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International Journal of Current Research
Vol. 9, Issue, 12, pp.62512-62515, December, 2017

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

TO STUDY THE EFFECT OF ADDITION OF NALBUPHINE TO INTRATHECAL BUPIVACAINE USED FOR ELDERLY PATIENT IN LOWER ABDOMINAL SURGERIES UNDER SPINAL ANAESTHESIA: A RANDOMISED DOUBLE BLINDED CONTROL STUDY

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ARTICLE INFO

Article History:
Received 08th September, 2017
Received in revised form
04th October, 2017
Accepted 27th November, 2017
Published online 27th December, 2017

Key words:
Spinal anaesthesia,
Nalbuphine,
Postoperative analgesia,
Bupivacaine,
Intrathecal.

ABSTRACT

Background and Objectives: The purpose of this study was: 1. To asses, evaluate and compare the analgesic effect of intrathecal nalbuphine when added to hyperbaric intrathecal bupivacaine and bupivacaine alone. 2. To evaluate the onset, quality and duration of sensory and motor blockade achieved with hyperbaric bupivacaine and nalbuphine combination when administered intrathecally for spinal anesthesia in lower abdominal surgery. 3. To study the effect of intrathecal nalbuphine on vital parameters. 4. To study any side effects and complication.

Methodology: 40 ASA I and II patients of age group 50-70 years, scheduled for below umbilicus surgeries were chosen for this study. Patients were randomized in two equal groups of 20 each by lottery method. Group I (Study Group) received 3 ml of hyperbaric bupivacaine 0.5 % + 0.5 ml inj. nalbuphine (0.5 mg) intrathecally. Group II (Control Group) received 3 ml of hyperbaric bupivacaine 0.5 % + 0.5 ml of inj. normal saline intrathecally. Assessment of motor and sensory blockade was done by Bromage scale and pin prick method. Pulse rate, BP, respiratory rate and SpO_2 were monitored throughout intraoperative period and 24hrs postoperative period.

Results: There is no significant difference between 2 groups for onset of motor and sensory blockade but mean time of postoperative analgesia in Study Group was highly significant than Control Group. No patient in our study developed any side effects.

Conclusion: Nalbuphine provides better quality of block as compared to bupivacaine alone. It also prolongs postoperative analgesia when used as adjuvant to spinal bupivacaine in elderly patients.

Citation: Dr. Sanjay P. Gadre and Dr. Asif Sayeed, 2017. "To study the effect of addition of nalbuphine to intrathecal bupivacaine used for elderly patient in lower abdominal surgeries under spinal anaesthesia: A randomised double blinded control study", *International Journal of Current Research*, 9, (12), 62512-62515.

INTRODUCTION

Spinal anaesthesia is now 100 years young and still the most popular regional anaesthesia technique. However the drug used for spinal anaesthesia doesn't have the advantage of post-operative analgesia. It is a challenge for anaesthesiologist as management of pain is his domain in the perioperative period. Many drugs have been used intrathecally as an adjuvant to local anaesthetic to prolong post-operative pain relief but have their own adverse effects. Nalbuphine is an opioid which is structurally related to oxymorphone. It is an opiod agonist antagonist with agonist action at kappa and antagonist action at mu receptors (Zarr *et al*., 1986; De Souza *et al*., 1988). Nalbuphine and other kappa agonists had provided reasonably potent analgesia in certain models of visceral nociception (Schmauss *et al*., 1982). Nalbuphine being an agonist antagonist is less likely to cause side effects like pruritus, respiratory depression, urinary retention, excessive sedation etc because of its action at kappa receptors. Previous studies have shown that epidural or intrathecal administration of nalbuphine produces a significant analgesia accompanied by minimal pruritus and respiratory depression (Lin, 1992; Fournier *et al*., 1998). Culebras *et al*. in 2002 used intrathecal nalbuphine in doses of 0.2, 0.8 and 1.6 mg with 10 mg of 0.5% hyperbaric bupivacaine in patients undergoing cesarean section under subarachnoid block (SAB) and found 0.8 mg of nalbuphine as an effective dose (Culebras *et al*., 2000). In search of an ideal agent we have studied the effect of nalbuphine added as an adjuvant to bupivacaine & compare it with effect of plain bupivacaine for post-operative analgesia and quality of block.

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MATERIALS AND METHODS

After approval from institutional ethical committee and written informed consent 40 patients of both genders ASA I & ASA II between ages 50-70 yrs posted for below umbilical lower abdominal surgeries were selected for the purpose of this

study. Pre-anesthetic checkup was done. Patients with contraindication to spinal anaesthesia were excluded from the study. Patients kept NBM for 6-8 hours. Randomization was done into two groups by lottery method.

Group I (Study group): Inj. Bupivacaine (0.5%) 3 ml + Inj. Nalbuphine (0.5mg) 0.5 ml intrathecally.

Group II (Control group): Inj. Bupivacaine (0.5%) 3 ml + Inj. Normal Saline 0.5 ml intrathecally.

Sedatives and hypnotics were avoided in pre, intra and post-operative period. IV line was secured with 20 G IV cannula. All patients were preloaded with Ringer lactate solution @ 10 ml/kg. Monitors were attached before performing the procedure (Pulse Oxymeter, NIBP, ECG). The study medication was prepared by the person who is not involved in the study to ensure blinding of the anaesthetist. Under all aseptic precautions, subarachanoid block was given using 26 G Quinke's Spinal Needle in sitting position. Respective agents were injected according to the group. The assessments of the haemodynamic parameters were noted. Onset of sensory block was judged by pin prick method and motor blockade was judged with Bromage scale.

Bromage scale

Score	Criteria
1.	Complete block (unable to move feet or knee).
2.	Almost complete block (able to move feet only).
3.	Partial block (just able to move knees).
4.	Detectable weakness of hip flexion while supine position.
5.	No detectable weakness of hip flexion while supine.
6.	Able to perform partial knee bend.

Height of sensory block was achieved up to T6 level.

Following parameters were observed: Time of onset of sensory blockade (T1), Time of onset of motor blockade (T2), Time of peak sensory blockade (T3), Time of peak motor blockade (T4), duration of post-operative analgesia (T5). Fall in MAP > 20 % of basal value was treated with Inj. Mepheteramine. Bradycardia i.e. HR > 15-20 % fall form basal value was treated with Inj. Atropine. Rescue analgesia with Inj. Tramadol 100 mg or Inj. Diclofenac 75 mg IM was given. Vital parameters were monitored every 5 min for 20 min then 10 min till end of surgery. Peri operatively patients were observed carefully for next 24hrs for the side effects like respiratory depression, nausea, vomiting, itching etc. Data was expressed as Mean +/- SD. ANOVA test was used for comparative analysis. P value <0.05 was considered as significant.

RESULTS

Demographic profile for all patients in group is present in Figure no. 1, 2 and 3. There was no statistically significant difference between two groups with respect to age, sex and ASA grading.

Mean onset of sensory blockade in nalbuphine group was 58 sec and in control group was 60 sec. p value is > 0.05 showing that there no statistically significant difference between two groups (Figure 4).

Mean onset of motor blockade in nalbuphine group was 110 sec and in control group was110 sec. p value is > 0.05 showing that there no statistically significant difference between two groups (Figure 5).

Time of peak sensory block in nalbuphine group was 380 sec and in control group was 380 sec. p value is > 0.05 showing that there no statistically significant difference between two groups (Figure 6).

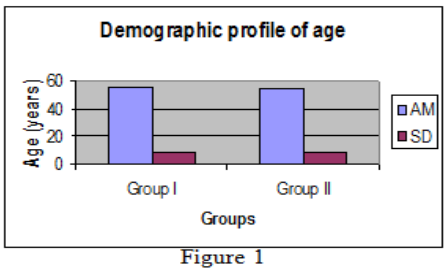
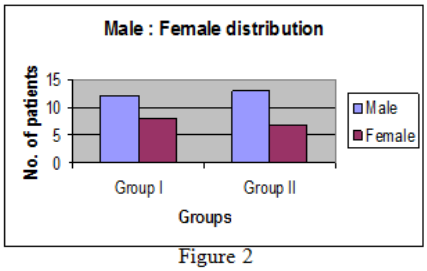


Figure 1



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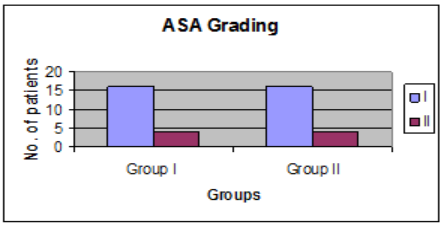

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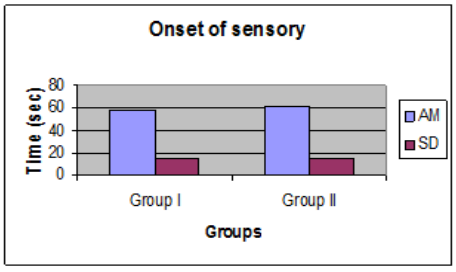
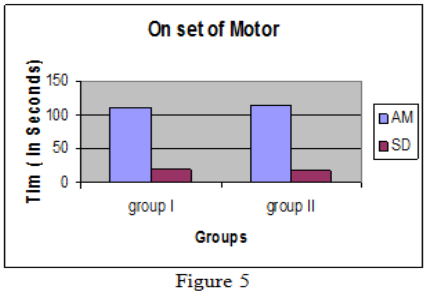


Figure 4



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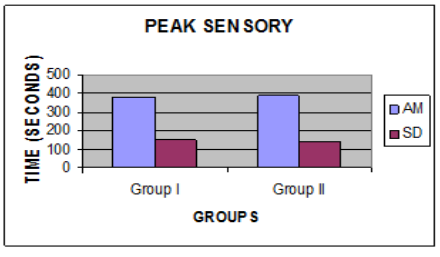

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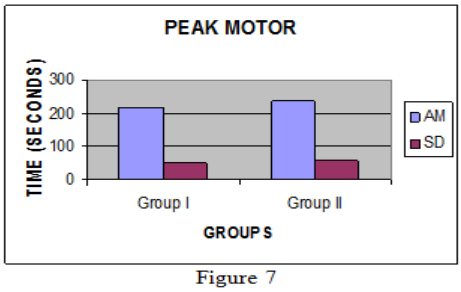

Figure 7

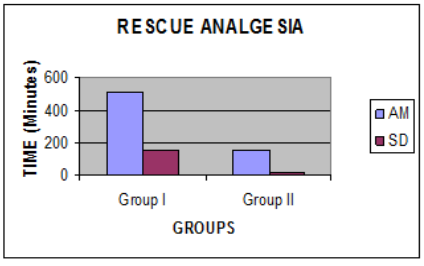

Figure 8

Time of peak motor block in nalbuphine group was 210sec and in control group was 220 sec. p value is > 0.05 showing that there no statistically significant difference between two groups (Figure 7). Duration of post-operative analgesia i.e. time between drug administration and request of first analgesic. In nalbuphine group duration of post-operative analgesia was 8 to 9hours (566+/-15.5min.) and in control group was 2 to 3 hours (159.5 +/- 18.42min.).p value is 0.000 which was highly significant statistically (Figure 8, Table 1).

Table 1. Duration of Analgesia

Parameter	Group i Am + sd	Group ii Am + sd	P value	Significance
Duration of analgesia	516 + 15.5	159.5 + 18.42	0.000	Highly significant

There was statistically significant difference in haemodynamic parameters like heart rate, mean, systolic and diastolic BP but clinically these parameters were within normal limits and did not required any intervention (Table 2).

Table 2. Comparison of Vital Parameters

Parameters	Group I (n= 20) (Mean ± SD)	Group II (n=20) (Mean ± SD)	p-value
HR	85.14 ± 10.75	75.7 ± 7.8	>0.001
SBP	126.86 ± 11.25	110 ± 2.4	
DBP	74 ± 7.66	65.1 ± 5.3	

*significant

Respiratory rate and SPO_2 were almost similar in both the groups. There was no side effects intra operatively and postoperatively in our study.

DISCUSSION

Subarachnoid block is technique of choice for lower abdominal and lower extremity surgeries. Since subarachnoid block with bupivacaine has post-operative analgesia for short period. Many adjuvants like fentanyl, morphine, buprenorphine, midazolam, clonidine have been used in past to prolong postoperative analgesia but having their own side effects. In present study we have used bupivacaine with nalbuphine as an adjuvent to see the duration of analgesia post operatively and any side effects. After subarachnoid block was given there is no significant difference between onset of sensory and motor block in both the groups. There is also no significant difference between peak sensory and motor block in both the groups but duration of post-operative analgesia in study group with added adjuvant nalbuphine was 8-9 hours and in control group with plain bupivacaine was 2-3 hours. Nalbuphine is a synthetic opioid with mu agonist and antagonist properties. Mechanism of analgesia by its agonistic action. nalbuphine stimulates kappa receptor. This inhibits release of neurotransmitter that mediates pain such as substance P. In addition it acts as post synaptic inhibitor on the interneuron and output neuron of spinothalamic tract which transports nociceptive information (Stanley F Malamed, 1986; Ready, 2000). In the nalbuphine group, almost 25% of elderly patients were controlled hypertensive. However no cardio pulmonary adverse effects were seen. It improves quality of block and prolonged and long lasting post-operative analgesia. No adverse effects like other opiods (respiratory depression, nausea, vomiting, and pruritus). It is also cost effective. Nalbuphine given systemically has a reduced incidence of respiratory depression and has been used to antagonize the side-effects of spinal opiates. There are a few studies of neuraxial administration of nalbuphine that have shown to produce a significant analgesia accompanied by minimal pruritus and respiratory depression.

A study comparing the different doses of nalbuphine was by Culebras *et al*., who studied intrathecal nalbuphine in doses of 0.2, 0.8 and 1.6 mg in 90 obstetric patients undergoing caesarean section and found 0.8 mg as the most effective dosage (Culebras *et al*., 2000). Lin *et al*. found that the addition of intrathecal nalbuphine 0.4 mg to hyperbaric tetracaine, compared with intrathecal morphine 0.4 mg for SAB, improved the quality of intraoperative and postoperative analgesia, with fewer side-effects (Fournier *et al*., 2000). In another study on 60 obstetric patients scheduled for caesarean section under SAB morphine 0.1 mg or nalbuphine 1 mg or morphine 0.1 mg with nalbuphine 1 mg in addition to 0.5% bupivacaine 10 mg was used and it was concluded that effective analgesia was prolonged in the morphine group and morphine with nalbuphine group, but the incidence of pruritus was significantly lower in the nalbuphine group, while the incidence of nausea and vomiting did not differ in the different groups (Yoon *et al*., 2002). In 2011 study by Tiwari and Tomar showed that nalbuphine hydrochloride (400 μg) significantly prolongs the duration of sensory blockade and postoperative analgesia without any side effect or complication when introduced intrathecally along with hyperbaric bupivacaine (Tiwari *et al*., 2011). A similar study showed that two-segment regression time of sensory blockade and duration of effective analgesia was prolonged in patients receiving 0.4 mg and 0.8 mg nalbuphine ($P<0.05$), and the incidence of side-effects was significantly higher in the latter group ($P<0.05$). The authors concluded that nalbuphine used intrathecally was a useful adjuvant in SAB and, in a dose of 0.4 mg, prolonged postoperative analgesia without increased side-effects (Yang *et al*., 1999; Mukherjee *et al*., 2011). Schimitz *et al* studied effect of intrathecal opiod medication for perioperative analgesia in handicapped children (Schmitz *et al*., 2010). There are some studies about use of intrathecal and intravenous opiods for pain relief (Sarantopoulos, 2000; Sarantopoulos and Fassoulaki, 1994). Another study compares intrathecal morphine with intrathecal nalbuphine in children (Krechel *et al*., 1995). Neuraxial use of nalbuphine is in modern anesthesia practice for more than 10 years. We are not aware of any reports of neurotoxicity of intrathecal nalbuphine since then. Some of the previous studies were even conducted with intrathecal nalbuphine in pregnant patients, but no neurotoxicity was reported in them (Mikuni *et al*., 2010; Tiwari *et al*., 2011; Yaksh and Birnbach, 2000; Rust *et al*., 1994). The FDA in 2005 advised that nalbuphine may be used during labor and delivery only if clearly indicated and if the potential benefits outweigh the risks. We are unaware of any definite caution in the use of nalbuphine by any statutory authority in non-pregnant patients and in subjects more than 18 years old. We included only middle to old aged patients in our study and obtained clearance from the local institutional ethical committee.

Concusion

Nalbuphine provides better quality of block as compared to bupivacaine alone. It also provides post-operative analgesia for almost 8-9 hours when used as an adjuvant to bupivacaine. From present study, we feel that addition of nalbuphine to bupivacaine is an effective measure of providing post-

operative analgesia without any adverse effects for patients undergoing infra-umbilical surgeries under Sub arachnoid Block.

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