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A Comparative Study between Intrathecal Clonidine and Neostigmine with Intrathecal Bupivacaine for Lower Abdominal Surgeries

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Abstract

Aim: This study was carried out to compare the effect of intrathecal clonidine 75 µg clonidine or 50 µg neostigmine added to intrathecal bupivacaine with respect to haemodynamic stability, side effects, sensory and motor characteristics. *Materials and Methods:* This study was carried out in 50 patients from November 2015 to October 2016, after obtaining approval from ethical committee. 60 patients were selected initially but 10 patients did not meet the inclusion criteria, hence they were excluded. 50 patients were divided into 2 groups of 25 each. *Group A patients (n=25):* Received bupivacaine with 50 µg neostigmine. *Group B patients (n=25):* Received bupivacaine with 75 µg clonidine. *Results:* Group A patients shows earlier mean onset time of sensory characteristics compared to group B. The cephalad spread was similar in both group A and B. The mean total duration of analgesia was more in group B compared to group A. Group A patients shows earlier mean onset time of motor characteristics compared to group B. The recovery time of motor blockade was earlier in group A when compared to group B. In both the groups, increase in heart rate was observed following spinal anesthesia with mean increase of 20 beats/minute noted at 6th minute in group A, whereas it showed an increase in heart rate of 16 beats/minute in group B. *Conclusion:* This study concluded that neostigmine enhanced the sensory onset, motor block without prolonging the analgesia duration compared to clonidine.

Keywords: Neostigmine; Clonidine; Motor Block.

Introduction

In the postoperative period, for managing pain, anesthesia is given to provide good analgesia and with muscle relaxation in a satisfactory way. To bring about early mobilization, satisfaction and comfort of patients, the morbidity and mortality may be decreased by successful management of postoperative period [1,2]. For elective and emergency procedures like cesarean sections, lower abdominal surgeries, orthopedic and urological surgeries, spinal anesthesia is one of the most accepted techniques, since its introduction in 1898. Its simple technique, rapid onset of action, drug cost being nominal and fewer side effects are the major advantages of spinal anesthesia along with patient being awake [3]. During subarachnoid block, the commonly used local anesthesia is bupivacaine intrathecally. When used alone, the insufficient duration of anesthesia and postoperative analgesia is the main disadvantage. For procedures lasting for 2 to 2 and half years, bupivacaine can be used, hence adjuvants can be added for surgeries which require more time. There is a risk of hypotension and bradycardia if the bupivacaine dose is increased to prolong the duration of the subarachnoid blockade. Hence, a number of adjuvants have been introduced to prolong the duration and postoperative analgesia [4]. The reduction in dose of local anesthesia and its reduced side effects are the other advantages. The pharmacological agents which are having little

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pharmacological effect by themselves, and they can enhance or potentiate the other drugs action when given at the same time are called adjuvants [5].

To find out the efficacy of both opioids and alpha 2 adrenergic agonists like clonidine as adjuvants to intrathecal bupivacaine, many studies have been conducted and was found to be effective. The absence of opioids related side effects like pruritis, nausea, vomiting, acute urinary retention, sedation are added advantage of alpha 2 adrenergic agonists.

The commonly used adjuvants added along with bupivacaine are clonidine and neostigmine. This study was carried out to compare the effect of intrathecal clonidine 75 µg clonidine or 50 µg neostigmine added to intrathecal bupivacaine with respect to haemodynamic stability, side effects, sensory and motor characteristics.

Materials and Methods

This study was carried out in 50 patients from November 2015 to October 2016, after obtaining approval from ethical committee. 60 patients were selected initially but 10 patients did not meet the inclusion criteria, hence they were excluded. 50 patients were divided into 2 groups of 25 each.

Group A patients (n=25): Received bupivacaine with 50 µg neostigmine.

Group B patients (n=25): Received bupivacaine with 75 µg clonidine.

Inclusion Criteria

Patients undergoing lower abdominal surgeries, who were above 18 years of age, who were not allergic to study drugs.

Exclusion Criteria

Patients with spinal anesthesia contraindications, with ischemic heart disease, with hypertension, with bronchial asthma, with diabetes mellitus, obese patients. On night before surgery, all the patients were premedicated with ranitidine and alprazolam. ECG, oxygen saturation(SPO_2), blood pressure were recorded. The study drugs were injected into the sub-arachnoid space at the rate of 1 mL in 3 seconds, after confirming the free flow of cerebrospinal fluid (CSF).

Results

Table 2 shows group A patients shows earlier mean onset time compared to group B. The cephalad spread was similar in both group A and B. The mean total duration of analgesia was more in group B compared to group A.

Table 3 shows group A patients shows earlier mean onset time compared to group B. The recovery time of motor blockade was earlier in group A when compared to group B. In both the groups, increase in heart rate was observed following spinal anesthesia with mean increase of 20 beats/minute noted at 6th

Table 1: Shows demographics and duration of surgery in both the groups

Parameter	Group A	Group B	P Value
Mean Age (Years)	30.58±8.32	40.11±3.56	<0.0001
Mean Weight (Kgs)	60.23±8.21	55.68±5.21	0.0598
Duration of surgery(mins)	58.47±12.36	59.63±15.98	0.8112

Extremely statistically significant =<0.0001.

Table 2: Shows sensory characteristics

Parameter	Group A	Group B	P Value
Mean Onset time(Seconds)	109±11	170±20	<0.0001
Mean total duration of analgesia	315±25	380±35	<0.0001
Median Cephalad spread	T4	T4	---

Table 3: Shows motor characteristics in both the groups

Parameter	Group A	Group B	P Value
Mean Onset time(Seconds)	170±26	220±14	<0.0001
Duration of motor blockade (mins)	180±45	219±55	<0.0001
Quality of motor blockade	Bromage grade	Bromage grade	---

minute in group A, whereas it showed an increase in heart rate of 16 beats/minute in group B.

Discussion

Many studies have been reported regarding the comparison of clonidine, neostigmine along with intrathecal bupivacaine.

A.Srikanth Reddy et al [6], conducted a study to compare the effect of intrathecal clonidine 75 µg or neostigmine 50 µg added to intrathecal hyperbaric bupivacaine, with respect to sensory characteristics, motor characteristics, haemodynamic stability and side effects. The prospective study included 60 patients who were admitted for lower abdominal surgeries. The patients were randomly divided into 2 groups, with 30 in each group. Group A patients received neostigmine 50 µg with 2.5 ml of intrathecal 0.5% hyperbaric bupivacaine and group B patients received intrathecal clonidine 75 µg and 2.5 ml of intrathecal 0.5% hyperbaric bupivacaine. The parameters for comparison of 2 groups included sensory characteristics, motor characteristics, haemodynamic stability and side effects. In Group B patients, there was a significantly enhanced onset of sensory and motor block and well maintained haemodynamics. Group A patients had prolonged analgesia. Perioperatively no serious adverse effects were noted in both the groups. Intrathecal clonidine with hyperbaric bupivacaine produces prolonged postoperative analgesia and intrathecal neostigmine with bupivacaine produces a good sensory and motor blockade for lower abdominal surgeries.

Dr B.N. Biswas et al [7], conducted a study in which the use of neuraxial opioids has gained popularity over the last few years; they may augment the analgesia produced by local anaesthetic through direct binding with the specific spinal receptors. Fentanyl, a lipophilic opioid has rapid onset of action, it does not tend to migrate intrathecally to the 4th ventricle in sufficient concentration to cause delayed respiratory depression. Forty healthy women of ASA grade I scheduled for elective Caesarean section were randomly allocated to receiver either 2 ml of 0.5% inj bupivacaine with 0.25 ml of normal saline (group A, n=20) or 0.25 ml (12.5 microgram) fentanyl with 2 ml of 0.5% inj bupivacaine (group B, n=20). Vital signs, sensory level, motor block, pain score and side effects were observed every 2 min for first 20 min, then at 15 min interval for remainder of operation, thereafter at 30 min interval until the patient complained of pain. Complete analgesia (time from injection to first report of pain) lasted longer in group B (183±9) than group A (129±9.5). The duration of effective analgesia (time from injection to first parenteral analgesic) was increased with the dose of intrathecal fentanyl 12.5 microgram (248±11.76). Pruritus was only 15% in fentanyl group.

Gabriela Rocha Lauretti et al [8], conducted a study in which opioids are considered mainstream for combined spinal-epidural anesthesia, but frequently limited by adverse effects. The aim of this study was to examine whether low-dose spinal neostigmine, epidural dexamethasone or their combination enhances analgesia from spinal bupivacaine without adverse effects. A total of 60 patients undergoing orthopedic surgery were randomized to one of four groups and evaluated for 24-h after surgery for analgesia (time to first rescue analgesic) and rescue analgesic consumption. Patients received 15 mg bupivacaine plus the test drug intrathecally (saline or 1 microgram (µg) neostigmine). The epidural test drug was either saline or 10 mg dexamethasone. The Control group (CG) received spinal and epidural saline. The Neostigmine group (NG), spinal neostigmine and epidural saline; the Dexamethasone group (DG), spinal saline and epidural dexamethasone; and the Neostigmine-dexamethasone group (NDG), spinal neostigmine and epidural dexamethasone. The CG (282 ± 163 min) and NG (524 ± 142 min) were similar in their times to first rescue analgesic and analgesic consumption. The time to first rescue analgesic was longer for the DG (966 ± 397 min) compared with CG and NG (P<0.0002), and the DG had less ketoprofen consumption and lower overall visual analogue scale-pain sores compared with CG and NG (P < 0.0005). Addition of 1 mg-neostigmine (NDG) resulted in longer time to rescue analgesic (1205±303 min; P < 0.02) and lower ketoprofen consumption (P < 0.05) compared to DG. Sporadic cases of vesical catheterization and emesis were observed, however adverse effects were similar among groups. Spinal 1 microgram (µg) neostigmine further enhanced analgesia from spinal bupivacaine combined with epidural dexamethasone, without increasing the incidence of adverse effects.

Mubasher Ahmad Bhat et al [9], conducted a study in which neuraxial administration of neostigmine alongwith local anaesthetics improves the quality of intraoperative analgesia and also provides postoperative pain relief for longer duration. The present study was conducted to study the efficacy and safety of intrathecal neostigmine with bupivacaine in two different doses. Ninety patients of ASA I and II undergoing lower abdominal and

lower limb surgeries under spinal anaesthesia were enrolled and divided into 3 groups of 30 each. Group A consisted of bupivacaine control group, Group B consisted of bupivacaine plus 50mcg neostigmine and Group C consisted of bupivacaine plus 150mcg neostigmine. Haemodynamic parameters, sensory and motor characteristics along with side effects were recorded. The post operative pain assessment was done by visual analogue scale score at hourly intervals for the first four hours, then two hourly intervals for the next 6 hours and thereafter at 24 hours. It was scaled from a score of 0 meaning no pain to a score of 100 meaning worst pain perceived. Time of two segment regression of sensory blockade and total duration of motor block was significantly prolonged in group B and C as compared to the control group. The mean total duration for analgesia was significantly prolonged in Group B (340±8.36) and Group C (700±8.65) when compared to group A (263.30±7.57) ($p<0.05$). This study concluded that intrathecal neostigmine results in effective postoperative analgesia prolonging sensory and motor block without hemodynamic and respiratory depression in the intra and postoperative period. N. Yoghanarasimha et al [10], conducted a study in which spinal anaesthesia requires a small volume of drug to produce profound reproducible sensory analgesia and motor blockade, but has limited duration of action. A properly chosen adjuvant to local anaesthetic agent produces the best way to achieve a better quality regional block. Hence, a study was conducted to compare the effect of intrathecal clonidine 75µg or neostigmine 50µg added to intrathecal hyperbaric bupivacaine, with regards to sensory characteristics, motor characteristics, haemodynamic stability and side effects. This was a prospective randomized experimental study in 50 patients posted for lower abdominal surgery belonging to ASA I and II status and aged between18 and 60 years. One group received intrathecal clonidine 75 µg and 2.5 ml (12.5 mg) of intrathecal 0.5% hyperbaric bupivacaine (group BC) and second group received neostigmine 50 µg with 2.5 ml (12.5mg) of intrathecal 0.5% hyperbaric bupivacaine (group BN) and they were compared with regards to sensory characteristics, motor characteristics, haemodynamic stability and side effects. Addition of 50 µg neostigmine significantly enhanced the onset of sensory block (BN - 90 ± 15 secs, BC-160 ± 20 secs, *P* value as <0.05) and motor block (BN-110±15 secs, BC-210±20 secs, *P* value as <0.05) compared to clonidine. Haemodynamics were well maintained in the neostigmine group. Group BC had prolonged analgesia (362 ± 36 mins) compared to BN group (300 ± 25 mins)($P < 0.05$) with no serious adverse effects noted perioperatively in either groups. Intrathecal clonidine with hyperbaric bupivacaine produces prolonged postoperative analgesia and intrathecal neostigmine with bupivacaine produces a good sensory and motor for the surgical procedure.

Conclusion

This study concluded that neostigmine enhanced the sensory onset, motor block without prolonging the analgesia duration significantly compared to clonidine.

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