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Research Article

Epidural ropivacaine combined with fentanyl or in combination with clonidine in infraumblical surgeries: a comparative study

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ABSTRACT

Background: The addition of an adjuvant, like clonidine and fentanyl, in epidural blockade has enhanced the effectiveness of local anaesthetics as they not only help in intensifying and prolonging the blockade effect but also help in the reduction of the dose of local anaesthetics.
Methods: 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. All the patients were randomly allocated into two groups. Group-I: Epidural ropivacaine 0.75% (14.5ml) + Fentanyl 50 µgm (1 ml) + 0.5 ml distilled water. Group-II: Epidural ropivacaine 0.75% (14.5ml) + Fentanyl 50 µgm (1 ml) + clonidine 50 µgm**.** Patients were monitored for sensory and motor blockade, hemodynamic parameters, rescue analgesia and adverse effects in perioperative period.
Results: Highest level of sensory and motor blockade was found to be insignificant ($p>0.05$) in both the groups. Mean time for regression of sensory blockade to T10 was significantly longer ($p<0.05$) in group II as compared to group I. The duration of motor blockade was significantly ($p<0.001$) higher in patients of Group-II as compared to Group-I. The addition of clonidine to epidural Ropivacaine and fentanyl (Group-II) produces longer duration of analgesia as compared to Group-I. Haemodynamically the patients in both the groups behaved similarly. The patients, in whom epidural fentanyl was used, had slightly higher incidence of nausea, vomiting, dry mouth and pruritus.
Conclusions: So this study re-established the fact, that the fentanyl and clonidine when added as adjuvant to epidural ropivacaine, significantly prolongs the analgesic duration without causing significant hemodynamic and respiratory changes.

Keywords: Epidural, Ropivacaine, Fentanyl, Clonidine

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 virtually at any level of the vertebrae, allowing more flexibility in its application to clinical practice. Its 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.

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. 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.[1-5] The very slow reversal of Na+ 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.[6,7]

The addition of an adjuvant has further enhanced the effectiveness of these local anaesthetics as they not only help in intensifying and prolonging the blockade effect but also help in the reduction of the dose of local anaesthetics.

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.[8] 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.[9] As fentanyl has no effect on sympathetic and motor neurons, it has advantages over local anaesthetics.

Clonidine a partial alpha-2 adrenergic agonist has been used as an adjuvant to epidural local anaesthetics and opioids to improve the quality of analgesia after major abdominal surgeries.[10] It can provide pain relief by an opioid independent mechanism as it directly stimulates pre- and postsynaptic 2α-adrenoceptors in the dorsal horn grey matter of the spinal cord, thereby inhibiting the release of nociceptive neurotransmitters.[11] Though at higher doses, it may further reduce the dose of local anaesthetic and prolong the analgesic duration, but at the same time can exert its toxic effects resulting in profound hypotension, bradycardia and deep sedation.[12]

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

METHODS

The present study on "Epidural Ropivacaine combined with Fentanyl or in combination with Clonidine in infraumblical 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) + Fentanyl 50 µgm (1 ml) + 0.5 ml distilled water.

Group-II: Epidural ropivacaine 0.75% (14.5ml) + Fentanyl 50 µgm (1 ml) +clonidine 50 µgm

All the patients were 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 were administered 14.5 ml solution of 0.75% ropivacaine and 50µgm of fentanyl, while group-II patients received 14.5ml of 0.75% ropivacaine, 50µgm of Fentanyl and 50µgm of clonidine. 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_{10} 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 T6-7 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_2 with the help of venturi mask. During the surgical procedure, any adverse event like anxiety, nausea, vomiting, pruritus, 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 analysed by Student's two tailed "t" test and chi square test. Student't' test was applied to analyse 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

1. Highest level of sensory block was found to be T6 in 7(46.6%) patients of Group-I, and 9(60%) patients of group-II (Table-3).
2. Mean time for regression of sensory blockade to T10 was significantly longer in group II (354 ± 55.10 minutes) as compared to group I (246 ± 33.92 minutes) (Table-4).
3. Highest level of motor blockade was found to be Bromage score-3 in 2 (13.33%) patients of group-II and group-II each (Table-5).
4. The duration of motor blockade was significantly (p<0.001) higher in patients of Group-II (236.33±42.65 minutes) as compared to Group-I (196±17.89 minutes) (Table-6).
5. The addition of clonidine to epidural Ropivacaine and fentanyl (Group-II) produces longer duration (413±41.51 minutes) of analgesia as compared to Group-I (317±32.80 minutes) (Table-7).
6. Haemodynamically the patients in both the groups behaved similarly (Table-8).
7. The patients in whom epidural fentanyl was used had slightly higher incidence of nausea, vomiting, dry mouth and pruritus (Table-9).

Table 1: Distribution of patients according to their demographic data.

	Group –I (Mean ± S.D.)	Group –II (Mean ± S.D.)
Age (years)	38.66 ± 13.27	39.16 ± 14.36
Height (cm)	159.36 ± 9.405	161.52 ± 6.724
Weight (kg)	55.06 ± 8.412	54.36 ± 7.212
Sex (M:F)	12:3	9:6

Table 2: Comparison of duration of surgeries in both the groups.

Groups	Total number of patients	Mean duration	S.D.	't' value	'p' value
Group-I	15	82.77	19.93	0.119	.905
Group-II	15	81.95	17.65		

Table 3: Comparison of upper level of sensory block after 20 minutes.

Block height	Group I		Group II	
	No.	%	No.	%
T6	7	46.66	9	60.0
T8	8	53.33	6	40.0
T10	-	-	-	-
Total	15	100	15	100

Table 4: Time to regress to T10 level in both groups.

	Mean ± S.D.	' t' value	' p' value
Group I	272.5 ± 23.51	5.09	<0.001
Group II	354 ± 55.10		

Table 5: Comparison of motor block (Bromage score) after 30 minutes in both groups.

Bromage score	Group I		Group II	
	No.	%	No.	%
1	0	0	0	0
2	13	86.66	13	86.66
3	2	13.33	2	13.33
4	0	0	0	0
Total	15	100	15	100

Table 6: Comparison of time for motor block recovery (Bromage score 1).

	Mean ± S.D.	' t' value	' p' value
Group I	196 ± 17.89	3.26	<0.01
Group II	236.33 ± 42.65		

DISCUSSION

Pasquale De Negri (2001) investigated the dose-response relationship for epidural clonidine when added to a continuous postoperative epidural infusion of ropivacaine. Analgesia was improved without any signs of increased sedation or other side effects. They found that epidurally administered clonidine enhances the quality and duration of postoperative analgesia when it is used as an adjunct to local anaesthetics in children.[13]

Table 7: Comparison of rescue analgesia (in minutes) in different groups.

	Mean ± S.D.	' t' value	' p' value
Group I	317 ± 32.80	7.076	<0.001
Group II	413.66 ± 41.51		

In our present study, we found that, the addition of clonidine to epidural ropivacaine and fentanyl (Group-II) produces longer duration (413 ± 41.51 minutes) of analgesia as compared to Group-I (317 ± 32.80 minutes).

Landau et al performed a study to determine the effects of clonidine with ropivacaine during epidural labour analgesia. They found that with addition of clonidine, duration of analgesia was increased (132 ± 48 min) [ropivacaine + clonidine group] versus (91 ± 44 min) [ropivacaine + Nacl 0.9% group].This study demonstrates the dose-sparing effect of clonidine when added to ropivacaine.[14]

Förste et al studied whether a small dose of clonidine added to a ropivacaine-fentanyl mixture improves epidural analgesia without provoking side effects typically related to larger amounts of epidural clonidine. They found that, the arterial pressure and heart rate were slightly lower in RFC Group as compared with the RF group throughout the study period.[15]

Table 8: Comparison of hemodynamic parameters in both groups at different intervals.

Time Interval	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	83.33 ±8.56	0.953	.348 !	83.73 ±9.91	0.540	.593 !	85.8 ±5.65	4.093	.0003 *	87.80 ±5.19	3.867	.0006
30 minutes	79.13 ±8.50	0.201	.844 !	79.93 ±11.04	0.433	.668 !	86.13 ±7.64	3.684	.001 *	87.33 ±6.36	3.795	.0007
60 minutes	76.53 ±9.63	0.873	.390 !	76.2± 9.75	1.443	.160 !	87.93 ±5.68	3.422	.0019 *	85.13 ±6.45	4.584	.0001
120 minutes	73.8± 10.02	1.561	.129 !	73.4± 7.18	2.442	.021 !	86.26 ±6.00	3.897	.0006 *	86.26 ±5.92	4.298	.0002

!- insignificant, *- significant

Table 9: Comparison of side effects in both groups.

Side effect	Group I	Group II
Immediate		
Nausea/vomiting	03	03
Hypotension	08	10
Bradycardia	00	00
Dry mouth	04	04
Shivering	04	06
Pruritus	02	03
Urinary Retention	02	02
Delayed		
Infection	00	00
Post-dural Puncture headache	00	01
Acute neurological Sequele	00	00

In this study, we found that the uppermost level of sensory blockade was found to be T6 in all the three groups, which is almost comparable to above study.

In the present study we found the results comparable to above study.

Kanai et al 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 regressions 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.[16] In our study

prolongation of mean time for regression of sensory blockade to T10 was highly significant ($p<0.001$) between groups I &II which is comparable to above study.

Singh Bajwa et al conducted a study and compare the clonidine-ropivacaine combination with fentanyl-ropivacaine in epidural anaesthesia. In their study they found that maximum sensory blockade level in different groups were T6-7 (ropivacaine + clonidine), T5-6 (ropivacaine + Fentanyl) & T6-7 (ropivacaine + clonidine + fentanyl).[17]

CONCLUSION

So this study re-established the fact, that the fentanyl and clonidine when added as an adjuvant to epidural ropivacaine, significantly prolongs the analgesic duration without causing significant haemodynamic and respiratory changes. The combination of fentanyl and clonidine with epidural Ropivacaine has more prolonged duration of analgesia without many side effects. And with this combination there is no significant change in the level of sensory and motor blockade. However, a more extensive study with larger population is needed to recommend the said combination routinely.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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