



## Epidural Ropivacaine Alone or Combined With Fentanyl in Infraumbilical Surgeries: A Comparative Study

### Authors

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### ABSTRACT

*Epidural blockade is becoming one of the most useful and versatile procedures in modern anaesthesiology. We compared intensity of sensory & motor blockade, duration of analgesia and hemodynamic changes in 45 patients belonged to ASA grade-I or II, between 20 and 55 years of age, among Gr-I ( 0.75% Ropivacaine) and Gr-II (0.75% Ropivacaine + 50 mcg Fentanyl), requiring central neuraxial blockade for infraumbilical surgeries. We concluded that the fentanyl when added as an adjuvant to epidural ropivacaine, significantly prolongs the analgesic duration without causing significant haemodynamic and respiratory changes. And with this combination there is no significant change in the level of sensory and motor blockade.*

**Key words-** ropivacaine, fentanyl, epidural

### INTRODUCTION

Epidural blockade is becoming one of the most useful and versatile procedures in modern anaesthesiology. It is unique in that it can be placed at virtually any level of the vertebrae, allowing more flexibility in its application to clinical practice. It's versatility, giving the clinician the opportunity to provide anaesthesia and analgesia, used to supplement general anaesthesia, decreasing the need for deep levels of general anaesthesia and therefore providing a more haemodynamically stable operative course. In such patients it can provide a relief from pain for a longer duration and the facility of further

top-ups and continuous infusion of the analgesic drugs through epidural catheter thus provides an uneventful and smooth recovery. In recent years, ropivacaine has increasingly replaced bupivacaine for the adequate post-op pain relief in patients undergoing lower abdominal surgeries, because of its similar analgesic properties, lesser motor blockade and decreased propensity of cardiotoxicity<sup>1</sup>.

Opioids, given by epidural route to relieve post-op pain, may provide adequate analgesia when given in low doses, but can also cause mental confusion, somnolence, nausea and vomiting, itching and respiratory depression when given in high doses<sup>2</sup>.

Local anaesthetic and opioid combination was shown to be more effective in epidural analgesia for post-op pain as their effects started rapidly and lasted longer when compared with local anaesthetics given alone<sup>3</sup>.

The main site of action of fentanyl is the substantia gelatinosa in the dorsal horn of spinal cord, where it blocks the neural fibres carrying pain impulses both at pre-synaptic and post synaptic levels<sup>4</sup>. As fentanyl has no effect on sympathetic and motor neurons, it has advantages over local anaesthetics. Addition of opioid to local anaesthetics gives the opportunity to use more diluted local anaesthetic solutions for better analgesia, and reduces systemic toxicity risk and motor block incidence of local anaesthetics<sup>5</sup>.

Keeping all these pharmacological interactions in consideration, we planned a prospective, randomized, double-blind, clinically controlled trial in our institute.

## REVIEW OF LITERATURE

In recent years, **ropivacaine** has been increasingly replacing bupivacaine for the epidural anesthesia and analgesia because of its similar analgesic properties.<sup>6,7</sup> lesser motor blockade<sup>6,7</sup> and decreased propensity of cardiotoxicity<sup>8,9</sup>. Ropivacaine is a long-acting amide local anaesthetic agent with high Pka, low lipid solubility and structurally related to Bupivacaine. It is first pure S (-) enantiomer, unlike Bupivacaine which is a racemate.

The greater safety of **ropivacaine** than bupivacaine may be related both, to the reduced toxicity of the single (S)-isomer and to the difference between the propyl- and butyl-N-piperidine substituent. The very slow reversal of Na<sup>+</sup> channel blockade after a cardiac action potential, which is a hallmark of bupivacaine, is considerably faster with ropivacaine. In addition to these electrical differences, the negative inotropic potency of ropivacaine on isolated cardiac tissue appears to be considerably less than that of bupivacaine<sup>10,11</sup>.

**Fentanyl** is a potent synthetic narcotic analgesic with a rapid onset and short duration of action. The main site of action of fentanyl is the substantia gelatinosa in the dorsal horn of spinal cord, where it blocks the neural fibres carrying pain impulses both at pre-synaptic and post synaptic levels<sup>12</sup>. Analgesic effects of epidural opioids are influenced by a number of pharmacokinetic factors including, the mode of drug delivery, with infusions resulting in lower dose requirements<sup>13</sup> the high lipophilicity of fentanyl, its rapid penetration across the dura,<sup>14</sup> its nonspecific binding in the spinal cord, its possible uptake by dural fat tissues, and its systemic absorption make its pharmacokinetics very complex when administered epidurally. Fentanyl (lipophilic opioid) is often preferred to morphine (hydrophilic opioid) because of its more limited rostral spread within the intrathecal space<sup>15</sup>.

**Scott DA et al (1999)** conducted a randomized, double-blinded study to compare the analgesic effectiveness and side effects of epidural infusions with ropivacaine 2 mg/mL alone and in combination with fentanyl 1microg/mL, 2microg/mL and 4microg/mL. They conclude that, after major abdominal surgery, an epidural infusion of ropivacaine 2mg/mL with fentanyl 4micro/mL provided significantly more effective pain relief over a 3-day period than ropivacaine alone or ropivacaine with lower concentrations of fentanyl<sup>16</sup>.

**David C. Campbell et al (1999)** conducted a prospective, randomized, double-blinded study designed to compare the efficacy of 20 mL of either 0.08% bupivacaine plus 2 µg/mL fentanyl or 0.08% ropivacaine plus 2µg/mL fentanyl to initiate ambulatory labour epidural analgesia. The results of their study indicate that dilute ropivacaine combined with fentanyl effectively initiates epidural analgesia while concurrently preserving maternal ability to void and ambulate<sup>17</sup>.

**Amanda J. Pinder et al (2000)** Meister et al. compared epidural analgesia with 0.125%

ropivacaine/fentanyl versus 0.125% bupivacaine/fentanyl during obstetric labor. The authors state that ropivacaine cannot be less potent than bupivacaine as less supplemental analgesia was needed in the ropivacaine group<sup>18</sup>.

**D J Buggy et al (2000)** compared patient-controlled epidural analgesia (PCEA) with ropivacaine alone or combined with fentanyl. They found that the incidence of motor weakness (Bromage grade 1 or higher) was 48% (11/23) at 8 h in group R compared with 13% (3/24) in group RF ( $P = 0.025$ ). So they concluded that, the caution should be exercised using ropivacaine PCEA after spinal bupivacaine for Caesarean section, because its reputed motor-sparing property may be unreliable<sup>19</sup>.

**Lee Wk et al (2003)** studied 210 patients undergoing lower abdominal or lower extremity surgery received epidural analgesia infusions at 7mL/hour, 105 with 0.1% ropivacaine and 105 with 0.1% ropivacaine plus 1 microg/mL fentanyl. They found that pain relief scores was significantly better in the ropivacaine/ fentanyl group after the first hour and this difference lasted for the remaining time<sup>20</sup>.

**Atienzar MC et al (2004)** concluded by their study that an epidural infusion of 0.1% ropivacaine with fentanyl 2 microg mL(-1) at 10 mL h(-1) provided adequate analgesia in the first stage of labour. The level of analgesia was similar to that obtained using 0.2% ropivacaine with fentanyl 2 microg mL(-1) and with no differences with regard to motor or sensory block<sup>21</sup>.

**Shirasaka T et al (2005)** conducted a study to investigate which dose of fentanyl in ropivacaine for epidural anaesthesia will provide effective analgesia with minimal side effects after caesarean section (CS). They concluded that continuous epidural administration of fentanyl 21 microg x hr(-1) with ropivacaine provides the optimum balance between pain relief and side effects compared with fentanyl 11 microg x hr(-1) with ropivacaine after CS<sup>22</sup>.

**Kanai A et al (2007)** concluded by their study that continuous epidural infusion of ropivacaine

may induce a slower regression of sensory blockade compared with bupivacaine and lidocaine. The addition of fentanyl to ropivacaine can enhance this prolonged analgesic effect with little effect on motor blockade<sup>23</sup>.

**Mikhail Y Kirov et al (2011)** conducted a study to assess the efficacy of thoracic epidural anaesthesia (EA) followed by postoperative epidural infusion (EI) and patient-controlled epidural analgesia (PCEA) with ropivacaine/fentanyl in off-pump coronary artery bypass grafting (OPCAB). They concluded that in OPCAB, EA with ropivacaine/fentanyl decreases arterial pressure transiently, optimizes myocardial performance and influences the perioperative fluid and vasoactive therapy. Postoperative EI combined with PCEA improves lung function and reduces time to extubation<sup>24</sup>.

## MATERIAL AND METHODS

present study on “*Epidural Ropivacaine alone or combined with Fentanyl in infraumbilical surgeries- A comparative study*” was conducted in Department of Anaesthesiology, Rural Institute of Medical Science and Research, Saifai, Etawah, U.P., India after approval by the ethical committee of the institution, a written consent was taken from the patients after explaining to them in detail about the implications of the anaesthetic and the surgical procedure.

Our study had 45 patients, all patients belonged to ASA grade-I or II, between 20 and 55 years of age requiring neuraxial blockade for lower abdominal surgeries. Patients having morbid obesity, pregnancy, psychiatric disease, history of drug abuse, expected duration of surgery >2.5 hours and any contraindication to regional anaesthesia were excluded from the study. Routine investigations were done preoperatively in all the patients.

All the patients were randomly allocated into two groups.

**Group-I** : Epidural ropivacaine 0.75% (14.5ml) +1.5 ml Distilled water.

**Group-II** : Epidural ropivacaine 0.75% (14.5ml) + Fentanyl 50 µgm (1 ml) + 0.5 ml distilled water

All the patients premedicated a night before and on the morning of the surgery with tablet ranitidine 150 mg and tablet alprazolam 0.25 mg. The patients were explained about the sequence of anaesthetic procedure and a good IV access was secured. All the patients were preloaded with 500 ml of 6% hydroxyl ethyl starch before administration of block and all monitoring devices were attached. The anaesthesia technician was given a written set of guidelines about preparation and blinding of drugs.

Patients were administered epidural block in sitting position/ left lateral position using standard epidural techniques followed by test dose injecting 3 ml of 2% lignocaine HCl solution containing adrenaline 1:200,000. After 4-6 minutes of test dose, patients in group-I received 14.5 ml of 0.75% ropivacaine only while Group-II patients were administered 14.5 ml solution of 0.75% ropivacaine and 50µgm of fentanyl.

The highest sensory level reached was noted after 20 minutes of administration of the block, it was done by using 25G hypodermic insulin needle. Similarly regression of sensory level block at the end of procedure was done. Time taken by highest level of block to recede to T<sub>10</sub> level was recorded in both groups. It was done at time interval of 10 minutes. Surgical procedures were initiated only after the establishment of adequate surgical anaesthetic effect with minimum level up to T<sub>6-7</sub> dermatome. Motor block onset and recovery was assessed by **Bromage scale** at 5, 10, 15, 20, 25, 30, 60, 90 and 120 minute intervals after the epidural administration of the drugs.

Hemodynamic parameters were monitored every 5 minutes until 30 minutes and at 10-minute intervals up to 60 minutes and then at 15-minute intervals for the next hour and finally at 30 minutes in the third hour.

Intravenous fluids were given as per the body weight and operative loss requirement, with no patient requiring blood transfusion. The patients

were given supplementary O<sub>2</sub> with the help of venturi mask. During the surgical procedure, any adverse event like anxiety, nausea, vomiting, pruritis, shivering, bradycardia, or hypotension was recorded and treated. Hypotension (defined as systolic arterial pressure falling more than 20% mm Hg) was treated with inj. mephenteramine 3-6 mg in bolus doses and HR<55 beats/min was treated with 0.3 mg of inj. atropine.

All the patients were kept for 8 hours in recovery room. Apart from vital parameters and any adverse event, all the patients were monitored for degree and duration of pain relief by pain scoring system. Assessment of analgesia was done by *analgesia score* (0 = No pain at rest or with movement, 1 =No pain at rest but pain during voluntary body movement, 2 = Pain at rest but tolerable, 3 = intolerable pain). Patients in both the groups were repeatedly assessed every 10 minutes for pain and rescue analgesic was given when they complained intolerable pain (score-3).

Comparability of the groups was analyzed by Student's two tailed "t" test and chi square test. Student 't' test was applied to analyze the parametric data (hemodynamic parameters and block characteristics). For all statistical analysis, the value of P<0.05 was considered as significant and p<.001 was considered most highly significant.

## RESULTS

Highest level of sensory block was found to be T<sub>6</sub> in 4(26.6%) patients of Group-I and 7(46.6%) patients of group-II. (Table-3)

Mean time for regression of sensory blockade to T<sub>10</sub> was significantly longer (Table-4) in group-II (272.5 ± 23.51 minutes) as compared to group I (246 ± 33.92 minutes).

Highest level of motor blockade was found to be Bromage score-3 in 1(6.66%) patients of Group-I, and 2 (13.33%) patients of group-II. (Table-5)

The duration of motor blockade was significantly (p<0.001) higher in (Table-6) patients of Group-II (196±17.89 minutes) as compared to Group-I (169±19.74 minutes).

The addition fentanyl (Group-II) produces longer duration ( $317 \pm 32.80$  minutes) of analgesia (Table-7) as compared to Group-I ( $214 \pm 28.42$  minutes). Haemodynamically the patients in both the groups behaved similarly. (Table-8)

The patients, in whom epidural fentanyl was used, had slightly higher incidence of nausea, vomiting, dry mouth and pruritis. (Table-9)

**Table -1** Distribution of patients according to their demographic data

	<b>Group -I</b> (Mean $\pm$ S.D.)	<b>Group -II</b> (Mean $\pm$ S.D.)
<b>Age(years)</b>	40.86 $\pm$ 12.03	38.66 $\pm$ 13.27
<b>Height(cm)</b>	160.44 $\pm$ 5.562	159.36 $\pm$ 9.405
<b>Weight(kg)</b>	52.35 $\pm$ 5.951	55.06 $\pm$ 8.412
<b>Sex (M:F)</b>	8:7	12:3

**Table-2** Comparison of duration of surgeries in both the groups

<b>Groups</b>	<b>Total number of patients</b>	<b>Mean duration</b>	<b>S.D.</b>	<b>'t' value</b>	<b>'p' value</b>
<b>Group-I</b>	15	80.57	22.45	0.284	0.778
<b>Group-II</b>	15	82.77	19.93		

**Table -3** Comparison of upper level of sensory block after 20 minutes

<b>Block height</b>	<b>Group I</b>		<b>Group II</b>	
	No.	%	No.	%
<b>T6</b>	4	26.66	7	46.66
<b>T8</b>	10	66.66	8	53.33
<b>T10</b>	1	6.66	-	-
<b>Total</b>	15	100	15	100

**Table -4** Time to regress to T10 level in both groups

	<b>Mean <math>\pm</math> S.D.</b>	<b>'t' value</b>	<b>'p' value</b>
<b>Group I</b>	246 $\pm$ 33.92	2.40	<0.05
<b>Group II</b>	272.5 $\pm$ 23.51		

**Table -5** Comparison of Motor block (Bromage score) after 30 minutes in both groups

<b>Bromage score</b>	<b>Group I</b>		<b>Group II</b>	
	No.	%	No.	%
1	0	0	0	0
2	14	93.33	13	86.66
3	1	6.66	2	13.33
4	0	0	0	0
<b>Total</b>	15	100	15	100

**Table-6** Comparison of time for Motor block Recovery ( Bromage score 1)

	<b>Mean <math>\pm</math> S.D.</b>	<b>'t' value</b>	<b>'p' value</b>
<b>Group I</b>	169 $\pm$ 19.74	3.79	< 0.001
<b>Group II</b>	196 $\pm$ 17.89		

**Table -7** Comparison of rescue analgesia time (in minutes) in different groups

	Mean ± S.D.	't' value	'p' value
<b>Group I</b>	214±28.42	9.192	< 0.001
<b>Group II</b>	317±32.80		

**Table-8** Comparison of hemodynamic parameters in both groups at different time interval

Time intervals	Pulse rate						Mean arterial blood pressure					
	Group I			Group II			Group I			Group II		
	Mean ± SD	't' value	'p' value	Mean ± SD	't' value	'p' value	Mean ± SD	't' value	'p' value	Mean ± SD	't' value	'p' value
15 minutes	87.06 ±5.94	2.276	.03 !	83.33 ±8.56	0.953	.348 !	87.40 ±5.53	4.373	.0002 *	85.8 ±5.65	4.093	.0003 *
30 minutes	83 ±6.31	0.902	.374 !	79.13 ±8.50	0.201	.844 !	87.60 ±4.71	4.478	.0001 *	86.13 ±7.64	3.684	.001 *
60 minutes	80.86 ±9.37	0.170	.866 !	76.53 ±9.63	0.873	.390 !	87.86 ±6.6	3.966	.0005 *	87.93 ±5.68	3.422	.0019 *
120 minutes	78 ±9.04	0.652	.519 !	73.8 ±10.02	1.561	.129 !	85.00 ±5.52	5.276	0.000 *	86.26 ±6.00	3.897	.0006 *

!- insignificant, \*- significant

**Table-9** Comparison of side effects in both the groups

Side effect	Group I	Group II
<b>Immediate</b>		
Nausea/vomiting	02	03
Hypotension	07	08
Bradycardia	00	00
Dry mouth	01	04
Shivering	05	04
Pruritis	00	02
Urinary Retention	01	02
<b>Delayed</b>		
Infection	00	00
Post-dural Puncture headache	01	00
Acute neurological Sequele	00	00

**DISCUSSION**

**Katz JA et al (1990)** studied 15 patients of ASA I or II for elective lower-extremity orthopedic procedures using a nonrandomized open-label design. Three groups of five patients each received either 0.5%, 0.75%, or 1.0% ropivacaine. Upper and lower levels of analgesia to pinprick were determined at frequent intervals until normal sensation had completely returned. They found that median maximum thoracic levels of analgesia achieved were 8, 6, and 5 for the 0.5%, 0.75%, and 1.0% groups, respectively, and occurred at 29 +/- 11, 37 +/- 21, and 30 +/- 9 min. Respective times to two-segment regression were 2.8 +/- 1.0,

3.0 +/- 0.5, and 2.9 +/- 0.6 hours. Total durations of sensory blockade were 5.4 +/- 0.7, 6.5 +/- 0.4, and 6.8 +/- 0.8 hours, respectively<sup>25</sup>.

In our study, In 20 out of 45 patients, T6 sensory blockade was achieved at 20 minutes, while 24 out of 45 patients achieved T8 sensory level. Time to regress to T10 level in all the three groups were 246 ±33.92, 272± 23.51, 354± 55 in group-I,II,III respectively. Thus our results were comparable with the above study.

**Kanai A et al (2007)** studies 80 patients, scheduled for orthopaedic procedures of the lower extremity under lumbar epidural anaesthesia. Following the operation, continuous infusion of a

randomized solution (0.2% ropivacaine, 0.125% bupivacaine, 0.5% lidocaine, or 0.2% ropivacaine with 2.5 microg/mL fentanyl) was commenced at a rate of 6 mL/h. The regression of sensory and motor blockade were compared among the groups. They found that the regression of sensory blockade was significantly prolonged in patients treated with ropivacaine. The addition of fentanyl to ropivacaine augmented this prolonged analgesic effect. So they concluded that epidural infusion of ropivacaine with fentanyl provides effective pain relief, possibly because of the maintenance of sensory blockade by ropivacaine and enhancement of this sensory blockade by fentanyl<sup>23</sup>.

In our study prolongation of mean time for regression of sensory blockade to T10 was significant ( $p < 0.05$ ) between group-I & group-II and highly significant ( $p < 0.001$ ) between groups II & III and I & III, which is comparable to above study.

**Meister G C et al (2000)** concluded that, the epidural ropivacaine 0.125% with fentanyl 2µg/mL produces similar labour analgesia with significantly less motor block than an equivalent concentration of bupivacaine/Fentanyl<sup>26</sup>. After statistical evaluation we found that difference in mean values between groups-I & II and in groups-I & III were most highly significant ( $p < 0.001$ ) while it was significant between Groups-II & II ( $p < 0.01$ ).

**Shirasaka T et al (2005)** conducted a study to investigate which dose of fentanyl in ropivacaine for epidural anaesthesia will provide effective analgesia with minimal side effects after caesarean section (CS). 58 patients scheduled for CS were randomly allocated into two groups according to fentanyl dose in epidural analgesia: group F1 (11 microg x hr<sup>-1</sup>); n=30) or group F2 (21 microg x hr<sup>-1</sup>); n= 28). Ropivacaine 0.2% 100 ml with fentanyl 400 or 800 microg was administered into the epidural space in the groups F1 and F2, respectively. They found that pain scores with cough or movement were significantly lower in the group F2 than the group F1 at twelve and twenty-four hours after CS and Bromage score at

twelve hours was lower in the group F2 than the group F1<sup>22</sup>.

In the present study, we found that, the duration of motor blockade was significantly ( $p < 0.001$ ) higher in group-II & III patients as compared to group-I. This is comparable to above study.

## CONCLUSION

So this study re-established the fact, that the fentanyl when added as an adjuvant to epidural ropivacaine, significantly prolongs the analgesic duration without causing significant haemodynamic and respiratory changes. And with this combination there is no significant change in the level of sensory and motor blockade.

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