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Comparison of Epidural Levobupivacaine 0.125% with Fentanyl 2 mcg/ ml and Levobupivacaine 0.125% Alone for Postoperative Pain Management

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Abstract

Introduction: The aim of the study was to compare effectiveness of single dose epidural 0.125% levobupivacaine with fentanyl 2 mcg/ml and 0.125% levobupivacaine alone in patients undergoing elective lower limb orthopaedic surgery. *Methodology:* We designed a prospective, randomized, double blind study, in which 60 patients with ASA1 and ASA2 were scheduled to undergo elective lower limb orthopedic surgery. Group A received single epidural block with 8 ml of 0.125% levobupivacaine and Group B received epidural block with 8 ml of 0.125% levobupivacaine and 2 mcg/ml fentanyl. Duration of analgesia, Quality of analgesia, Degree of motor blockade, sedation score, hemodynamic changes and side effects were assessed. *Results:* Duration of postoperative analgesia for group B (366±39.70 min) was longer as compared to group A (236±34.99 min). Quality of anaesthesia was significantly better in group B as compared Group A. *Conclusion:* We conclude that addition of fentanyl 2 mcg/ml to epidural 0.125% levobupivacaine produces significantly better quality and longer duration of postoperative analgesia, good hemodynamic stability and no side effect as compared to 0.125% levobupivacainealone in patient undergoing elective lower limb orthopedic surgeries.

Keywords: Levobupivacaine; Fentanyl; Postoperative Pain.

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Introduction

Lower limb orthopedic surgeries are common in many elderly patients and these surgeries are considerably more painful than other general surgeries. The pain can cause immense suffering to the patient and also alter physiological functions induced by hormonal changes. The increased sympathetic nervous system activity can stress the heart due to high blood pressure and/or rapid heart rate. This can increase the risk of myocardial ischemia because the myocardial oxygen

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demand exceeds its supply. For this reason, early postoperative pain control should improve the outcome of lower limb orthopedic surgery.

The advantages of effective postoperative pain management include patient comfort and therefore satisfaction, earlier mobilization, fewer pulmonary and cardiac complications, a reduced risk of deep vein thrombosis, faster recovery with less likelihood of the development of neuropathic pain and reduced cost of care. The failure to provide good postoperative analgesia is multifactorial. Insufficient education, fear of complications associated with analgesic drugs, poor pain assessment, and inadequate staffing are among its causes. Poorly controlled acute postoperative pain may be an important predictive factor in the development of pathologic long-term chronic pain after surgery [4,5]. Control of acute postoperative pain may improve long-term recovery or patient-oriented outcomes (e.g., quality of life). Patients whose pain is controlled in the early postoperative period (especially with use of continuous epidural or peripheral catheter techniques) may be able to actively participate in postoperative rehabilitation, which may improve short- and long-term recovery after surgery [6,7]. Epidural analgesia is one of the most effective regimens for post-operative pain relief after lower limb surgeries. Epidural infusion of local anesthetic alone may be used for postoperative analgesia. However, epidural local anaesthetic administered alone have never become widely used for routine postoperative analgesia because of the significant failure rate resulting from regression of the sensory block and the unacceptable incidence of motor blockade and hypotension [8]. A variety of adjuvants may be added to epidural infusions to enhance analgesia while minimizing the side effects and these include mainly Opiates, Ketamine, Clonidine, Benzodiazepines etc. But no single drug has proved to be devoid of any side effect. Search for an ideal adjuvant still continues that could result in reliable prolongation of postoperative pain relief without side effects. Levobupivacaine is a pure 5 - enantiomer of racemic bupivacaine [9]. They were developed mainly to overcome the fatal cardiotoxicity associated with bupivacaine, which is a well-established local anaesthetic whose one of the main use is postoperative pain management through epidural route. The benefits of addition of opiate to postoperative epidural levobupivacaine infusion is controversial. Fentanyl has emerged as a suitable opioid for infusion into epidural space. Advantages of fentanyl over other opioids are that it easily crosses lumbar dura and quickly penetrates the lipid phase of underlying tissue of the cord as it is more lipophilic. Since not many studies have been done to compare the effects of adding fentanyl to epidural levobupivacaine 0.125% for postoperative analgesia after major orthopedic surgery. Therefore we conducted this study in order to evaluate epidural levobupivacaine 0.125% with fentanyl 2µg/ml is compared with levobupivacaine 0.125% alone with regard to the effectiveness in postoperative analgesia, onset of action and hemodynamic changes in patient undergoing elective lower limb orthopaedic surgery.

Aims and Objectives

To compare the effectiveness of epidural 0.125% levobupivacaine with fentanyl 2µg/ml and 0.125% levobupivacaine alone in patients posted for elective major orthopaedic surgeries regarding: Duration of analgesia, Quality of postoperative analgesia, Hemodynamic changes: blood pressure and heart rate, Any adverse effects.

Material and Methods

This prospective randomized double blind study was conducted on 60 patients aged between 20-60 years of either sex belonging to ASA class I and class II posted for elective major orthopedic surgeries at M.G.M. Medical College, Kamothe, Navi Mumbai were selected for the study. The study was conducted from January 2016 to January 2017. The study population was randomly divided into two groups with 30 patients in each group (n=30). Group A: Epidural block with 8 ml of 0.125% levobupivacaine, Group B: Epidural block with 8 ml of 0.125% levobupivacaine + 2 µg/ml fentanyl. Preoperative assessment was done for each patient and informed consent was taken. Intravenous line was obtained with 18 G i.v cannula and was preloaded with ringer lactate 500 ml half an hour before anaesthesia. The patients were randomly divided into two groups as designed above and demographic data was noted. Baseline vital parametres were noted. After pre anaesthetic checkup patient were kept fasting from previous night and premedicated with tablet ranitidine 150 mg and tablet alprazolam 0.5 mg. Patients were placed in sitting position. Under aseptic precautions, epidural space was identified at L2-L3 using 16G Tuohy's needle by loss of resistance technique, epidural catheter inserted into the epidural space and fixed 3 cm inside epidural space. The epidural catheter will be tested for intravascular or subarachnoid placement

with 3 ml of 2% lidocaine containing 1:200000 epinephrine. After epidural catheter insertion, spinal anaesthesia was given with 0.5% hyperbaric bupivacaine 10-12 mg. Once surgery is completed patient was shifted to postoperative room, pain was assessed using visual analogue scale (0= no pain till 10= maximum pain) and motor blockade assessed using modified Bromage scale. Once the patient gives VAS score as 4, the test drug was injected through epidural catheter. Now patient is evaluated for post-operative pain at rest and upon movement using VAS score. Sensory block was assessed bilaterally by pin prick method with a short bevelled 27G needle. Haemodynamic changes and motor blockade checked every 5 mins upto 30 min and every half hour thereafter. The following parameters were assessed postoperatively At the end of the operation, the quality of analgesia was assessed according to the VAS score: Time taken for reappearance of VAS score 4 from the time of injection was considered as total duration of post-operative analgesia. Degree of Motor Blockade was assessed according to modified Bromage scale. Modified Bromage scale. The level of sedation was assessed using the sedation score described by Chernik et al a follows: Grade 0: Wide awake, Grade I: Sleeping comfortably, responding to verbal commands., Grade II: Deep sleep, but arousable, Grade III: Deep sleep, not arousable. The parameters such as heart rate, non invasive blood pressure, ECG and Spo2 were periodically monitored every 5 mins upto 30 min and every half hour thereafter.

Statistical Analysis All the collected data was entered in Microsoft Excel sheet and then transferred to SPSS software ver. 17 for analysis. Qualitative data was presented as frequency and percentages and analysed using chi-square test. Quantitative data was presented as mean and SD and compared by t-test. P-value < 0.05 was taken as level of significance.

Results

Table 1: Preoperative hemodynamic parameters amongst different study population

Preoperative	Group A	Group B	P value
SBP	124.73 ± 9.8	125.3 ± 6.4	0.38
DBP	78 ± 9	80.83 ± 5.9	0.17
Pulse	80.3 ± 9	85.13 ± 10	0.056
RR	13.37 ± 1.3	12.87 ± 0.9	0.101
SpO2	99.53 ± 0.73	99.43 ± 0.7	0.597

Both groups were comparable in respect to mean age, sex, height, weight, ASA grading. There was no significant changes in systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR) and peripheral oxygen saturation (SpO_2) of the patients in both groups pre and post operatively (Table 1).

Table 2: Duration of action amongst different study population

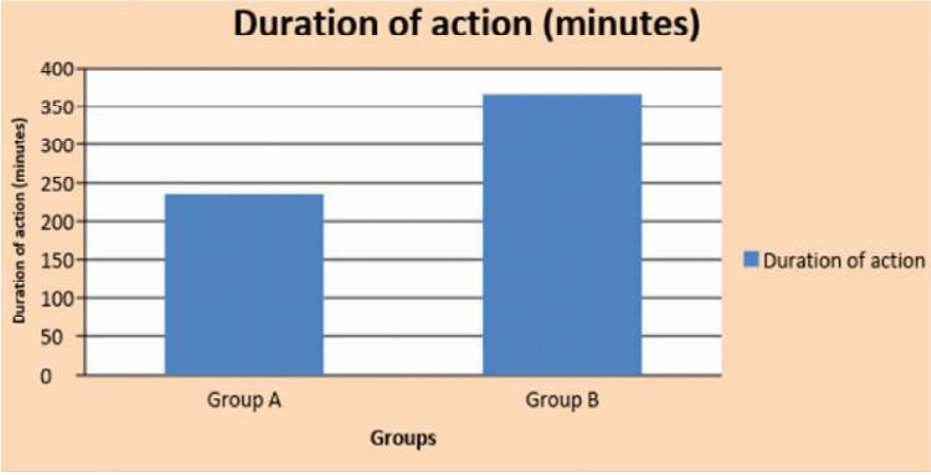
Duration of action	Group A	Group B	P value
Duration of action	236.00 ± 34.99	366 ± 39.7	0.0001

As seen in the above table 2, duration of action was significantly longer in group B (366±39.70 min) as compared to Group A (236±34.99 min). (Graph 1)

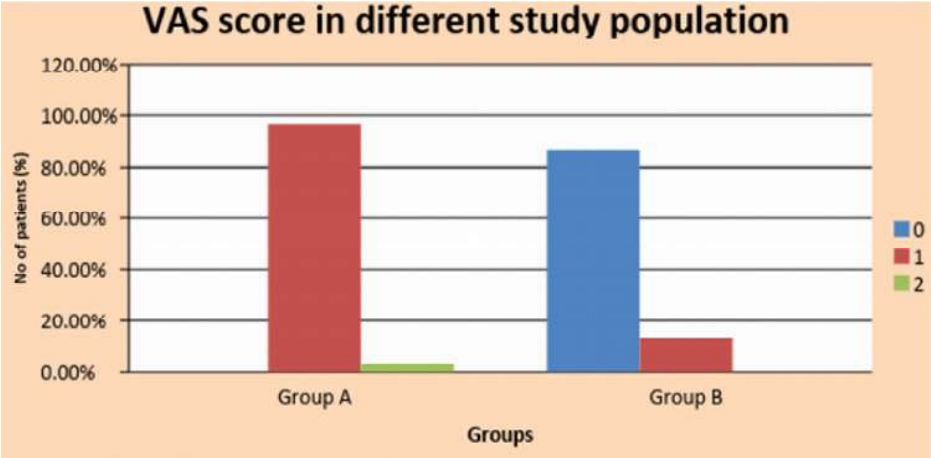
Table 3: Quality of analgesia amongst different study population

VAS Score	Group A	Group B	Total
0	0 (0%)	26 (86.7%)	26 (43.3%)
1	29 (96.7%)	4 (13.30%)	33 (55%)
2	1 (3.3%)	0 (0%)	1 (1.7%)
Total	30 (100%)	30 (100%)	60 (100%)

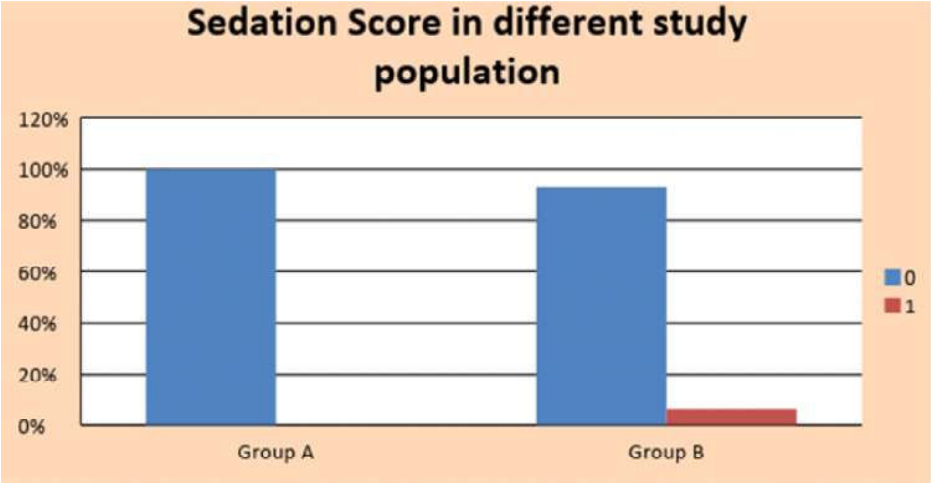
As seen in the above table 3, quality of analgesia



Graph 1: Duration of action amongst different study population



Graph 2: Quality of analgesia amongst different study population



Graph 3: Sedation Score amongst different study population

was better in Group B as compare to Group A. No motor blockade was noted in either of the groups. (Graph 2)

Table 4: Sedation Score amongst different study population (Graph 3)

Sedation Score	Group A	Group B	Total
0	30 (100%)	28 (93.3%)	53 (96.67%)
1	0 (0%)	2 (6.70%)	7 (3.3%)
Total	30 (100%)	30 (100%)	60 (100%)

Discussion

The benefits of adequate postoperative analgesia are many and include a reduction in the postoperative stress response, a reduction in postoperative morbidity and in certain types of surgeries postoperative analgesia leads to improvement in surgical outcome [10,11]. Other benefits of effective regional analgesic techniques include reduced pain intensity, decrease in the incidence of side effects from analgesics and improved patient comfort [12]. Orthopedic surgery associated with intraoperative and postoperative pain can stimulate the stress response and autonomic system. It may cause various complications such as myocardial ischemia, thromboembolic phenomena, impaired pulmonary function, ileus, fatigue and muscle catabolism.

Role of epidural analgesia is well known. It provides satisfactory analgesia and very minimal side effect. It is very effective in relieving intraoperative and postoperative pain after major upper abdominal, thoracic and orthopedic surgeries. Epidural analgesia technique has welcomed in labour analgesia because it reduces the pain and sympathetic response without any motor deficit. Epidural analgesia provides analgesia and helps in early mobilization in postoperative period

and allow to resume early routine activity. Epidural analgesia for postoperative analgesia will give specific advantages like reduced requirement for systemic opioids hence less side effect associated with it and leads to early return of bowel function. The side effects or complications associated with epidural analgesia might be related to procedure or drug like dural perforation, epidural hematoma, infection, urinary retention, hypotension, pruritus and respiratory depression. The benefit of adequate epidural analgesia includes improved respiratory function, decrease in postoperative cardiac complication, decreased chances of deep vein thrombosis. Most commonly used local anaesthetic for epidural analgesia in India are bupivacaine and Lignocaine. Drawback of lignocaine is its intermediate duration of action and bupivacaine is its cardiotoxicity. Though bupivacaine has fair safety profile, currently it is replaced by newer local anesthetics: levobupivacaine and ropivacaine. These newer local anesthetics have less risk for cardiac and central nervous system toxicity and less postoperative motor blockade [13,14]. Levobupivacaine is a long acting local anaesthetic and the pure S (-) enantiomer of racemic bupivacaine, is an effective and safer alternative local anaesthetic in epidural analgesia. Levobupivacaine has a lower risk of cardiovascular and CNS toxicity than bupivacaine [15]. Various studies have been done using different concentration of levobupivacaine like in study by De Negri et al., compared epidural bupivacaine, levobupivacaine and ropivacaine on postoperative analgesia and motor blockade in patient undergoing hypospadias surgery and found that there is no motor blockade associated with 0.125% levobupivacaine whereas bupivacaine associated with postoperative motor blockade in 20% of patient. Good quality of analgesia was observed in patient given 0.125% levobupivacaine [16].

S.J.V. Kameshwara Rao et al., in their study compared 0.5% bupivacaine with 0.75% ropivacaine and 0.5% levobupivacaine in sub umbilical surgeries under epidural anaesthesia and found high concentrations of these drugs were associated with significant hypotension, motor blockade and high incidence of side effects [17]. We chose levobupivacaine concentration of 0.125% because low concentration of local anaesthetic is not associated with unwanted postoperative motor blockade, provide satisfactory analgesia and less incidence of side effects. Use of combined local anaesthetic and an opioid in epidural analgesia may have advantages over local anaesthetic or opioid alone. It provides better postoperative analgesia, prolongs sensory block, decreases the dose of local anaesthetic and incidence of side effects are also reduced [18]. It is unclear whether the analgesic effect of local anaesthetic and opioid in the epidural analgesia is additive or synergistic. The choice of opioid also varies, although many clinicians choose to use a lipophilic opioid fentanyl 2 mcg/ml. Cooper DW, Turner G et al., in their study concluded that combination of epidural local anesthetic and fentanyl has better analgesic actions and reduces the requirements of each individual agent. Therefore we have combined local anaesthetic along with fentanyl [19]. Gaurav S. Tomar et al., in their study concluded that addition of fentanyl 2 mcg/ml to 0.125% bupivacaine decreases the time of onset of analgesia and prolonged duration of analgesia along with better level of maternal satisfaction during labour as compare to 1 mcg/ml fentanyl [20]. Hence in our study we chose to evaluate the effect of adding inj fentanyl 2mcg/ml to epidural 0.125% levobupivacaine will result in no motor blockade with adequate analgesia and lesser incidence of side effect. Thus the aim of this investigation was to compare the effect of a postoperative single epidural dose of these two local anaesthetic drugs on motor blockade and pain relief after lower limb orthopedic surgery. Duration of Post Operative Analgesia: All patients were given bolus dose of epidural after appearance of VAS score of 4 and the VAS score was again assessed after giving bolus dose of epidural. Following the dose, VAS score reduced to either 0,1 or 2 in most of the patients among both the groups. In the present study, duration of postoperative analgesia for group A was 236±34.99 min and for Group B 366±39.70 min. Hence, the mean duration of postoperative analgesia was significantly longer in Group B as compared to Group A. Our findings correlate well with the studies conducted by Gaurav S. Tomar et al., [20] and Danyalönal et al, [21] in which levobupivacaine with opioid group had longer duration of postoperative analgesia after surgery as compared to levobupivacaine group alone.

Quality of Analgesia: In our study, VAS score of 1 and 2 was observed in 96.7% and 3.3% patients in Group A respectively while in group B 86.7% patients had VAS score of 0 and 13.3% patient had VAS score 1 following epidural bolus. Thus the difference was statistically significant. Lee Wai- Keung et al. [22] and Bayazit EG et al. [23], concluded that pain relief was significantly better in the ropivacaine/fentanyl group after the first hour and this difference lasted for the remaining time. The quality of analgesia was significantly improved

by addition of fentanyl 1 µg/ml to local anaesthetic in their study. This findings is in agreement with the study conducted by Paraskevi Matsota et al. [24]. it was concluded that the combination of ropivacaine 0.15% with fentanyl 2 µg/ml appeared superior as it provided higher patient satisfaction. Sedation Score: In our study, in group A all patients were wide awake whereas In group B 76.7% patients were wide awake and 6.7% patients had grade 1 sedation score. This difference was statistically not significant. This result well correlates with study conducted by Kopacz et al. [25].

Motor Blockade: No motor block was observed in any patient in both the groups. De Negri P et al., concluded that significantly less unwanted motor blockade was associated with postoperative epidural analgesia of 0.125% levobupivacaine in children after hypospadias repair as compared with a similar infusion of bupivacaine [16].

Haemodynamic Changes: There was no significant difference amongs two group with respect to Systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate and SpO_2 at any time interval. None of the patients showed systolic pressure decrease of more than 20% of the value after epidural bolus [26].

Side Effect: None of our patients experienced respiratory depression, headache, urinary retention. In our study, side effect like Pruritus and nausea was observed 6.7% and 10% in group B respectively and no patient in group A complained of prutritus or nausea. This difference was statistically not significant [27,28].

Conclusion

We conclude that addition of fentanyl 2 mcg/ml to epidural 0.125% levobupivacaine produces significantly both quality and longer duration of postoperative analgesia as compared to 0.125% levobupivacaine alone in patient undergoing for elective lower limb orthopedic surgeries.

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