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Comparison of Tramadol Vs Butorphanol added to Epidural Ropivacaine for Postoperative Pain Relief in Abdominal Hysterectomy

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Abstract

Background and Objectives *Aim of this study was to compare the efficacy in providing post operative analgesia in abdominal hysterectomy by epidurally administered combination of ropivacaine with tramadol vs. ropivacaine with butorphanol. The study was done to compare the onset time of analgesia, the duration of analgesia, and the side effects of the combination of drugs (ropivacaine-tramadol & ropivacaine-butorphanol) when administered epidurally*

Methods: *This study was done among two groups of patients belonging to ASA1 &11,who underwent abdominal hysterectomy. They are comparable with regards to age, height and weight. Patients were allocated in to two study groups, named A and B using computer generated randomization. Group A received 8 ml of Ropivacaine (0.20%) with 50 mg (1 ml) Tramadol and Group B received 8 ml of Ropivacaine (0.20%) with 1 mg (1 ml) Butorphanol epidurally. (The groups were later redesignated as group RT (group A) and group RB (group B)).*

Results: *The mean time of onset of analgesia in group RT is 9 ±1.6 min, and in group RB it is 6.1±1.7 min. There is statistically significant difference ($p<0.001$) between the time of onset of analgesia between the two groups. The duration of analgesia is 4.3±0.1hours in group RT and 5.1±0.4 hours in group RB. Side effects like nausea, vomiting, hypotension and head ache are more in RT group. Sedation was more in group RB. No significant difference in motor blockade was observed in either group No serious side effects were observed in both the groups*

Conclusion: *Epidural bolus injection of both 0.2 % ropivacaine with 50 mg tramadol and 0.2 % ropivacaine with 1 mg butorphanol are effective for relieving post operative pain after abdominal hysterectomy. However faster onset of analgesia, longer duration of analgesia and less adverse reactions are observed when butorphanol is used as an adjuvant with 0.2%ropivacaine.*

Keywords: *epidural, ropivacaine, tramadol, butorphanol.*

Introduction

Post-operative pain warrants rapid and effective pain management. Post-operative analgesia in patients undergoing abdominal hysterectomy is usually provided by parenteral medication or epidural analgesia.

Epidural analgesia is a common method for post-operative pain relief. Drugs belonging to various groups are given via epidural catheter for this purpose.

Epidural administration of local anaesthetics is one of the methods for post-operative analgesia. For many years, bupivacaine (an amide local

anaesthetic) has been used because of its longer duration of action. Compared with older local anesthetics, bupivacaine provides better analgesia without significant motor block. In addition, there is less tachyphylaxis with its prolonged administration. However, bupivacaine is more cardio toxic than other local anesthetics[1].

Ropivacaine is an amide type long acting local anesthetic. Its use may address some of the concerns related to bupivacaine. It exists in the pure levorotatory form. At higher concentration it produces both motor and sensory blockade and at lower concentration it produces analgesia (sensory blockade) with limited and non-progressive motor blockade. Compared to bupivacaine the motor block is slower in onset, shorter in duration and less intense. Also ropivacaine produces less cardiac and CNS toxicities[2,3,4,5,6,,].

Adjuvants are drugs that improve the efficacy and potency of other drugs when given concurrently. Neuraxial adjuvants are used to improve the quality of block or prolong analgesia and decrease the adverse effects associated with high doses of a single local anaesthetic agent. In addition to their effect on dose reduction, neuraxial adjuvants are also utilized to increase speed of onset of neural blockade (ie to reduce latency), improve quality and prolong duration of neural blockade.

Epidural tramadol is widely used for post-operative analgesia as an adjuvant. Tramadol is a synthetic codeine analog that is a weak μ receptor agonist. Its affinity for μ receptor is only 1/6000 that of morphine. But the primary O-demethylated metabolite of tramadol is 2-4 times as potent as parent drug and may account for part of its analgesic effect. It is supplied as a racemic mixture which is more effective than either enantiomer alone. Part of its analgesic effect is produced by inhibition of uptake of norepinephrine and serotonin. The (+) enantiomer binds to the μ receptor and inhibit the uptake of serotonin. The (-) enantiomer inhibit nor epinephrine[6] uptake and stimulate ∞2 adrenergic receptors. The unique pharmacological profile of tramadol makes it an attractive drug for postoperative pain management. In several clinical trials, tramadol has been proved to be a safe and effective drug for epidural analgesia [7,8]

Butorphanol is a synthetically derived opioid agonist –antagonist analgesic of phenanthrene series. It is a mixed agonist-antagonist with low intrinsic activity at receptors of the mu (μ) type. It is also an agonist at κ(kappa) opioid receptors. Kappa-receptors appear to be involved in somatic as well as visceral pain modulation and are thus useful in reducing postoperative pain after abdominal hysterectomy, which has a somatic as well as visceral component. Epidural butorphanol has been used effectively for labor analgesia and postcesarean section analgesia[9,] and no neurotoxic effects have been reported so far in humans.

Materials and Methods

This study was done under the department of Anaesthesiology, Govt. T.D. Medical College Hospital, Alappuzha, Kerala from November 2013-June 2014 after obtaining approval from institutional research committee and institutional ethics committee

Study Design

A double blind prospective randomized controlled study.

Patients were allocated in to two study groups, named A and B using computer generated randomization.

Group A- Receives 8 ml of Ropiva-caine (0.20%) with 50 mg(1 ml) Tramadol

Group B–Receives 8 ml of Ropiva-caine (0.20%) with 1 mg(1 ml) Butorphanol

Study Subjects

Inclusion Criteria

- Patients undergoing elective abdominal hysterectomy under spinal anaesthesia
- ASA physical status I and II
- Age between 40 to 60 years
- Height between 145 to 165 cm
- Weight between 48 to 70 Kg

Exclusion Criteria

- Patients who are not willing to participate in this study

- Patients with contraindication to epidural anaesthesia
- Patients with history of drug allergy
- Patients who required intraoperative supplemental epidural analgesia

Sample Size

50 patients undergoing elective total abdominal hysterectomy under combined spinal epidural anaesthesia in gynaecology operation theatre. They were allocated in to two study groups of 25 each named A and B, according to computer generated randomization

Methodology

Clearance has been obtained from institute research and ethics committee. Study subjects were patients in the age group 40 to 60 years of ASA I and II who underwent elective abdominal hysterectomy under spinal anaesthesia. A written infor-med consent was obtained from the patients. Preoperatively all patients were explained about visual analogue scale (VAS) for post-operative pain assessment.

They were given Tab. Alprazolam 0.25 mg, Tab. Ranitidine 150 mg and Tab. Metoclopramide 10 mg on pre operation day at night time and on the day of surgery at 6 am.

When the patient reached operation theatre, intravenous line was established using 18G cannula and maintenance fluid was started .ECG leads and pulse oximeter probe were attached. Noninvasive blood pressure monitoring was done using appropriate sized cuff. Patients were given premedication with Inj. Midazolam (0.02 mg /Kg Body Weight).Preloading was done with 500 ml of normal saline (NS).

Under strict aseptic condition and under local anaesthesia 18G epidural catheter was inserted at L1-L2 intervertebral space using 18G Tuohy needle after identifying the epidural space using loss of resistance technique and catheter is fixed with 3 cm placed inside the epidural space. 3ml of 2% Lignacaine with 5 microgram/ml of Adrenaline was given as a test dose via epidural catheter to check for the intravascular or intrathecal placement of catheter. All patients were given subarachnoid blockade with 3.4 ml of 0.5% bupivacaine (Heavy) to obtain a sensory block up to T6 level for surgery by lumbar puncture at L2-L3 intervertebral space using 23 G QB needle. Patient's pulse rate, ECG, non-invasive blood pressure and respiratory rates were monitored during surgery.

After the surgery, in the Post OP ICU patients were monitored. Pain intensity is assessed by using a 100-mm linear visual analog scale (VAS) marked such that 0=no pain and 100=worst imaginable pain. A baseline pain intensity was measured on patient's arrival and was recorded as VAS at 0 hours. when the patient complained of pain with severity of >30 in VAS , either 8 ml of Ropivacaine (0.20%) with 50 mg Tramadol (total 9 ml)or 8 ml of Ropivacaine(0.20%) with 1 mg Butorphano l(total 9 ml) was given via the epidural catheter. As per the randomization the guide prepared the study drug and the investigator administered the drug. All patients were assessed at 5, 10, 15, 30,60 and 90 minutes and at 2 ,3,4,5,6,8,12,24 hours. when the patient appreciated pain of severity >30 in VAS, analgesia was provided by Injection Diclofenac 75 mg IV Q 8^{th} hourly and monitoring continued for 24 hours.

The following parameters were monitored for 24 hours

- Pulse rate
- ECG
- Non invasive arterial blood pressure
- Respiratory rate
- O2 saturation by finger pulse oximeter

The following parameters were assessed

- **Pain score using VAS**
- **Onset of analgesia**
  It is the time from completion of epidural injection till complete pain relief
- **Duration of analgesia**
  It is the time from completion of epidural injection of study drug to the time of first request by patient for additional pain medication. (When pain severity >30 in VAS)

Sedation score using Ramsay score

RAMSAY SCALE	
1	Patient anxious and agitated or restless or both
2	Patient co-operative, oriented and tranquil
3	Patient responds to commands only
4	Brisk response to a light glabellar tap or loud auditory stimulus
5	Sluggish response to a light glabellar tap or loud auditory stimulus
6	No response to the stimuli mentioned in item 4 and 5

A score >4 is considered sedated.

Motor blockade using Bromage score

GRADE	CRITERIA	MOTOR BLOCK
0	No motor block (able to lift extended leg at hip)	Nil
1	Inability to raise extended leg; able to move knees and feet	Partial
2	Inability to raise extended leg and move knee; able to move feet	Almost complete
3	Complete motor block of limb	Complete

- **Adverse drug reactions:**
  - nausea
  - vomiting
  - sedation
  - dizziness
  - arrhythmias
  - hypo/hypertension
  - dry mouth
  - head ache
  - seizure

If patients complained of pain even after 15 minutes of epidural injection of study drug, rescue analgesia is provided by Injection Diclofenac 75 mg IV.

Hypotension is defined as systolic BP less than 90 mmHg

Hypotension will be treated with Inotropes and Vasopressors.

Bradycardia is defined as heart rate less than 50 beats per minute.

Bradycardia will be treated with Atropine 0.01mg/Kg IV.

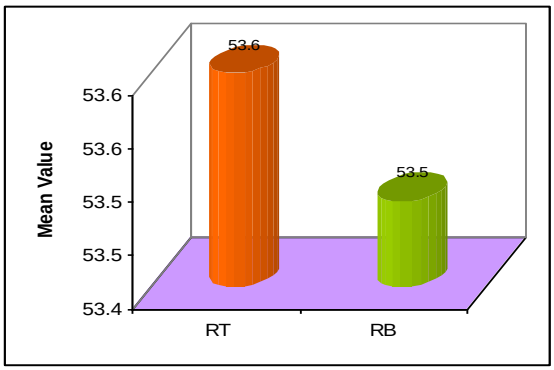
Statistical Analysis

Base line data were entered in Microsoft Excel sheet. Qualitative variables has been summarized using proportions with 95% C I .Quantitative variables has been summarized using mean with standard deviation. Test of significance using independent t test for quantitative variables and Mann Whitney U test for qualitative variables has been done.

Observation and Analysis

Table 1 Comparison of age

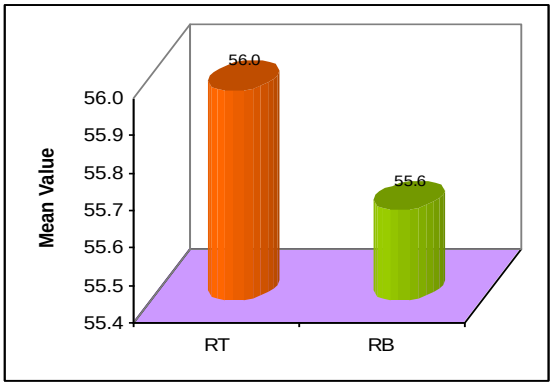
Group	Mean	SD	N	T	p
RT	53.6	4.0	25	0.1	0.917
RB	53.5	4.1	25		



As there were no statistical difference (P>0.05) between two groups, the two groups were comparable or age matched

Table 2 Comparison of weight

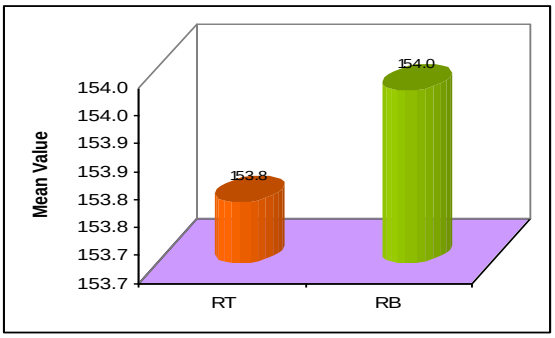
Group	Mean	SD	N	T	p
RT	56.0	4.0	25	0.32	0.752
RB	55.6	3.1	25		



As there were no statistical difference (P>0.05) between two groups, the two groups were comparable or weight matched

Table 3 Comparison of height

Group	Mean	SD	N	T	P
RT	153.8	3.3	25	0.2	0.839
RB	154.0	3.6	25		

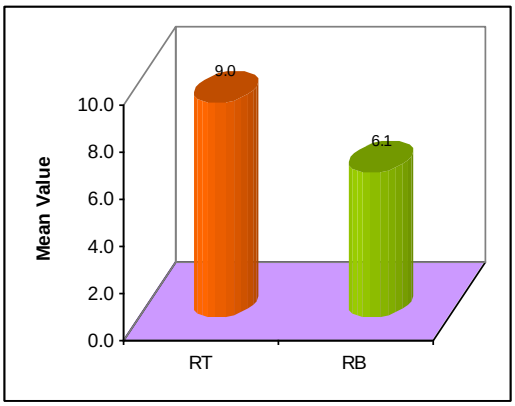


Height distribution of the two study groups are given in table 3 and figure 3. As there were no statistical difference (P>0.05) between two groups, the two groups were comparable or height matched

Table 4 Comparison of Onset of analgesia (time at which pain becomes 0 by VAS) based on group

Group	Mean	SD	N	t	p
RT	9.0	1.6	25	6.19**	0.000
RB	6.1	1.7	25		

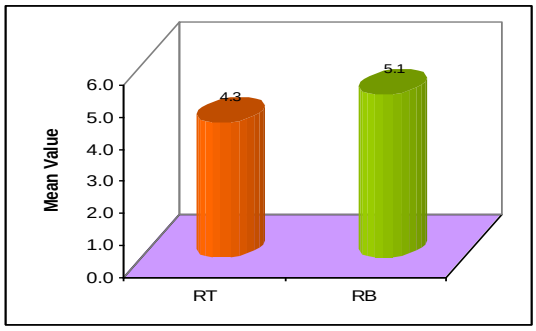
**: -Significant at 0.01 level



Mean time of onset of analgesia is shown in table 4 and figure 4. In group RT is 9.0 min and in group RB is 6.1 min. There was statistically significant difference (p<0.001) between the time of onset of analgesia between the two groups.

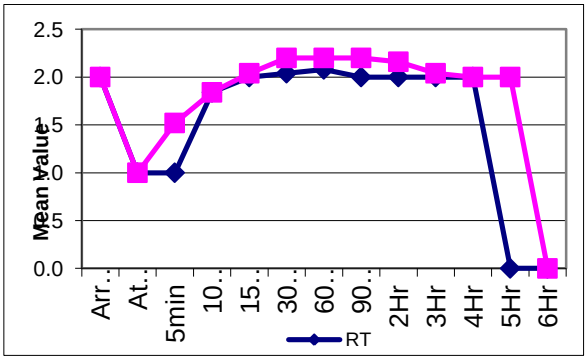
Table 5 Comparison of duration of analgesia in hours based on group

Group	Mean	SD	N	T	p
RT	4.3	0.1	25	0.02	0.984
RB	5.1	0.4	25		



Mean duration of analgesia of in group RT is 4 hours and in group RB is 5.1 hours. The mean duration of analgesia is significantly higher (p<0.001) in group RB compared to group RT.

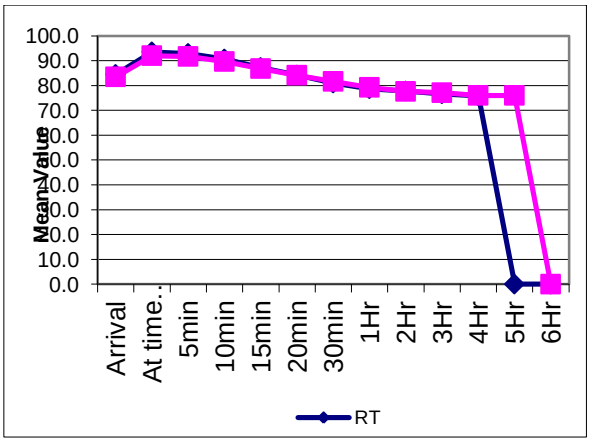
Comparison of sedation



Time line chart showing the distribution of mean values of sedation for both the groups

Sedation score at various interval are analysed using Mann Whitney U test. It shows sedation is more in group RB

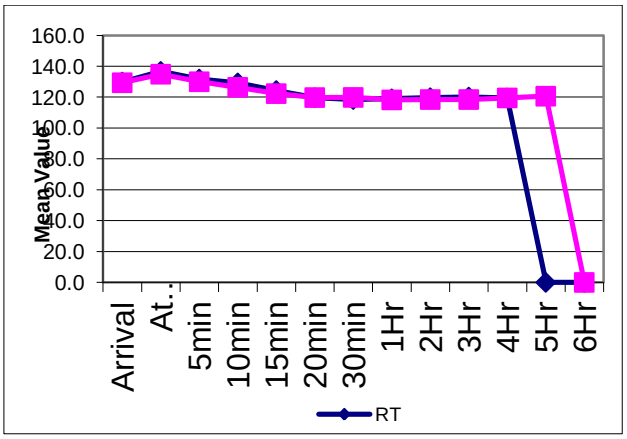
Comparison of pulse rate



Time line graph showing the distribution of mean pulse rates for the two groups.

Mean pulse rate at various time interval are anylysed using independent t test. It shows no significant difference between the two groups

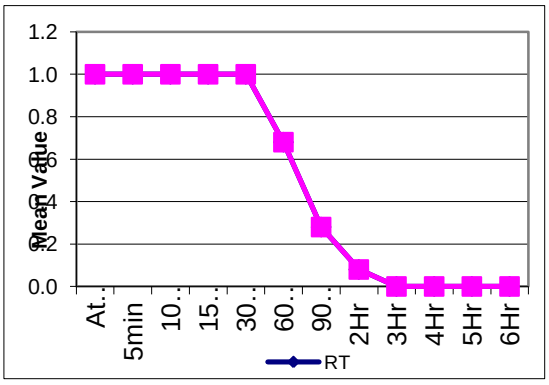
Comparison of systolic blood pressure



Time line graph showing the distribution of mean systolic blood pressure of the two groups

Mean systolic blood pressure at various time interval are analysed using independent t test. It shows no significant difference between the two groups

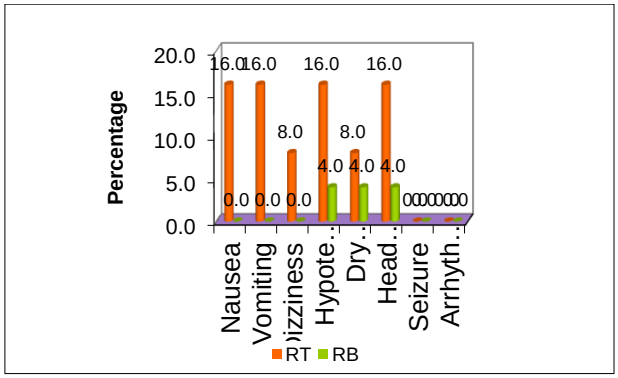
Comparison of Motor Blockade



Time line graph showing the distribution of motor blockade of the two different groups.

Motor blockade was studied using Mann-Whitney U Test.it shows no significant difference between the two groups.

Adverse Drug Reaction



Multiple bar diagram showing the percentage distribution of adverse reactions in the two groups.

The incidence of nausea, vomiting, headache and hypotension are more in group RT compared with group RB

Discussion

Inadequate treatment for pain can result in short and long term morbidity. So the provision of post operative analgesia is mandatory during the administration of any anaesthesia.

In this study, epidural bolus injection of either 0.2% ropivacaine 8ml with 50 mg tramadol (1ml) or 0.2% ropivacaine 8 ml with 1 mg butorphanol (1ml) were used for providing analgesia after abdominal hysterectomy.

Only patients of ASA 1 & 2 undergoing elective abdominal hysterectomy were included in this study. This may avoid variations in the duration of surgery, anaesthesia technique and haemodynamic status when compared to an emergency surgery. No other analgesics were administered in the post operative period, when the test drug was given to the patient, to avoid additive effects.

This study was done among two groups of patients who underwent elective abdominal hysterectomy and are comparable with regards to age, height and weight.

The mean time of onset of analgesia in group RT is 9±1.6 min and in group RB it is 6.1±1.7 min .There was statistically significant difference ($p<0.001$) between the time of onset of analgesia between the two groups.

Bharti N[117] compared two mg of butorphanol in 10 mL of normal saline (Group 1), two mg of butorphanol in 10 mL of 0.125% bupivacaine (Group 2), or two mg of butorphanol in 10 mL of 0.25% bupivacaine (Group 3) administered epidurally for post operative analgesia after abdominal hysterectomy.Onset time for group1 was 14.1±2.6 min ,7±2.1 min for group 2 and 7.1±3.4 min for group 3.Duration of analgesia in that study is 4.4±0.7, 8.7±0.8 and 9.8±0.5 hours respectively in group 1, 2 and 3.Compared to that onset time of analgesia in ropivacaine butorphanol group in the present study is 6.1±1.7 min.

The duration of analgesia is 4.3±0.1 hours in group RT and 5.1±0.4 hours in group RB. Eventhough the duration ofanalgesia is more in ropivacaine –butorphanol group,it is not statistically significant($p>0.05$)

The duration of analgesia with ropivacaine – tramadol combination is low when compared with some studies done in children for abdominal surgery[118]. It may be due to the higher dose and volume of drugs that was used (Tramadol 2mg/kg, ropivacaine0.2% and total volume 0.7 ml/kg).

No significant increase in motor blockade as measured by bromage scale is observed in both the group due to the administration of study drug. The motor blockade observed in the beginning is due to the residual effect of spinal anaesthesia.

The sedation score is more in RB (ropivacaine – butorphanol) group.

Incidence of nausea and vomiting in this study is 16% in group RT and 0% in group RB. It is statistically and clinically significant. Incidence of hypotension in this study is 16 % in group RT and 4% in group RB. Incidence of dizziness in this study is 8% in group RT and 0% in group RB. Incidence of headache is in this study is16% in group RT and 4% in group RB No incidence of seizure, arrhythmia, respiratory depression or fever are observed in the present study.

Conclusions

Epidural bolus injection of both 0.2 % ropivacaine with 50 mg tramadol and 0.2 % ropivacaine with 1 mg butorphanol are effective for relieving post operative pain after abdominal hysterectomy. However faster onset of analgesia, longer duration of analgesia and less adverse reactions are observed when butorphanol is used as an adjuvant with 0.2%ropivacaine .

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