http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v8i12.16

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

A Comparative Study of Post Operative Analgesic Efficacy of Levobupivacaine 0.1% versus Ropivacaine 0.1% Combined with Fentanyl under Epidural for Abdominal Surgeries

Authors
Arun Kumar P[1*], Kalyan Chakravarthy P[2], Pradeep Kumar Das[3], Preethi Vaddi[4]
[1]Postgraduate, Department of Anaesthesiology, GEMS.
[2]Professor &HOD Department of Anaesthesiology, GEMS
[3]Assistant Professor, Department of Anaesthesiology, GEMS
[4]Senior resident, GEMS
*Corresponding Author
Arunkumar P.
Postgraduate, Department of Anaesthesiology, GEMS

Abstract
Background: *Levobupivacaine and Ropivacaine are pure S (-) Enantiomer of Bupivacaine. Both these new local anaesthetics 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. In our study we compare the clinical efficacy and adverse effects of epidural Levobupivacaine with Ropivacaine both combined with Fentanyl following major abdominal surgery.*
Methodology: *All sixty patients after appropriate premedication and insertion of epidural catheter were allowed to undergo scheduled surgery under general anesthesia and 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 µg/ml or Ropivacaine 0.1% with fentanyl 2 µg/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 adverse effects between the two groups.*
Conclusion: *the study concludes that both local anaesthetics in combination with fentanyl provided satisfactory analgesia with minimal adverse effects.*
Keywords: *Epidural, Levobupivacaine, Ropivacaine, Fentanyl.*

Introduction

Optimal dynamic pain relief after major abdominal surgery is a prerequisite for early postoperative recovery and rehabilitation. Epidural anaesthetic technique improves the surgical outcome by reducing the central sensitization, pain-induced surgical stress response and subsequently organ dysfunction.[1]

Low concentration of an epidural local anaesthetic 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.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 anaesthetic 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 found to have better postoperative analgesia and reduced incidence of motor blockade.[5]

Levobupivacaine, S(-) enantiomer – stereoisomer form of racemic bupivacaine, an amide local anaesthetic with better safety profile in terms of decreased cardiac toxicity, a favourable sensory-motor blockade ratio was introduced and found to have less adverse effects compared to racemic bupivacaine.[6]

In terms of onset of 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 anaesthetics 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]

Combination of local anaesthetic-opioid for epidural infusion is the most commonly used epidural technique for post-operative analgesia.[9]

Hence the present study was undertaken to compare the clinical efficacy of epidural Levobupivacaine 0.1% and Ropivacaine 0.1% both combined with fentanyl in patients undergoing elective intra-abdominal surgery

Material and Methods

This prospective, randomized, double blind study was designed to compare local anaesthetics combined with opioid in epidural anaesthesia for abdominal surgery. After obtaining institutional ethics committee approval and written, informed consent from 60 patients admitted at Great Eastern Medical School and Hospital scheduled for major abdominal surgery belonging to ASA physical status I and III of either sex aged between 18 to 65 years, were studied. The duration of the study was 6 months.

Inclusion Criteria

1) Patients posted for elective upper and lower abdominal surgery under general anaesthesia.
2) Age between 18 to 65 years of either sex.
3) Written informed consent.
4) ASA physical status between I and III.

Exclusion Criteria

1) Emergency surgeries
2) Known hypersensitivity to local anaesthetics.
3) History of active neurological, cardiac, respiratory and renal diseases.
4) Blood dyscrasia, clotting disorders and platelet count 100 kilograms, height 185cms and age >65 years.

Preoperative Assessment and Premedication

Every patient underwent a pre-anaesthetic check-up a day before surgery, including a detailed history, complete general physical and systemic examination, and relevant investigations.

All the patients were educated about the 10 points visual analogue pain scale (VAPS) at the preoperative visit (0 – no pain, 10 – worst imaginable pain). All patients received adequate

fasting orders preoperatively according to the surgery planned.

Study Method

The patient was shifted to the operating room. 18G IV cannula was secured. IV fluids were connected. Monitors such as ECG, pulse oximetry, NIBP were connected. Baseline values were noted.

The patients were positioned in the sitting position. Under strict aseptic conditions, the epidural space was identified at the L2-3 or L3-4 space using a loss of resistance to air technique using an 18G Tuohy needle. A 20 G catheter was then advanced into the epidural space for 5cm. A standard test dose of 2-3 ml of 2% lignocaine with adrenaline was given to verify the catheter's correct placement. Then the patient received the appropriate study drug epidurally, slowly over 5 minutes.

General anaesthesia was induced with propofol 1-2mg/kg body weight iv. 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.

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

The initial bolus dose and the subsequent infusion dose was calculated on the basis of height of the patient as follows:- -

-<160cm-8ml

- 160-170 cm-12ml

->170cm-15ml

Observations and Results

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

The demographic data of two groups are listed in table 1, which shows that there was no significant difference in the two groups (p>0.05) with respect to age, sex, weight and height.

Table 2: Max sensory level achieved

		Group		Total
		Group 1	Group 2	
Max sensory level	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 0.0%	1 1.7%
Total		30 100.0%	30 100.0%	60 100.0%

Maximum level of sensory block attained between the groups is shown in Table 2.

Among 60 patients, 30 patients (50%) had sensory block at T8, 18 patients had sensory block at T6, 11 patients had sensory block till T10 and one patient had sensory block tillT9.

Visual Analogue scale score at different time intervals between the two groups

Time interval	Group 1 (n=30)	Group 2 (n=30)	P Value
0 hours	5.33±1.918	5.17±1.510	0.710
4 hours	3.60±1.192	3.80±0.551	0.408
8 hours	3.30±1.022	3.57±0.626	0.228
12 hours	3.30±0.915	3.50±0.572	0.314
16 hours	3.17±0.834	3.53±0.730	0.075
20 hours	3.23±0.971	3.37±0.556	0.517
24 hours	3.23±1.006	3.47±0.730	0.308
28 hours	3.10±0.845	3.40±0.770	0.156
32 hours	3.10±0.845	3.37±0.765	0.205
36 hours	3.03±0.805	3.37±0.765	0.116
40 hours	3.33±1.398	3.27±0.583	0.810
44 hours	3.17±0.913	3.30±0.596	0.506
48 hours	3.17±0.913	3.27±0.583	0.615

VAS scores were higher among Group 2 compared to Group 1 at different time intervals but was statistically insignificant.

Table 5: Residual motor blockade at 24.00 hours between the two groups

Residual motor blockade	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%)	

Table 6: Residual motor blockade at 48.00 hours between the two groups

Residual motor blockade	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%)	

Two patient had residual motor blockade in Group 1 at 4 hours compared to 3 patients in 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 7: Systolic blood pressure at different time intervals between the two groups

Time interval	Group 1 (n=30)	Group 2 (n= 30)	P Value
0 Hours	137±22.96	130±18.92	0.182
4 Hours	121.33±24.179	111.67±24.927	0.133
8 Hours	123±20.123	115.80±18.891	0.111
12 Hours	117.33±24.464	112.37±26.534	0.454
16 Hours	122.07±20.185	115.37±18.440	0.185
20 Hours	121.97±19.168	108.77±33.256	0.065
24 Hours	122.00±15.803	113.07±27.428	0.128
28 Hours	118.70±23.486	116.67±17.450	0.705
32 Hours	118.47±26.452	115.93±17.422	0.663
36 Hours	124.13±17.815	118.33±17.167	0.204
40 Hours	124.27±17.512	118.37±18.068	0.204
44 Hours	124.57±16.952	148.23±16.418	0.428
48 Hours	124.37±16.134	119.43±16.821	0.251

Overall, the mean systolic blood pressure was on the lower side in Group 2 in comparison with Group 1 at different time intervals, but was statistically insignificant

Table 8: Heart rate at different time intervals between the two groups

Time interval	Group 1 (n=30)	Group 2 (n= 30)	P Value
0 Hours	91.83±15.347	84.10±11.917	0.033#
4 Hours	89.23±15.099	107.13±12.63	0.446
8 Hours	86.03±12.634	76.47±21.471	0.040#
12 Hours	84.27±11.154	75.47±21.855	0.054#
16 Hours	84.50±11.599	80.90±8.946	0.183
20 Hours	83.70±10.551	80.13±9.902	0.182
24 Hours	82.33±11.321	79.93±8.956	0.366
28 Hours	82.70±11.689	78.90±15.302	0.284
32 Hours	83.17±10.544	77.83±16.989	0.149
36 Hours	83.17±11.706	80.00±8.404	0.234
40 Hours	83.70±10.790	80.07±7.978	0.143
44 Hours	82.50±10.075	80.80±9.076	0.495
48 Hours	80.90±7.928	80.90±7.928	0.226

The mean heart rate was significantly ($p<0.005$) lower in Group 2 than group 1 at 0, 8 and 12 hours interval. There is no statistically significant difference in mean heart rate between the two groups other time intervals. None of the patients required Atropine for bradycardia.

Table 9: Adverse events

Adverse events	Group1	Group 2	P value
Nausea& vomiting	1(3.33%)	1(3.33%)	1.000
hypotension	0(0%)	3(10%)	0.092
pruritis	0(0%)	0(0%)	0
Resp depression	0(0%)	0(0%)	0

There is no statistically significant difference between the two groups among the occurrence of adverse events.

Discussion

Epidural analgesia is one of the most effective regimen for postoperative analgesia. Epidural local anaesthetic or combined local anaesthetic-opioid techniques are the most effective technique for providing dynamic pain relief after major surgical procedures. 1

Continuous epidural local anaesthetics 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.[(10)] 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 anaesthetic agent for postoperative epidural analgesia.[(11)] Addition of an opioid to epidural local anaesthetic agent may affect its analgesic potency and duration of action, in fact displaying a synergistic action.

The main goals of postoperative analgesia in major abdominal surgeries along with 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.[12]

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 2µg/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.

The mean VAS score was less than 4 throughout the study period in both the groups which was similar to the findings of Senard and colleagues8 who found no difference between ropivacaine 0.1% and levobupivacaine 0.1% with added background morphine infusion over 48-hour period except fewer patients who experienced motor weakness in ropivacaine group. Pouzeratte et al.have demonstrated that addition of sufentanyl 0.5µg/ml to epidural Ropivacaine 0.125% provides better postoperative analgesia in abdominal surgery than Ropivacaine 0.2% alone. They concluded that combination of Ropivacaine and Sufentanyl group as more effective in postoperative analgesia. However this study differed from the present study with respect to use of higher concentration of local anaesthetics in both the groups as well as use of sufentanyl for combination with Ropivacaine.

In a similar study by Smet et al. 30 in patients undergoing total hip or knee replacement surgery using patient controlled epidural analgesia with ropivacaine 0.165% or levobupivacaine 0.125% for postoperative analgesia and found satisfactory analgesia with both local anesthetics but they found consumption of higher volumes in the ropivacaine group despite its higher concentration. They suggested use of lower concentration of ropivacaine as unwise as it could increase the total opiate dose consumed due to higher patient demand.

Heart rate and systolic blood pressure remained stable and were comparable between the two groups in the 48hour postoperative period. The results obtained are comparable to previous studies where the incidence of hypotension was infrequent.

However, in our study, there was significant reduction in heart rate ($p<0.05$) in the Ropivacaine group at 0, 8 and 12 hours after the epidural infusion. There was no incidence of bradycardia in the two groups. One incidence of hypotension was reported in both the groups which responded well to crystalloid infusion. The lower concentration of local anaesthetic usage could be the reason for less incidence of hypotension.

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.

Conclusion

In conclusion, continuous epidural infusion of Levobupivacaine 0.1% and Ropivacaine 0.1%, both combined with fentanyl 2µg/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.

References

1. Kehlet H, Holte K. Effect of postoperative analgesia on surgical outcome. Br J Anaesth 2001; 87: 62-72.
2. Jayr C, Beaussier M, Gustafsson U, et al. Continuous epidural infusion of ropivacaine for postoperative analgesia after major abdominal surgery: comparative study with

i.v. PCA morphine. Br J Anaesth 1998; 81: 887-92.
3. Scott DA, Beilby DS, McClymont C. Postoperative analgesia using epidural infusions of fentanyl with bupivacaine. A prospective analysis of 1,014 patients. Anesthesiology 1995; 83: 727-37.
4. McClure JH. Ropivacaine. Br J Anaesth 1996; 76: 300-7. Review.
5. Liu SS, Moore JM, Luo AM, Trautman WJ, Carpenter RL. Comparison of three solutions of ropivacaine/fentanyl for postoperative patient-controlled epidural analgesia. Anesthesiology 1999; 90: 727-33.
6. Casimiro C, Rodrigo J, Mendiola MA, Rey F, Barrios A, Gilsanz F. Levobupivacaine plus fentanyl versus racemic bupivacaine plus fentanyl in epidural anesthesia for lower limb surgery. Minerva Anestesiol 2008; 74: 381-91.
7. Murdoch JA, Dickson UK, Wilson PA, Berman JS, Gad-Elrab RR, Scott NB. The efficacy and safety of three concentrations of levobupivacaine administered as a continuous epidural infusion in patients undergoing orthopedic surgery. Anesth Analg 2002; 94: 438-44.
8. Senard M, Kaba A, Jacquemin MJ, et al. Epidural levobupivacaine 0.1% or ropivacaine 0.1% combined with morphine provides comparable analgesia after abdominal surgery. AnesthAnalg 2004; 98(2): 389-94. 67.
9. Wheatley RG, Schug SA, Watson D. Safety and efficacy of postoperative epidural analgesia. Br J Anaesth 2001; 87: 47-61
10. Bajwa SJS, Kaur J. Clinical profile of levobupivacaine in regional anesthesia: A systematic review. *Journal of Anaestheisology Clinical Pharmacology* 2013; 29:530-9.
11. Kuthiala G, Chaudhary G. Ropivacaine: Review of its pharmacology and clinical use. *Indian J Anaesth*2011; 55: 104-10.
12. Etches RC, Writer WD, Ansley D, Nydahl PA, et al. Continuous epidural ropivacaine 0.2% for analgesia after lower abdominal surgery. *AnesthAnalg*1997;84: 784-90.