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Original research article

Epidural Analgesia After Abdominal Surgery: A Comparative Study of Levobupivacaine 0.1% Versus Ropivacaine 0.1% Combined with Fentanyl

Dr. Garima Gaurav[1], Dr. Kumar Akash[2], Dr. H.D. Singh[3]

[1]Senior Resident, Department of Anaesthesiology. DMCH Darbhanga

[2]Ex Senior Resident, Department of Surgery, DMCH Darbhanga

[3]Associate Prof. & Head. Department of Anaesthesiology. DMCH Darbhanga

Corresponding Author: Dr. Kumar Akash

Abstract

Background: Levobupivacaine and Ropivacaine are pure S (-) Enantiomer of Bupivacaine. Both these new local anesthetics have the advantage of lower degree of motor blockade, lesser cardio toxicity, thus making them a safer alternative to Bupivacaine. Fentanyl has been used commonly with Levobupivacaine and Ropivacaine for further improvement in analgesia without intensifying adverse effects.

Methodology: All sixty patients after appropriate premedication and insertion of epidural catheter were allowed to undergo scheduled surgery under general anesthesiaand extubated at the end of surgery. They were randomly allocated in to two groups to receive postoperative epidural infusion of either Levobupivacaine 0.1% with Fentanyl 2 g/ml or Ropivacaine 0.1% with fentanyl 2 g/ml for 48 hours. The efficacy was compared in terms of onset, quality of analgesia and residual motor blockade and any other adverse events.

Results: Pain scores were similar between the two groups. Mean VAS scores were consistently below 4 throughout the study period with no significant residual motor blockade($p>0.05$). There was no significant hemodynamic changes and adverseeffects between the two groups.

Conclusion: The study concludes that both local anesthetics in combination withfentanyl provided satisfactory analgesia with minimal adverse effects.

Keywords: Levobupivacaine, Ropivacaine, Fentanyl, Epidural analgesia.

Introduction

Optimal dynamic pain relief after major abdominal surgery is a prerequisite for early postoperative recovery and rehabilitation. Epidural anesthetic techniqueimproves the surgical outcome by reducing the central sensitization, pain-induced surgical stress response and subsequently organ dysfunction.[1] Low concentration ofan epidural local aesthetic agent alone or more commonly in combination with epidural opioids, provides adequate analgesia, also minimizes individual doses of each drug and their adverse effects than when used alone.[2] Epidural infusion of racemic bupivacaine is most commonly used for postoperative analgesia.

Addition of epidural opioids such as fentanyl provides better pain relief than bupivacaine alone. Bupivacaine is a racemic mixture of R(+) and S(-) enantiomers. Increased affinity of R(+) enantiomer to sodium channels of neural and cardiac tissues accounts for its greater toxicity.[3] Ropivacaine is an amino amide local anesthetic introduced in 1957, a pure S(-)enantiomer, with additional properties such as long duration of action, less cardiotoxicity and greater sensory-motor separation when compared to racemic bupivacaine.[4] Epidural Ropivacaine in concentrations less than 0.2% in combination with epidural opioids such as fentanyl have been studied and found to have better postoperative analgesia and reduced incidence of motor blockade.[5] Levobupivacaine, S(-) enantiomer – stereoisomer form of racemic bupivacaine, an amide local anesthetic with better safety profile in terms of decreased cardiac toxicity, a favorable sensory-motor blockade ratio was introduced and foundto have less adverse effects compared to racemic bupivacaine.[6] In terms of onset time of action, duration of sensory and motor blockade and dermatomal spread, Levobupivacaine has comparable clinical efficacy to racemic bupivacaine. By addition of epidural opioids to lower concentration of epidural Levobupivacaine, adequate analgesia without motor blockade can be achieved.[7] The concentration of local anesthetics used for epidural analgesia can be reduced by the addition of small dose of an epidural opioid. Thus smaller concentrations of epidural Ropivacaine or Levobupivacaine solutions combined with opioids (morphine or fentanyl) provides effective postoperative analgesia and also reduces the incidence of undesired motor blockade.[8] Making a decision on choice of drug to achieve an adequate level of pain relief, providing effective analgesia as well as early mobilization and rapid recovery are the daily challenges for most of the anesthesiologists. Combination of local anesthetic-opioid for epidural infusion is the most commonly used epidural technique for post-operative analgesia.[9]

Objectives

To compare the clinical efficacy of the postoperative epidural analgesia withlevobupivacaine 0.1% and ropivacaine 0.1% with fentanyl 2g/ml. To study the adverse effects of epidural ropivacaine 0.1% and levobupivacaine 0.1%,both combined with fentanyl 2g/ml.

Review of Literature

Kehlet *et al*., (2001) reviewed data from various randomized controlled trials on different modalities of analgesic techniques for postoperative analgesia such as patient controlled analgesia(PCA), nonsteroidal anti-inflammatory drugs, epidural techniques and also surgical outcome and morbidities with each technique. They found that epidural analgesic techniques were most effective in reducing the postoperative morbidity by blunting the surgical stress response, autonomic reflex response and subsequently the organ dysfunction. They concluded that, continuous epidural analgesia with local anaesthetic alone or in combination with epidural opioids reduces postoperative pulmonary morbidity, cardiac morbidity, thromboembolic complications as well as paralytic ileus and thus influences postoperative recovery and rehabilitation.[1] Wheatley *et al*., (2001) in a review article based on a computerized search of literature from 1976 to 2000 on safety and efficacy of postoperative epidural analgesia, documented multiple factors for effective as well as safe epidural techniques. They found that efficacy of epidural analgesia depends on choice of the local anesthetic as well as opioids, whether used alone or in combination, site of insertion of the catheter in relation to surgical site and method of drug delivery. They also mentioned about the associated complications which are of major concerns such as, serious neurological complications, dural puncture, direct trauma to spinal cord, transient neuropathy, spinal hematoma, catheter migration, risk of infection and drug errors, CNS and cardiovascular toxicities.[9] Scott *et al*.,(1995) studied epidural infusion of Bupivacaine with Fentanyl for postoperative analgesia in 1016 patients undergoing major abdominal surgery and reported incidence of side effects such as sedation,

nausea, vomiting, pruritus and respiratory depression attributed to epidural opioids and lower limb motor blockade (3.0%), hypotension (6.6%) associated with use of epidural local anesthetic. They concluded that epidural bupivacaine with fentanyl provides adequate postoperative analgesia and requires careful monitoring in postoperative surgical units.[3] Schug *et al*.,(1996) undertook a study to find out the optimal dose of epidural Ropivacaine for postoperative analgesia . In their prospective randomized double blind study involving 36 ASA I-III patients undergoing upper abdominal surgery, they studied the effect of continuous extra dural infusion of 3 different concentrations of Ropivacaine (0.1%,0.2% and 0.3%) on postoperative analgesia. Patients also had access to i.v. PCA Morphine. They found that Ropivacaine group consumed less Morphine compared to saline group over 21-hour infusion period and motor blockade was negligible. They concluded that patient satisfaction was higher in 0.2% and 0.3% Ropivacaine group than in the other two groups.[10] Etches *et al*.,(1997) in a prospective randomized double blind study involving 125 patients studied lumbar epidural infusion of 0.2% Ropivacaine 6,8,12,14 ml/hour following lower abdominal surgery for effective analgesia, incidence of motor blockade and also adverse effects with epidural infusion. Patients had availability of PCA Morphine for supplemental analgesia. They found that Morphine consumption was less in 10 & 12,14 ml infusion groups when compared with saline groups. They concluded that though Ropivacaine 0.2% epidural infusion reduced parenteral consumption of Morphine, it has minimal effect on pain scores and is associated with significant motor blockade.[11] Scott *et al*., (1999) in their study compared the analgesic effectiveness and side effects of epidural infusions with Ropivacaine 2 mg/mL alone and in combination with Fentanyl. It was a prospective, randomized, double-blinded study. 259 patients undergoing major abdominal surgery were randomized into four groups, to receive Ropivacaine 2 mg/mL alone, and in combination with Fentanyl 1 μg/mL, 2 μg/mL, and 4 μg/ml for up to 72 hours and found that hypotension, nausea, and pruritus were more common with the larger dose of Fentanyl. They concluded that epidural infusion of Ropivacaine 2 mg/mL with Fentanyl 4 μg/mL was most effective.[12]

Material and methods

This prospective, randomized, double blind study was designed to compare local anesthetics combined with opioid in epidural anesthesia for abdominal surgery. After obtaining institutional ethics committee approval and written, informed consent from 60 patients admitted at Darbhanga medical college and Hospital, Lahaeriasarai, Biahr. The study duration of Two years. scheduled for major abdominal surgery belonging to ASA physical status I and III of either sex agedbetween 18 to 75 years, were studied.

Inclusion criteria

Patients posted for elective upper and lower abdominal surgery under generalanesthesia.
Age between 18 to 75 years of either sex. Written informed consent. ASA physical status between I and III.

Exclusion criteria

Emergency surgeries, Known hypersensitivity to amide local anesthetics.
History of active neurological, cardiac, respiratory and renal diseases. Blood dyscrasia, clotting disorders and platelet count <100000 mm^3. Patients with cutaneous infections or anatomical malformation of the spine. Weight > 100 kilograms, height <150cms or >185cms and age > 75 years.
A detailed history and pre anesthetic evaluation was done on the first visit before the surgery. Routine investigations like hemoglobin, blood grouping and typing, blood urea, serum creatinine, blood sugar and platelet count, coagulation test were done. Electrocardiogram

(ECG) and chest X ray whenever indicated was takento rule out the presence of any active cardiac disease. Preoperative vital parameters such as pulse rate, respiratory rate and blood pressure values were noted. The day before surgery, written, informed consent was obtained from all the patients. They received verbal instructions regarding the nature of study and they were familiarized with a 10 cm visual analogue scale (VAS) device for pain intensity assessment. Patients were kept nil oral for at least 6 hours before the day of surgery. All the patients were premedicated with Diazepam 0.1mg/kg on the night before surgery. Patients were shifted to the operation theatre and pulse oximeter, non-invasive blood pressure and electrocardiography monitors were connected. Baseline parameters like heart rate, oxygen saturation (SpO_2) and non- invasive blood pressure were recorded. General anesthesia was induced with propofol 1-2mg/kg body weight i.v. Oro tracheal intubation was facilitated with vecuronium 0.1 mg/kg body weight. Fentanyl up to 2µg/kg i.v. was used for intraoperative analgesia. Adequate intraoperative muscle relaxation obtained with vecuronium. Isoflurane was delivered with oxygen and nitrous oxide for maintenance of depth of anesthesia and lungs were mechanicallyventilated. General anesthesia was maintained till the end of surgery, patient were reversed with neostigmine 0.05mg/kg i.v. glycopyrrolate 0.01mg/kg i.v. and were allowed to emerge from general anesthesia and then extubated when they met the clinical criteria. Hemodynamic parameters like HR, SBP, DBP and MAP was analyzed using ANOVA. Sensory and motor block characteristics were analyzed with t-test. Chi square test was used to analyze the peak sensory level attained adverse effects between the two groups.

$p < 0.01$ statistically highly significant ($p < 0.01$)
$p < 0.05$ statistically significant ($*p < 0.05$)
$p > 0.05$ statistically not significant ($p > 0.05$)

Results

Sixty patients, who underwent elective abdominal surgery at Darbhanga medical college and Hospital, Laheriasarai. were randomly assigned into 2 groups. No cases had accidental dural puncture during the procedure. No difference was observed in the duration of surgery and management of general anesthesia. At the time of surgery, all patients received same amount of analgesic, i.e., i.v. fentanyl. The epidural catheter was inserted at T7-T9 level for upper abdominal surgery and T9-T11 level for lower abdominal surgery. None of the patients had surgical complications during or following the surgery.

Group 1- Levobupivacaine 0.1%. with fentanyl 2g/ml epidural
Group 2- Ropivacaine 0.1% with fentanyl 2g/ml epidural

Table 1: Demographic data

	Group 1(N=30)	Group 2(N=30)	P Value
Age (yrs)	51.53□11.92	51.4□12.29	0.966
Height (Cms)	155.03□5.014	155.47□3.674	0.704
Weight (Kgs)	56.03□7.708	57.33□5.215	0.447
Male/Female Ratio	6/24	7/23	0.754

Values are in mean SD

Table 2: Max sensory level achieved

	Group	

		Group 1	Group 2	Total
max sensorylevel	T10	6 20.0%	5 16.7%	11 18.3%
	T6	8 26.7%	10 33.3%	18 30.0%
	T8	15 50.0%	15 50.0%	30 50.0%
	T9	1 3.3%	0 .0%	1 1.7%
Total		30 100.0%	30 100.0%	60 100.0%

Values are number of patients in (%).

Table 3: Residual motor blockade at 24.00 hours between the two groups.

Residual MotorBlockade	Group 1 (n=30)	Group 2 (n=30)	P Value
0	29 (96.7%)	29 (96.7%)	0.368
1	0 (0.00%)	1 (3.3%)	
2	1 (3.30%)	0 (0.00%)	
3	0 (0.00%)	0 (0.00%)	

Values are in number of patients in (%)

Table 4: Residual motor blockade at 48.00 hours between the two groups.

Residual MotorBlockade	Group 1 (n=30)	Group 2 (n=30)	P Value
0	29 (96.7%)	30(100%)	0.313
1	0 (0.00%)	0 (0.00%)	
2	1 (3.30%)	0 (0.00%)	
3	0 (0.00%)	0 (0.00%)	

Values are in number of patients in (%)
Two patient had residual motor blockade in Group 1 at 4 hours compared to 3 patientsin group 2. However, no patients had residual motor blockade at 24 and 48 hours in Group 2 where as one patient had residual motor blockade at similar rime interval in Group 1. But, there is no statistically significant difference in the residual motor blockade at various time interval between the two groups.

Table 5: Adverse events

Adverse events	Group 1 (n=30)	Group 2 (n= 30)	P Value
Nausea & Vomiting	1 (3.33%)	1 (3.33%)	1.000
Hypotension	0 (0%)	3 (10%)	0.092
Pruritus	0 (0%)	0 (0%)	0
Resp depression	0 (0%)	0 (0%)	0

Table 6: Adverse events

	p value
Nausea& vomiting	1.000

Hypotension	0.092
Resp Depression	0
Pruritus	0

here is no statistically significant difference between the two groups among theoccurrence of adverse events.

Discussion

Epidural analgesia is one of the most effective regimen for postoperative analgesia.[13] Epidural local anesthetic or combined local anesthetic-opioid techniques are the most effective technique for providing dynamic pain relief after major surgical procedures.[1] Continuous epidural local anesthetics alone or in combination with opioids have been demonstrated to reduce postoperative pulmonary and cardiac morbidity, risk of thromboembolic episodes and gastrointestinal complications, facilitates early mobilization and shorter duration of hospital stay following various major thoracic, abdominal and lower body procedures.[1,3] Levobupivacaine, the S(-) enantiomer of racemic bupivacaine with less undesirable side effects on cardiac and central nervous system has emerged as an alternative to bupivacaine. Ropivacaine, another pure S(-)enantiomer of bupivacaine with additional characteristic such as lower incidence of motor blockade, reduced cardiac and neurotoxicity make it an attractive alternative long acting local anesthetic agent for postoperative epidural analgesia.[14] Addition of an opioid to epidural local anesthetic agent may affect its analgesic potency and duration of action,in fact displaying a synergistic action.[15] The main goals of postoperative analgesia in major abdominal surgeries alongwith good analgesia, are no or minimal motor blockade for early ambulation and minimal need for rescue opioids and other analgesics along with permissible adverse effects. [11] This prospective, randomized, double-blinded study has shown that, there were no significant difference in onset, analgesic quality, residual motor blockade, along with similar hemodynamic changes and minimal adverse effects between epidural levobupivacaine 0.1% or ropivacaine 0.1%, both combined with fentanyl 2g/ml in postoperative patients who underwent major abdominal surgery. The quality of analgesia was satisfactory without significant motor blockade and adverse effects in both the groups. Demographic data with respect to age, sex distribution, height and weight of the patients were comparable in both groups and there was no statistically significant difference among the groups. The onset time of sensory block was ranging between 6 to 14 minutes with a mean value of 11 minutes at T8 level in majority of the patients of both the groups. All the patients achieved adequate level of blockade appropriate for surgical procedure and none of the patients were excluded in our study due to inadequate blockade. Patients reported similar pain scores in both the groups till 48 hours of postoperative period. In contrast, Schug et al.[10] demonstrated that continuous extradural infusion of 0.1%, 0.2% and 0.3% ropivacaine after abdominal surgery resulted in lower VAS scores, negligible motor blockade. However, they reported less patient satisfaction with 0.1% ropivacaine and more consumption of i.v. PCA morphine in this group compared to other two groups. Scott et al.[12] suggested 4g/ml fentanyl for epidural infusion for effective postoperative analgesia along with ropivacaine, In our study, we did not find any statistically significant difference between levobupivacaine and ropivacaine group in motor blockade. Among both the groups, one patient had residual motor blockade with Bromage score of 1 in Ropivacaine group and 2 in the levobupivacaine group from the beginning of epidural infusion till the end of first twenty-four hours. However, Bromage score two block was present at the end of 48 hours in the same patient in levobupivacaine group but was statistically insignificant. This findings correlates well with Pouzeratte et al.[16] They noticed that there was no significant difference between Ropivacaine 0.125% and Sufentanyl

and Ropivacaine 0.2% groups in the occurrence of motor blockade in spite of using higher concentration of Ropivacaine in comparison to our study. Nausea and vomiting were the other adverse events noted in our study. We noticed one patient (3.33%) in each group with no statistical significance($p>0.05$). There was no incidence of respiratory depression and pruritus in both the groups. Limitations of our study might be the relative low sample size. Especially the variations in hemodynamic parameters and the frequency of adverse effects could have altered if studied on a large group. In addition, even though VAS scores show nodifference between the two groups, the study would have been further enhanced by employing an additional questionnaire on patient satisfaction with postoperative pain relief.

Conclusion

continuous epidural infusion of Levobupivacaine 0.1% and Ropivacaine 0.1%, both combined with fentanyl 2g/ml in major abdominal surgery provides satisfactory postoperative analgesia in the concentrations used along with minimal or no adverse effects. Hence we conclude that, these drugs can be used as a safer alternative to Bupivacaine for postoperative epidural analgesia in major abdominal surgery.

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