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EVALUATION OF EFFECT OF INTRATHECAL NEOSTIGMINE AS AN ADJUVANT TO BUPIVACAINE IN SPINAL ANAESTHESIA FOR POST-OPERATIVE ANALGESIA

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ABSTRACT

To study the effect of neostigmine as an adjuvant to bupivacaine in spinal anaesthesia on onset and duration of sensory and motor block , duration of post-operative analgesia, perioperative hemodynamic parameters and complications. 80 patients of ASA I & II scheduled for lower abdominal or lower limb surgery were included in double blind randomized comparison of 40 patients in each group. Group A patients were given injection neostigmine 100 µg + bupivacaine and group B patients were given only bupivacaine. We recorded time of onset and duration of sensory and motor block, duration of analgesia, hemodynamic changes and side effects in both groups. Post-operative pain is less in group A (study group) compared to group B (control group) and pain relief is significant highly ($p < 0.001$) in study group. Duration of motor and sensory blockade is also prolonged in study group. Intrathecal neostigmine produces prolonged postoperative analgesia and produces a good sensory and motor for the surgical procedure.

Key words: Intrathecal, Neostigmine, Bupivacaine, Analgesia.

INTRODUCTION

Pain is an unpleasant sensory and emotional experience associated with actually or potential tissue damage or can be described in terms of such damage. Modern anaesthesiologists are not only concerned about pre-operative and intra-operative care of the patient but also with post-operative welfare of the patient. Post-operative pain can lead to pulmonary, circulatory, gastrointestinal, urinary-dysfunction, impairment of muscle function, thrombo embolic process and undesirable psychological and emotional reaction. Hence a critical need exists for effective prophylaxis and treatment of post-operative pain.

Incidence of post-operative pain varies with the individual patient and also varies with site and nature of operation. Requirement of post-operative analgesia is more in first 24 to 48 hrs of surgery. As the pain differs from patient to patient and time to time there are different methods of post-operative pain relief.

Systemically administered NSAIDS and narcotic analgesics as round the clock basis (if properly prescribed) remain the mainstay of therapy for effective post-operative pain relief. However it is often given "too little and too late." As patient is the only one who can assess his or her pain and judge whether it has been satisfactorily relieved, "patient controlled analgesia" with opioid was introduced. However in India it is not a practice as solution due to the increased cost and high-tech machinery.

The regional anaesthesia has much to offer to the patient, surgeon and anaesthetist due to simplicity of its administration, preservation of consciousness, good

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analgesia and least side effects. Local anaesthetics used epidurally for post-operative pain relief may also produce undesirable side effects including hypotension, sensory and motor blockade, nausea and urinary retention. Opioids also produce respiratory depression, nausea, and urinary retention. Hence new drugs have been searched for postoperative pain relief. A number of non-opioid substances given intrathecally or epidurally in alternative to interrupt the spinal pain pathways at other receptor viz, ketamine, clonidine, benzodiazepines.

Recent research has focused on non-opiate spinal cord receptors like NMDA, adrenergic receptors and cholinergic receptors that inhibit transmission of pain signals. In adrenergic system, alpha-2 agonist clonidine given systemically or neuraxially provide analgesia but it also produces hypotension.

There is a high density of muscarinic cholinergic receptors in the dorsal horn cells of spinal cord, in substantia gelatinosa (lamina II and III) and in lamina IV. Intrathecal injection of cholinergic agonist produces analgesia by muscarinic mechanism. Intrathecal neostigmine inhibits breakdown of an endogenous spinal neurotransmitter acetylcholine that has been shown to cause analgesia in animals and preliminary clinical trials [1-23].

Here is my study I have used 100 µg neostigmine with bupivacaine intrathecally in 40 patients of study group and bupivacaine alone in 40 patients in control group undergone surgery on the lower abdomen and lower limbs and have studied the effects of neostigmine on vital parameters and on post-operative pain.

MATERIALS AND METHOD

This study is carried out to evaluate the effects of neostigmine given along with Bupivacaine intrathecally before surgery for post-operative pain relief.

The study consisted of 80 patients of either sex between the ages 14 to 60 years of ASA risk I & II in whom lumbar spinal anaesthesia was planned for surgery. Pre-anaesthetic evaluation of each patient was done on the day before the surgery. All the patients were explained regarding the type of anaesthesia and procedure and an informed consent was taken.

The patients were divided into 2 main groups:

Group A (study group): Inj. Bupivacaine (0.5%) with 100µg neostigmine.

Group B (control group): Inj. Bupivacaine (0.5%)

On the day of surgery, the patients were examined in the preoperative room and pulse rate, blood pressure and respiratory rate were noted. On the table with the patient in supine position peripheral intravenous line was taken and 500-1000 ml ringer lactate was infused. Then the patients were placed either in sitting or lateral position and lumbar puncture was performed under strict aseptic precautions using a fine bore lumbar puncture needle. Intrathecal drug was used depending upon the duration of surgery. Later the patients were positioned supine and pulse rate, blood pressure and respiratory rate were monitored. Onset and the level of sensory block were assessed by pinprick and motor block was determined by Bromage scale. Intraoperatively pulse rate, blood pressure and respiratory rate were monitored every 15 minutes till the end of surgical procedure. Complications such as bradycardia (pulse rate <60 min) were treated with Inj. Atropine and hypotension was treated with Inj. Mephentramine when necessary. Nausea and vomiting was treated with Inj. Metoclopramide.

After completion of surgery in post-operative period patient were observed for pulse rate, blood pressure and respiratory rate. Whenever patient complained about pain, time for arrival of pain was noted, Duration of sensory block (analgesia) and motor block was noted.

Table 1. The degree of pain was determined by Magill's scale

Degree of Pain	Score
No pain	0
Slight pain	1
Discomfort	2
Unbearable pain	3
Excurciating pain	4

Side effects like nausea, vomiting, bradycardia, increased salivation, sweating, nystagmus, respiratory depression, pruritus and retention of urine (if not catheterized) were looked for and treated accordingly.

The results of the study were stastically analysed Whether they are significant or not.

OBSERVATION AND RESULTS

In study group 7 patient had nausea and 5 patient had vomiting intra operatively which was treated with inj. Metoclopramide. There was bradycardia in 3 patients which was treated with inj. Atropine. One patient complained about increased salivation while one patient had anxiety which was treated with inj. Midazolam.

Table 1. Drug wise distribution :There are two main group, Study Group (Group-A) and Control Group (Group-B).

Group	Drug given	No. of pts.
A	Inj. Bupivacaine (0.5% with 100 µg Neostigmine	40
B	Inj. Bupivacaine (0.5%)	40

Table 2. Demographic data

Parameters		Group A	Group B	p-Value
Age (Yrs) (Mean ± SD)		37.13 ± 14.14	37.2 ± 12.89	>0.05
Sex	Male	28 (70 %)	29 (72.50%)	
	Female	12 (30 %)	11 (27.50%)	>0.05
ASA Grade	I	24 (60 %)	22 (56.67 %)	
	II	16 (40%)	18 (43.33%)	>0.05

Table 3. Onset of analgesia

Onset (Minutes)	Group A	Group B
<1	-	-
1-2	-	-
2-3	9	18
3-4	9	2
4-5	2	-
≥5	-	-
Total	20	20
Mean `	3.15	2.6
S.D.	0.35	0.20

Table 4. Degree of analgesia after 3 ½ hr

Analgesia (Magill's scale)	Group A	Group B
0	15	1
1	4	3
2	1	6
3	-	9
4	-	1

Table 5. Duration of analgesia

Duration(hours)	Group A	Group B
<2	-	-
2 – 3	-	3
3 – 4	-	16
4 – 5	4	1
5 – 6	4	-
6 – 7	9	-
≥7	3	-
Total	20	20
Mean	6.05	3.4
S.D.	0.51	0.32

Duration of analgesia is highly significant (P<0.001) in study group.

Table 6. Duration of Motor block

Duration (hours)	Group A	Group B
<2	-	8
2 – 3	-	12
3 – 4	7	-
4 – 5	11	-
≥5	2	-
Total	20	20
Mean	4.25	3.1
S.D.	0.33	0.105

Duration of motor block is differed highly significantly at P<0.001 in study group.

Table 7. Change in heart rate

Heart rate (hour)	Group A (Study gp) (Mean±S.D.)	Group B (Control gp) (Mean±S.D.)	P value
Pre-operative	89.75±3.58	92.0±3.63	P >0.05
1hr	78.75±5.23	78.0±3.63	P > 0.05
2 hr	79.75±3.57	80.25±3.58	P >0.05
3 hr	80.00±3.58	81.25±3.60	P >0.05
4 hr	79.5±5.39	82.75±3.68	P >0.05
6 hr	80.75±5.46	83.0±3.76	P >0.05
8 hr	81.75±5.61	84.0±3.80	P >0.05
12 hr	83.5±3.75	84.25±2.27	P >0.05
18 hr	85.25±3.95	86.75±2.31	P >0.05
24 hr	87.0±2.33	92.0±3.63	P >0.05

Table 8. Changes in blood pressure

Blood Pressure (hour)	Group A (Study group) (Mean±S.D.)	Group B (Control gp) (Mean±S.D.)	P value
Pre-operative	95.00±1.60	91.5±2.46	P >0.05
1 hr	96.25±2.29	87.0±2.00	P > 0.05
2 hr	90.75±2.55	84.8±2.26	P >0.05
3 hr	91.25±2.49	76.62±3.24	P >0.05
4 hr	91.00±2.52	89.25±2.55	P >0.05
6 hr	92.5 ±2.36	90.25±3.58	P >0.05
8 hr	93.5 ± 2.30	93.3 ± 3.74	P >0.05
12 hr	96.25 ± 2.29	93.5 ± 2.30	P >0.05
18 hr	98.0 ±2.41	96.0±2.36	P >0.05
24 hr	100.0±2.66	98.0±2.40	P >0.05

Table 9. Incidence of complications

Complication	Group A (Study)	Group B (Control)
Nausea	7 (17.5%)	1 (2.5%)
Vomiting	5 (12.5%)	-
Bradycardia	3 (7.5%)	-
Hypotension	-	2 (5.0%)
Anxiety	1 (2.5%)	-
Retension of urine	-	1 (2.5%)
Increased salivation	1 (2.5%)	-
Total (percentage)	17 (42.5%)	4 (10%)

DISCUSSION

Postoperative pain is a very distressing symptom and may have deleterious effect on body function and hinder early mobilization and recovery. Therefore adequate pain relief indicated not only on humanitarian ground but also for ameliorate some of the harmful effects.

Despite advances in treatment of postoperative pain, many patients suffer from pain after surgery probably due to difficulty in balancing the postoperative pain treatment regimen with acceptable side effects. There is high density of muscarinic cholinergic receptors in the dorsal horn of spinal cord. Intrathecal injection of cholinergic agonist produces analgesia by muscarinic mechanism. In 1994 Naguib and Yaksh performed the first study on neostigmine, given intrathecally inhibits the metabolism of spinally released Acetylcholine and produce analgesia without some dangerous side effects which are common to spinal opioids [24-26].

This study was undertaken to assess the efficacy of intrathecal neostigmine for postoperative pain relief and to evaluate the incidence of side effects. 80 patients of ASA grade I & II were divided into two group, group-A study group and group-B control group. Study group was received inj. Bupivacaine with 100µg Neostigmine. Control group was received only inj. Bupivacaine.

Study group and control group did not differ significantly in age, sex, weight, type of surgery and duration of surgery.

The onset of analgesia was delayed significantly in study group that might be because of dilution of local anaesthetic drug with neostigmine.

In this study we reported a prolonged analgesia due to effect of neostigmine. Patients were evaluated for

efficacy of post-operative analgesia using Magill's scale. In our study duration of analgesia was 7.3±0.69 hrs with study group (bupivacaine + neostigmine) compared to 3.8±0.8 hrs. in control group (only bupivacaine) which was also highly significant (P<0.001). Duration of motor blockade was prolonged in study group and that was also significant.

The groups receiving neostigmine did not differ in blood pressure, heart rate, respiratory rate from their control group. Haemodynamic stability has an obvious impact on the clinical utility of the given drug.

Intrathecal neostigmine prevents or diminishes hypotension due to intrathecal bupivacaine. In our study, with dose of 100 µg neostigmine intrathecally hypotension was not found.

Neostigmine's adverse effects included intense nausea and vomiting, salivation, nystagmus, dizziness, agitation and bradycardia. In this study incidence of nausea and vomiting was 12 out of 40 patients (30%) little is known about neural mechanism underlying the gastrointestinal effects of intrathecal neostigmine. Eisenach et al described the vomiting is due to action of neostigmine on the brainstem, since a hyperbaric solution of this drug produces analgesia without nausea and vomiting. In our study as hyperbaric local anaesthetic was used with 100µg neostigmine, ;incidence of nausea and vomiting was less. Only one patient had increased salivation. 3 patients had bradycardia, treated with iv atropine 0.6 mg. bradycardia could be explained by neostigmine's (cholinergic agonist) cephalic spread and its high polarity.

The above study had proved intrathecal neostigmine significantly reduces pain and analgesic requirement in postoperative period.

CONCLUSION

In our study we came to following conclusions after comparing both study group and control group.

1. Post-operative pain is less in group-A (study group) compared to group-B (control group) and pain relief is significant highly (P<0.001). Requirement of rescue analgesia is minimal.
2. Duration of motor blockade was also prolonged in study group compared to control group.
3. There were no significant change in blood pressure (mean arterial pressure) and heart rate in both groups at different time intervals.
4. High incidence of adverse effects like nausea and vomiting.

Hence it can be concluded that the intrathecal neostigmine with bupivacaine significantly reduces postoperative pain without dangerous side effects.

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