COMPARATIVE EVALUATION OF BUTORPHANOL AND FENTANYL FOR EPIDURAL ANALGESIA IN LOWER LIMB SURGERIES

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ABSTRACT

BACKGROUND

Epidural and spinal blocks are major regional techniques with a long history of effective use for a variety of surgical procedures and pain relief. Epidural block with the catheter technique gives a better control of the level of analgesia and can be used for providing post-operative pain relief by opioids or local anaesthetic agents.

The purpose of the present study was to compare the safety and efficacy of epidural butorphanol versus epidural fentanyl as adjuvants to bupivacaine for lower limb surgeries.

MATERIALS AND METHODS

100 patients were randomised into two groups with 50 patients in each group: Group BB- epidural administration of 20 mL 0.5% plain bupivacaine with [1 mg (1 mL) butorphanol + 1 mL NS= 2 mL]. Group BF- epidural administration of 20 mL 0.5% plain bupivacaine with 100 mcg (2 mL) of fentanyl.
Settings and Design- Randomised double-blind trial.

RESULTS

The mean onset of sensory blockade and time for maximum sensory blockade was observed to be significantly reduced with the addition of fentanyl to bupivacaine as compared to butorphanol and bupivacaine. The results showed statistically significant increase in the duration of analgesia with the addition of fentanyl to bupivacaine as compared to butorphanol and bupivacaine.

CONCLUSION

We can conclude that butorphanol and fentanyl were effective adjuvants to bupivacaine when used epidurally in patients undergoing lower limb surgery. Although, epidural fentanyl with bupivacaine produces significantly faster onset of sensory blockade compared to epidural butorphanol; however, epidural butorphanol with bupivacaine produces significantly prolonged duration of analgesia compared to epidural fentanyl.

KEYWORDS

Fentanyl, Butorphanol, Epidural, Bupivacaine.

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BACKGROUND

Epidural and spinal blocks are major regional techniques with a long history of effective use for a variety of surgical procedures and pain relief. Epidural block with the catheter technique gives a better control of the level of analgesia and can be used for providing post-operative pain relief by opioids or local anaesthetic agents.[1]

Local anaesthetics are the mainstay of therapy for obtaining analgesia or anaesthesia with an epidural. Specifically, factors such as surgical location and duration desire to have a sensory and/ or motor block or the expected potency and duration of a specific local anaesthetic agent should be considered prior to placing an epidural block.[2]

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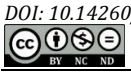


Local anaesthetics act by producing a reversible blockade of sodium channels in nervous tissue preventing the transmission of electrical impulses and produce sympathetic blockade.[2]

Adjuvant analgesics (co-analgesics) contribute significantly to pain relief when used either alone or in combination with other analgesics. Neuraxial adjuvants are used to improve or prolong analgesia and decrease the adverse effects associated with high doses of a single local anaesthetic agent. In addition to their dose sparing effects, neuraxial adjuvants are also utilised to increase the speed of onset of neural blockade (reduce latency), improve the quality and prolong the duration of neural blockade. Sedation, stable haemodynamics and an ability to provide prolonged post-operative analgesia are the main desirable qualities of an epidural adjuvant. Butorphanol is a potent analgesic with both opioid agonist and antagonist effect. Butorphanol and its major metabolites are agonist at kappa-opioid receptors and mixed agonist-antagonists at mu opioid receptors.[3]

Fentanyl, a highly lipid soluble, pure mu agonist with rapid onset and short duration of action has been used with various local anaesthetics for wide variety of surgical

procedures. Fentanyl is highly lipophilic, rapidly diffuses out of epidural space and much of fentanyl analgesic effect is mediated by systemic absorption rather than spinal receptor binding. These highly lipid soluble agents as fentanyl are associated with rapid dermatomal spread, rapid onset and low incidence of pruritis or nausea and can be potentiated by epinephrine.[4] Epidural fentanyl caused segmental analgesia when administered as a bolus and non-segmental systemic analgesia when administered continuous infusion.

The purpose of present study was to compare the safety and efficacy of epidural butorphanol versus epidural fentanyl as adjuvants to bupivacaine for lower limb surgeries.

MATERIALS AND METHODS

After Institute's Ethical Committee approval and informed written consent from patients, 100 patients of both genders aged 18 - 60 years, ASA grade I and II admitted for lower limb surgeries were enrolled into the present study. Those patients who had any anatomical abnormalities of spine, local skin infection or cellulitis, coagulation disorders or associated neurological or cardiovascular disorders were excluded from the study.

Study Design- Randomised controlled double-blind trial.

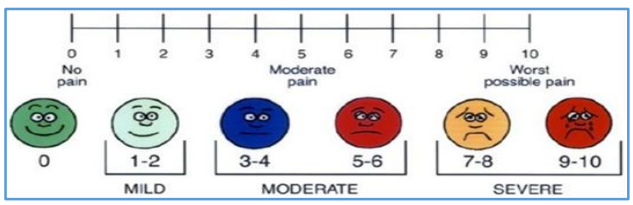
Randomisation

Eligible patients underwent randomisation after providing written informed consent. The random sequence of allocation code (Intrathecal analgesia group or systemic analgesia group) was obtained from a random number table of integers. This random number table of integers was constructed using a computer generated random number function in Libre Office Calc version 5.0.3.2. Randomised and blinded allocation of patients to the study drugs was achieved by assigning concealed random number codes to patients at the time of enrolment. Labels indicating intrathecal analgesia group or systemic analgesia group were sealed in opaque, numbered envelopes. The concealed randomised allocation codes (patient's group assignment) was known only to the principal investigator and the anaesthesia care givers, but not to the post-operative assessors or the patients or the statistician.

100 patients were randomised into two groups with 50 patients in each group: Group BB- epidural administration of 20 mL of 0.5% plain bupivacaine with [1 mg (1 mL) butorphanol + 1 mL NS = 2 mL]. Group BF- epidural administration of 20 mL 0.5% plain bupivacaine with 100 mcg (2 mL) of fentanyl.

Patients were familiarised with the visual analogue scale (VAS) (0- No pain, 10- Worst pain) 1 day before surgery and asked to grade their pain on this scale.

Visual Analogue Scale (VAS)[5]



During pre-anaesthetic check-up, a detailed history and thorough general, physical and systemic examination (CVS, chest, CNS, renal) was done. Patients were advised overnight fasting and Tab. Ranitidine 150 mg and Tab. Lorazepam 1 mg orally was given as premedicants 6 am in the morning on the day of surgery. In the operation room, after attaching routine monitors (Electrocardiogram, non-invasive blood pressure, pulse oximeter), intravenous access was secured with 18-G cannula. All patients were preloaded with 20 mL/kg of Ringer's lactate solution.

After proper positioning, back was cleaned with antiseptic solution and draped. Local anaesthetic 1 - 2 mL of 2% xylocaine was injected subcutaneously at L3 - L4 space. Sise introducer was introduced and taken out. The epidural space was identified using 18-G disposable Tuohy's needle with loss of resistance technique at L3 - L4 interspace. Then 18-G Portex epidural catheter will be passed through the epidural needle in upward direction and threaded 3 - 4 cm inside the epidural space. The needle was withdrawn slowly, and the catheter was fixed to the back using adhesive tape. A test dose of 3 mL of 2% lignocaine with adrenaline was given after initial negative aspiration for blood and cerebrospinal fluid. Then, 20 mL of 0.5% plain bupivacaine along with one of the two study drugs was injected into the epidural space.

Group BB- Epidural administration of 20 mL 0.5% plain bupivacaine with [1 mg (1 mL) butorphanol + 1 mL NS= 2 mL].

Group BF- Epidural administration of 20 mL 0.5% plain bupivacaine with fentanyl 100 mcg [2 mL].

Blood pressure (systolic, diastolic and mean), heart rate, respiratory rate and peripheral oxygen saturation (SpO_2) were recorded 5 minutes before the epidural injection (0) and at 5, 10, 15, 20, 25 and 30 minutes after the injection, and subsequently every 15 minutes till the end of surgery. Hypotension (defined as systolic blood pressure of less than 90 mmHg or less than 20% of baseline blood pressure) was treated with intravenous fluid initially and appropriate doses of intravenous mephentermine, if required. Bradycardia (defined as heart rate of less than 60) was treated with intravenous 0.6 mg atropine sulfate.

Sensory block was assessed by pinprick method. The level of sensory blockade was assessed every two minutes till blockade at L_1 level was achieved.

Onset of Sensory Blockade

It was taken from the completion of injection of study drug till the patient does not feel pinprick at L_1 level.

Time for Maximum Sensory Blockade

It was taken as the time from the completion of injection of study drug to maximum sensory blockade attained (i.e. till two consecutive readings of sensory block remain the same, i.e. highest cephalad spread of sensory block occur).

Onset of motor blockade was assessed at 5-minute intervals till 30 mins (i.e. B5, B10, B15, B20, B25 and B30) according to the Modified Bromage Scale[6]:

1- Complete block (Unable to Move Feet or Knees).
2- Almost complete block (Able to Move Feet Only).
3- Partial block (Just able to Move Knees).
4- Detectable weakness of hip flexion while supine (Full Flexion of Knees).

5- No detectable weakness of hip flexion while supine.
6- Able to perform partial knee bend.

Onset of Motor Block
It was taken from the completion of the injection of study drug till the patient developed Modified Bromage Scale grade 4 motor blockade.

Time for Maximum Motor Blockade
It was taken from the completion of the injection of study drug till the patient developed Modified Bromage Scale grade 1 motor blockade.

Grade of sedation during surgery was assessed by the Modified Ramsay's Sedation Scale[7] every 5 mins till 30 mins and then every 15 mins till end of surgery.

Post-operatively, assessment of pain was done with the help of VAS score, every hour till 6 hrs. and every 2 hrs. till 24 hrs. and vitals were recorded at the same time intervals. Duration of analgesia was taken as the time from onset of analgesia upto time when VAS reached 5. Patient was then given rescue analgesic (Butorphanol 2 mg in 10 mL of normal saline in BB Group and fentanyl 100 mcg in 10 mL of normal saline in BF Group) through epidural catheter and study in that patient was ceased. The epidural catheter was kept for 24 hrs. in post-operative period and post-operative analgesia will be maintained with epidural top-ups on patient's demand. Complications such as nausea, vomiting, urinary retention, headache, pruritus and respiratory depression were noted and treated accordingly.

Statistical Analysis: Analysis was conducted using IBMM SPSS Statistics (version 22.0). Numerical data was expressed as mean and standard deviation and statistical analysis was done using the independent 't' test, chi-square test and Mann-Whitney U test to compare the two groups. The 'p' value of <0.05 was considered statistically significant and the 'p' value of < 0.001 was considered statistically highly significant.

Sample size was estimated based on pilot study. We see that mean difference in SBP in 2 groups was 5.3 with SD of 9.05. With this our sample size n= 46 per group at a power of 80% and confidence interval of 95%. For possible dropouts, it was decided to include 50 patients per group. Alpha= 0.05, z(1-alpha/2)=1.95996, beta= 0.20 Power= 1-beta= 0.80, z(1-beta)= 0.84162, sigma= 9.05, delta= 5.3 n= 46 per group. N=(Z alpha/2+Zβ)2 *2*σ2 / d2, where Z alpha/2 is the critical value of the normal distribution at /2, Zβ is the critical value of the normal distribution at β, σ2 is the population variance and d is the difference between 2 means.

RESULTS
A total of 100 patients for lower limb surgery were enrolled for the study and were randomly divided into two groups. The demographic characteristics in both the groups exhibited marked similarities and did not show any statistical significant difference (p > 0.05). Table 1 shows the demographic profile of various patients.

As shown in Table 2, the onset of sensory block was faster in Group BF with mean 4.92 ± 1.14 as compared to Group BB with mean 5.80 ± 0.95 and this difference was statistically highly significant as the 'p' value was < 0.001**.** The time for maximum sensory block was faster in Group BF with mean 15.60 ± 1.39 as compared to Group BB with mean 17.60 ± 1.76 and this difference was statistically highly significant as the 'p' value was < 0.001. The onset in Group BF was 21.10 ± 1.13 minutes and in Group BB was 20.84 ± 1.69 and time for maximum motor blockade was 29.32 ± 2.13 in Group BF and 29.56 ± 1.75 minutes and the difference was statistically not significant as the 'p' value was < 0.05. In Table 3 duration of analgesia was 7.64 ± 1.39 in Group BB and 6.04 ± 1.29 in Group BF and it was statistically highly significant as the 'p' value was < 0.001.

Demographic Characters	Group BB	Group BF	P value
Age (year)	39.34 ± 12.69	39.16 ± 13.27	0.939
Height (cm)	164.12 ± 4.99	162.57 ± 5.93	0.160
Weight (kgs)	68.74 ± 5.00	67.96 ± 5.74	0.471
Male/ Female	41/9	37/13	0.334
Mean Duration of Surgery (mins)	105.10 ± 15.40	107.40 ± 13.52	0.429

Table 1. Demographic Profile

Block Characteristics	Group BB	Group BF	P value
Onset of sensory block (mins)	5.85 ± 0.95	4.92 ± 1.14	<0.001
Maximum duration of sensory block (mins)	17.60 ± 1.76	15.60 ± 1.39	<0.001
Onset of motor block (mins)	20.84 ± 1.69	21.10 ± 1.13	0.553
Maximum duration of motor block (mins)	29.32 ± 2.13	29.56 ± 1.75	0.763

Table 2. Comparison of Sensory and Motor Block Characteristics

Groups	Group BB	Group BF	P value
Duration of Analgesia	7.64 ± 1.39	6.04 ± 1.29	< 0.001

Table 3. Duration of Analgesia (hrs.)

DISCUSSION
Epidural anaesthesia offers superior pain relief and early mobilisation. It also improves the post-operative outcome and attenuates the physiological response to surgery, in particular significant reductions in pulmonary infections, pulmonary embolism, ileus, acute renal failure and blood loss. Addition of opioids to bupivacaine leads to faster onset of sensory blockade and prolonged duration of analgesia. The dose-sparing action of local anaesthetics and stable cardiovascular parameters make it a very effective adjunct in regional anaesthesia.

In present study, mean time for onset of sensory block was 5.80 ± 95 mins In BB Group and 4.92 ± 1.14 mins in BF Group. Statistically, the difference in time of onset of analgesia was highly significant [p value < 0.001]. Our results are in concordance with Kaur et al comparing epidural butorphanol AND fentanyl as adjuvants in the lower abdominal surgery. It was shown that mean time for onset of sensory block in BB (Bupivacaine Butorphanol group) was 5.50 ± .91 mins AND BF was 4.92 ± 1.03 mins.[8] Similar results were obtained by Kumar et al,[9] Sharma et al[10] and Nupoor et al.[11]

In present study, time for maximum sensory block was 17.6 ± 1.76 mins in BB Group and 13.9±20 mins in BF Group. Statistically, the difference in time for maximum sensory block was highly significant [p value < 0.001]. Kaur et al in 2014 compared butorphanol 1 mg and fentanyl 100 mcg as

adjuvants to bupivacaine in lower abdominal surgeries and demonstrated time for maximum sensory blockade (Completion of analgesia) was 11.80 ± 1.63 mins in butorphanol group and 10.80 ± 1.25 mins in fentanyl group. However, their definition of time for maximum sensory blockade is different from our study. They defined it as time from the onset of analgesia to maximum sensory blockade attained, whereas we defined it as time from the completion of injection of study drug to maximum sensory blockade attained.[8] Our results are in concordance with those given by Hunt et al.[12]

In present study, mean time of onset of motor blockade was 20.84 ± 1.69 mins in butorphanol group and 21.10 ± 1.13 in fentanyl group, which was statistically non-significant. Kaur et al in 2014 compared epidural butorphanol and fentanyl as adjuvants in lower abdominal surgery and found mean onset of motor block in butorphanol group was 20.56 ± 2.04 mins and fentanyl (100 ug) was 20.76 ± 1.6 mins.[8] The results of present study were consistent with Kumar et al and Chattopadhyay et al. The time for maximum motor blockade in present study in butorphanol group was 29.32 ± 2.13 mins and 29.56 ± 1.75 mins in fentanyl group. The difference in mean value of these two groups is non-significant.

In study conducted by Kaur et al, the mean time for maximum motor blockade was 8.68 ± 1.06 mins in butorphanol group and 8.72 ± 0.79 mins in fentanyl group. The results of our study are not in concordance with the above study, because in Kaur et al study time for maximum motor blockade was taken from onset of motor blockade, while in our study it was taken from injection of study drug.

In present study, mean duration of analgesia in butorphanol group was 7.64 ± 1.39 hrs. and in fentanyl group was 6.04 ± 1.29 hrs. Statistically, the difference is highly significant with 'p' value (< 0.001). Thus, fentanyl prolongs duration of analgesia more than butorphanol. Similar to our study, Kaur et al in 2014 compared epidural butorphanol and fentanyl as adjuvants in lower abdominal surgery and concluded mean duration of analgesia in butorphanol group was 7.64 ± 1.41 hrs. and 5.96 ± 1.30 hrs. in fentanyl group.[8]

Our results are in concordance with Naulty et al in 1985 observed duration of analgesia with epidural fentanyl 100 mcg to be about 4.6 hrs.[13]

CONCLUSION

The mean onset of sensory blockade and time for maximum sensory blockade was observed to be significantly reduced with the addition of fentanyl to bupivacaine as compared to butorphanol to bupivacaine. The results showed statistically significant increase in the duration of analgesia with the addition of fentanyl to bupivacaine as compared to butorphanol to bupivacaine. However, haemodynamic parameters and level of sedation was comparable in both groups.

So, we can conclude that butorphanol and fentanyl were effective adjuvants to bupivacaine when used epidurally in patients undergoing lower limb surgery. Although, epidural fentanyl with bupivacaine produces significantly faster onset of sensory blockade compared to epidural butorphanol; however, epidural butorphanol with bupivacaine produces significantly prolonged duration of analgesia compared to epidural fentanyl.

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