ORIGINAL ARTICLE

A randomized, double blind, control study of the effects of adding nalbuphine to spinal bupivacaine for lower abdominal surgeries in elderly patients

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ABSTRACT

Background and objectives: The purpose of this study was 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 as well as efficacy of nalbuphine for postoperative analgesia and its side effects if any.

Method: 40 ASA I and II patients of age group 50-70 years, scheduled for below umbilicus surgeries were chosen for this study. Patients were randomised 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.

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.

Key words: Spinal anesthesia; Nalbuphine; Postoperative analgesia; Bupivacaine

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INTRODUCTION

Spinal anesthesia was introduced about 100 years back and it is still the most popular regional anesthesia technique. However, the local anesthetic drugs used for spinal anesthesia don't have the advantage of prolonged postoperative analgesia. It is a continuous challenge for the anesthesiologists as perioperative pain management is their domain.

Many drugs have been used intrathecally as an adjuvant to local anesthetic to prolong postoperative pain relief with variable effects, but have their own adverse effects. Nalbuphine is an opioid, structurally related to oxymorphone. It is highly lipid soluble opioid with an agonist action at the kappa and an antagonist activity at the mu opioid receptors.[1,2] Nalbuphine and other kappa agonists had provided reasonably potent analgesia in certain models of visceral nociception.[3]

They have a short duration of action consistent with their lipid solubility and rapid clearance compared with other opioids like morphine. 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.[4,5] 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.[6]

In search of an ideal agent we studied the effect of nalbupine added as an adjuvant to bupivacaine and compared it with plain bupivacaine for quality of block and postoperative analgesia.

METHODOLOGY

After approval from institutional ethical committee and written informed consent, 40 patients of both genders, ASA I & ASA II, in the age range of 50-70 years, posted for below umbilicus, lower abdominal surgeries were selected for the purpose of this study. Duration of study was 6 months, at Dr. D.Y Patil Medical College and Research Centre, Pimpri, Pune. Pre-anesthetic check up was done. Patients with contraindication to spinal anesthesia were excluded from the study. Patients were kept nil per orum for 6-8 hours. Randomization was done into two groups by lottery method.

Group I (Study group): Inj. bupivacaine hyperbaric 0.5% 3 ml + inj. nalbupine 0.5 mg intrathecally

Group II (Control group): Inj. bupivacaine hyperbaric 0.5% 3 ml + inj. normal saline 0.5 ml intrathecally

Sedatives and hypnotics were avoided in pre, intra- and postoperative period. An IV line was secured with 18G IV cannula. All patients were preloaded with 10 ml/kg of Ringer's lactate solution. Monitors were attached before performing the procedure (pulse oxymeter, NIBP and ECG). The study medication was prepared by the person who was not involved in the study to ensure blinding of the anesthetist. Under all aseptic conditions, SAB was given using 26G Quinke 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.

Following observations were made:

T0 - Time of spinal anesthesia.

T1 - Time of onset of sensory block.

T2 - Time of onset of motor block.

T3 - Time of peak sensory block.

T4 - Time of peak motor block.

T5 - Time of two segment regression of sensory block.

T6 - Time to first dose of post-operative rescue analgesia.

Two segment regressions were noted. Postoperative analgesic drugs were given when patient's VAS score reached >7 (this time was taken as the time of wear off of analgesia). Inj. diclofenac 75 mg was given intramuscularly as rescue analgesia.

Height of sensory block was achieved upto T6 level.

Fall in MAP >20 % of basal value was treated with inj. mepheteramine. Bradycardia i.e. heart rate >15-20 % fall form basal value was treated with inj. atropine. Rescue analgesia with inj. diclofenac 75 mg IM was given. Vital parameters were monitored every 5 min for 20 min then every 10 min till end of surgery. Perioperatively, patients were observed carefully for the side effects like respiratory depression, nausea, vomiting, itching etc.

VAS score was calculated on a 10 cm long scale with '0' on one end, meaning 'no pain at all', while '10' on the other end representing 'worst pain imaginable'. Patient rated the degree of pain by making a mark on the scale. Thus the pain score was obtained by measuring the distance from the '0' end to the indicated mark.

Statistical Analysis : Data were analyzed using Student's t-test (paired and unpaired), one-way ANOVA and Fisher's test with the help of Epical C2000 software. A P value less than 0.05 was considered statistically significant.

RESULTS

The demographic variables e.g. age, weight, height, sex ratio and the duration of surgery were comparable in both of the groups and statistically not significant

Table 1: Demographic data and duration of surgery

Variable	Group I	Group II	F test	p-value
Age(yrs)	59.9 ± 11.14	60.3 ± 10.67	0.525	0.666
Weight(kg)	64.9 ± 5.21	66.0 ± 10.38	0.244	0.865
Height(cm)	164.3 ± 5.72	166.0 ± 3.08	0.396	0.756
Sex(M:F)	12:8	10:10		0.929
Duration of surgery (min)	119.1 ± 17.10	120.9 ± 26.46	0.060	0.981

Mean onset of sensory blockade was 58 sec and 60 sec in nalbuphine group and control group respectively (p value > 0.05). Mean onset of motor blockade was 110 sec and time of peak sensory block was 380 sec in both of the groups (p > 0.05). Time of peak motor block was 210 sec and 220 sec in nalbuphine group and control groups respectively (p > 0.05).

Two-segment regression time of sensory blockade was prolonged in Group I (116.23±9.17 min) compared to Group II (104.43±17.75 min). Duration of postoperative analgesia i.e. time of drug administration to request for first analgesic was 8 to 9 hours (566 ± 15.5 min) in nalbuphine group duration of postoperative analgesia compared to 2 to 3 hours (159.5 ± 18.42 min) in control group (p-value = 0.0001; significant statistically).

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 require any intervention (Table 2).

Table 2: Comparison of vital parameters (Mean ± SD)

Parameters	Group I (n= 20)	Group II (n=20)	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. No side effects or complications were noted introperatively 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 postoperative analgesia for short period. Many adjuvants like fentanyl, morphine, buprenorphine, midazolam, clonidine have been used in past to prolong postoperative analgesia but everyone has its own side effects.

In the present study we have used bupivacaine with nalbuphine as an adjuvent to see the duration of analgesia postoperatively and any side effects. After subarachnoid block was given there was no significant difference between onset of sensory and motor block in both of the groups.

There was also no significant difference between peak sensory and motor block in both the groups but duration of postoperative 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 is by its agonistic action on this receptor. It also stimulates kappa receptors. 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. In the nalbuphine group, almost 25% of elderly patients were controlled hypertensive. However, no cardiopulmonary adverse effects were seen. It improves quality of block and offers prolonged and long lasting postoperative analgesia. It has low incidence of adverse effects known for other opioids (respiratory depression, nausea, vomiting, 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.[7-18]

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.[8]

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.[9]

In 2011study 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.[11] 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 later 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.[10-12]

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.[7,10,15,18] 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 nonpregnant 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

Intrathecal nalbuphine added to hyperbaric bupivacaine

provides better quality of block as compared to bupivacaine alone. It also prolongs postoperative analgesia for almost 8-9 hours when used as adjuvant to bupivacaine without any significant adverse effects for patients undergoing infra-umbilical surgeries under subarachnoid block.

REFERENCES

1. Zarr GD, Werling LL, Brown SR, Cox BM. Opioid ligand binding sites in the spinal cord of the guinea-pig. Neuropharmacology 1986;25:47-80. [PubMed]
2. De Souza EB, Schmidt WK, Kuhar MJ. Nalbuphine: An autoradiographic opioid receptor binding profile in the central nervous system of an agonist/antagonist analgesic. J Pharmacol Exp Ther 1988;244:391-402. [PubMed]
3. Schmauss C, Doherty C, Yaksh TL. The analgesic effects of an intrathecally administered partial opiate agonist, nalbuphine hydrochloride. Eur J Pharmacol 1982;86:1-7. [PubMed]
4. Lin ML. The analgesic effect of subarachnoid administration of tetracaine combined with low dose of morphine or nalbuphine for spinal anesthesia. Ma Zui Xue Za Zhi 1992;30:101-5. [PubMed]
5. Fournier R, Gamulin Z, Macksay M, Van Gessel E. Intrathecal morphine versus nalbuphine for post operative pain relief after total hip replacement. Anesthesiology 1998;89:867. [PubMed]
6. Culebras X, Gaggero G, Zatloukal J, Kern C, Marti RA. Advantages of Intrathecal nalbuphine, compared with intrathecal morphine, after Cesarean delivery: An evaluation of postoperative analgesia and adverse effects. Anesth Analg 2000;91(3):601-5. [PubMed] [Full Free Text]
7. Mikuni I, Hirai H, Toyama Y, Takahata O, Iwasaki H. Efficacy of intrathecal morphine with epidural ropivacaine infusion for postcesarean analgesia. J Clin Anesth. 2010 Jun;22(4):268-73. doi: 10.1016/j.jclinane.2009.09.003. [PubMed]
8. Fournier R, Van Gessel E, Macksay M, Gamulin Z. Onset and offset of intrathecal morphine versus nalbuphine for postoperative pain relief after total hip replacement. Acta Anaesthesiol Scand. 2000 Sep;44(8):940-5. [PubMed]
9. Yoon JY, Jee YS, Hong JY. A Comparison of Analgesic Effects and side effects of intrathecal morphine, nalbuphine and morphine-nalbuphine mixture for pain relief during a caesarean section. Korean J Anaesthesiol 2002;42:627-33. [KOMCI]
10. Yang T, Breen TW, Archer D, Fick G. Comparison of 0.25 mg and 0.1 mg intrathecal morphine for analgesia after cesarean section. Can J Anaesth 1999;46:856-60. [PubMed]
11. Tiwari AK, Tomar GS, Agrawal J. Intrathecal Bupivacaine in Comparison With a Combination of Nalbuphine and Bupivacaine for Subarachnoid Block: A Randomized Prospective Double-Blind Clinical Study. Am J Ther. 2011, Sep 8 [Epub ahead of print] [PubMed]
12. Mukherjee A, Pal A, Agrawal J, Mehrotra A, Dawar N. Intrathecal nalbuphine as an adjuvant to subarachnoid block: What is the most effective dose?. Anesth Essays Res 2011;5:171-5 [Publisher website] [Free Full Text]
13. Schmitz A, Salgo B, Weiss M, Dillier CM, Frotzler A, Gerber AC. Intrathecal opioid medication for perioperative analgesia in severely handicapped children undergoing spinal operations. Anaesthesist. 2010 Jul;59(7):614-20. doi: 10.1007/s00101-010-1733-7. [PubMed]
14. Sarantopoulos C. Intravenous lidocaine and intrathecal opioids. Anesth Analg. 2000 Oct;91(4):1042. [PubMed]
15. Yaksh T, Birnbach DJ. Intrathecal nalbuphine after cesarean delivery: are we ready? Anesth Analg. 2000 Sep;91(3):505-8. [PubMed] [Free Full Text]
16. Krechel SW, Helikson MA, Kittle D, Eggers GW Jr. Intrathecal morphine (ITM) for postoperative pain control in children: a comparison with nalbuphine patient controlled analgesia (PCA). Paediatr Anaesth. 1995;5(3):177-83. [PubMed]
17. Sarantopoulos C, Fassoulaki A. Systemic opioids enhance the spread of sensory analgesia produced by intrathecal lidocaine. Anesth Analg. 1994 Jul;79(1):94-7. [PubMed] [Free Full Text]
18. Rust LA, Waring RW, Hall GL, Nelson EI. Intrathecal narcotics for obstetric analgesia in a community hospital. Am J Obstet Gynecol. 1994 Jun;170(6):1643-6; discussion 1646-8. [PubMed]

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