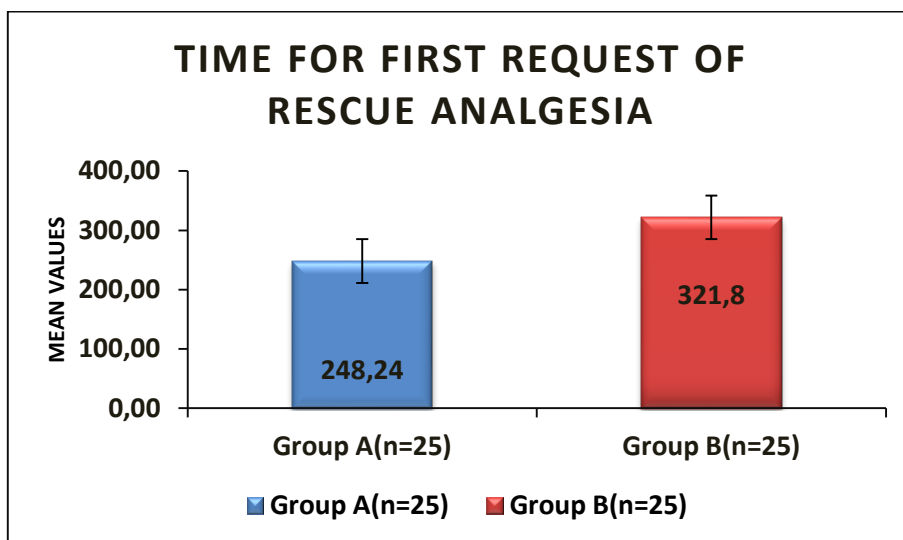


Figure 4. Time for first request of rescue analgesia

GROUP A: Intrathecal Bupivacaine 12.5 mg (2.5 ml) + Fentanyl 20 µg (0.4 ml)+0.1 ml Normal Saline GROUP B: Intrathecal Bupivacaine 12.5 mg (2.5 ml) + Fentanyl 20 µg (0.4 ml) + Neostigmine 1µg (0.1 ml)

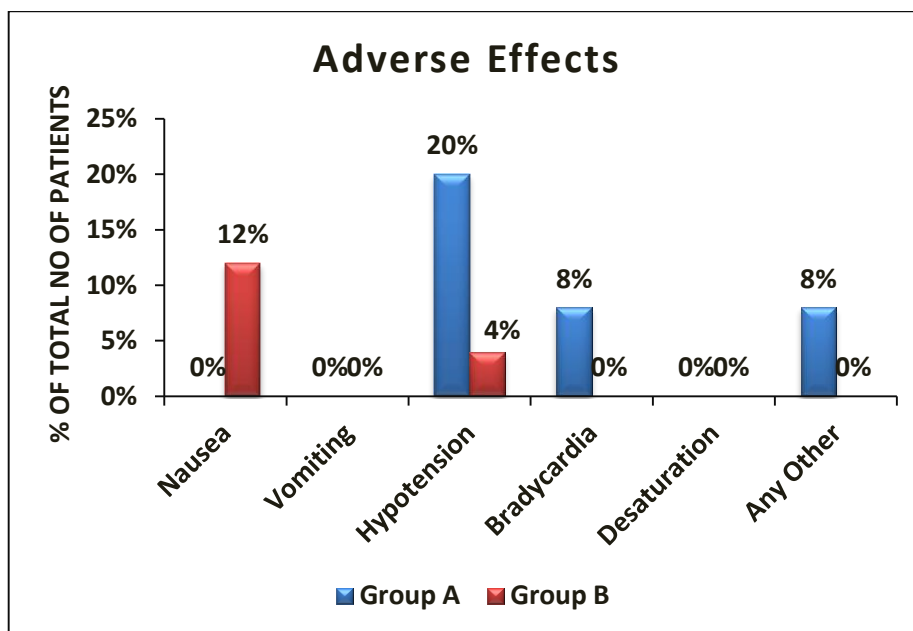


Figure 5

GROUP A: Intrathecal Bupivacaine 12.5 mg (2.5 ml) + Fentanyl 20 µg (0.4 ml)+0.1 ml Normal Saline GROUP B: Intrathecal Bupivacaine 12.5 mg (2.5 ml) + Fentanyl 20 µg (0.4 ml) + Neostigmine 1µg (0.1 ml)