VOLUME-7, ISSUE-5, MAY-2018 • PRINT ISSN No 2277 - 8160

Original Research Paper

Anaesthesiology

COMPARISON OF EPIDURAL BUTORPHANOL VERSUS NALBUPHINE AS ADJUVANTS WITH BUPIVACAINE FOR ABDOMINAL HYSTERECTOMY: A PROSPECTIVE RANDOMIZED DOUBLE-BLIND CONTROLLED CLINICAL STUDY

Dr. Ankita Junior Resident, Deptt. Of Anesthesiology,rims,ranchi

Dr. Usha suwalka Hod, Deptt. Of Anesthesiology,rims,ranchi

Dr. Mukesh kumar* Associate Prof., Deptt. Of Anesthesiology, rims,ranchi *Corresponding Author

Dr.Harish kumar Senior Resident, Deptt. Of Anesthesiology,rims,ranchi

ABSTRACT

Introduction: Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. The main goal of anesthesia is to provide adequate pain relief in the intraoperative and postoperative period. Epidural anesthesia is used for all the surgical procedures carried on lower abdomen, pelvis and lower limbs. Narcotic analgesics are used as adjuvants to local anesthetics in epidural anesthesia. They hasten the onset, improve the quality of block as well as prolong the duration of analgesia.

Aims & objectives: To evaluate the postoperative analgesic benefits in patients administered butorphanol and nalbuphine as adjuvants with bupivacaine for abdominal hysterectomy under epidural anesthesia and to compare their postoperative efficacy with respect to increase in duration of analgesia, reduction in total requirements of analgesics postoperatively and to study the side effects and complications.

Materials & methods: The prospective randomized double blind study was done in 90 patients of ASA 1 & 2 in the age group of 30-60 years, randomly divided into three groups of 30 each according to the epidural medications they received:Group C (n=30): Inj. bupivacaine 0.5% (20 ml),Group B (n=30): Inj. bupivacaine 0.5% (19 ml)+Inj. butorphanol 1mg (1 ml),Group N (n=30): Inj. bupivacaine 0.5% (19 ml)+Inj. nalbuphine 10mg (1 ml). Hemodynamic parameters and various block characteristics were observed and recorded. Sensory block was assessed by pin-prick method, motor block was assessed by Bromage Scale and pain was assessed on VAS scale. Rescue analgesic 0.5% 2.5 ml bupivacaine and normal saline diluted to make 10 ml when VAS score is 4 till 24 hrs. Complications were noted and treated accordingly. Sedation was assessed by Wilson's sedation scoring. Statistical analysis was done by unpaired t test and chi square test. A 'P' value <0.05 was considered as statistically significant.

Result: The mean time of onset and completion of sensory block was statistically significant among the three groups and even better in nalbuphine group compared to butorphanol group.The duration of analgesia was maximum in nalbuphine and minimum in bupivacaine group.There was statistically significant difference in the total dose of rescue analgesic required in 24 hours between the three groups, with maximum requirement in bupivacaine group and minimum in nalbuphine group.

Conclusion:The addition of opioids like butorphanol and nalbuphine as adjuvants to bupivacaine for epidural anesthesia decrease the time of onset and completion of sensory block, the quality of analgesia is better, with lesser side effects and requiring lesser dose of rescue analgesic in postoperative period.

KEYWORDS : Butorphanol,nalbuphine,abdominal Hysterectomy,epidural,analgesia

Introduction:

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. The main goal of anesthesia is to provide adequate pain relief in the course of surgical procedure and also in the postoperative period.Epidural anesthesia is well established regional anesthetic technique and commonly used for all surgical procedures carried on lower abdomen, pelvis and lower limbs. It is also an effective treatment of intraoperative and postoperative pain, blunts autonomic, somatic and endocrine responses. The epidural anesthesia has advantages over general anesthesia by blocking nociceptive impulses from the operative site, reduced blood loss and decreased incidence of deep vein thrombosis but there is always a possibility of local anesthetic toxicity due to use of larger volumes of epidural local anesthetic solution.[1, 2]It has become a common practice to use polypharmacy approach for treatment of intra and postoperative pain without associated side effects.[3]

Various adjuvants have been added to local anesthetics in an attempt to further minimize the side effects of the local anesthetics and prolong the duration of intraoperative and postoperative analgesia. Narcotic analgesics are commonly used as adjuvants to local anesthetics in epidural anesthesia. Narcotic analgesics hasten the onset, improve the quality of the block as well as prolong the duration of analgesia.

Butorphanol is a lipid-soluble synthetically derived narcotic with weak μ-receptor agonist and antagonist activity and strong k-receptor agonism.[4]It has strong analgesic and sedative properties without respiratory depression and frequently used for postoperative analgesia and labor analgesia. It has lower addiction potential, lesser nausea, vomiting, pruritus and urinary retention.[5,6,7] Nalbuphine, a derivative of 14-hydroxymorphine which is structurally related to oxymorphone and naloxone is a strong analgesic with mixed k-agonist and μ-antagonist properties. It exhibits a ceiling effect on respiratory depression. Sedation is commonly seen when used in postoperative period as an analgesic.[8] This study was undertaken to evaluate the postoperative analgesic benefits in patients administered epidural butorphanol and nalbuphine as adjuvants with bupivacaine for abdominal hysterectomy under epidural anesthesia and to compare their postoperative efficacy with respect to increase in duration of analgesia, reduction in total requirements of analgesics postoperatively and to study the side effects and complications, if any attributable to these drugs.

Materials & methods:

This study was conducted at Rajendra Institute of Medical Sciences, Ranchi after approval from institutional ethical committee.Study eligibility included 90 female patients aged 30-60 years, weighing 40-70 kgs, ASA physical status I and II, posted for elective abdominal hysterectomy under epidural anesthesia who gave consent to participate in the study. Patients with severe anemia, coagulation abnormalities and bleeding disorders, previous history of surgeries on spine, spinal deformity, history of chronic backache & active skin lesions over the lumbosacral area were excluded.

This was a randomized, double-blind, controlled clinical study. A thorough preanesthetic evaluation was conducted with special emphasis on cardiorespiratory system, nervous system and

endocrinal abnormalities. Previous anesthetic exposure and drug sensitivity were enquired. A thorough general and systemic examination was carried out for baseline parameters and airway assessment. Patients were advised to be nil orally from 10 pm onwards and were pre-medicated with oral alprazolam 0.25 mg on the previous night before surgery.A written informed consent was taken and following investigations were confirmed. The investigations pertaining to Hb%, BT, CT, blood sugar, blood urea, serum creatinine, urine analysis for albumin, sugar and microscopy, ECG 12 leads and chest X-ray was conducted on all patients. On the day of surgery, IV access was obtained on the forearm with 20G IV cannula and IV fluid given. All patients were premedicated with inj. ranitidine 50 mg i.v., inj. glycopyrrolate 0.2 mg i.v., and inj. Metoclopramide 10 mg i.v., 30 minutes before.The patients were preloaded with Ringer's lactate 10 ml/kg over 15-20 mins prior to epidural block in preoperative area. HR, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), RR and SpO2 was monitored and noted every 5 min until the end of surgery.

With proper positioning and under all aseptic precautions, epidural space was identified in L3-4 intervertebral space using 18G Tuohy's needle with the loss of resistance to water technique. Epidural catheter was be threaded 4-7 cm inside the epidural space and fixed. A test dose of 3 ml of 2% lignocaine with adrenaline was given after initial negative aspiration for blood and cerebrospinal fluid.The study drugs were prepared by a trained anesthesia technician and the anesthesiologist giving the epidural block and making the observations in intraoperative as well as postoperative period were unaware of the drug used. The drug was administered accordingly- Group C (n=30): Inj. bupivacaine 0.5% (20 ml), Group B (n=30): Inj. bupivacaine 0.5% (19 ml) + Inj.butorphanol 1mg (1 ml), Group N (n=30): Inj.bupivacaine 0.5% (19 ml) + Inj. nalbuphine 10mg (1 ml). During procedure/operation hypotension (SBP<90 mm Hg or DBP<60 mm Hg) was treated with rapid infusion of ringer lactate and if hypotension persist bolus dose of mephenteramine 6 mg i.v. given.

The various block characteristics were observed including:-

- Sensory block was assessed by pin-prick method using a blunt needle.
- Onset of sensory block: Time from injection of LA solution up to feeling of warmth or loss of pin-prick sensation in any dermatome.
- Completion of sensory block: Time from initial onset of analgesia up to the time when analgesia attained its maximum dermatomal level, with no further rise for 5 min.
- Level of sensory block: Assessed in the midline from symphysis pubis going upward and the highest dermatome showing analgesia is taken as level of analgesia.
- Quality of analgesia:

Good - No complaint of pain or discomfort during the procedure.

Fair- Pain or discomfort felt only during specific stage of procedure like traction on viscera/peritoneum.

Poor-Pain during the surgery and needed top up with epidural LA.

- Duration of analgesia: total duration till demand of first rescue analgesia.
- Motor block was be assessed by using Bromage Scale.
- oOnset of motor block: Time from the injection of LA solution up to the time when the patient feels heaviness in the lower limbs.
- Completion of motor block: Time between the initial onset of motor block until the time when the patient will be unable to move his or her toes or raise lower limbs.
- Regression of motor block: Time when the patient will be unable to move his or her toes or lower limbs until the time when the patient start moving his or her toes or lower limbs.
- Sedation was assessed by Wilson's sedation scoring: 1=awake and alert, 2=awake but drowsy, 3=eyes closed but arousable to command, 4=eyes closed but arousable to mild physical stimulation, 5=eyes closed but unarousable to mild physical stimulation.

Sensory block was assessed at 0, 2, 5, 10, 20 and 30 min post-drug injection into the epidural space. Motor block was measured at 0, 10, 20 and 30 min post-drug administration and every hour post-surgery until the regression of the motor block. The surgery was started 30 mins after the drug injection. Those patients who were able to move her toes or raise lower limbs 30 mins after drug injection were excluded from the study population. Sedation was assessed by Wilson sedation scoring every 0, 10, 20 and 30 mins post drug administration and every hour until the end of the surgery. Respiratory rate will be assessed and rate <10/min was taken as respiratory depression.

In the post-operative period, pain scores was assessed on the VAS scale every hour till 6 h and then every 2 h till 24 h. Vitals and sedation was recorded every hour till 6 hours, every 2 hour till 12 hours and every 4 hour till 24 hrs. Duration of analgesia was taken as the time from the onset of analgesia up to the time when the VAS reached 4. Patient was then be given analgesic 0.5% 2.5 ml bupivacaine + normal saline diluted to make 10 ml and repeated when VAS score is 4 till 24 hours. Complications such as, nausea and vomiting, urinary retention, headache, pruritus, respiratory depression was noted and treated accordingly.

Statistical analysis:

The data obtained was compiled by using an excel sheet. The significance of differences between duration of sensory or motor block in two groups was analysed by calculating the standard error of difference between two means and by unpaired 't' test. For comparison of incidences of side effects in two group Chi-square test was used. A 'P' value <0.05 was considered as statistically significant.

Results:

TABLE:1 Demographic profile

Variables Our study	Age (years) Mean(± SD)	Weight(kgs) Mean(± SD)	Height(cms) Mean(± SD)	ASA gr (%) Gr 2
Group C	44.5(± 10.25)	58.2 (± 8.8)	151(±5.06)	53.3%
Group B	42.8 (± 8.0)	57.3(± 7.0)	152.08(±6.83)	50%
Group N	40.8 (± 8.7)	60.6 (± 8.1)	151.24(±5.88)	30%
P value	0.238, NS	0.255, NS	0.249, NS	0.144, NS

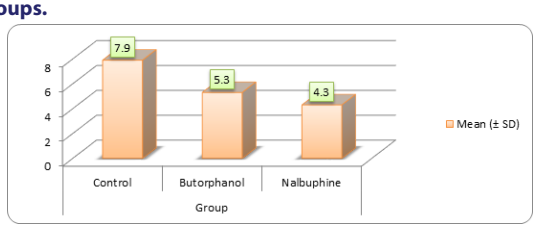
Hemodynamic parameters

Pre-operative HR, RR, SBP, DBP and SpO2 were also comparable in the groups. There was no statistically significant change in the hemodynamic parameters in any group throughout the study period.

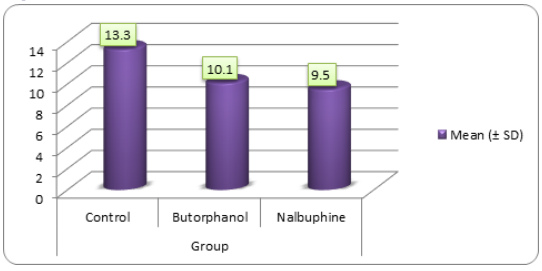
TABLE:2 Block characteristics in three groups

Block characteristic	Group C	Group B	Group N	P value
Time of onset of sensory block(mins)	7.9(±2.0)	5.2(±1.6)	4.3(±1.2)	0.000,sig
Time of completion of sensory block (mins)	13.3(±2.5)	10.1(±2.9)	9.5(±2.2)	0.000,sig
Time of onset of motor block(mins)	15.02(±1.02)	14.08(±1.04)	14.60(±1.9)	0.297,NS
Time of completion of motor block (mins)	30.0(±0.92)	29.45(±0.84)	27.89(±1.02)	0.345,NS
Duration of analgesia(hrs) or time for first rescue analgesic	4.96(±1.11)	6.64(±1.12)	7.08(±1.03)	0.000,sig
Intraoperative quality of analgesia-Good Fair	70% 30%	93.3% 6.7%	93.3% 6.7%	0.012,sig
Total rescue analgesic in 24 hours (ml)	40.12(±8.2)	36.8(±7.01)	31.3(±8.1)	0.007,sig

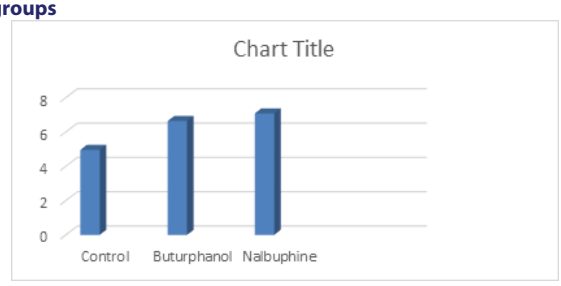
GRAPH:1 Time of onset of sensory block in different study groups.



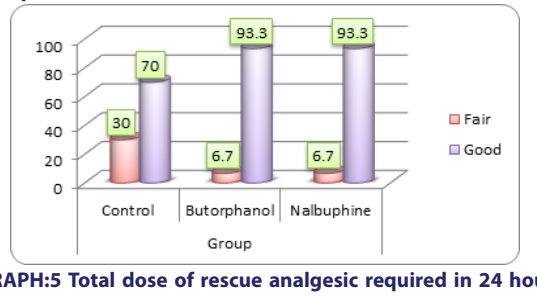
GRAPH:2 Time of completion sensory block in different study groups



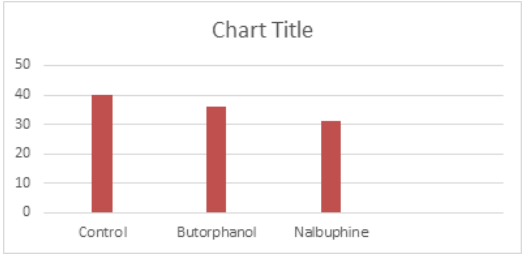
GRAPH:3 Time for first rescue analgesic in different study groups



GRAPH:4 Intraoperative quality of analgesia in different study groups



GRAPH:5 Total dose of rescue analgesic required in 24 hours (ml)



Discussion:

Our results demonstrate that the addition of butorphanol and nalbuphine to bupivacaine quicken the onset as well as completion of sensory block. Administration of 20 ml of 0.5% plain bupivacaine showed mean time of onset of sensory block 7.9 mins and the block was completed in mean time of 13.3 mins. The onset of analgesia was more rapid (mean 4.3 mins) and was completed in mean 9.5 mins with the addition of 10mg of nalbuphine to 19 ml 0.5% plain B as compared to butorphanol group where the mean time of onset of sensory block was 5.2 mins and was completed in mean 10.1 mins consistent with the study by **Moore et al** [9] addition of 1 mg butorphanol to 20 ml 0.5% plain bupivacaine reduced the latency of onset of analgesia to 5-9 min and the completion of analgesia occurred earlier (9-14 min; mean 11.80). **Abboud et al**[12] studied epidural butorphanol for the relief of postoperative pain after caesarean section and reported the time of onset of pain relief with 1 mg butorphanol to be 15 min. In a study by **Kaur et al**[10], 75 adult patients of either sex of ASA I and II, aged 20-60 years, undergoing lower abdominal surgery under epidural anesthesia were randomly divided into three groups of 25 each: bupivacaine (B), bupivacaine and butorphanol (BB) and bupivacaine and fentanyl (BF). B (0.5%) 20 ml was administered epidurally in all the three groups with the addition of 1 mg butorphanol in BB group and 100 µg fentanyl in the BF group. Onset and completion of sensory analgesia was earliest in BF group, followed by BB and B group. The duration of analgesia was significantly prolonged in BB group followed by BF as compared with group B.

In our study the mean time of onset of motor block among group C was 15.02min, 14.80 min in group B and 14.60 min among group N. The mean time of completion of motor block among group C was 30.0 min, 29.45 min in group B and 27.89 min in group N. There was no statistically significant difference in the motor block level of the three groups consistent with study by **Kaur et al**[10] ,addition of butorphanol and fentanyl to bupivacaine had no effect on the time of onset, completion and regression of motor block. Butorphanol provides a significantly prolonged post-operative analgesia.

The quality of the sensory block was significantly improved with the addition of both the opioids to Bupivacaine. Majority of the patients, 93.3% in each group B and group N had good quality of analgesia. No patient received any supplemental analgesic during the surgery. The pain scores as assessed on the VAS were low and remained low for a significant time in the post-operative period with the addition of nalbuphine to bupivacaine compared to butorphanol.

The duration of analgesia was also significantly prolonged with the addition of opioids to LA. We observed duration of analgesia with 20 ml 0.5% bupivacaine alone to be 2-7 h (mean 4.96) in consistent with other studies given by **Malik et al**[14] have also reported in their study that butorphanol provides a longer duration of analgesia than fentanyl, similar to our study.

In a study by **Kaur et al**[10], butorphanol provides a significantly prolonged post-operative analgesia, consistent with study by **Ahmed et al**[11], they concluded that the combination of intrathecal bupivacaine with nalbuphine significantly prolonged postoperative analgesia as compared to the control group and 1.6 mg dose of nalbuphine administered intrathecally showed the best results among all other study groups.

Narcotic analgesics are well-known for the potential side effects such as pruritus, nausea, vomiting, urinary retention and respiratory depression. Delayed respiratory depression is the most troublesome of these side effects. The patients were continuously observed for respiratory depression with SpO2 (< 90%) and RR (< 10). No case of respiratory depression was observed in any group, consistent with study by **Malik et al**[14]. The incidence of pruritus was higher in group BF (25%) as compared to group (BB). Previous studies have documented the incidence of pruritus with epidural fentanyl to be 23%, 41% and 46.7%.Pruritus has been observed in few patients receiving epidural butorphanol in previous studies, 1.4% and 3% Three cases in group BF and one in group BB had nausea.

The total dose of rescue analgesic required in 24 hours was 40.12 ml in control group >36.8 ml in butorphanol group >31.3 ml in nalbuphine group. **Banerjee et al**[7] conducted a study on 75 patients belonging to age groups 18-60 years who were scheduled for surgeries of lower abdomen were randomly divided into groups of 25 each. Epidural technique was adopted for surgery of the lower abdomen for all patients with 0.5% bupivacaine. In the post-operative period, the study drug was given through epidural

catheter. Group A received butorphanol 2 mg, Group B received fentanyl 100 µg, and Group C received nalbuphine 10 mg with 0.125% bupivacaine diluted to 10 ml in normal saline each. All patients in fentanyl group and nalbuphine group required analgesic supplementation within first 2 – 4 hours and 4 – 6 hours respectively.

Conclusion:

The mean time of onset of sensory block and mean time of completion of sensory block was better in nalbuphine group followed by butorphanol group followed by control. The mean onset of motor block was also comparable between the three groups, the pain score was better in nalbuphine group followed by butorphanol group compared to control group. Side effects were higher in control group than the butorphanol and nalbuphine groups. The mean duration of analgesia was highest in nalbuphine group followed by butorphanol and then control group. The total dose of rescue analgesic required in 24 hours was minimum in nalbuphine group followed by butorphanol and control group.We can conclude that addition of opioids like butorphanol and nalbuphine as adjuvants to bupivacaine for epidural decrease the time of onset and completion of sensory block, the quality of analgesia is better,with lesser side effects and requiring lesser dose of rescue analgesic in postoperative period.

References:

1. Agarwal S, Gupta K, Gupta PK, Bansal M, Sharma R, Buchh A, Clonidine versus fentanyl as adjuvant to 0.75% ropivacaine for epidural anesthesia for lower limb surgeries a comparative evaluation, Int J Res Med Sci. 2016 Aug;4(8):3606-3610.
2. Liu S, Carpenter RL, Neal JM. Epidural anesthesia and analgesia-Their role in postoperative outcome. Anesthesiology. 1995;82:1474-506.
3. Sirvinskas E, Laurinaitis R, Vimantite R, Dumcius M, Bieliunas A. Magnesium sulfate usage for patients during cardiopulmonary bypass. Medicina (Kaunas):2002:38 Suppl (2):209-12.
4. Hunt CO, Naulty JS, Malinow AM, Datta S, Ostheimer GW. Epidural butorphanol-bupivacaine for analgesia during labor and delivery. Anesth Analg 1989;68:323-7.
5. Bharti N, Chari P. Epidural butorphanol-bupivacaine analgesia for postoperative pain relief after abdominal hysterectomy. J Clin Anesth 2009;21:19-22.
6. Shrestha CK, Sharma KR, Shrestha RR. Comparative study of epidural administration of 10 ml of 0.1% bupivacaine with 2 mg butorphanol and 10 ml of 0.25% plain bupivacaine for analgesia during labor. JNMA J Nepal Med Assoc 2007;46:1-6.
7. Banerjee S, Pattnaik SK, A comparative study between epidural butorphanol, Nalbuphine and fentanyl for post operative analgesia in lower abdominal surgeries, Asian J Pharm Clin Res, Vol 10, Issue 5, 2017, 383-388.
8. Gunion MW, Marchionne AM, Anderson TM. Use of the mixed agonist - antagonist nalbuphine in opiod based analgesia. Acute Pain 2004;6:29 – 39.
9. Moore RA, Bullingham RE, McQuay HJ, Hand CW, Aspel JB, Allen MC, *et al*. Dural permeability to narcotics: *In vitro* determination and application to extradural administration. Br J Anaesth 1982; 54:1117-28.
10. Kaur J, Bajwa SJS. Comparison of epidural butorphanol and fentanyl as adjuvants in the lower abdominal surgery: A randomized clinical study. *Saudi Journal of Anaesthesia*. 2014;8(2):167-171. doi:10.4103/1658-354X.130687.
11. Ahmed F, Narula H, Khandewal M, Dutta D, A comparative study of three different doses of nalbuphine as an adjuvant to intrathecal bupivacaine for post operative analgesia in abdominal hysterectomy, Indian J Pain 2016;30:23-8.
12. Abboud TK, Moore M, Zhu J, Murakawa K, Minehart M, Longhitano M et al. Epidural butorphanol for the relief of post-operative pain after caesarean section. Anaesthesiol 1986;65:A397.
13. Mok MS, Tsai YJ, Ho WM. Effi cacy of epidural butorphanol compared to morphine for the relief of post-operative pain. Anaesthesiol 1986;65:A175
14. Malik P, Manchanda C, Malhotra N. Comparative evaluation of epidural fentanyl and butorphanol for post-operative analgesia. J Anesthesiol Clin Pharmacol 2006;22:377-82.