Original Research Article

Comparative study of epidural bupivacaine plus buprenorphine versus bupivacaine with fentanyl in lower limb surgeries

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Abstract

Background: Acute postoperative pain is a complex physiological reaction to tissue injury, visceral distension and disease. Managing the patient postoperatively by multimodal analgesia methods will improve pain relief, improve functionality, help in early mobilization and reduce physical, psychological and emotional morbidity. The present study was designed to compare the efficacy of epidural bupivacaine with buprenorphine and bupivacaine with fentanyl in lower limb surgeries.
Material and Methods: Present study was single-center, prospective, comparative study, conducted in patients aged between 18-60 years, of either sex, with ASA Grade I and II, selected for elective lower limb surgeries Patients were randomly divided into two groups: Group A (Buprenorphine with Bupivacaine) and Group B (Fentanyl With Bupivacaine)
Results: General Characteristics such as age, gender, height, weight, BMI, ASA grade, duration of surgery (minutes) were comparable in both the groups and difference was not statistically significant. It is observed that onset of analgesia in Group-A was 6.70 min and in group-B was 6.60 min, which was statistically insignificant (P<0.05). In Group A the highest level achieved maximally was T8 in 16 (53%) patients and in Group B the highest level reached was also T8 in 17 (56.7%) patients. The mean time to attain complete motor blockade in Group A was 17.83 mins and in Group B was 18.63mins this difference was statistically insignificant. The time to achieve a Bromage scale of 2 in Group A was 12.67mins and in Group B was 14.47 mins which was found to be statistically significant, thus a quicker partial blockade was achieved in Group A which is the buprenorphine group. The VNS scale was statistically significant between the groups throughout post operative period except at 12,18 and 20 hours. The mean time until need for rescue analgesia in Group A was 12.66hrs and in Group B was 7.72 hrs. There was a statistically significant difference between the duration of analgesia between the two groups.
Conclusion: Addition of buprenorphine epidurally increased the duration and quality of analgesia to a greater extent compared to fentanyl. Thus it can be concluded that buprenorphine can be used to provide longer duration of analgesia without any hemodynamic instability.
Keywords: buprenorphine, epidural, fentanyl. postoperative analgesia

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Received Date: 19/07/2021 Revised Date: 13/08/2021 Accepted Date: 07/09/2021
DOI: https://doi.org/10.26611/10152023

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 07 November 2021

INTRODUCTION

Pain is an unpleasant sensory and emotional experience associated with either actual or potential tissue damage. Over the years alleviation of pain has become one of the prime responsibilities of the anaesthesiologists as good pain relief prevents the patient from any psychological trauma and helps in a smooth and comfortable hospital stay.[1,2] Acute postoperative pain is a complex physiological reaction to tissue injury, visceral distension and disease. Managing the patient postoperatively by multimodal analgesia methods will improve pain relief, improve functionality, help in early mobilization and

How to site this article: Manasi Panat, Sayali Mhabdi, Sanjay Gadre. Comparative study of epidural bupivacaine plus buprenorphine versus bupivacaine with fentanyl in lower limb surgeries. *MedPulse International Journal of Anesthesiology.* November 2021; 20(2):55-59. http://medpulse.in/Anesthsiology/index.php

reduce physical, psychological and emotional morbidity.[2] Regional anaesthesia techniques provide for a smooth operative time as well as reduced mortality and morbidity for the patient. The advantages of regional techniques as compared to General Anaesthesia include lesser airway manipulation, an awake patient, early food intake by patient, good sensory and motor blockade, lower incidences of postoperative nausea and vomiting and ability to provide prolonged analgesia.[3,4] Epidural anaesthesia provides prolong duration of action, postoperative analgesia, maintains hemodynamic stability and aids in the early recovery from surgery. A local anaesthetic–opioid combination provides superior analgesia during perioperative and postoperative period.[3] This combination limits rapid regression of sensory blockade and possibly decreases the dose of local anaesthetic administered. The present study was designed to compare the efficacy of epidural bupivacaine with buprenorphine and bupivacaine with fentanyl in lower limb surgeries

MATERIAL AND METHODS

Present study was single-center, prospective, comparative study, conducted in Department of Anaesthesia, JMF'S ACPM Medical College, Dhule, India. Study duration was of 2 years (July 2018 to June 2019). Study was approved by institutional ethical committee.

Inclusion criteria: Patients aged between 18-60 years, of either sex, with ASA Grade I and II, selected for elective lower limb surgeries

Exclusion criteria: Pregnant women. Patients with H/o Cardio-Respiratory disorders. Patients with Hepatic and Renal diseases. Patients with H/o convulsions and neurological deficits. Patients with Spinal deformities and Psychiatric diseases. Patients with ASA Grade III and above. Patients with contra-indications for epidural anaesthesia.

60 Patients posted for elective lower limb surgeries were randomly selected for the study. All patients underwent a thorough pre-anaesthetic evaluation a day before surgery and were explained in detail regarding the anaesthetic procedure. Study was explained and patients were educated about the Verbal numerical scale that would be used for assessment of pain. Pain scores with 0 correspond to no pain and 10 to the worst imaginable pain. Written informed consent was obtained. All patients received Tab. Alprazolam 0.25 mg orally on the previous night of surgery as anti-anxiety medication. Patients were advised nil orally for a period of 6 hours prior to their surgery.

Patients were randomly divided into two groups:

Group A Buprenorphine with Bupivacaine group - 0.5% Bupivacaine 15ml (75mg) with 0.5ml (150 ug) Buprenorphine (preservative free) with 0.5ml sterile water for injection made to a total of 16ml.

Group B Fentanyl With Bupivacaine group- 0.5% Bupivacaine 15ml (75mg) with 1ml (50ug) Fentanyl (preservative free).

Patients were shifted to operating room, connected to multi para monitor and baseline heart rate, non-invasive blood pressure (systolic and diastolic) and Spo2 was recorded. Under strict aseptic precautions, in sitting position, in L2-L3 interspace local anaesthetic solution was injected, epidural catheter was inserted and continuous monitoring was done. 16ml of study drug was injected depending on patient study group through epidural catheter and patient was made to lie supine. After adequate blockade (T10) patient was repositioned based on surgical requirements. The onset time and the time for maximum motor and sensory block and the maximum level of sensory and motor block were recorded. Motor blockade in the lower limbs was assessed using modified Bromage scale. Vital parameters such as the heart rate, blood pressure, respiratory rate were continuously monitored for every 5 min for first 15min and every 15min throughout surgery during intraoperative period and every half an hour in the post-operative period for 2 hours. Intra-operatively and postoperatively complications, like nausea, vomiting, bradycardia, hypotension, respiratory depression and pruritus were noted, treated and tabulated. Duration of post-operative analgesia, Quality of post-operative analgesia (VNS)., Hemodynamic monitoring (MAP and HR), need for rescue analgesic supplementation, side effects if any were recorded. The data was coded and entered into Microsoft Excel spreadsheet. Analysis was done using SPSS version 20 (IBM SPSS Statistics Inc., Chicago, Illinois, USA) Windows software program. Descriptive statistics included computation of percentages, means and standard deviations. The unpaired t test (for quantitative data to compare two independent two groups) was used for quantitative data comparison of all clinical indicators. Chi-square test and fisher exact test were used for qualitative data whenever two or more than two groups were used to compare. Level of significance was set at $P \leq 0.05$.

RESULTS

General Characteristics such as age, gender, height, weight, BMI, ASA grade, duration of surgery (minutes) were comparable in both the groups and difference was not statistically significant.

Table 1: General Characteristics

Characteristics	group A (mean ± SD)	group B (mean ± SD)	p value
Age (years)	44.33 ± 8.774	39.93 ± 10.435	0.08
Gender			---
Male	27 (90 %)	27 (90 %)	
Female	3 (10 %)	3 (10 %)	
Weight (kgs)	57.73 ± 9.659	57.03 ± 7.819	0.75
Height (cms)	163.17 ± 8.313	166.67 ± 8.434	0.11
BMI	21.62 ± 2.88	20.47 ± 1.81	0.07
ASA			0.27
I	18 (60 %)	22 (73.3 %)	
II	12 (40 %)	8 (26.7 %)	
Duration of surgery	146.17 ± 26.577	148.67 ± 14.794	0.65

The table shows various surgeries attempted under epidural anaesthesia. The results are comparable but show no statistical significance.

Table 2: Comparison of surgical procedures done

Surgery	group A (%)	group B (%)	p value
AMP	9 (30 %)	4 (13.3 %)	13 (21.7 %)
DHS plating	7 (23.3 %)	8 (26.7 %)	15 (25 %)
ORIF	0	1 (3.3 %)	1 (1.7 %)
ORIF with bone graft	0	1 (3.3 %)	1 (1.7 %)
ORIF with DHS plating	0	1 (3.3 %)	1 (1.7 %)
ORIF with IMIL nailing	0	1 (3.3 %)	1 (1.7 %)
ORIF with LCP	9 (30 %)	1 (3.3 %)	10 (16.7 %)
ORIF with plating	5 (16.7 %)	9 (30 %)	14 (23.3 %)
Split thickness S	0	3 (10 %)	3 (5 %)
TBW and ORIF with	0	1 (3.3 %)	1 (1.7 %)

It is observed that onset of analgesia in Group-A was 6.70 min and in group-B was 6.60 min, which was statistically insignificant (P<0.05).

Table 3: Sensory level achieved (MINS)

Sensory level achieved (MINS)	group A (mean ± SD)	group B (mean ± SD)	p value
T12	6.70 ± 3.131	6.60 ± 2.372	0.89
T10	10.30 ± 3.030	10.20 ± 2.809	0.89
T8	12.53 ± 5.835	12.50 ± 5.118	0.98
T6	5.80 ± 8.495	5.67 ± 8.343	0.95

In Group A the highest level achieved maximally was T8 in 16 (53%) patients and in Group B the highest level reached was also T8 in 17 (56.7%) patients. The cephalad spread of the block was thus similar in both groups and not statistically significant.

Table 4: Highest Sensory Level Achieved

Sensory level	group A (%)	group B (%)	Total
T10	4 (13.3 %)	3 (10 %)	7 (11.7 %)
T6	10 (33.3 %)	10 (33.3 %)	20 (33.3 %)
T8	16 (53.3 %)	17 (56.7 %)	33 (55 %)

P value=0.91

The mean time to attain complete motor blockade in Group A was 17.83 mins and in Group B was 18.63mins this difference was statistically insignificant. The time to achieve a Bromage scale of 2 in Group A was 12.67mins and in Group B was 14.47 mins which was found to be statistically significant, thus a quicker partial blockade was achieved in Group A which is the buprenorphine group.

Table 5: Motor Level (Using Bromage Scale)

Motor Level (Using Bromage Scale)	group A (mean ± SD)	group B (mean ± SD)	p value
0	5.07 ± 2.586	6.67 ± 2.023	0.01 (s)
1	9.13 ± 2.636	10.13 ± 2.360	0.12
2	12.67 ± 2.617	14.47 ± 3.082	0.01 (S)
3	17.83 ± 3.425	18.63 ± 3.253	0.35

The VNS scale was statistically significant between the groups throughout post operative period except at 12,18 and 20 hours.

Table 6: Visual Numerical Scale

Post-operative period (hours)	group A (mean ± SD)	group B (mean ± SD)	P value
1	.500 ± .0000	.667 ± .4011	0.02 (S)
2	.500 ± .0000	.983 ± .6497	0.001 (S)
4	.600 ± .2034	1.467 ± .9908	0.001 (S)
6	.867 ± .6008	2.250 ± 1.2714	0.001 (S)
8	1.267 ± .7849	3.567 ± 1.4840	0.001 (S)
10	2.333 ± 1.4933	3.150 ± 1.4922	0.03 (S)
12	2.717 ± 1.3814	2.733 ± 1.7798	0.96
14	3.300 ± 1.3493	1.817 ± .4822	0.001 (S)
16	3.117 ± 1.4244	1.900 ± .7474	0.001 (S)
18	.833 ± .6343	1.033 ± .8996	0.32
20	.750 ± .2543	.633 ± .2249	0.06

The mean time until need for rescue analgesia in Group A was 12.66hrs and in Group B was 7.72 hrs. There was a statistically significant difference between the duration of analgesia between the two groups.

Table 7: TIME UNTIL RESCUE ANALGESIA

	Mean	*Std. Deviation*	*P VALUE*
Group A	12.66	2.91	0.001 (S)
Group B	7.72	2.43	

The incidence of vomiting was in 11 (36.7%) patients from Group A and 2 (6.7%) patients from Group B, which was found to be statistically significant. The number of patients with pruritus was 0 in Group A and 10 in Group B which is a statistically significant difference.

Table 8: Side effects

Side effects	group A (%)	group B (%)	Total	P VALUE
Nausea, vomiting	11 (36.7 %)	2 (6.7 %)	13 (21.7 %)	0.005 (S)
Pruritus	0	10 (33.3 %)	20 (33.3 %)	0.001 (S)

DISCUSSION

Analgesia is a primary component of anaesthesia. It is found that operative pain is more severe after surgery and gradually diminishes over the next 24 hours. The pain in the postoperative period demands relief not only on humanitarian grounds but also to reduce physical morbidity following the operation. The advantages of Epidural Anaesthesia are it provides effective surgical anaesthesia and can meet the extended duration of surgical needs, prolonged post-operative analgesia, reduces the incidence of hemodynamic changes as a result of sympathetic blockade as it can produce segmental anaesthesia unlike subarachnoid block anaesthesia and no PDPH as the dura is not pierced. Buprenorphine is a thebaine derivative, it is 33 times more potent than morphine, and it is mu-receptor partial agonist and antagonist. It is effective in relieving moderate to severe pain, when placed in epidural space.[5] Fentanyl is a phenylpiperidine-derivative synthetic opioid agonist; it is 75 to 125 times more potent than morphine.[6] Boas RA *et al.*[7] in their study on clinical actions of Fentanyl and Buprenorphine, the significance of receptor binding. Receptor binding assays were undertaken in an attempt to elucidate the opioid binding characteristics of fentanyl and buprenorphine, and to investigate some of the differences between them. Buprenorphine showed slow receptor association (30 min), but with high affinity to multiple sites from which dissociation was very slow (T ½ = 166 min) and incomplete (50% binding after 1 h). This contrasted with the receptor binding of fentanyl, which achieved rapid equilibrium (within 10 min) and dissociated equally rapidly (T 1/2 = 6.8 min) and completely (100% by 1 h). SA Lytle,[8] noted that continuous infusions of fentanyl at concentrations of 50 mcg for a period of 72 hours did not produce respiratory depression compared to epidural morphine.17 Hayashi H *et al.* studied postoperative pain relief by continuous epidural infusion in 2 groups in which buprenorphine and fentanyl were epidurally administered postoperatively. There was no significant difference between the two groups in the analgesic efficacy. However, compared with buprenorphine group, the incidence of nausea or vomiting and dizziness was significantly less in the fentanyl group. These results implied that the major site of action of epidurally administered fentanyl is the spinal cord. In contrast, analgesic effect of epidural buprenorphine appeared to be enhanced by the supraspinal action. They concluded that fentanyl was superior to buprenorphine for postoperative pain relief by continuous epidural infusion. There is ceiling in the respiratory depression induced by buprenorphine but not by fentanyl. In conclusion, buprenorphine was more favorable compared with fentanyl with respect to

ventilatory control. Buprenorphine caused limited respiratory depression with a ceiling effect at higher doses, while fentanyl caused dose-dependent respiratory depression with apnea at high dose levels. In the rare instance of respiratory depression, reversal was possible with a sufficient and continuous infusion of naloxone.[9,10] Scott DA *et al.*[11] concluded in their study that, epidural infusions of Fentanyl with bupivacaine after major abdominal surgeries were found to be effective in management of postoperative pain relief with minimal complications. Longer duration of action and analgesia efficacy of epidural buprenorphine can be explained by its high affinity for spinal receptors, high lipid solubility, strong opioid receptor binding and intense and prolonged activity was responsible for longer duration of action.[12] Limitations of present study were small sample size, elective surgeries, further larger studies are required to confirm findings of present study.

CONCLUSION

Addition of buprenorphine epidurally increased the duration and quality of analgesia to a greater extent compared to fentanyl. Thus it can be concluded that buprenorphine can be used to provide longer duration of analgesia without any hemodynamic instability.

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Source of Support: None Declared
Conflict of Interest: None Declared