Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 01, 2023

A comparative study of epidural ropivacaine with nalbuphine and ropivacaine with butorphanol in lower abdominal surgeries

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Received: 06/10/2022 Revised: 02/12/2022 Accepted: 19/01/2023

ABSTRACT

Introduction: Epidural analgesia has been the gold standard and extensively preferred technique for providing postoperative analgesia in lower abdominal surgeries where complications are very less as compared to spinal anaesthesia. Epidural analgesia has been shown to accelerate post operative recovery, faster mobilization, reduce the pulmonary morbidity, reduces the pain score, and minimizes patient distress. Both Butorphanol and Nalbuphine are partial agonist–antagonists, acting as agonists on the kappa receptor while acting as antagonists or partial agonists on the mu receptor. **Aims and Objectives:** To compare the efficacy of analgesic effect of epidural 0.75% ropivacaine with 10mg nalbuphine and 0.75% ropivacaine with 2mg butorphanol in patients posted for lower abdomen surgeries under epidural anesthesia. Also, to observe side effects like bradycardia, hypotension, nausea, sedation, shivering.

Materials and methods: A total of 60 adult patients of either sex of ASA physical status I and II, aged 18-60 years, undergoing lower abdominal surgeries under epidural anaesthesia were enrolled into the study. Patients were randomly divided into two groups of 30 each: 0.75% ropivacaine + 10 mg Nalbuphine (group RN) and 0.75% ropivacaine + 2 mg butorphanol (group RB). The hemodynamic parameters as well as onset of pain relief and duration of analgesia were noted. Adverse events were also noted.

Result: Duration of sensory analgesia ($p < 0.001$) and motor blockade ($p < 0.001$) was significantly prolonged in nalbuphine group than butorphanol group. Onset of sensory and motor blockade was earlier in nalbuphine group. VAS scores were better in nalbuphine group postoperatively. Perioperative hemodynamic parameters and the adverse side effects including bradycardia, hypotension, nausea and vomiting, sedation and shivering were comparable between the two groups .

Conclusion: Nalbuphine as an epidural adjuvant to ropivacaine provides better overall perioperative analgesia compared to butorphanol with comparable hemodynamic alterations and very minimal side effects for patients undergoing lower abdominal surgeries.

Keywords: Postoperative analgesia; Ropivacaine; Nalbuphine; Butorphanol.

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INTRODUCTION

Major abdominal surgeries are commonly performed under general anaesthesia due to the need for controlled respiration and adequate muscle relaxation. However, general anaesthesia, especially in high-risk patients, is associated with a high incidence of cardiorespiratory complications. Epidural administration of various analgesics gained increasing popularity following the discovery of opioid receptors in the spinal cord capable of producing potent analgesia as reported by Taksh and Rudy in 1976.[1] Numerous studies have demonstrated that epidural analgesia does inhibit the stress response. This effect seems to be greatest when epidural anaesthesia is continued in the post operative period.It is now clear that epidural administration of opioids is superior to traditional intravenous and intramuscular injections of opioids. Postoperative epidural infusion of local anaesthetic drug has shown more analgesic efficacy than parenteral opioids, especially during mobilization, and may reduce either postoperative morbidity or length of hospital stay. [2] However, because of excessive doses, low individual toxic thresholds or unrecognized intravascular injections of local anesthetic drug like bupivacaine toxic adverse side effects have been reported. [3] Therefore, it is important that the analgesia regimens do not expose patients to toxic doses of local anesthetic drug leading to serious adverse effects.[4] Ropivacaine acts as a safer substituent.

Ropivacaine is a long-acting regional anaesthetic that is structurally related to Bupivacaine. It is a pure S(-)enantiomer, unlike Bupivacaine, which is a racemate, developed for the purpose of reducing potential toxicity and improving relative sensory and motor block profiles.[5]

Ropivacaine blocks conduction by decreasing or preventing the large transient increase in the permeability of excitable membranes to Na^+ that normally is produced by a slight depolarization of the membrane. This action is due to the direct interaction with voltage-gated Na^+ channels. As the anesthetic action progressively develops in a nerve, the threshold for electrical excitability gradually increases, the rate of rise of the action potential declines, impulse conduction slows, and the safety factor for conduction decreases. These factors decrease the probability of propagation of the action potential, and nerve conduction eventually fails.[6]

Ropivacaine has a few properties that make it unique. Ropivacaine is less lipophilic compared to other local anesthetics, such as bupivacaine, and is less likely to penetrate large myelinated motor fibers. It, therefore, selectively acts on the nociceptive A, B, and C fibers over the AB (motor) fibers. Ropivacaine is also manufactured as a pure S(-) enantiomer; the S(-) enantiomer has significantly less cardiotoxicity and neurotoxicity. [7,8]

Nalbuphine is an opioid, synthetically prepared with mixed μ antagonist and κ agonist properties provides potent analgesia of visceral nociception. [9] It is a widely used opioid in regional anesthesia as it acts as an effective adjuvant to local anesthetic drug. Nalbuphine when administered intrathecally binds to kappa receptors in the spinal cord and brain producing analgesia and sedation without μ adverse effects. It has minimal respiratory depressant effect and low abuse potential compared to other centrally acting opioid analgesics. Side effects like shivering, nausea, vomiting and urinary retention are infrequent with nalbuphine hydrochloride.[10] It is a mixed synthetic agonist-antagonist, which attenuates the μ-opioid effects and enhances the κ-opioid effects. [11]

Nalbuphine, if given systemically, has a reduced incidence of respiratory depression and has been used to antagonize the side effects of spinal opiates. [12] Intrathecal nalbuphine produces

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lesser adverse effects like pruritus, nausea, and vomiting when compared to intrathecal morphine and does not cause any significant hemodynamic or respiratory complications. [13]

Butorphanol is also synthetically derived narcotic agonist and antagonist, acts as a partial agonist or weak antagonist at mu receptor and strong agonist at kappa receptor. Activation of these receptors causes both supraspinal and spinal analgesia, sedation, dysphoria with low abuse potential. It is relatively safer drug than pure agonist opioids because of its ceiling effect on respiratory depression, lower addiction potential, lesser side effects like nausea, vomiting, pruritus, and urinary retention. The analgesic potency of butorphanol can be compared with the gold standard opioid analgesic morphine but studies have shown that it produces sedation more than that of morphine, which is desired in postoperative period.[14]

Aim: To compare the onset & duration of analgesia of epidural 0.75% ropivacaine with 10mg nalbuphine and 0.75% ropivacaine with 2mg butorphanol in patients posted for lower abdomen surgeries.

MATERIALS AND METHODS

This is a prospective randomized double-blind study. was conducted in the Department of Anesthesia, Tertiary care Teaching Hospital over a period of 1 year. Present study was conducted amongst 60 American Society of Anesthesiologist (ASA) status I-II patients of either sex in age group of 18-60 years coming to hospital for lower Abdominal surgeries performed under epidural anesthesia.

Inclusion Criteria: 1)Either gender patients in age group of 18-60 years.
2)Patients classified as ASA grade I and II .
3) Patients who gave consent to participate in study.

Exclusion Criteria1)Patients with severe systemic disease, metabolic disorder, neurological, congenital or cardiovascular disease
2) Patients with coagulation disorders.
3)Local sepsis at site of epidural insertion.
4)Patients allergic to local anesthetics.
5) Patients refusal for epidural anaesthesia**.**

Patients were randomly divided into two groups of 30 each: 0.75% ropivacaine + 10 mg Nalbuphine (RN) and 0.75% ropivacaine + 2 mg butorphanol (RB).

Pre-anesthetic evaluation: All patients were thoroughly examined and assessed pre-operatively for any cardiovascular, respiratory or any other systemic illness.
All the patients had the following investigations done.
a. Haemoglobin percentage
b. Urine examination for albumin and sugar
c. Bleeding time and clotting time
d. Blood sugar
e. Blood urea
f. Serum creatinine
g. Serum electrolytes
h. HIV and HBSAG
Chest X-ray and electrocardiogram were taken when required.

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The patients were explained about the epidural technique with catheter in situ and its advantages and disadvantages. Grading of post operative pain was done using Visual analog Scale(VAS).The patient would be asked to quantify their pain using VAS pain scale, giving a score of 0 to10, with 0- indicating no pain and 10 indicating the worst possible pain.

Written informed consent was obtained. All patients received premedication at 10p.m on the night before surgery with Tab. Alprazolam 0.25mg and Tab. Ranitidine 150mg and thereafter advised nil per oral.

Anaesthesia: Epidural anaesthesia technique was adopted for surgery of the lower abdomen for all patients. On the day of surgery patients were shifted to the operating room, and multiparameter monitors were connected. The base line heart rate, SpO2 and blood pressure (systolic, diastolic and MAP) were recorded. An 18G iv cannula was inserted and patients were preloaded with 10ml/kg of Ringer lactate over 15-30minutes prior to epidural block.The anaesthesia machine, airway equipment's and emergency drugs were kept ready.

Patients were positioned in right lateral decubitus posture. Observing sterile precautions L1-L2 space was identified. Skin was infiltrated with local anesthetic inj. 2% lignocaine 2ml. Epidural space was identified with an 18G Tuohys needle, by using loss of resistance to air technique and a 19G epidural catheter was inserted about 5cms into the epidural space and secured in place. Throughout the procedure patient's vitals were monitored. A test dose of 3ml of 1.5% lignocaine with adrenaline (1:2,00,000) was given to rule out intravascular or intrathecal placement of the catheter. The patient was made to lie supine. After confirming correct placement of the catheter, epidural anesthesia was activated using 18 ml bolus dose of 0.75% ropivacaine with 10 mg nalbuphine in RN group and 18 ml bolus of 0.75% ropivacaine with 2 mg butorphanol in RB group. Subsequent top up doses were given depending on the duration of surgery and intensity of pain. No intravenous analgesics or sedation were administered during the surgery.
Fluid management: The patients were infused and maintained with crystalloids and colloids. Blood was transfused only when indicated. The following observations were made.

Intraoperative:

- Onset of sensory blockade
- Onset & duration of motor blockade
- Duration of sensory analgesia
- BP monitoring (NIBP).
- Heart rate (HR).
- Respiratory rate (RR) and SpO2.

Postoperative:
VAS scores between the two groups.

Duration of surgery was also noted.

Onset of sensory blockade: is taken as the time from the completion of the injection of the study drug till loss of sensation at T10 level.

Onset of motor blockade: is taken from the completion of the injection of study drug till the patient develops modified Bromage scale grade 1 motor blockade.

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Duration of motor block: is taken from the time of injection till the patient attains complete motor recovery (Bromage 0).

Duration of sensory analgesia: The time interval between onset of analgesia (VAS score <5), till patient complained of pain (VAS score >5) when rescue medication was administered.

During intraoperative period, NIBP, HR, RR, and SpO2 were recorded before activating epidural anesthesia and subsequently at every 5 minutes till the end of the surgery.

After the surgery, the patients were shifted to recovery room and monitoring was continued. When patients recovered from motor blockade, they were shifted to post-operative ward.

Post-operative period: In the post-operative period, when the patients first complained of pain, intensity of pain was assessed using VAS scale. When the VAS score was >5, study drug was given through epidural catheter after confirming its proper position.

The intensity of pain and pain relief was assessed using VAS every hourly at 1 hr,2hrs up to 8 hrs postoperatively. As and when the patient complained of pain during the period of observation, intensity of pain was assessed again using VAS to know the effect of the study drug given earlier. If it was >5, an intramuscular non-opioid analgesic as per the institutionally approved protocol was given.
VAS consisted of a 10 cm line, marked at 1 cm each on which the patient makes a mark on the line that represents the intensity of pain he/she was experiencing. Mark "0" represents no pain and mark "10" represents worst possible pain. The numbers marked by the patient was taken as units of pain intensity.

Bradycardia was defined as fall of HR by 20% from the basal HR.

Hypotension was defined as a fall of systolic BP by 20% from basal systolic BP.

Statistical Analysis
After completion of the study, the results were compiled and statistically analyzed using Chi Square test for non-parametric data and ANOVA for parametric data. Post hoc students paired t test was applied wherever indicated using SSPS 22.0 software. We have used means and standard deviations to represent the average and typical spread of values of variables and median to represent various scores. p value of less than 0.05 was considered significant and less than 0.001 as highly significant.

RESULTS
Study of 60 patients was completed study successfully. Demographic profile and baseline hemodynamic parameters were comparable between two groups (Table 1).

Table 1: Comparison of demographic data and baseline parameters between two groups [mean ± SD]

Parameters	Group RN	Group RB	p value
Age (in years)	41.31 ±17.10	40.39 ± 16.98	0.89
Weight(kgs)	63.54 ± 9.69	64.61 ± 8.00	0.49

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Sex	**Male (n)**	18	14	0.89
	Female (n)	12	16	
Baseline HR (in bpm)		79.99 ± 6.029	81.15 ± 7.89	0.29
Baseline NIBP SBP/DBP (in mmhg)		114.64±12.35/74.64 ± 10.5	115.71±12.24/72.64 ± 9.25	0.63

Table 2: Comparison of block characteristics and post op analgesia between two groups [mean ± SD]

Parameters	Group RN	Group RB	P value
Time of onset of sensory block in mins	8.09±3.08	10.84±0.99	<0.001
Time of onset of motor block in mins	10.43±3.79	13.08±2.35	<0.001
Duration of motor block in mins	238.69±34.53	204.29±24.63	<0.001
Duration of sensory analgesia in mins	398.68±33.28	320.65±30.85	<0.001

Time of onset of sensory block was earlier in group RN than group RB (8.09±3.08 vs 10.84±0.99 mins) and this was significant between two groups ($p < 0.001$). Time of onset of motor block was earlier in group RN than group RB (10.43±3.79 vs13.08±2.35 mins) and this was also significant between two groups ($p < 0.001$). (Table 2).

Duration of sensory analgesia was significantly higher in group RN than group RB (398.68±33.28 vs. 320.65±30.85 min) ($p < 0.001$) (Table 2). Duration of motor block was more in group RN than group RB (238.69±34.53 vs. 204.29±24.63 min) and this was highly significant between two groups ($p < 0.001$) (Table 2).

Table 3: Comparison of mean heart rate (bpm) at different intervals between two groups [mean ± SD]

	Group RN	Group RB	P value
Time interval in mins			
Pre-op	79.99 ± 6.029	81.15 ± 7.89	0.29
5 min	77.34 ± 5.02	79.10 ± 6.28	0.34
10 min	76.24 ± 4.34	77.25 ± 4.10	0.75
15min	76.10 ± 3.10	76.23 ± 5.10	0.45
30 min	75.12 ± 4.02	75.45 ± 6.89	0.12
45 min	72.89 ± 5.30	71.85 ± 4.50	0.33
60 min	71.80 ± 3.30	70.15 ± 5.50	0.07
75 min	70.29 ± 4.30	69.91 ± 4.83	0.12
90 min	70.18± 3.45	69.15 ± 4.40	0.11
105 min	71.68 ± 4.56	71.15 ± 5.55	0.42
120 min	70.79 ± 5.05	70.25 ± 7.29	0.07

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Table 4: Comparison of mean arterial pressure (mmhg) at different intervals between two groups [mean ± SD]

	Group RN	Group RB	P value
Time interval in mins			
Pre-op	92.74 ±4.45	91.55 ±3.20	0.38
5 min	89.56 ±3.44	89.45 ±3.14	0.66
10 min	87.68 ±5.20	88.64 ±4.20	0.38
15min	85.89 ±3.66	84.89 ±2.66	0.27
30 min	83.50 ±2.88	84.30 ±3.88	0.29
45 min	82.22 ±4.77	82.15 ±4.71	0.07
60 min	81.38 ±3.80	80.20 ±4.82	0.24
75 min	80.44 ±3.56	80.22 ±5.24	0.36
90 min	80.69 ±3.78	80.77 ±3.50	0.46
105 min	80.19 ±4.10	79.65 ±5.50	0.98
120 min	80.20 ±3.20	79.48±2.24	0.28

Intra-operative and postoperative hemodynamic parameters were comparable between two groups.

Table 6: The Mean Post-Operative Pain Scores(VAS) At different intervals between RN & RB groups[mean ± SD]:

Time interval in hours	Group RN	Group RB	P value
1	0.14 ±6.45	0.94 ±5.40	<0.05
2	0.56 ±3.32	1.58 ±2.44	<0.05
3	0.88 ±4.20	2.10 ±4.24	<0.05
4	1.89 ±3.40	3.59 ±4.66	<0.05
5	2.80 ±3.88	3.8 ±2.20	<0.05
6	3.50 ±3.75	4.32 ±5.2	<0.05
7	4.38 ±2.80	5.45 ±2.78	<0.05
8	5.24 ±2.88	6.44 ±3.87	<0.05

Group RN showed lesser VAS scores compared to Group RB for a significant longer duration of time**.**

Table 5: Comparison of side effects between groups

Parameters	Group RN		Group RB		p value
	No.	%	No.	%	
Bradycardia	3	10%	4	13.33%	0.73
Hypotension	6	20%	7	23.33%	
Nausea	2	6.6%	3	10%	
Sedation	3	10%	3	10%	
Shivering	2	6.6%	4	13.33%	

The observed side effects included bradycardia, hypotension, nausea and vomiting, sedation and shivering were comparable between the two groups (Table 5).

DISCUSSION

Opioids are being extensively used as adjuvants to local anaesthetics to improve the quality of the block and to produce dose-sparing effect. Epidural administration of various analgesics

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 01, 2023

have gained popularity following the discovery of opioid receptors in the spinal cord. The use of epidural techniques also offer the advantage of post-operative analgesia. There are a number of studies to prove the efficacy of adding opioids to local anaesthetics. Opioid receptors are found to be highly specific receptors located in specific regions of central nervous system and peripheral nervous system. The opioid receptors located in the dorsal horn of spinal cord mediate both pre and post synaptic effects modulating the nociceptive input without sensory or motor blockade. Epidural administration of opioids have found to be superior than intravenous or intramuscular injection of opioids.

Effective post-operative epidural analgesia with local anesthetic drug combined with opioids has reduced the incidence of cardiac and pulmonary morbidity and mortality in majority of patients undergoing major abdominal surgery.

Butorphanol, a mixed opioid agonist/antagonist, acts as a mu (μ) agonist/antagonist and kappa agonist, produces effective analgesia, associated with fewer side effects and also low abuse potential. Its high lipid solubility and high affinity for opioid receptors are other factors that contribute to lesser 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 sedation. It commonly finds its place in clinical practice as it has a ceiling effect on respiratory depression.

In the present study we compared the efficacy of analgesic effect of epidural 0.75% ropivacaine with 10mg nalbuphine and 0.75% ropivacaine with 2mg butorphanol in patients posted for lower abdomen surgeries under epidural anesthesia in intraoperative and post operative period.

Time of onset of sensory block was earlier in group RN than group RB(8.09±3.08 vs 10.84±0.99 mins)and this was significant between two groups ($p < 0.001$). Time of onset of motor block was earlier in group RN than group RB(10.43±3.79 vs13.08±2.35 mins) and this was also significant between two groups ($p < 0.001$).

Duration of sensory analgesia was significantly higher in group RN than group RB (398.68±33.28 vs. 320.65±30.85 min) ($p < 0.001$) (Table 2). Duration of motor block was more in group RN than group RB (238.69±34.53 vs. 204.29±24.63 min) and this was highly significant between two groups ($p < 0.001$) (Table 2).

Intra-operative and postoperative hemodynamic parameters were comparable between two groups. Group RN showed lesser VAS scores compared to Group RB for a significant longer duration of time. Side effects included bradycardia, hypotension, nausea and vomiting, sedation and shivering were comparable between the two groups

Hala Mostafa Gomaa found that an intrathecal adjuvant of nalbuphine 0.8mg to hyperbaric bupivacaine for cesarean delivery intensified postoperative analgesia compared to fentanyl with hyperbaric bupivacaine . [15] Swarna Banerjee concluded that addition of nalbuphine 10 mg to 0.125% hyperbaric Bupivacaine prolonged duration of postop analgesia compared to Butorphanol with 0.125% bupivacaine. [16]

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Veena Chatrath. found that 10mg nalbuphine as epidural adjuvant to 0.25% bupivacaine has significant larger duration of analgesia compared to 100mg tramadol.[17] Oinam Bisu Singh demonstrated that nalbuphine as epidural adjuvant to ropivacaine had prolonged duration of postoperative analgesia for more than 6 hours.[18] Babu S found that addition of nalbuphine as epidural adjuvant to ropivacaine has duration of analgesia for more than 6 hours. [19] The above observations were similar to our study results. Hence, we conclude that nalbuphine has an advantage of prolonged duration of perioperative analgesia when used as adjuvant to ropivacaine compared to butorphanol for epidural postop analgesia at equipotent doses.

CONCLUSION

Nalbuphine as an epidural adjuvant to ropivacaine provides better intraoperative as well as postoperative analgesia compared to butorphanol. Hence nalbuphine can be used with local anesthetics for providing safe ,effective and reliable epidural anesthesia for perioperative pain relief.

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