



**Comparative study of the epidural Ropivacaine with Butorphanol & Ropivacaine with Nalbuphine for post operative analgesia in lower extremity surgeries**

<sup>1</sup>Dr Sumita Mohanty. Assoc Prof, <sup>2</sup>Dr Khageswar Raut. Assoc Prof

<sup>3</sup>Dr Sidharth Sraban Routray, Assoc Prof, <sup>4</sup>Dr Vijaye Partha Ray. Postgraduate student, <sup>5</sup>Dr Soumyakant Mallick, Postgraduate student

<sup>1</sup>Department of Anaesthesiology, Pain and Palliative Care, Acharya Harihar Regional Cancer Research Centre, Cuttack, Odisha, India.

<sup>2,3,4,5</sup>Department of Anaesthesiology, S C B Medical College, Cuttack, Odisha, India.

**Correspondence Author:** Dr Khageswar Raut .Department of Anaesthesiology, S C B Medical College, Cuttack, Odisha, India.

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**Abstract**

**Background and aim:** Opioids in epidural route act through the spinal cord receptors and improve the quality and duration of analgesia produced by local anaesthetics. Our aim of the study was to compare the efficacy and safety profile of butorphanol and nalbuphine when used as adjuvant to epidural ropivacaine.

**Materials and Methods:** A total of 50 adult patients of either sex of American Society of Anesthesiologist physical status I and II, aged 20-70 years, posted for lower extremity surgery under epidural anesthesia were enrolled into the study. Patients were randomly divided into two groups of 25 each. Group a received epidural ropivacaine and butorphanol and group B received epidural ropivacaine and nalbuphine. The block characteristics like onset and duration of sensory and motor blockade, hemodynamic parameters and various side effects were observed and compared.

**Results:** Onset of sensory and motor block was earlier in B group, compared A group. The duration of sensory and motor blockade was significantly prolonged in B group

compared with group A. No significant side effects were observed in any group.

**Conclusion:** Both butorphanol and nalbuphine as adjuvant to epidural ropivacaine are equally safe and provide comparable stable haemodynamics. Nalbuphine with ropivacaine provides both early onset of sensory motor block and significantly prolonged post-operative analgesia compared to butorphanol with ropivacaine.

**Keywords-**Epidural,ropivacaine,butorphanol,nalbuphine

**Introduction**

Pain is an unpleasant sensory, emotional & psychological response associated with potential tissue damage or described in such terms<sup>1</sup>. Pain after surgery is inevitable. In perioperative scenario, pain is now taken up as the sixth vital sign. Hence, relieving pain is one of the fundamental responsibilities of anaesthesiologists and evaluation and alleviation of pain is one of the primary goals.

Acute post operative pain is associated with lots of adverse events like increased sympathetic activity predisposing to myocardial ischemia.<sup>2</sup> Administration of opioids through the epidural route is a more popular

technique for postoperative pain management. Advantages of the combination include better pain relief, motor sparing & reduced overall toxicity of local anaesthetics. Amongst the opioids, morphine, pethidine, fentanyl, sufentanyl, buprenorphine and butorphanol are commonly used drugs through epidural route.<sup>3</sup> Nalbuphine is used sometimes. In the present study, nalbuphine and butorphanol have been selected for evaluation and comparison of postoperative analgesia.

Butorphanol is a synthetic agonist-antagonist opioid analgesic. It is an agonist on  $\kappa$  receptor and either antagonist or partially agonist on  $\mu$  receptor. Epidural butorphanol has been employed successfully for the relief of postoperative pain. It is considered safer than pure agonist opioids because of its ceiling effect on respiratory depression, lower addiction potential, lesser nausea, vomiting, pruritus and urinary retention.<sup>4</sup> Nalbuphine is an agonist-antagonist opioid analgesic which is synthetically derived.<sup>5</sup> Few studies are there in literature comparing nalbuphine and butorphanol in epidural route. The aim of our study is to evaluate postoperative analgesic benefits in patients administered epidural butorphanol and nalbuphine as adjuvants with local anaesthetics in epidural anaesthesia.

### **Methods**

This prospective study was conducted in a tertiary care hospital in Odisha, India. Written informed consent was obtained from all the patients. A total of 50 patients of age ranging from 20- 70 years of ASA I and ASA II were selected for the study. This study was conducted from September 2015 to October 2017 in patients posted for surgeries of lower extremity. Patients having local infection, known allergy to study drugs, coagulopathies, vertebral anomalies neurological diseases, renal insufficiency were excluded

from study. Patients were randomly divided into two groups of 25 each

Group A – received 15ml of 0,5% ropivacaine and butorphanol 2mg (1ml)

Group B – received 15ml of 0,5% ropivacaine and nalbuphine 10mg (1ml)

A detail clinical history was taken and detail general and systemic examinations were done. Basic laboratory investigations like complete haemogram, bleeding time, clotting time, blood sugar, blood urea, serum creatinine and urine analysis, ECG, chest X Ray were carried out in all patients. The patients were explained about the epidural technique and the usage of linear visual analogue scale (VAS) for assessment of the intensity of postoperative pain and were instructed to mark on the scale at the point which he/she felt was representative of their level of discomfort. All patients were given Tablet Alprazolam 0.5 mg on the night before the surgery. Patients were also kept nil orally for 8 hrs before surgery. All patients had an intravenous line with 18G cannula after arriving in the operation theater and ringers lactate was started. Base line heart rate, blood pressure, ECG, respiratory rate, SpO<sub>2</sub> were recorded. The drugs were prepared by an anaesthesiologist who was not involved in the study. Epidural anaesthesia was administered in sitting position with 18G Tuohy needle in L<sub>2-3</sub> space. After negative aspiration test for blood and CSF, 3 ml of inj. Lignocaine hydrochloride 2% with adrenaline (1:200000) was administered and epidural catheter was introduced. Then study drug was slowly injected in small increments and the patients were made supine. Monitoring of vital signs was continued throughout the procedure. Group A (n=25) patients received 15ml of 0,5% ropivacaine and butorphanol 2mg (1ml). On the other hand, Group B (n=25) received 15ml of 0,5% ropivacaine and nalbuphine 10mg (1ml). Onset of

sensory block was assessed by pin prick method at every minute's interval. Onset time duration was assessed from local anaesthetic solution injection to epidural space to start of loss of pain sensation to pin prick .Duration of sensory block was assessed every 15 minutes postoperatively by pin prick method. Onset of motor block was assessed by modified Bromage scale as follows: 0 - no paralysis,1-inability to raise extended leg.2-inability to flex knee,3-Inability to flex ankle joint.<sup>6</sup> Duration of Analgesia was assessed every 15 minutes postoperatively by 10 cm Visual Analogue Scale (VAS)17. 0 - no pain,10 - worst possible pain.Rescue analgesic injection iv paracetamol 1gm was given intravenously when VAS score >5.<sup>7</sup>

Haemodynamic parameters like heart rate, systolic BP, diastolic BP, respiratory rate were noted at 0, 15, 30, 60, 75, 90, 120, and at 240 mins from administration of epidural anaesthesia. Side effects like nausea, vomiting, hypotension, sedation, shivering ,respiratory depression and headache were noted.Sedation was assessed on 4 point sedation scale.0-awake and alert,1-mildly sedated,2-moderately sedated,3-deeply sedated.<sup>8</sup>

**Statistical evaluation**

Sample size calculation was done by taking duration of analgesia as primary outcome variable of interest. It was estimated that n = 23 ( recruitment target achieved - n = 30 in each group) will be required per group to detect 60 minutes difference in this parameter with 80% power and 5% probability of Type I error. This calculation assumed a standard deviation of 75 minutes in duration of analgesia. For statistical analysis, raw data entered into a MS Excel spread sheet and analyzed by SPSS 21 (statistical software version 21). Unpaired student's t- test was used to compare normally distributed numerical variables. All analysis were two-tailed and p value <0.05 was taken to be statistically significant.

**Result**

Table 1: Demographic characteristics

Parameters	GROUP A (mean±SD )	GROUP B (mean±SD )	P value
Mean Age (years)	35.80±8.32	35.13±8.24	0.204
Sex distribution (m/f)	16/9	15/10	0.345
Weight (kg)	58.26±6.46	57.46±7.9	0.225
Height (cm)	154.3±9.45	154.80±10.1	0.128
Duration of surgery (min)	120.86±34.2	124.2±33.26	0.223

The table 1 shows distribution of demographic parameters in different groups of patients which comparable.

Table 2: Epidural block characteristics

Block characteristics	Group A (mean±SD )	Group B (mean±SD )	P Value
Onset time of sensory block at T 10 (mins)	7.95±2.4	5.81±3.45	0.02
Time to max sensory block (mins)	13.94±3.56	10.84±3.24	0.03
Time for complete motor block (mins)	16.52±5.12	13.26±6.64	0.02
Maximum sensory block level achieved	T6	T6	0.59

Table 3:Postoperative block characteristics

Block characteristics	Group A (mean±SD )	Group B (mean±SD )	P Value
Mean time to sensory regression at S 1(mins)	278.78±30.25	345.32±32.14	0.0001

Mean time to regression to bromage 1(mins)	254.42±28.26	285.62±28.94	0.0001
Time to first rescue top up (mins)	315.4±26.15	380.66±25.8	0.0001

Addition of nalbuphine to epidural ropivacaine produced an earlier onset of sensory block in group B compared to group A which was statistically significant. There was no statistical difference in height of block achieved. Complete motor blockade was achieved earlier in group B compared to group A which was statistically significant.(table-2,3)Time regression at S1 was earlier in group A compared to group B which was statistically significant. Duration of motor block was prolonged in group B compared to group A which was statistically significant. Time to 1<sup>st</sup> dose of rescue analgesia was delayed in group B compared to group A.

Figure-1: Height of block attained in the groups

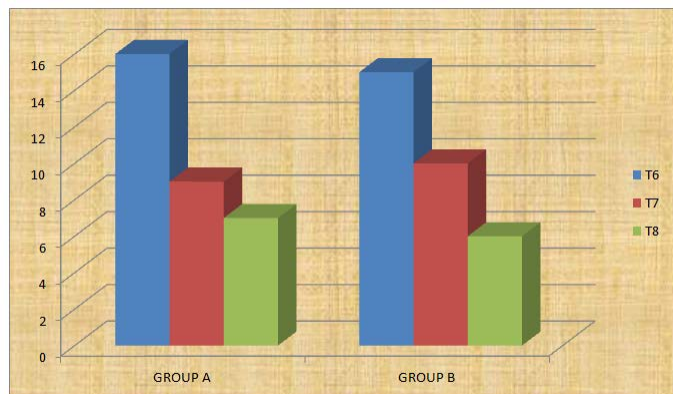


Fig 1 shows the maximum height of block attained in the groups. The heights of block in two groups are comparable.

Figure-2: Change in mean pulse rate between two groups

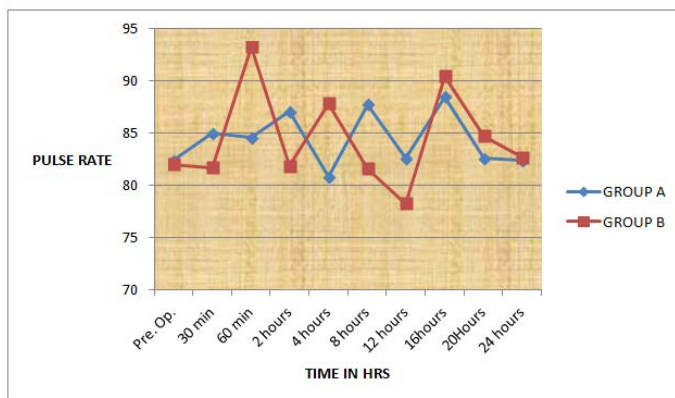
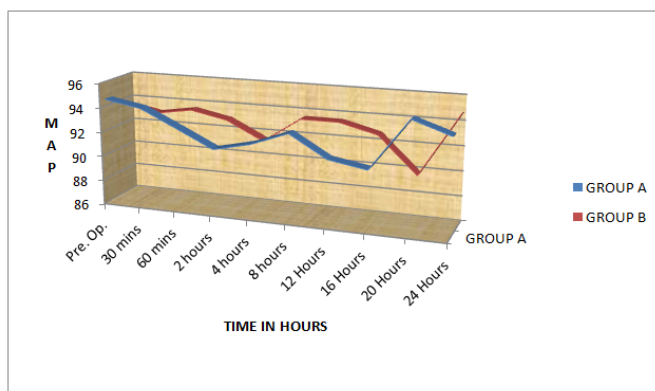


Figure 2 shows the mean pulse rate trend in the groups which were comparable.

Figure-3: Change in mean arterial pressure between two groups (MAP)



In terms of incidence of hypotension, the two groups were comparable and there was no significant difference among the two groups.(fig 3)

Fig- 4: Comparison of VAS score between two groups (postoperatively).

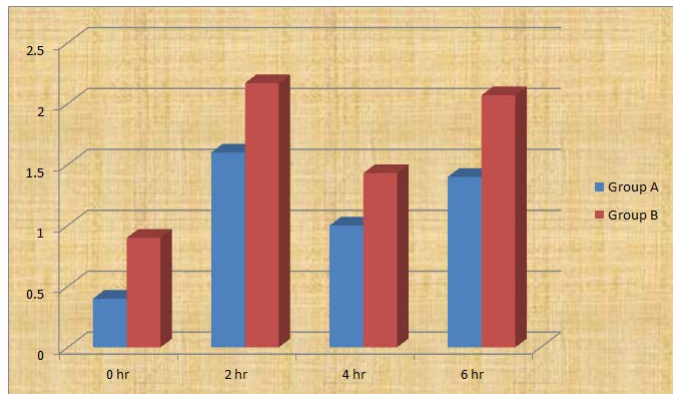


Figure 4 and 5 shows that in group A, VAS score was more in comparison to group B and no of top up doses of rescue analgesia requirement was more in group A compared to group B which was statistically significant.

Figure-5 :Total no. of analgesic top up

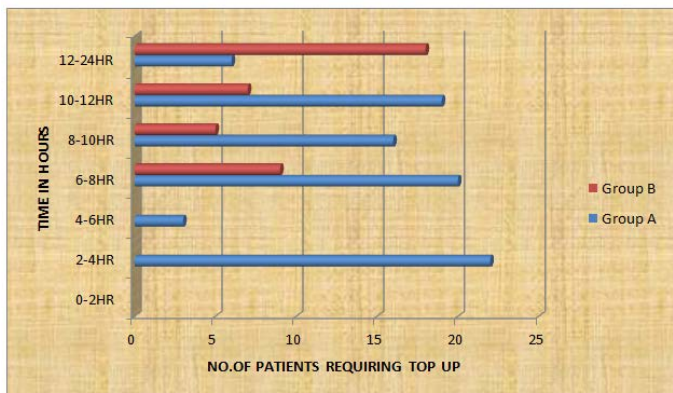
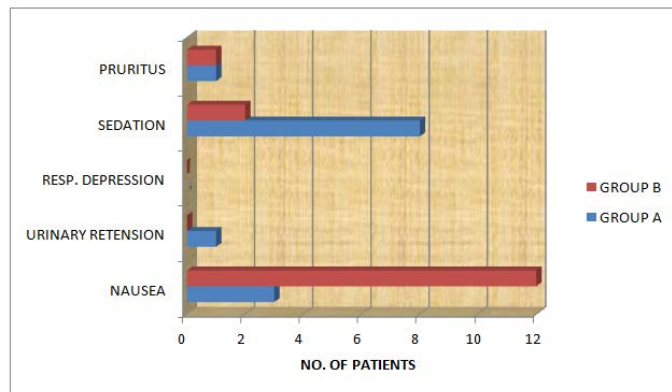


Figure 6 depicts the complications which occurred in the groups as enumerated below. There no significant difference among the two groups in terms of incidence of urinary retention, respiratory depression and pruritus. There is significant difference among the groups in the incidence of nausea and sedation.

Figure 6: Complications



### Discussion

Postoperative pain can be detrimental and very much disturbing to the patients.<sup>9</sup> So effective pain relief of the patients undergoing surgery is essential and is of paramount importance to reduce many postoperative complications. Inadequate control of pain may result in increased catecholamine secretion in response to pain, which may in turn increase myocardial oxygen demand. A number of studies in the past have proved that improved postoperative analgesia may reduce the incidence of cardiac and pulmonary morbidity and mortality in patients undergoing major abdominal surgery.<sup>10</sup>

Since the discovery of opioid receptors in the spinal cord, the action of narcotics through opioid receptors has become more clearly understood.<sup>11,12</sup> One of the opioid receptors, kappa are mainly involved with the mediation of visceral pain. After this, achieving satisfactory postoperative analgesia with epidural and intrathecal administration of narcotics has been the subject of much research. The use of epidural opioids had become an increasingly popular technique for management of acute postoperative pain in recent times.<sup>13,14</sup> However, there are disadvantages associated with narcotics as they are not always simple to use and may be associated with some unpleasant adverse effects, like nausea and vomiting (PONV), pruritus, respiratory depression and urinary

retention. Stimulation of spinal opiate receptors ( $\kappa$ ) can also produce spinal analgesia but with fewer side effects.<sup>15,16</sup> Therefore, a drug such as butorphanol, a mixed narcotic agonist/antagonist, acts as a  $\mu$  ( $\mu$ ) agonist/antagonist and  $\kappa$  agonist, also produces analgesia, associated with fewer side effects like sedation and also low abuse potential. Its high lipid solubility and high affinity for opioid receptors are additional factors that contribute to paucity of side effects with its use. Nalbuphine is an agonist-antagonist, equipotent to morphine also has a low abuse potential. It is known to produce profound analgesia and is known to be associated with side effects like nausea and vomiting.<sup>17,18</sup> The present study is a prospective randomized controlled comparative study done to assess the efficacy and safety of epidural butorphanol and epidural nalbuphine, each combined with ropivacaine for the management of postoperative pain. All the two groups were comparable in terms of age, sex and weight. Babu S et al has compared butorphanol and nalbuphine with epidural ropivacaine in thoracic epidural anaesthesia and concluded that nalbuphine has better analgesic profile compared to butorphanol.<sup>19</sup>

In our study, postoperative pain was assessed using VAS scale. The study drugs were given when the VAS score is  $>5$  in the immediate postoperative period. Furthermore, the need of rescue analgesia was higher in the A group than B group during the first 6 hrs only. This shows that ropivacaine with nalbuphine having an earlier onset of action and provided prolonged analgesia than ropivacaine with butorphanol. There was decreased need of rescue analgesia in the immediate postoperative period in nalbuphine group. Our study results on quality of analgesia are similar to the previous studies by Gupta R et al<sup>20</sup>, Chatrath V et al<sup>21</sup>, and Kaur J et al<sup>22</sup> where addition of nalbuphine to local anesthetics provided effective

postoperative epidural analgesia when compared to other opioids.

### Conclusion

Opioid analgesics with local anesthetics are extremely safe, effective and reliable method of postoperative pain relief. Nalbuphine produces faster onset of analgesia and longer duration of analgesia than butorphanol when given epidurally along with Ropivacaine. Butorphanol administered epidurally produced adverse effect like sedation more than that of Nalbuphine where as Nalbuphine produced adverse effect like nausea and vomiting more than that of Butorphanol.

### References

1. B Jyothi, Shruthi Gowda, Safiya I Shaikh. A comparison of analgesic effect of different doses of intrathecal nalbuphine hydrochloride with bupivacaine and bupivacaine alone for lower abdominal and orthopedic surgeries. Indian J Pain 2014 ; 28(1) : 18-23.
2. Kenneth H, Jerry V Young. The safety & efficacy of Intrathecal opioid analgesia for acute post operative pain; Anaesthesia & analgesia 1999, 88: 599-604.
3. B Jyothi, Shruthi Gowda, Safiya I Shaikh. A comparison of analgesic effect of different doses of intrathecal nalbuphine hydrochloride with bupivacaine and bupivacaine alone for lower abdominal and orthopedic surgeries. Indian J Pain 2014 ; 28(1) : 18-23.
4. Ahluwalia P, Ahluwalia A, Varshney R, Thakur S, Bhandari S. A Prospective Randomized Double Blind Study to Evaluate the Effects of Intrathecal Nalbuphine in Patients of Lower Abdominal Surgeries

- Under Spinal Anaesthesia. *Int J Sci Stud* 2015;3(3):19-23.
5. Hala Mostafa Gomaa a, Nashwa Nabil Mohamed a,\* ,A Comparison Between Post operative analgesia after Intrathecal Nalbuphine with Bupivacaine and Intrathecal Fentanyl with Bupivacaine after Caesarean Section. *Egyptian Journal of Anaesthesia* (2014) 30, 405–410
  6. 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;44:940-5.
  7. 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* 2013;20:592-5.
  8. Babu S, Gupta BK, Gautam GK. A Comparative Study for Post Operative Analgesia in the Emergency Laparotomies: Thoracic Epidural Ropivacaine with Nalbuphine and Ropivacaine with Butorphanol. *Anesthesia, Essays and Researches*. 2017;11(1):155-159.
  9. Hwang KB, Chung CJ, Lee JH, Lee SC, Oh SH. Comparison of Butorphanol and Fentanyl for Patient-Controlled Epidural Analgesia after Gastrectomy. *Journal on Korean Pain Soc* 2004 Jun; 17(1): 24-48.
  10. Soto RG, Fu ES. Acute pain management for patients undergoing thoracotomy. *Ann Thorac Surg*. 2003;75:1349–57.
  11. Beaussier M, Genty T, Lescot T, Aissou M. Influence of pain on postoperative ventilatory disturbances. Management and expected benefits. *Ann Fr Anesth Reanim*. 2014;33:484–6.
  12. Wilkinson KM, Krige A, Brearley SG, Lane S, Scott M, Gordon AC, et al. Thoracic epidural analgesia versus rectus sheath catheters for open midline incisions in major abdominal surgery within an enhanced recovery programme (TERSC): Study protocol for a randomised controlled trial. *Trials*. 2014;15:400.
  13. Förster JG, Rosenberg PH. Clinically useful adjuvants in regional anaesthesia. *Curr Opin Anaesthesiol*. 2003;16:477–86.
  14. Bromage PR. The price of intraspinal narcotic analgesics: Basic constraints (Editorial) *Anaesth Analg*. 1989;68:323–7.
  15. Schmauss C, Doherty C, Yaksh TL. The analgetic effects of an intrathecally administered partial opiate agonist, nalbuphine hydrochloride. *Eur J Pharmacol*. 1982;86:1–7.
  16. 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.
  17. Gunion MW, Marchionne AM, Anderson TM. Use of the mixed agonist-antagonist nalbuphine in opioid based analgesia. *Acute Pain*. 2004;6:29–39.
  18. Bharti N, Chari P. Epidural butorphanol-bupivacaine analgesia for postoperative pain relief after abdominal hysterectomy. *J Clin Anesth*. 2009;21:19–22.
  19. Kato A, Koitabashi T, Masuda S, Masuda Y, Ouchi T, Serita R. Comparison of the efficacy of ropivacaine and that of levobupivacaine for postoperative epidural analgesia in patients undergoing gynecological open abdominal surgery. *Masui*. 2013;62:1160–5.
  20. Saravana Babu M, Verma AK, Agarwal A, Tyagi CM, Upadhyay M, Tripathi S. A comparative study in the post-operative spine surgeries: Epidural ropivacaine with dexmedetomidine and ropivacaine with clonidine for post-operative analgesia. *Indian J Anaesth*. 2013;57:371–6.

21. Gupta R, Kaur S, Singh S, Aujla KS. A comparison of epidural butorphanol and tramadol for postoperative analgesia using CSEA technique. *J Anaesthesiol Clin Pharmacol*. 2011;27:35–8.
22. Chatrath V, Attri JP, Bala A, Khetarpal R, Ahuja D, Kaur S. Epidural nalbuphine for postoperative analgesia in orthopedic surgery. *Anesth Essays Res*. 2015;9:326–30.
23. Kaur J, Bajwa SJ. Comparison of epidural butorphanol and fentanyl as adjuvants in the lower abdominal surgery: A randomized clinical study. *Saudi J Anaesth*. 2014;8:167–71.