

## Comparative Evaluation of two Doses of Epidural Butorphanol with Bupivacaine for Postoperative Analgesia

Sukhvir Singh<sup>1</sup>, Navreet Kaur<sup>2</sup>

**Author's Affiliation:**<sup>1</sup>Consultant, Department of Anesthesiology, Max Hospital Mohali, Punjab 160055. <sup>2</sup>Medical Officer, PCMS, Punjab 160062, India.

### Abstract

**Background:** Postoperative analgesia is very important to prevent subjective discomfort, early mobilization and shortened hospital stay. Opioids addition to local anesthetics improve the quality of analgesia. Present study was designed to evaluate and compare the duration and efficacy of two different doses of epidural Butorphanol for postoperative analgesia.

**Patients and Methods:** This prospective, randomized double blinded study was conducted on 75 patients in the age group of 20-60 years of either sex, with ASA class I and II scheduled for elective lower limb orthopedic surgeries under combined spinal epidural anesthesia after taking the informed consent and approval from hospital ethical committee. Group allocation, group I (n=25) received epidural 0.25 % bupivacaine, group II (n= 25) patients received 0.25% epidural Bupivacaine and 1 mg Butorphanol, group III (n= 25) patients received 0.25% epidural Bupivacaine and 2 mg Butorphanol. Postoperatively VAS, sedation score, vitals & side effects were observed. Injections were given on achieving VAS>3.

**Results:** Onset of analgesia was significantly shorter in group III as compare to group II and group I. Duration of analgesia was longest in group III 9.95±0.43 hour which was significantly greater than group I 3.90±0.32 hours and group II 6.06±0.26 hours. Postoperative VAS scores at different intervals were lower in group III than group II and group I (group III< group II< group I). Sedation scores were significantly higher in butorphanol group with no major adverse effects.

**Conclusion:** Butorphanol 2 mg with 0.25% bupivacaine appears to be the optimal dose to produce a more rapid onset and longer duration of analgesia with no adverse effects.

**Keywords:** Epidural; Postoperativanalgesia; Butorphanol.

### Introduction

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.<sup>1</sup> Postoperative pain can be a major source of fear and anxiety in hospitalized patients. The most terrible period as far as pain is concerned is the first 24 hours, when the severity of pain and vital signs are fluctuating. Use of postoperative regional

analgesia not only decreases the cost of patient care through shorter intensive care units stays, but also decreases the rate of complications and increases patient satisfaction.<sup>2</sup> Combined spinal epidural aims at providing the benefits of spinal anesthesia with flexibility of an indwelling epidural catheter to extend the duration of analgesia into postoperative period.<sup>3</sup> Combination of local anesthetic with opioids result in prolonged postoperative analgesia.

### How to cite this article:

Sukhvir singh, Navreet Kaur/ Comparative Evaluation of Two Doses of Epidural Butorphanol with Bupivacaine for Postoperative Analgesia/ Indian J Anesth Analg. 2021;8(3): 363-367.

**Corresponding Author: Sukhvir Singh**, Consultant, Department of Anesthesiology, Max Hospital Mohali, Punjab 160062, India.

**Email:** [drsukhvirsingh@gmail.com](mailto:drsukhvirsingh@gmail.com)



This work is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0.



Butorphanol, a synthetic morphine derivative is a mixed agonist and antagonist non-narcotic opioid analgesic. Butorphanol and its metabolites are agonist at kappa receptors and mixed agonists antagonists at mu receptors.<sup>4</sup> Receptor specificity of butorphanol has been used to limit respiratory depression, gastrointestinal side effects and reduce risk of dependency.<sup>5</sup> Present study was conducted to compare and evaluate duration and efficacy of two different doses of epidural butorphanol and to find out the most suitable analgesic dose with minimal side effects for postoperative analgesia.

## Methods

The present prospective, randomized double blinded study was conducted on 75 patients in the age group of 20-60 years of either sex, with American society of anaesthesiologists (ASA) class I and II admitted to tertiary care hospital of north India after obtaining institutional ethical committee clearance and scheduled for elective lower limb orthopaedic surgeries of duration more than one hour under combined spinal epidural anaesthesia. After taking the informed consent patients were randomly divided into three groups of 25 each based on computer generated random numbers (figure 1). Group I patients received 10 ml of 0.25% epidural Bupivacaine. Group II patients received 9 ml of 0.25% epidural Bupivacaine and 1 ml of 1 mg Butorphanol. Group III patients received 9 ml of 0.25% epidural Bupivacaine and 1 ml of 2 mg Butorphanol. All injections were

prepared to make a final volume of 10 ml in all groups. After routine pre anesthetic checkup patients were moved to operation theatre. A sealed envelope with drug code was given to the attending anesthesiologist who was unaware of study design and study groups. Baseline vitals were recorded and monitored. Under all aseptic precautions combined spinal epidural anaesthesia was administered. Subarachnoid block was given with 2.5 ml of 0.5% heavy bupivacaine. Spinal needle was then withdrawn, epidural catheter was inserted, secured and its patency checked. Level of sensory blockade was checked by pinprick and motor blockade by Bromage's criteria (1=unable to move feet or knees, 2=able to move feet only, 3=just able to move knees, 4=full flexion of knees and feet). The operation was started when full surgical anaesthesia was attained. In the postoperative period, at visual analogue scale >3, a bolus of one of the three study drugs was injected through an epidural catheter. Patients were assessed at 5, 10, 15, 30, 60 and 90 minutes and then at 2, 3, 4, 5, 6, 8, 12 and 24 hours after epidural injection for intensity of pain, heart rate, systolic and diastolic blood pressure, respiratory rate and sedation score. Time from epidural injection to complete pain relief was recorded as onset of analgesia. Duration of analgesia was defined as time from epidural injection to time of request of rescue analgesia. Additional rescue analgesia was given with Diclofenac sodium 75 mg. Sedation score (0 - Fully awake, 1- Slightly drowsy, 2- Asleep but easily arousable, 3- Fully asleep but

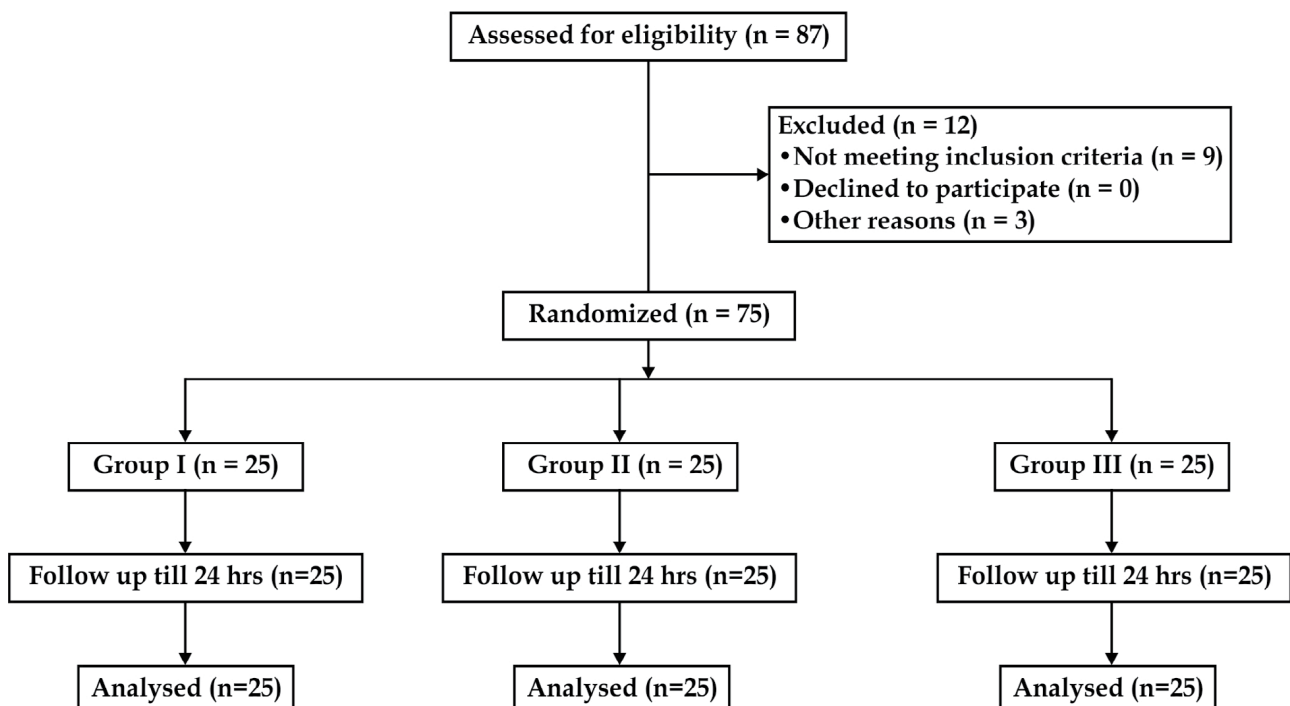


Fig. 1: Consort flow diagram.

arousable, 4- Sleeping and not arousable) was assessed. Side effects such as nausea, vomiting, pruritis, hypotension and bradycardia if any were recorded. Data was calculated in terms of mean  $\pm$  standard deviation ( $\pm$ SD). Comparison of data between groups was done by using ANOVA with Post Hoc Tukey HSD for inter group comparison of parametric data and chi square test for non-parametric data. A p value of less than 0.05 was considered significant and less than 0.001 was considered highly significant.

**Results**

Demographic variables were comparable between three groups (table 1). ASA grading, mean duration of surgery and sensory level achieved were comparable between three groups. There was no statistically significant difference between baseline vitals in three groups. Open reduction and internal fixation of femur and tibia was the most common surgery performed among all the three groups. The difference in the mean postoperative pulse rate, blood pressure at different time intervals in between groups was found to be insignificant.

**Table 1:** Demographic data of three groups.

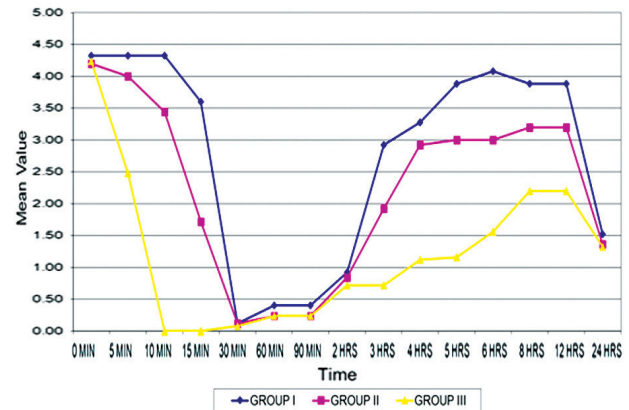
Demographic variable	Group I	Group II	Group III	P value
Age (years)	45.28 $\pm$ 7.10	43.48 $\pm$ 10.81	44.56 $\pm$ 11.36	0.813
Sex (F:M)	8:17	7:18	7:18	0.938
ASA grade (I: II)	17:8	16:9	18:7	0.832
Duration of surgery	141.40 $\pm$ 14.47	137.80 $\pm$ 20.05	143.40 $\pm$ 20.80	0.563
Sensory level achieved	T9.20 $\pm$ 1.16	T9.12 $\pm$ 1.17	T9.60 $\pm$ 1.14	0.353

**Table 2:** No. of Injections of rescue analgesia (Values are Mean  $\pm$  SD).

Group I	Group II	Group III	P value Group I VS II	P value Group I VS III	P value Group II VS III
2.72 $\pm$ 0.46	1.16 $\pm$ 0.37	1.04 $\pm$ 0.20	<0.001	<0.001	0.471

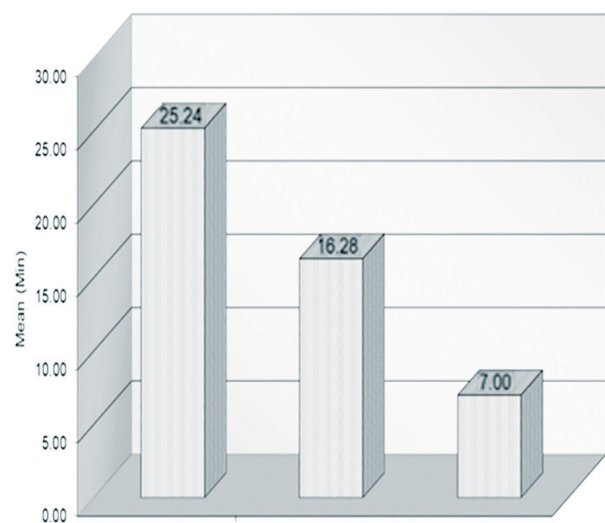
The mean oxygen saturation, respiratory rate in three groups was calculated at different intervals. The difference between the three groups was found to be insignificant statistically ( $p > 0.05$ ). The mean VAS score was calculated in three groups (figure 2). The VAS at '0' minute was found to be insignificant ( $p > 0.05$ ) between the groups, it was highly significant ( $p < 0.001$ ) at 5, 10, 15 minutes and at 3, 4, 5, 6, 8 and 12 hours ( $p < 0.001$ ). VAS at 30, 60, 90 and 2 hours was found to be insignificant statistically ( $p > 0.05$ ). This data shows that patients in group III and group II had significantly lower VAS scores.

The mean duration of onset of analgesia in group I was 25.24 $\pm$ 4.12 minutes, group II was 16.28 $\pm$ 1.51 minutes and group III was 7.00 $\pm$ 0.81 minute (figure 3). The difference in groups was found to be highly significant statistically. Thus, indicating that group III had a shorter onset of analgesia as compared to group II and group I.



**Fig. 2:** Comparison of postoperative visual analogue scale in three groups.

The mean duration of analgesia in Group I was 3.90 $\pm$ 0.32 hours, in Group II was 6.06 $\pm$ 0.26 hours and in Group III was 9.95 $\pm$ 0.43 hours (figure 4). This difference in groups was found to be highly significant statistically ( $p < 0.001$ ). Thus, indicating that group III had a longer duration of analgesia as compared to group II and group I. Mean no. of injections of rescue analgesia was 2.72 $\pm$ 0.46 in group I, 1.16 $\pm$ 0.37 in group II and 1.04 $\pm$ 0.20 in group III (table 2). The difference in group I and II, group I and III was found to be highly significant statistically ( $p < 0.001$ ). Total consumption of Diclofenac sodium injections was less in patients in group II and III as compare to group I.



**Fig. 3:** Comparison of onset of analgesia in three groups.

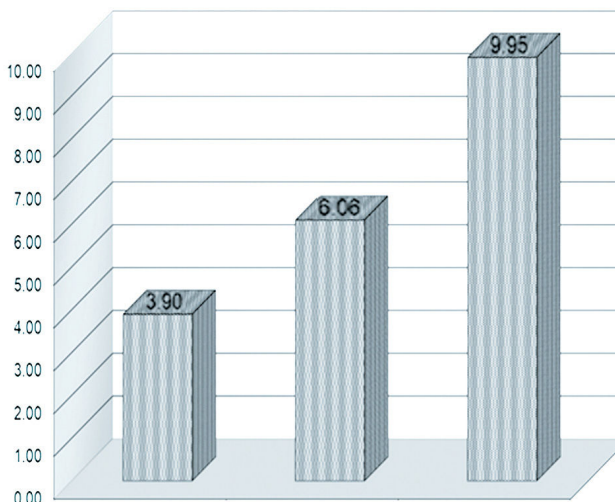


Fig. 4: Comparison of duration of analgesia in three groups.

There was no patient who was having sedation at '0' minutes thus mean difference of sedation was also found to be insignificant statistically ( $p > 0.05$ ) and at other time intervals sedation score was found to be highly significant at 5 minutes to 12 hours, except 24-hour interval where it was insignificant among three groups. Thus, indicating that group III has more incidence of sedation than group II and group I (figure 5). Nausea was seen in 4 patients of group I which was statistically significant. Vomiting was seen in 3 patients of group I which was also statistically significant as none of patient in group II and group III has episode of vomiting. None of the patient had pruritis and respiratory depression in three groups.

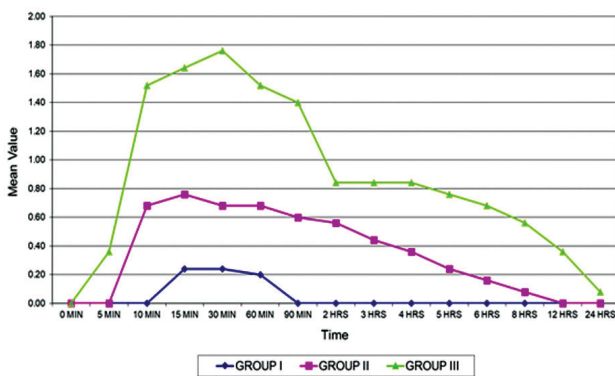


Fig. 5: Comparison of sedation scores in three groups.

## Discussion

Combined spinal epidural anesthesia finds a common place for perioperative management of orthopedic surgery. Various opioids have been used with bupivacaine for postoperative epidural analgesia like morphine<sup>6</sup>, fentanyl<sup>7</sup>, pethidine<sup>8</sup>, tramadol<sup>9</sup>, buprenorphine<sup>10</sup>, methadone<sup>11</sup> and butorphanol<sup>12</sup>. Butorphanol is a strong  $\kappa$ -receptor

agonist and a weak  $\mu$ -receptor agonist-antagonist, thus it has significant analgesic potency and narcotic antagonistic properties. The analgesic potency of butorphanol has been found to be greater than morphine and pethidine. Butorphanol unlike morphine exhibits a ceiling effect on respiratory depression.<sup>13</sup> In this study we evaluated and compared the duration and efficacy of two different doses of epidural butorphanol for postoperative analgesia in patients undergoing lower limb orthopaedic surgeries.

In our study it was observed that group I has onset of analgesia time of  $25.24 \pm 4.12$  minutes. Time of onset of analgesia decreased to  $16.28 \pm 1.51$  minutes in group II and to  $7.00 \pm 0.82$  minutes in group III, this difference in onset time was highly significant ( $p < 0.001$ ). High lipid solubility and high affinity for opioid receptors of butorphanol is the reason for rapid onset of analgesia. Our results were in accordance with study conducted by Hunt et al<sup>14</sup>, they reported that complete pain relief was present in  $21.3 \pm 5.2$  minutes when no butorphanol was added to the 0.25% bupivacaine. Time of onset decreased to  $16.5 \pm 3.6$  minutes and to  $6.9 \pm 3.6$  minutes with addition of 1 mg and 2 mg of butorphanol to 0.25% bupivacaine respectively. In our study duration of analgesia in group III was  $9.95 \pm 0.43$  hours which was significantly higher ( $p < 0.001$ ) than group II ( $6.06 \pm 0.26$  hours) and group I ( $3.90 \pm 0.32$  hours). A dose dependent reduction in rescue analgesic requirements was also noted in our study in group III and group II as compare to group I. Abboud et al<sup>15</sup> showed that addition of one or two mg of butorphanol to 0.25% bupivacaine epidurally produces significantly longer duration of labor analgesia ( $139 \pm 11$  minutes and  $141 \pm 14$  minutes, respectively) than does bupivacaine alone ( $96 \pm 6$  minutes). In a dose response study of a combination of epidural butorphanol with zero, one, two or three mg of butorphanol, Hunt et al<sup>14</sup> reported significantly greater duration of labor analgesia ( $137 \pm 18.4$  minutes) with addition of two mg of butorphanol to 0.25% bupivacaine as compared with bupivacaine alone ( $59 \pm 12.3$  minutes). Although these studies reported increased duration of analgesia with the addition of butorphanol to epidural bupivacaine than with bupivacaine alone, duration of analgesia was only about 140 minutes in the combination group. In our study duration of analgesia was  $9.95 \pm 0.43$  hours in two mg of butorphanol- bupivacaine combination group and  $6.06 \pm 0.26$  hours in one mg of butorphanol- bupivacaine combination group. Our findings are consistent with their findings but the differences in duration may be due to different study populations

as we compared postoperative analgesia after orthopedic lower limb surgeries rather than labor analgesia. In our study, mean VAS scores at the time of epidural administration were similar in all the three groups. VAS scores at 5, 10, 15 minutes and at 3, 4, 5, 6 and 8 hours were significantly ( $p < 0.001$ ) lower in butorphanol bupivacaine combination group than the bupivacaine alone group. At 30, 60, 90 minutes and two hours VAS scores were insignificant between groups. Similarly N. Bharti, P. Chari<sup>16</sup> also found median VAS scores were significantly lower in butorphanol bupivacaine combination group. Palacios et al<sup>17</sup> also found median pain scores significantly lower in butorphanol group. Sedation was significantly higher in group III ( $0.08 \pm 0.28$  to  $1.76 \pm 0.60$ ) and group II ( $0.08 \pm 0.28$  to  $0.76 \pm 0.60$ ) in our study and this was statistically highly significant ( $p < 0.001$ ) as compare to group I. Mild sedation is considered desirable as in group III and group II. Malik P et al<sup>18</sup> also found sedation scores significantly higher in butorphanol group ( $0.97 \pm 0.68$  to  $2.03 \pm 0.87$ ) at all postoperative intervals over 24 hours. There was no statistical difference in changes of respiratory rate and SpO<sub>2</sub> at different time interval between the three groups. Butorphanol has a ceiling effect on respiratory depression<sup>13</sup>, although no clinical evidence of respiratory depression with epidural butorphanol has been reported thus far, a transient depression of carbon dioxide response curve was observed by Abboud et al<sup>15</sup> after 1.5 hrs in patients receiving two to four mg of epidural butorphanol. We were unable to document any respiratory depressant effect of epidural butorphanol, also none of the patient had pruritis, nausea, vomiting and other adverse events.

## Conclusion

From the present study we conclude that both 1 mg and 2 mg of butorphanol in combination with 0.25% bupivacaine can be used for postoperative analgesia via epidural route in patients undergoing lower limb orthopedic surgeries with effective postoperative analgesia without fear of nausea/vomiting, pruritis and respiratory depression. Butorphanol 2 mg with 0.25% bupivacaine appears to be the optimal dose to produce a more rapid onset and longer duration of analgesia with no adverse effects.

## Reference

- Merskey H, Fessard DG, Bonica JJ. Pain terms: a list with definition and terms of usage. *Pain* 1979; 6: 249-52.
- Wu CL. Acute postoperative pain. In: Miller RD editor. *Anesthesia*. 6th ed.
- Pennsylvania: Churchill Livingstone; 2005.p.2729-62.
- Soresi AL. Episubdural Anaesthesia. *Anesth Analg* 1937; 16:306-10.
- Ameer B, Salter FJ. Drug therapy reviews: Evaluation of butorphanol tartarate. *Am J Hosp Pharm* 1979; 36:1683-91.
- Voyelsang J and Haynes SR. Butorphanol tartrate(stadol): A review. *J Post Anaesth Nurs* 1991; 6(2): 129-35.
- Behr M, Olshwang D, Magora F, Davison JT. Epidural morphine in the treatment of pain. *Lancet* 1979; 1: 52.
- Naulty JS, Johnson M, Burger GA, Datta S. Epidural fentanyl for post cesarean delivery pain management. *Anaesthesiology* 1983; 59(3):415.
- Cousins MJ, Mather LE, Glynn CJ, Wilson PR, Graham JR. Selective spinal analgesia. *Lancet* 1979 May 26; 1(8126):1141-2.
- Gupta R, Kaur S, Singh S, Aujla K.S. A Comparison of epidural Butorphanol and tramadol for postoperative analgesia using CSEA technique; *J Anaesth Clin Pharmacol* 2011; 27(1):35-8.
- Srivastava S. Epidural buprenorphine for postoperative pain relief. *Anaesthesia* 1982; 37:699.
- Bromage PR, Camporesi EM, Chestnut D. Epidural narcotic for post op analgesia. *Anaesth Anal* 1980; 59:473-80.
- Ackerman WE, Juneja MM, Colclough GW. A comparison of epidural fentanyl, buprenorphine and butorphanol for the management of cesarean section pain. *Anaesthesiology* 1988; 69: 401.
- Talbert RL, Peters JJ, Sorrels SC, Simmons RS. Respiratory effects of high dose butorphanol. *Acute care* 1988; 12(Suppl):47-56.
- Hunt OC, Naulty S, Malinow AM, Datta S, Ostheimer GW. Epidural butorphanol-bupivacaine for analgesia during labor and delivery. *Anaesth Analg* 1989; 68:323-7.
- Abboud TK, Afrasiabi A, Zhu J, Mantilla M, Khoo N, Reyes A et al. Epidural morphine or butorphanol augments bupivacaine analgesia during labor. *Reg Anaesth* 1989; 14:115-20.
- Bharti N, Chari P. *Journal of Clinical Anesthesia* 2009; 21:19- 22.
- Palacios QT, Jones MM, Hawkins JL. Post caesarean section analgesia. A comparison of epidural butorphanol and morphine. *Can J Anaesth* 1991; 38:24-30.
- Malik P, Manchanda C, Malhotra N. Comparative evaluation of epidural fentanyl and butorphanol for postoperative analgesia. *J Anaesth Clin Pharmacol* 2006; 22(4):377-82.

