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Intrathecal Buprenorphine for Post-Operative Analgesia: a Prospective Randomized Double Blind Study

Dr. Vishal Joshi | Assistant professor, Department of Anesthesia, GAIMS, Bhuj

ABSTRACT

Background: The use of intrathecal narcotics for pain relief is now an established technique, the drug most used being Morphine. Buprenorphine is a mixed agonist antagonist narcotic with high affinity at both μ and k opiate receptors. This study was conducted to assess the efficacy of intrathecal buprenorphine for postoperative pain relief and to study the incidence of side-effects.

Patients & Methods: A prospective randomized double blind study was conducted in 100 patients, who underwent surgery of the lower abdomen and lower extremities. One group received (Control Group) 15 mg of heavy bupivacaine (0.5%), while the other group (Study Group) received 15 mg of heavy bupivacaine (0.5%) with 1 μg kg-1 buprenorphine intrathecally upto a maximum of 50 μg.

Results: Prolonged post-operative analgesia was observed in the study group (475.6 ± 93.7 min) compared with Control Group (195.2 ± 29.52 min). The side effects were minimal.

Conclusion: This study shows that buprenorphine is an effective analgesic suitable for the management of post-operative pain.

KEYWORDS | Buprenorphine, Intrathecal Anaesthesia, Postoperative Analgesia.

INTRODUCTION:-

Pain is a presenting feature of many conditions and complicates peri-operative care following major surgery. Opioids are commonly used to treat post-operative pain and intrathecal morphine is a routine method that provides prolonged post-operative analgesia. Side effects such as nausea, vomiting, itching and possible respiratory depression have been reported in a number of cases. The use of conventional local anaesthetics like bupivacaine and lignocaine has been unable to provide anaesthesia for longer surgery or analgesia for longer duration.

To overcome these difficulties, many drugs have been added to local anaesthetics to prolong the duration of intrathecal anaesthesia. Buprenorphine, because of its high lipid solubility, high affinity for opiate receptors6 and prolonged duration of action seems to be suitable choice for intrathecal administration.

This study was performed to compare intrathecal bupivacaine with intrathecal bupivacaine and buprenorphine for postoperative pain-relief and to study the incidence of side effects.

PATIENTS & METHODS:-

A prospective randomized double blind study was conducted on 100 patients of A.S.A. Grade 1 and 2 between the age group of 18-60 years, who underwent surgery of the lower abdomen and lower extremities. Written informed consent was obtained from the patients. Exclusion criteria were patient having infection at the site, bleeding disorders and allergic reaction to any anaesthetic drug.

The patients were randomly allocated into one of 2 groups of 50 each. The allocation of the patients in the two groups and the preparation of the solution were carried out by an anaesthesiologist, who was not involved in the study. Both patient and anaesthesia provider were blinded for the drug.

Patients belonging to controlled Group (Group A) received 15 mg heavy bupivacaine 0.5 %+ 0.2 ml of normal saline. Patients belonging to study group (Group B) received 15 mg heavy bipivacaine + 1μg kg-1 of buprenorphine 0.2ml (max 50 μg). All the patients were kept nil orally for 6 hours prior to surgery. No premedication or sedative was administered to the patient. An intravenous line was started and Ringer Lactate 500 ml was given before the procedure. Lumbar puncture was performed with a standard technique at L2-L3 or L3-L4 interspace. After the subarachnoid injection, pulse rate, blood pressure and respiration rate were monitored immediately, at 5 min & then every 10 minutes for the first half hour. Then the vital signs were recorded half hourly for the rest of surgical procedure.

Onset of sensory blockade & duration of sensory blockade were noted. Pain was assessed by visual analogue scale. Sedation was assessed by 3 point objective score based on eye opening. Incidence of side effects like nausea, vomiting, urinary retention and itching were monitored & recorded. Post-operatively, vital signs were monitored on every two hourly basis upto 8 hours, 12 and 24 hours respectively. Rescue analgesic was inj. Diclofenac 1.5 mg Kg-1.

Statistical Analysis:-

Interval data are expressed as mean and standard deviation. The Z-test was used for comparing the 2 groups; Chi-Square Test was used for analysis of categorized data. A "P" value was said to be statistically significant, if it was less than 0.05.

RESULTS:-

The mean value of age, sex and weight were comparable and the difference was not statistically significant. Table 1 shows the comparison of sensory onset in both the groups. In control group, the sensory onset duration was between 2 to 6 minutes with the average duration of onset was 3.78 ± to 0.97 min and in study group the duration of sensory onset was 2 to 5 minutes with an average of 3.66 ± 1.002 mins. This difference was not statistically significant.

Table 2 shows the comparison of pulse rate in both the groups. In control group, the mean pulse rate with SD at 0 min was 81.3 ± 7.91 and in Study group was 79.16 ± 6.156 and the difference in pulse rate at 0, 5, 10, 30 and 60 min-

utes respectively between both the groups were not statistically significant. There was no statistical difference between both the groups in systolic blood pressure, diastolic blood pressure and respiration at intervals of 0,5, 10, 20, 30 and 60 minutes respectively.

In control group, there were 5 cases of hypotension and one case of nausea-vomiting while in study Group there were 6 cases of hypotension, 2 cases of nausea vomiting and 2 cases of shivering (Table 3). There was no statistically significant difference observed in both the groups.

This Table 4 shows that mean duration of surgery in control group was 90.2 ±33.7 mins and in study group was 99.18 ± 44.03 mins. There was no statistical difference in the duration of surgery between the groups. In control group the duration of analgesia was 195.2 ± 29.52 min with a range of 135-300 min. In study group the mean duration of analgesia was 475.6 ± 93.7 mins with a range of 310-700 mins. Here Z value is 20.18 and p value is < 0.001 which is highly significant (Table 5). Therefore, the duration of analgesia was much longer in study group compared to control group.

Table 1
Comparison of Sensory onset

Group	Sensory onset in mins	Range
A	3.78 ± 0.97	2-6 mins
B	3.66 ± 1.002	2-5 mins

Table 2
Comparison of Pulse Rate

Time	Gp A	Gp B	Z	Significance
0	81.3±7.91	79.16 ± 6.156	1.51	NS
5	81.4 ±5.54	80.16 ± 7.89	0.87	NS
10	80.2 ±5.77	79.84 ± 8.28	0.255	NS
20	79.1 ± 7.14	79.76 ± 8.70	0.465	NS
30	81 ± 5.69	82.44 ± 5.775	1.09	NS
60	82.6 ± 6.21	82.66 ± 5.228	0.045	NS

Table 3
Incidence of Complication

Complication	Gp A – (n = 50)	Gp B (n=50)
Hypotension	5	6
Nausea vomiting	1	2
Shivering	0	2

Table 4
Surgical Duration

Duration in mins	A	B
30 – 60	16	12
61 – 120	27	24
121 – 180	7	14

Mean ± SD 90.2 ± 33.7 99.18 ± 44.03

SD – Standard Deviation

Z = 1.146 P > 0.05

Table 5
Comparison of duration of analgesia

Group	Range of analgesic Duration in mins	Mean duration in mins	SD
A	135 – 300	195.2	29.52
B	310 – 700	475.6	93.7

SD – Standard Deviation

Z = 20.10 P < 0.001

DISCUSSION:-

Numerous studies since the first clinical use of intrathecal morphine in 1979 have confirmed the efficacy of spinally administered opioids for post-operative pain relief. However, opioids do not remain localized to the site of epidural and or intrathecal injection. After spinal administration, opioids undergo redistribution by rostral spread, which explains the occurrence of nausea and vomiting in 15-35% of patients, respiratory depression and the spread of hypoalgesia.

Opioids reach the cistern of brain 3-6 hours after intrathecal administration and then the respiratory centers through the ventral pons. A lipid soluble non-ionized drug like buprenorphine passes rapidly via the arachnoid granulation into venous and lymphatic vessels, which allow a minimal increase of cerebrospinal fluid concentration with a minor risk of respiratory depression.

The present clinical study was a prospective randomized double blind study conducted on 100 patients who underwent surgery of lower abdomen and lower extremities. This study was performed to compare intrathecal bupivacaine & bupivacaine with buprenorphine for postoperative pain relief and to study the incidence of side effects.

The mean value of age, sex and weight were comparable and the difference was not statistically significant. The onset of analgesia in control group was average of 3.78 ± 0.97 mins and in study group was average of 3.66 ± 1.002 min. There was no statistical difference between both the groups. This is in contrast with study of Thomas et al.

The duration of analgesia was much longer in a study group (475.6 ± 93.7 min) compared to control group (195.2 ± 29.52 mins). Our findings are consistent with many other studies. Since the first clinical use of Intrathecal opioids by Wang et al, 3 numerous other studies have confirmed the efficacy of intrathecal opioid for post-operative analgesia.

In our study, there was no significant haemodynamic difference between both the groups. There was no significant change in respiratory rate intraoperatively and post-operatively in both the groups. The average sedation score in control group was 1.06 ± 0.24 and in study Group was 1.3 ± 0.47%. And this difference was statistically significant.

Buprenorphine has been shown to produce more drowsiness than morphine. The sedative effect could be considered desirable in the intra-operative and postoperative period. All the patients were arousable on verbal commands. We observed that low dose of intrathecal buprenorphine (1µg Kg-1) provided good post-operative analgesia without any significant increase in side effects. Using high doses of intrathecal buprenorphine, a high incidence of hypotension, bradycardia, vomiting and drowsiness have been reported.

Buprenorphine, because of its high lipid solubility, high affinity for opioids & prolonged duration of action is a suitable choice for intrathecal administration. Studies on tissue compatibility indicate that buprenorphine may be safely administered intra-

thecally with a mixture of buprenorphine. The main advantage of spinal opioid is the absence of sympathetic blockade and postural hypotension, allowing the patients to ambulate earlier. The intrathecal route has also the advantage of greater technical ease and a single injection produces pain relief of sufficient duration.

In the present study, intrathecal buprenorphine provided prolonged post-operative analgesia without any significant increase in side effects. The quality of surgical anaesthesia and post-operative analgesia were excellent. Thus, we conclude that intrathecal buprenorphine is a suitable drug for post-operative analgesia. We suggest intrathecal buprenorphine for post-operative analgesia