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Original Research Article

Comparison of epidural Ropivacaine 0.75% and Ropivacaine 0.75% Plus Buprenorphine (0.5 ml) for total knee replacement surgery

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Abstract

Aim and Objectives: To assess the comparison between ropivacaine and combination of ropivacaine with buprenorphine in terms of onset and duration of analgesia, cardiorespiratory effects, side effects and post-operative analgesia.
Methods: Total 60 adult patients of either sex, ASA grade I - II, schedule for total knee replacement surgery were enrolled in the study and randomized into two groups. Group R: received 14.5ml of 0.75% plain Ropivacaine + 0.5ml Normal saline (NS) making volume 15ml. Group RB: received 14.5ml of 0.75% plain Ropivacaine + Buprenorphine 150 mics (0.5ml) making volume 15ml. Onset of sensory-motor block, hemodynamic variables (HR, SBP, DPB, MAP, RR), duration of analgesia were recorded.
Results: The onset of sensory blockade was earlier in group R as compared to in group RB. The motor onset time was similar in both the groups. The mean hemodynamic parameters were comparable in both the groups. Duration of analgesia was prolonged in group RB as compared to group R. Group RB had more incidences of post-op vomiting (36.67%) and pruritus (3.3%) as compared to group R.
Conclusion: The addition of buprenorphine to epidural ropivacaine is a well tolerated, effective method for epidural anesthesia in patients undergoing unilateral total knee replacement surgery.
Keywords: Ropivacaine, Buprenorphine, Epidural Cardiorespiratory effects, Post-operative analgesia, Knee replacement surgery.

1. Introduction

Epidural anesthesia is the most commonly used technique for providing not only peri-operative surgical anesthesia but post-operative analgesia in lower abdominal and limb surgeries [1]. It provides dynamic analgesia, allowing patient to resume normal activities unlimited by pain [2]. Local anesthetics and opioids remain the most commonly used drugs in regional anesthesia either by single shot or continuous infusion technique. The sole use of local anesthetics agent is less popular at present because there is delay in onset of sensory block and inadequate analgesia. The discovery of opioid receptors has opened up a new horizon in pain management.

The new amide local anesthetic ropivacaine has minimal cardiovascular and central nervous system toxicity as well as less propensity of motor block during post operative epidural analgesia. The most important attribute of ropivacaine, however, is its increased margin of safety as compared to with bupivacaine when given in equal doses.

Also the incidence of motor block after epidural analgesia with amide local anesthetic and opioids is approximately 4-12% which itself defeats the novel purpose of early rehabilitation [3].

Buprenorphine is most widely used epidural opioid analgesic for orthopedic surgeries. It is 30 times more potent than morphine and is agonist-antagonist with lipid solubility about 5 times greater than that of morphine has been used epidurally for post operative analgesia. It has been associated with lower incidence of delayed respiratory depression, because there is no rostral spread [4]. It has low potential for abuse. It is readily available without a narcotic license.

Though ropivacaine has been used with many opioids for neuraxial blocks but there is very few studies available to compared the effects of addition of epidural buprenorphine to ropivacaine for total knee replacement surgery. Therefore this prospective, randomized, double blind study was designed to compares the epidural ropivacaine 0.75% with a combination of epidural ropivacaine and buprenorphine for total knee replacement surgery with emphasis on onset, intensity, duration of the block, cardiorespiratory effects and post-operative analgesia. We chose only epidural route because there have been no studies comparing these drugs through epidural route solely.

2. Material and Method

After obtaining Institutional Ethical Committee approval and patient's written informed consent, this prospective, randomized, double blind study was conducted in 60 adult patients of ASA grade I or II, aged 18–85 years, weight and height between 45kg – 85kg and 4. 150cm – 180cm respectively and were scheduled for total knee replacement surgery. Patients with known hypersensitivity to any of the study drug, ASA grade III and above**,** having history of backache or spine surgery, presence of spinal deformities, local infection at the site of epidural injection patients who needed induction of general anesthesia, surgical or anesthetic complication requiring intubation**,** evidence of severe cardiovascular, renal, hepatic, h**e**matological, neurological, or psychiatric illness, chronic pain syndrome, alcoholism, drug abuse or mental retardation were excluded from the study. All the patients were randomly divided into two equal groups. Group R: received 14.5ml of 0.75% plain Ropivacaine + 0.5ml Normal saline (NS) making volume 15ml and group RB: received 14.5ml of 0.75% plain Ropivacaine + Buprenorphine 150 micrograms (0.5ml) making volume 15ml. One patient from group R was excluded from the study due to inadequate effect of the study drug.

A pre-anesthetic evaluation including proper history, general and systemic examination, airway assessment and all relevant investigations were done for all the patients. The technique of epidural anesthesia and nature of the study were explained to the patient and a written informed consent was obtained. All patients received thromboprophylaxis (inj. Enoxaparin 0.6mg SC) 24 hours prior to surgery. Next dose was given 48 hours after the first dose. Epidural catheter removal was done 12 hours after the second dose. All patients were fasted for 8 hrs and premedicated with ranitidine 150mg on the night before and 1hr before surgery with sips of water. Anti-platelet agents (Aspirin and Clopidgrel) were stopped 7 days before surgery**.** Morning dose of anti-hypertensive drug was given with sips of water 1 hour before surgery.

In operation theatre, an intravenous access was secured using 20G IV cannula and patient pre-loaded with Ringers lactate solution (10 ml/kg body weight). The multipara monitors such as pulse oximeter, Cardio scope, NIBP were attached to the patients and baseline readings of heart rate, blood pressure, SpO_2%, ECG, respiratory rate were recorded. Under due aseptic and antiseptic precautions and with patient in sitting position, a skin wheal was raised at L3-L4 inter space with 2ml of 2% lidocaine. The epidural space was identified using an 18G Touhy needle with 20G catheter in the midline with loss of resistance to air technique. The catheter was advanced 5cm into the epidural space in cephalic direction. The patient was given supine position after securing the epidural catheter in position. A test dose of 3ml of 2% lidocaine containing epinephrine (1:200,000) was administered to detect intrathecal or intra-vascular injection. After negative response, 14.5ml of 0.75% ropivacaine with 0.5ml of buprenorphine (Group RB) or 0.5ml Normal saline (Group R) was administered @ 3ml / 10sec. The study drug solutions were prepared by an anaesthetist who was given written instructions and was unaware of the study design. Supplementation with bupivacaine was required for adequate surgical anesthesia.

Sensory block was assessed every 2.5 minutes till 30 minutes or till two consecutive same readings were achieved using a pin-prick method. Motor block was assessed by Modified Bromage scale at every 5 minutes till 30 minutes after completion of epidural injection or till two consecutive same readings were achieved. Heart rate, blood pressure, oxygen saturation and respiratory rate were recorded every 5 minutes for the first 30 minutes and thereafter every 15 minutes till the end of surgery. All patients received oxygen at 2 L/minute by nasal cannula during the surgery. The patients were monitored for adverse effects viz. nausea and vomiting, respiratory depression and pruritis. We could not monitor urinary retention, a side-

effect, as all the patients were catheterized. Nausea and vomiting was treated with injection ondansetron 4 mg and pruritis was treated with chlorpheniramine 10 mg intravenously. Further sedation was provided with IV boluses of midazolam 0.03-0.05 mg/kg during surgery to patients who experienced discomfort and were anxious at any time during surgical procedure. Patient and surgeon satisfaction was noted with anesthesia technique after the surgery using the two point scale: 1. Satisfactory [if necessary, I would have the same anesthetic again], 2. Unsatisfactory [I would prefer a different anesthetic]

In the recovery room, all patients were assessed for sensory and motor blocks every 30 minutes for 4 hours after injection.

2.1 Statistical Analysis

Software SPSS version 15 and Sigmaplot Version 11 was used for data analysis. Quantitative data was presented as mean, standard deviation, median and IQR, comparison among study groups were done using Unpaired T test or Mann-Whitney test as per the results of Normality test. Also comparison was done with the help of Paired T test or Wilcoxon sign rank test. Qualitative data was presented as frequency and percentage, association among study group was assessed using Chi-Square test. The results were considered statistically significant at $P < 0.05$ and highly significant at $P < 0.005$ level.

3. Observations and Results

Table 1 show the demographic data and mean duration of surgery, there was no statistically significant difference between two groups with regard to age, weight; height, sex, ASA physical status and duration of surgery.

Table 1: Demographic data and duration of surgery

Variables	Group R	Group RB	P-value
Age (years)	61.72 ± 8.40	62.93 ± 7.81	0.569
Height (cm)	162.93 ± 8.79	161.42 ± 7.00	0.466
Weight (kg)	70.38 ± 9.61	70.57 ± 8.76	0.938
Sex (M/F)	13/16	9/21	-
ASA grade I/II	10/19	16/14	-
Duration of surgery (min)	74.59 ± 11.69	79.73 ±13.19	0.119

The time taken for achieving sensory block at T12 level was higher in group RB (20.25 ± 2.31 minutes) as compared to that in group R (17.67 ± 2.00 minutes). Complete motor block was achieved in 25.95 + 1.23 minutes in group R and 26.58 + 1.55 minutes in group RB ($p = 0.086$) and it was comparable in both the groups. The mean duration of post-operative analgesia was longer in group RB (297.33 ± 12.08 minutes) as compared to that of group R (259.3 ± 12.08 minutes), the difference being statistically significant (Table 2).

Table 2: Comparison of Anesthetic Parameters between two groups

Parameters	Group R	Group RB	P-value
Onset for T 12	17.67 ± 2.00	20.25 ± 2.31	0.00**
Complete block (3)	25.95 ± 1.55	26.58 ± 1.23	0.086
Post op-analgesia (min)	259.31±12.08	297.33±12.08	0.00**

***P<0.05 – significant**
****P<0.005 – highly significant**

The pulse rate during the surgery till 90 minutes was comparable in both the groups. It was higher in group RB at 105 minutes (mean PR = 89.00) which was statistically significant. The systolic blood pressure in both the groups was comparable throughout the intra-operative period. The diastolic blood pressure was higher in group RB at 5, 25, 45, 60, 90, 105 minutes while mean arterial pressures were higher at 5, 25, 90 minutes which was statistically significant (Figure 1). The respiratory rate was comparable throughout the intra-operative period in both the groups (Figure 2). There was no statistically significant difference in intra-op oxygen saturation in two groups. The sedation score was higher in group RB at 30, 45, 60 and 75 minutes which was statistically significant.

Figure 1: Comparison of haemodynamic parameters (pulse rate, systolic, diastolic and mean blood pressure) between two groups

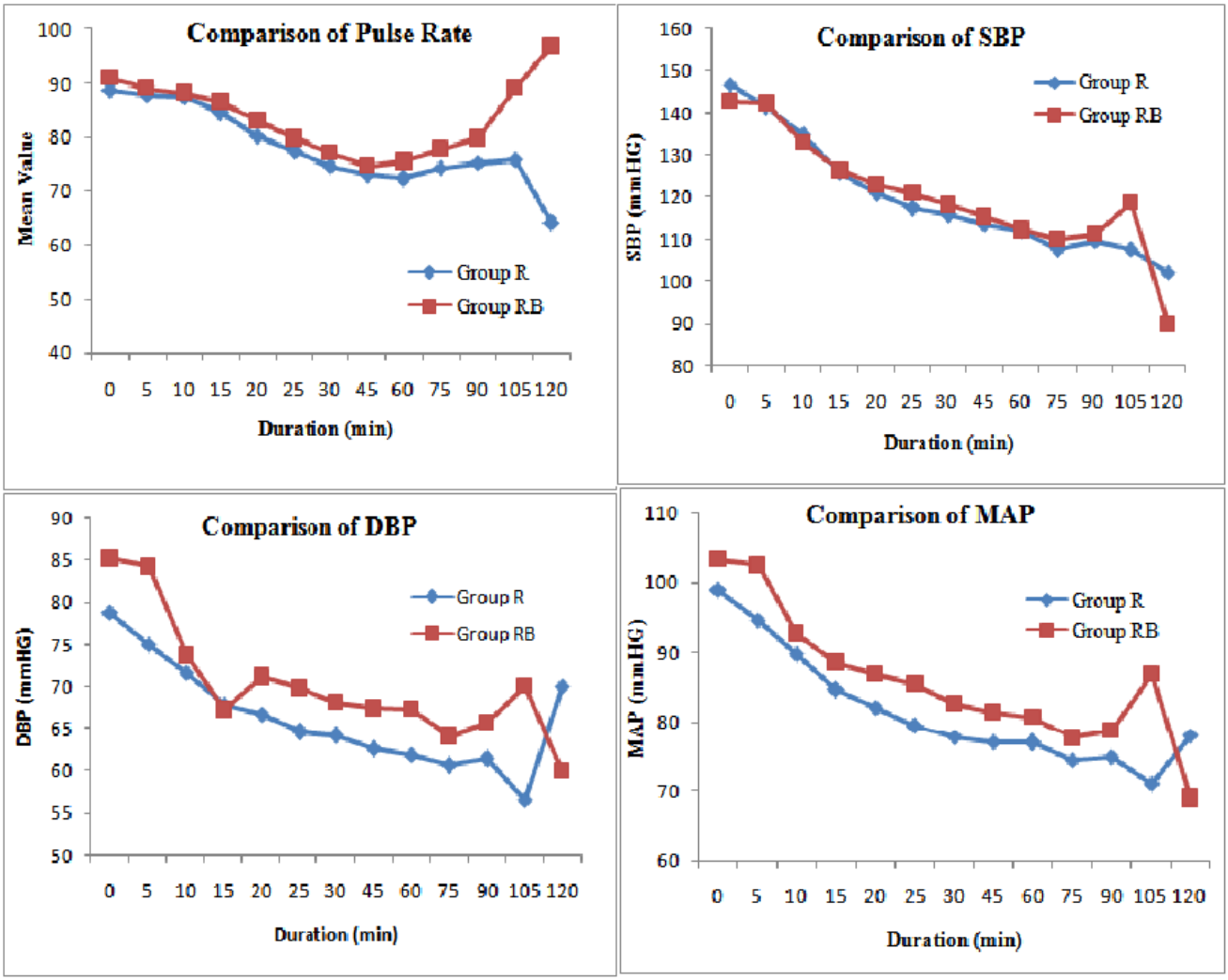
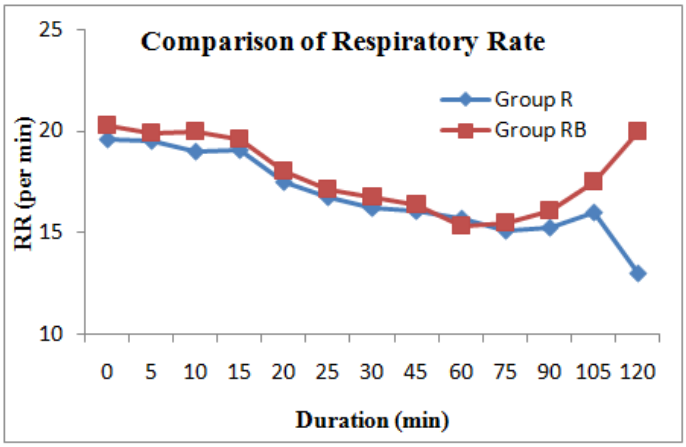


Figure 2: Comparison of respiratory rate between two groups



The haemodynamic parameters (pulse rate, systolic, diastolic and mean blood pressure) were comparable in post operative period. Except for diastolic BP was higher in group RB at 30 minutes which was statistically significant. The respiratory rate in group RB was higher at 1hr postoperatively which was statistically significant. It was observed that the group RB had more incidences of post-op vomiting (36.67%) and pruritus

(3.3%) as compared to Group R, association of which was statistically significant.

4. Discussion

Total knee replacement with continuous passive motion for postoperative rehabilitation may cause more severe pain and thus may require a higher local anaesthetic concentration than that required for pain due to rehabilitation after total hip replacement. To our knowledge, there are no data available on the epidural combination of ropivacaine with buprenorphine after total knee replacement. Hence, the present study was designed to compare the qualitative and quantitative aspects of epidural block, hemodynamic effects, and post operative pain relief of ropivacaine Vs its combination with buprenorphine in 60 adult patients of ASA physical status I and II undergoing unilateral total knee replacement surgery. The demographic data (age, sex, height and weight) and duration of surgery being comparable and seems that it has no influence on outcome of the study.

Time of onset of sensory block to T12 dermatome in group R (17.67 + 2.00 min) was found to be earlier than group RB (20.25 + 2.31 min) and difference was found to be statistically highly significant (p = 0.00). Maximum block height achieved was T6 in both the groups. This shows that addition of buprenorphine to ropivacaine delayed the onset of sensory block. These results were in concordance with the results of Katz JA *et al* [5] and Peduto *et al* [6]. In the study of Katz JA *et al* [5] dose of ropivacaine used was more (20 ml) as compared to our study (15 ml), thereby explaining lower sensory block height in lesser time in their study. The mean time taken to achieve complete motor block (modified Bromage scale 3) was comparable in two groups, difference was found to be statistically insignificant and which was similar to the results of Katz JA *et al* [5] and Tuttle AA *et al* [7]. The mean duration of post-operative analgesia was longer in group RB (297.33 ± 12.08 minutes) as compared to that of group R (259.3 ± 12.08 minutes), the difference being statistically significant. This shows that addition of buprenorphine to ropivacaine delayed the onset of sensory block but prolonged the duration of analgesia in the post-operative period. None of the patients in either group required additional epidural top-up dose during the surgery. Our finding compared with the previous studies [5,8-11]. The addition of buprenorphine to the local anesthetic used for brachial plexus block in present study provided a 3-fold increase in the duration of postoperative analgesia. However in other studies [5,8,9], the dose of buprenorphine administered was higher (3 micrograms/kg and 300 micrograms), resulting in longer duration of analgesia as compared to our study (150 micrograms). Previous studies [5,8-11] suggest that combination of ropivacaine with buprenorphine is more beneficial than ropivacaine alone as a local anesthetic agent for post-operative analgesia.

In present study the pulse rate during the surgery till 90 minutes was comparable in both the groups. It was higher in group RB at 105 minutes (mean PR = 89.00) which was statistically significant. This may be due to less number of patients in both the groups at 105 minutes. The systolic blood pressure was comparable in both the groups throughout the intra-operative period. The diastolic blood pressure was significantly higher in group RB at 5, 25, 45, 60, 90, 105 minutes while mean arterial blood pressure was higher at 5, 25 and 90 minutes as compared to that in group R. This can be due to delayed onset of anesthetic effect on autonomic nervous system in group RB resulting in higher diastolic and mean arterial pressures. The cardiovascular parameters were correlated with the study of McGlade DP *et al* [12]. The respiratory rate and oxygen saturation was comparable in both the groups throughout the intra-operative period showing that there was no respiratory depression due to buprenorphine administration in our study and compare with Ichiishi N.*et al* [13].

The sedation score was higher in group RB at 30, 45, 60 and 75 minutes which was statistically significant. Nine patients in group RB and 1 patient in group R were given IV Midazolam 1mg as they experienced anxiety regarding the environment of the operation theatre. There was no pain experienced at this time as seen by stable hemodynamic parameters (no tachycardia, hypertensive response). Our results compare with the study of Shin K *et al* [14]. Post-operative vomiting was seen in 11 patients in group RB while none of the patients had complained the same in group R. Pruritis was seen in one patient in group RB which was not seen in any of the patients in group R. Cases of urinary retention could not be assessed, as patients were catheterized prior to surgery. This suggests the significant occurrence of adverse effects after administration of epidural buprenorphine with ropivacaine. Similar effects were observed in study of Ita Takashi *et al* [15]. Patient and surgeon satisfaction was comparable in both the groups in our study; this was similar to the study of Tuttle AA *et al* [7].

The present study demonstrated that ropivacaine is a well tolerated regional anesthetic, effective for surgical anesthesia as well as the relief of postoperative pain. Clinically adequate doses of ropivacaine appear to be associated with a lower incidence or grade of motor block. Addition of buprenorphine prolongs the duration of post-operative analgesia. Thus ropivacaine, with its efficacy, lower propensity for motor block and reduced potential for CNS toxicity and cardiotoxicity, appears to be an important option for regional anesthesia and for the management of

postoperative pain. Further studies will be carried out with this aspect in consideration. Epidural buprenorphine dose can be increased to 300 micrograms with local anesthetic agent to further prolong the post-operative analgesia but with an anti-emetic given pre-operatively and continued in the post-operative period to prevent post-operative nausea and vomiting.

5. Conclusion

The addition of buprenorphine to epidural ropivacaine delays the onset of sensory blockade and prolongs the duration of analgesia. Also, epidurally administered opioids have gradual and prolonged analgesic action without hampering the motor power of the lower limbs. This provides early post-operative mobilization and rehabilitation reducing the chances of muscle stiffness and deep vein thrombosis. Thus addition of buprenorphine to epidural ropivacaine is a well tolerated, effective method for epidural anesthesia in patients undergoing unilateral total knee replacement surgery. It can be reasonably recommended as epidural anesthetic agent in ASA I and II adult patients for intra-operative anesthesia and post-operative analgesia as well.

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Reference

[1]. Grass JA. The role of epidural anesthesia and analgesia in postoperative outcome. *Anesthesiology Clinics of North America.* 2000 Jun; 18(2): 407-28.

[2]. Choi P, Bhandari M, Scott J, Douketis J. Epidural analgesia for pain relief following hip or knee replacement. *Cochrane Database Syst Rev*. 2003; 3(3).

[3]. Dene Simpson, Monique P. Curran, Vicki Oldfield, Gillian M. Keating. Ropivacaine – A review of its use in regional anesthesia and acute pain management. *Adis drug evaluation Drugs* 2005; 65(18):2675-717.

[4]. Henry J. Mc Quay. Epidural analgesics in Pairic D. Wall, Ronald Melzack. Text Book of Pain. 3rd edition, Churchill Livingstone, 1994; 1025-26.

[5]. Katz JA, Knarr D, Bridenbaugh PO. A double-blind comparison of 0.5% Bupivacaine and 0.75% Ropivacaine administered epidurally in humans. *Reg. Anesth* 1990; 15(5): 250-2.

[6]. Peduto VA, Baroncini S, Montanini S, Proietti R, Rosignoli L, Tufano R, Casati A. A prospective, randomized, double-blind comparison of epidural levobupivacaine 0.5% with epidural Ropivacaine 0.75% for lower limb procedures. *Eur J Anaesthesiol* 2003; 20(12):979-83.

[7]. Tuttle AA, Katz JA, Bridenbaugh PO, Quinlan R, Knarr D. A double-blind comparison of the abdominal wall relaxation produced by epidural 0.75% Ropivacaine and 0.75% Bupivacaine in gynecologic surgery. *Reg Anesth*. 1995; 20(6):515-20.

[8]. Bazin JE, Massoni C, Bruelle P, Fenies V, Groslier D, Schoeffler P. The addition of opioids to Local Anaesthetics in brachial plexus block: The comparative effects of morphine, buprenorphine and sufentanil. *Anesthesia* 1997; 52:858-62.

[9]. Kenneth D. Candido, Carlo D. Franco, Mohammad A. Khan, Alon P. Winnie, Durre S. Raja. Buprenorphine added to the local anesthetic for brachial plexus block to provide postoperative analgesia in outpatients. *Reg Anesth Pain Med* 2001; 26:352-6.

[10]. Candido KD, Winnie AP, Ghaleb AH, Fattouh MW, Franco CD. Buprenorphine added to the local anesthetic for axillary brachial plexus block prolongs postoperative analgesia. *Reg Anesth Pain Med* 2002; 27(2):162-7

[11]. Hirabayashi Go, Uchino Hiroyuki *et al*. Comparison of thoracic epidural Ropivacaine or Ropivacaine / Buprenorphine infusions for post-thoracotomy pain. *Pain Clinic* 2006; 27(12):1581-5.

[12]. McGlade DP, Kalpokas MV, Mooney PH, Buckland MR, Vallipuram SK, Hendrata MV, Torda TA. Comparison of 0.5% Ropivacaine and 0.5% Bupivacaine in lumbar epidural anesthesia for lower limb orthopaedic surgery. *Anaesth Intensive Care.* 1997; 25(3):262-6.

[13]. Ichiishi N. Hiraishi T, Hara O *et al*. Effect of epidural Buprenorphine on post operative respiratory function. *Masui* 1992; 41(10): 1574-9.

[14]. Shin K, Choe H, Han Y, Kim D, Song H. Efficacy of the Epidural Buprenorphine for Postoperative Pain Control after Upper Abdominal Surgery. *J Korean Pain Soc.* 1993; 6(2):213-219.

[15]. Ito Takashi, Takahashi Hitoshi, Kinoshita Mayumi, Matsuura Naomi. Side Effects Caused by Epidural Buprenorphine in Young Patients Undergone Knee Surgery of about One Hour Duration. *J Clin Anesth.* 2000; 24(7):1117-21.