European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 10, Issue 01, 2023

ORIGINAL RESEARCH

Evaluation Of Post-Operative Analgesic Effect Of Combined Use Of Fentanyl And Neostigmine As An Adjunct To Bupivacaine In Lower Abdominal Surgeries

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Received Date: 11/11/2022 Acceptance Date: 08/01/2023

ABSTRACT

Background: Spinal anaesthesia requires a small volume of drug to produce profound sensory and motor blockade but has limited duration of action. An adjunct to local anaesthetic produces a better-quality regional block. The present study was aimed to evaluate the study and tolerability of combined use of intrathecal neostigmine and fentanyl as an adjunct to bupivacaine for postoperative analgesia in patients posted for abdominal surgeries under spinal anaesthesia. Material and Methods: Present study was single-center, prospective, comparative, observational study, conducted in patients of age group of 20-60 years, of either gender, ASA grade I/II, Elective patients undergoing Lower Abdominal Surgeries. 60 patients were divided by computer assisted randomization table into 2 groups of 30 subjects each as GROUP B (BUPIVACAINE Group) & GROUP C (COMBINED Fentanyl Neostigmine Group). Results: There was no significant difference in age distribution, gender distribution & ASA grade in two groups. ($p>0.05$). The mean duration of sensory block was found to be 194.16 ±21.43 minutes in group C while 153.03 ±19.19 minutes in group B, difference was statistically highly significant. ($P <0.0001$). The mean duration of motor block was found to be 197.18 ±21.78 minutes in group C while 169.26 ± 19.38 minutes in group B, difference was statistically highly significant. ($P <0.0001$) There was no difference when two groups were compared statistically for complications. ($p>0.05$) post-operative analgesia remained for longer duration in Group C, 7.40 ± 1.21 hours as compared to 5.32 ± 1.21hours in Group B, difference was statistically significant ($P <0.05$). Conclusion: Spinal neostigmine added to bupivacaine and fentanyl provided a significantly longer surgical analgesia and insignificant adverse effects who had lower abdominal surgery under spinal anaesthesia**.**

Keywords: neostigmine, bupivacaine, fentanyl, post-operative analgesia, lower abdominal surgery, spinal anaesthesia.

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INTRODUCTION

Pain is one of the main postoperative adverse outcomes especially after abdominal surgeries. Regional analgesia techniques reduce neuroendocrine stress response, thromboembolic phenomenon and requirement of parenteral analgesics in the postoperative period.[1] Spinal anaesthesia requires a small volume of drug to produce profound sensory and motor blockade but has limited duration of action. An adjunct to local anaesthetic produces a better-quality regional block.[1]

Single Opioids as additives result in urinary retention, sedation and pruritis,[2] whereas, non-opioids such as clonidine, ketamine, neostigmine, tramadol, midazolam and dexmedetomidine have been evaluated as epidural adjuvants. [3] Intrathecal neostigmine has been used as an adjunct to spinal anaesthesia for the prevention of acute perioperative pain. It has been shown to potentiate opioid analgesia.[4] Intrathecal neostigmine inhibit the breakdown of spinally released acetylcholine thereby enhancing the descending control of afferent nociceptive stimuli and provides new approach for enhancement of desirable analgesia with few dose related side effects.[5]

Issue related to the side effects caused by neuraxial use of neostigmine was still important, considering this fact we have used lower dose of fentanyl and neostigmine combination as an adjunct to Bupivacaine to minimize the side effects along with better postoperative analgesia.[6] The present study was aimed to evaluate the study and tolerability of combined use of intrathecal neostigmine and fentanyl as an adjunct to bupivacaine for postoperative analgesia in patients posted for abdominal surgeries under spinal anaesthesia.

MATERIAL AND METHODS

Present study was single-center, prospective, comparative, observational study, conducted in, Department of Anaesthesiology, SRTR Government Medical College and Hospital, Ambajogai, India. Study duration was of 2 years (October 2018 to December 2020). Study approval was obtained from institutional ethical committee.

Inclusion criteria

- Patients of age group of 20-60 years, of either gender, ASA grade I/II, Elective patients undergoing Lower Abdominal Surgeries, willing to participate in present study.

Exclusion criteria

- Any contra-indications to spinal anaesthesia, obese patients > 90 kg, short stature patients <150 cm, patients allergic to drugs.
- Patients with impaired renal, hepatic & biliary function, impaired respiration, head injury and peripheral neuropathy.
- Prior history of opioid & other substance abuse, patients on tranquilizers, hypnotics, sedatives & other CNS depressant drugs.
- Obstetric patient

Patients were evaluated for any systemic diseases and laboratory investigations recorded. Preanesthetic check-up was done one day prior to the surgery. Study was explained to patients in local language & written consent was taken for participation & study. Preparation of patients included period of overnight fasting. Patients were premedicated with tab. Diazepam 0.2 mg/kg orally, the night before surgery.

On the day of surgery, in operation theater, 60 patients were divided by computer assisted randomization table into 2 groups of 30 subjects each as.

1. GROUP B (BUPIVACAINE Group): Received normal saline as 1ml solution

2. GROUP C (COMBINED Fentanyl Neostigmine Group): Received combination of fentanyl 20 mcg and neostigmine 20micg as 1 ml solution.

In the operating room, IV access was be obtained on the forearm with no.18 G IV cannula and all patients were preloaded with 20 ml/kg Ringer's Lactate before the surgery. Baseline vitals were recorded. Under strict asepsis, using 23 G Quincke lumber puncture needle, lumbar puncture was performed at L3–L4 interspace in left lateral position. A total volume of 4ml was injected intrathecally, at the rate of 0.25ml/sec as per group allocation. Patients were placed in the supine position immediately after spinal injection.

Intraoperatively pulse rate, non-invasive blood pressure, electrocardiogram, SpO2 was recorded. Time of onset of sensory block, maximum cephalic spread of sensory block, time of onset of motor block, time to complete motor block (by Modified Bromage Scale), total duration of sensory & motor block, duration of surgery, duration of Rescue analgesia, total number of rescue analgesics administered in 24 hrs., postoperative assessment findings were noted in proforma,

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi- square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

RESULTS

The mean age in group C was 38.53±13.88 years and group B was 38.96±11.41 years. There was no significant difference in age distribution, gender distribution & ASA grade in two groups. (p>0.05).

Table 1: Demographic profile

Characteristics		**Group C (n=30)**	**Group B (n=30)**	**P Value**
Mean age (Yrs.)		38.53 ±13.88	38.96 ±11.41	0.783
Sex	Male	23	21	0.71
	Female	07	09	
ASA	I	12	17	0.42
	II	09	06	
	III	09	07	

The mean time for onset of sensory block was found to be 4.13 ±1.32 minutes in group C while 4.57 ±1.46 minutes in group B, difference was statistically significant (P <0.05). The mean time to achieve maximum sensory block was found to be 12.03 ±3.12 minutes in group C while 13.19 ±3.41 minutes in group B, difference was statistically significant (P <0.05). The mean duration of sensory block was found to be 194.16 ±21.43 minutes in group C while 153.03 ±19.19 minutes in group B, difference was statistically highly significant. (P <0.0001). The mean time for onset of motor block was found to be 5.13 ±0.58 minutes in group C while 5.63 ±0.92 minutes in group B, difference was statistically significant. (P <0.5). The mean duration of motor block was found to be 197.18 ±21.78 minutes in group C while 169.26 ± 19.38 minutes in group B, difference was statistically highly significant. (P <0.0001)

Table 2 Anaesthesia characteristics

Parameters	**Group C**	**Group B**	**P value**
Onset of Sensory block (mins.)	4.13 ±1.32	4.57 ±1.46	0.02
Time to achieve maximum sensory block (minutes)	12.03 ±3.12	13.19 ±3.41	0.01
Duration of sensory block (minutes)	194.16 ±21.43	153.03 ±19.19	<0.0001
Onset of motor block (mins.)	5.13 ±0.58	5.63 ±0.92	0.02

Duration of motor block (min)	197.18 ±21.78	169.26 ±19.38	<0.0001

Out of total 60 patients, it was observed that in maximum patients' level of sensory block reached was T6; 16 (53.33%) and 14 (46.67%) patients among Group C and Group B respectively. There was no difference in level of sensory block when two groups were compared statistically. (p>0.05)

Table 3: Maximum level of sensory block:

Level	Group C	Group B	P value
T4	08	06	X2=1.44; DF=3; P=0.69
T6	16	14	
T8	05	08	
T10	01	02	
Total	30	30	

Out of total 60 patients, it was observed that maximum intensity of motor block was Bromage 3; 28 (93.33%) and 30 (96.67%) patients among Group C and Group B respectively. There was statistically no significant difference in intensity of motor blockade when two groups were compared. (p>0.05)

Table 4 Intensity of motor blockade

Intensity	Group C	Group B	P value
Bromage 1	00	00	P=0.31*
Bromage 2	02	0	
Bromage 3	28	30	

The baseline characteristics were noted before giving induction doses of both the drugs. Mean heart rate in Group C and Group B was 81.52 ±7.13 and 80.36 ±6.54 respectively. Mean systolic blood pressure in Group C and Group B was 128.32±11.12and 126.38±10.36 mm of Hg respectively. Mean diastolic blood pressure in Group C and Group B was 78.73±5.18and 79.84±5.43 mm of Hg respectively. Mean O2 saturation in Group C and Group B was 99.68±0.28and 99.76±0.3 % respectively. Mean arterial pressure in Group C and Group B was 94.25 ±4.57 and 95.41 ± 3.76mm of Hg respectively.

Table 5: Showing baseline characteristics:

Characteristics (Mean)	Group C	Group B	P value
Heart rate(beats/min)	81.52 ±7.13	80.36 ±6.54	0.72*
Systolic blood pressure(mmHg)	128.32±11.12	126.38±10.36	0.68*
Diastolic blood pressure(mmHg)	78.73±5.18	79.84±5.43	0.75*
Mean arterial pressure (mmHg)	94.25 ±4.57	95.41 ± 3.76	0.83*
O2 Saturation(%)	99.68±0.28	99.76±0.32	0.91*
Respiratory rate(breaths/min)	17.60±1.68	17.78±1.79	0.89*

There were 2 cases of headache, one from each Group C & B There were 19 cases of Nausea, 12 from Group C and 7 from Group B. There were 2 cases of vomiting and pruritus each, both of which were seen in Group C There were 5 cases of hypotension, 1 in Group C and 4 in Group B. There were 3 cases of bradycardia, all in Group C. There was no difference when two groups were compared statistically for complications. (p>0.05)

Table 6. Showing complications among various group:

Complication	Group C (n=30)	Group B (n=30)
Headache	01	01
Nausea	12	7

Vomiting	2	0
Pruritus	2	0
Hypotension	1	4
Bradycardia	3	0

Post-operative analgesia remained for longer duration in Group C, 7.40 ± 1.21 hours as compared to 5.32 ± 1.21hours in Group B, difference was statistically significant (P <0.05). Numbers of post-operative analgesics were required less in Group C, 2.5 ± 1.2 as compared to 4.2± 1.8 in Group B, difference was statistically significant (P <0.05). Group C patients get early ambulated with early discharge compared to Group B, difference was statistically significant (P <0.05).

Table 7: Postoperative characteristics

Postoperative characteristics	Group C (n=30)	Group B (n=30)	P value
Duration of postoperative analgesia (Hrs.)	7.40 ± 1.21	5.32 ± 1.41	<0.05 (S)
Number of post operative rescue analgesics required	2.5 ± 1.2	4.2 ± 1.8	<0.05 (S)
Length of stay (Days)	1.20 ±0.32	1.83 ±0.41	<0.05 (S)
Time to ambulation (min)	225.23 ±56.11	265.18 ±58.23	<0.05 (S)

DISCUSSION

Relief of pain during surgery and postoperative period is one of the mainstays of balanced anaesthesia. Spinal anaesthesia remains one of the basic techniques in modern anaesthesia despite variable popularity over many years since its introduction into clinical practice. Various drugs have been tried in subarachnoid block along with local anaesthetics with the aim of improving the quality of intra operative and post-operative pain relief.

Bupivacaine is a long-acting local anaesthetic, to the ambulatory setting by using smaller doses. However, the duration of the block remains prolonged with these smaller doses, and they may provide insufficient anaesthesia.

Single analgesics, either opioid or non-steroidal anti-inflammatory drugs (NSAIDs) are not able to provide pain relief without side effects such as nausea, vomiting, sedation or bleeding. Intrathecal neostigmine has been used as an adjunct to spinal anaesthesia for the prevention of acute perioperative pain.

In the present study, the mean age in group C was 38.53±13.88years and group B was 38.96±11.41 years. In other similar studies Jain A et al.,[4] & Lauretti GR et al.,[7] noted no differences with regard to age was noted among groups. (P > 0.05).

Out of total 60 patients, there were 23 (76.67%) and 21 (70%) male patients among Group C and Group B respectively. There were 7 (23.33%) and 9 (30%) females in Group C and Group B respectively. There was no gender difference when two groups were compared statistically (p>0.05)

In the study, the mean time for onset of sensory block was found to be 4.13 ±1.32 minutes in group C while 4.57 ±1.46 minutes in group B. The difference in mean time for onset of sensory block was statistically significant which is 0.02 (P <0.05). Similar findings were noted by Jain A et al.,[4] while in study by Lauretti GR et al.,[7] various groups showed no differences regarding onset of sensory time. (P>0.05) This was in contrast to present study.

In the present study, out of total 60 patients, it was observed that in maximum patients level of sensory block reached was T6; 16 (53.33%) and 14 (46.67%) patients among Group C and Group B respectively. There was no difference in level of sensory block when two groups were compared statistically. (p>0.05) Jain A et al.,[4] noted that the maximum level of sensory block in Group I was T7 and Group III was T6 with no statistical significant difference which is comparable to present study. Similar findings were noted by Lauretti GR et al.,[7]

The mean time to achieve maximum sensory block was found to be 12.03 ±3.12 minutes in group C while 13.19 ±3.41 minutes in group B. The difference in mean to achieve maximum sensory block was statistically significant. (P <0.05) In study by Jain A et al.,[4] maximum sensory block to achieve in Group I was 11.8 ± 4.2 minutes and Group III was 13 ± 3.2 with statistical significant difference. This finding was comparable to present study. while in study by Lauretti GR et al.,[7] various groups showed no differences regarding time to achieve maximum sensory lock. (P>0.05) This was in contrast to present study.

The mean duration of sensory block was found to be 194.16 ±21.43 minutes in group C while 153.03 ±19.19minutes in group B. The difference in mean duration of sensory block was statistically highly significant. (P <0.0001). Similar findings were noted by Jain A et al.,[4] as the duration of sensory lock in Group I was 141.4 ± 21.4 minutes and Group III was 269 ± 35.5 with statistical significant difference. While in study by Lauretti GR et al.,[7] various groups showed no differences regarding duration of sensory block. (P>0.05) This was in contrast to present study.

The mean time for onset of motor block was found to be 5.13 ±0.58 minutes in group C while 5.63 ±0.92 minutes in group B, the difference in mean time for onset of motor block was statistically significant. (P <0.5). In study by Jain A et al.,[4] duration of complete motor block in Group I was 9.6 ± 4.1 minutes and Group III was 11 ± 3.4 minutes with statistical significant difference. This finding was comparable to present study.

There were 2 cases of headache, one from each Group C & B. There were 19 cases of Nausea, 12 from Group C and 7 from Group B. There were 2 cases of vomiting and pruritus each, both of which were seen in Group C. There were 5 cases of hypotension, 1 in Group C and 4 in Group B. There were 3 cases of bradycardia, all in Group C. There was no difference when two groups were compared statistically for complications. (p>0.05) In study by Akinwale MO et al.,[8] incidence of adverse effects such as hypotension, bradycardia, nausea and vomiting were not statistically significant in both groups, p > 0.05. Almeida et al.,[9] demonstrated a trend toward more nausea with doses higher than 1 mcg in patients undergoing major gynecological surgeries. These observations are further supported by the present study.

The post-operative analgesia remained for longer duration in Group C, 7.40 ± 1.21 hours as compared to 5.32 ± 1.21hours in Group B. Significant difference was seen between the duration of post-operative analgesia in the two groups. (p< 0.05) study. Similar findings were noted by Akinwale MO et al.,[8] as 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.

The numbers of post-operative analgesics were required less in Group C, 2.5 ± 1.2 as compared to 4.2± 1.8 in Group B. Significant difference was seen between the numbers of post-operative analgesics required in the two groups. (p< 0.05) In study by Akinwale MO et al.,[8] total analgesic consumption 12 hours post-intrathecal injection was also less in the neostigmine group.

Thus, spinal neostigmine added to hyperbaric bupivacaine and fentanyl provided a significantly longer surgical analgesia and insignificant adverse effects who had lower abdominal surgery under spinal anaesthesia.

CONCLUSION

The present study concludes that, spinal neostigmine added to bupivacaine and fentanyl provided a significantly longer surgical analgesia and insignificant adverse effects who had lower abdominal surgery under spinal anaesthesia.

REFERENCES

1. Apfelbaum JL, Chen C, Mehta SS, Gan TJ. Posteoperative pain experience: Results from a national survey suggest postoperative pain continues to be undermanaged. AnesthAnalg 2003:97;534-40

2. Horlocker TT. Complications of regional anesthesia and acute pain management.AnesthesiolClin 2011;29:257-78
3. Bakshi U, Chatterjee SK, Sengupta S, Gupta D. Adjuvant drugsin central neuraxial analgesia- A review. Internet J Anesthesiol 2010;26 Suppl 1:1-4. Available from http://isup.com/IJA/26/1/6383. [Last accessed on 2014 Sep 29]
4. Jain A, Jain K, Bhardwaj N. Analgesic efficacy of low-dose intrathecal neostigmine in combination with fentanyl and bupivacaine for total knee replacement surgery. Journal of Anesthesiology Clinical Pharmacology 2012;28(4):486-490.
5. Chung CJ, Kim JS, Park HS, Chin YJ. The efficacy of intrathecal neostigminne, intrathecal morphine and their combination for post-caesaren section analgesia. AnesthAnalg 1998:87:341:346.
6. BK Sodhi GS et al. Comparative evaluation of different doses of intrathecal neostigmine as an adjunct to bupivacaine for pandeyV ,Mohindra Anesth Essays Res 2016;10(3):538-545
7. Lauretti GR, Mattos AL, Reis MP, Pereira NL. Combined intrathecal fentanyl and neostigmine:: Therapy for postoperative abdominal hysterectomy pain relief. Journal of clinical anesthesia. 1998 Jun 1;10(4):291-6.
8. Akinwale MO, Sotunmbi PT, Akinyemi OA. Analgesic effect of intrathecal neostigmine combined with bupivacaine and fentanyl. African journal of medicine and medical sciences. 2012 Jun 1;41(2):231-7.
9. Almeida RA, Lauretti GR, Mattos AL. Antinociceptive effect of lowdose intrathecal neostigmine combined with intrathecal morphine following gynecological surgery. Anesthesiology 2003;98:495-8.