Original Research Article

Received in revised form : 13/12/2023

Bupivacaine, Buprenorphine, Fentanyl,

Email: Niralijoshi07@gmail.com

DOI: 10.47009/jamp.2024.6.1.261

Conflict of Interest: None declared

Received

Accepted

Keywords.

Lower Limb.

Corresponding Author:

Source of Support: Nil,

Int J Acad Med Pharm

2024; 6 (1); 1314-1320

Dr. Nirali Joshi,

: 05/10/2023

: 29/12/2023

COMPARATIVE ANALYSIS BETWEEN EPIDURAL BUPIVACAINE 0.5% WITH BUPRENORPHINE AND EPIDURAL BUPIVACAINE 0.5% WITH FENTANYL REGARDING PERIOPERATIVE ANALGESIA IN LOWER ABDOMINAL AND LOWER LIMB SURGICAL PROCEDURES

Sravya Vemuri¹, Neel Rana², Devarsh Thakar³, Nirali Joshi⁴

¹Assistant professor, Department of Anaesthesiology, IKDRC, Ahmedabad, Gujarat, India ²Assistant professor, Department of Anaesthesiology, Smt. NHL Municipal Medical College, Ahmedabad, Gujarat, India

³Anesthesiologist, Kaizen hospital, Ahmedabad. Gujarat, India

⁴Tutor, Department of Anaesthesiology, B.J. Medical College and Civil hospital, Ahmedabad, Gujarat, India

Abstract

Background: Epidural anesthesia/analgesia is one of the best accepted techniques for lower abdominal and lower limb surgeries as it provides good sensory and motor block with contracted bowels retaining adequate spontaneous respiration, haemodynamic stability and also an indwelling catheter facilitates further administration of analgesic doses for postoperative period. Present study was done with an aim to compare the perioperative analgesic efficacy of these two lipophilic drugs along with epidural bupivacaine in lower abdominal and lower limb surgeries. Materials and Methods: This prospective, randomized, double-blind, comparative study was conducted at Tertiary Care Teaching Institute of India after obtaining approval from the hospital institutional review board. In this study, the efficacy of 0.5% bupivacaine (15ml) with 150 mcg buprenorphine and 0.5% bupivacaine (15ml) with 50mcg fentanyl given epidurally was compared in providing adequate perioperative analgesia. 100 patients in the age group of 20-60 years belonging to ASA I - II posted for elective lower abdominal/gynaecological/ genitourinary/lower limb surgeries were studied. Side effects: Like nausea, vomiting, hypotension, respiratory depression and pruritus allergic reaction were looked for. Vital parameters such as the HR, BP, RR and oxygen saturation were continuously monitored for every 5 min for first 15min and every 15min throughout intraoperative period or for first 3 hours. Duration of the surgery was recorded. Result: Mean duration of surgery in Group A was 2.15±0.7 hours. Mean duration of surgery in Group B was 2.09±0.65 hours. The difference in heart rate in between the groups is insignificant, there is a significant difference at 135, 150, 165 minutes. Both the groups maintained hemodynamic stability, there were no significant changes with respiratory parameters in either of the groups in perioperative period. Duration of analgesia was significantly prolonged in Group A (761.6 min) compared to Group B (461 min) with significant P value. Conclusion: Both inj. Buprenorphine 150 µg and inj. fentanyl 50 µg given epidurally with 15ml of 0.5% bupivacaine, as a single shot provided excellent operative conditions and satisfactory postoperative analgesia in both the groups.

INTRODUCTION

Pain is defined as "unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage", by International Association for the study of Pain (IASP). "Surgery" to anyone stands synonymous to "pain" hence treatment of pain after surgery is central to the care of postoperative patients. Other than psychological trauma, pain is shown to affect the physiology of almost all the systems including respiratory, cardiovascular and metabolic profile there by increasing the morbidity.^[1] Pain is derived from Latin word "ponea".^[2]

Epidural anesthesia/analgesia is one of the best accepted techniques for lower abdominal and lower

limb surgeries as it provides good sensory and motor block with contracted bowels retaining adequate spontaneous respiration, haemodynamic stability and also an indwelling catheter facilitates further administration of analgesic doses for postoperative period.^[3]

Epidural anesthesia is the most commonly used technique for providing not only surgical anesthesia but also postoperative analgesia in surgical patients.^[4] Early postoperative mobilization, rehabilitation, minimal pain and discomfort are the most desirable features of the modern surgery.^[5-7]

In the context of "Augmentation strategies" for epidural and intrathecal analgesia, the discovery of opioid receptors in the spinal cord and subsequent development of technique of epidural and intrathecal opioid administration has opened a new horizon in the pain management in perioperative period and gained significance in the past three decades. Numerous studies have demonstrated that epidural analgesia does inhibit stress responses. This effect seems to be greatest when epidural analgesia is continued in postoperative period and is superior to traditional intravenous and intramuscular injection opioids. Local anesthetic agents like bupivacaine, lignocaine with or without adrenaline are in use and are the gold standard drugs.^[8,9]

Epidural opioids have their own side effects; the most dangerous side effects are delayed respiratory depression, nausea and vomiting which were seen with morphine due to its hydrophilic nature and its rostral spread. On invention of buprenorphine, which is 30 times more potent than morphine, is an agonistantagonist with lipid solubility about 5 times greater than that of morphine, has been used epidurally for perioperative analgesia and has been associated with low incidence of respiratory depression because there is no rostral spread but was associated with urinary retention.^[10] Arrival of a new synthetic lipophilic opioid, fentanyl which has a shorter duration of action and time of onset as compared to pethidine and morphine has revolutionised its use in the past 3 decades.

An effort is made in this study to compare the perioperative analgesic efficacy of these two lipophilic drugs along with epidural bupivacaine in lower abdominal and lower limb surgeries.

MATERIALS AND METHODS

After obtaining the Institutional Review Board approval, a Prospective, randomized, double-blind, comparative study was conducted. Written informed consent of patients was obtained before including in the study. Adult patients undergoing lower abdominal/gynaecological/urological/lower limb elective surgeries under epidural block during the study period were recruited after meeting the inclusion and exclusion criteria.

www.randomizer.org generated random allocation of 2 groups of 50 each. This allocation was followed for

assigning the patients blinded medications. Double blinding was done with the help of faculty in anesthesia department. Blinded drug coded A could contain Bupivacaine with buprenorphine/fentanyl. Blinded drug coded B could contain Bupivacaine with fentanyl/ Buprenorphine.

From available literature we see that 40% more patients experience better quality of analgesia (lower VAS score) during surgery with buprenorphine compared to fentanyl as an adjuvant to bupivacaine in epidural anesthesia. This difference is at 120 minutes time point from administration of drugs through epidural catheter.11 In our study if we need to show a difference in proportion of patients of 40% we will need 28 patients in each treatment group. We assume a 10-15% drop out due to failed insertion of epidural catheter, cancellation of surgery or prolonged surgery needing general anesthesia. Hence, we chose to randomize 100 patients (50 in each group) for this study.

Inclusion Criteria

ASA physical status I and II

Age between 20 to 60 years of both sexes. Weight of the patients between 40 to 70 kg.

Height of the patients between 150 to 180 cm.

Exclusion Criteria

Patients refusal.

Patients with spinal deformities.

Patients with bleeding and clotting disorders.

Patients with neurological deficits.

Patients with local sepsis around the site for epidural needle insertion.

Patients with history of cardiorespiratory disorders, hepatic, renal disease, convulsions and neurological deficits.

Patients of weight less than 40 kg and above 70 kg.

Patients of height less than 150 cm and above 180 cm. Patient Complaining of pain at the site of surgery or recorded VAS scores of > 4. Time for duration of analgesia was measured in minutes. A total 60 patients of both sexes between the ages 20-60 years were selected randomly. All patients were visited on the day prior to surgery and explained in detail regarding the anesthetic procedure. A detailed preanesthetic evaluation with detailed history, systemic and general examination was carried out, patients having pregnancy, respiratory, cardiovascular and metabolic disorders were ruled out.

The surgeries included were

Gynecological: Abdominal and vaginal hysterectomy.

General surgeries: Hernioplasty, open appendicectomy.

Urological procedures, lower limb surgeries.

All the patients had the following investigations done.

Haemoglobin percentage.

Urine examination for albumin and sugar.

Bleeding time and clotting time.

Blood sugar. Blood urea.

Serum creatinine.

HIV and HBSAg.

Serum electrolytes – if needed.

Chest X-ray and electrocardiogram were taken when required. Procedure was explained and the patients were taught to assess the intensity of pain using the visual analogue scale (VAS). In the visual analogue scale the patients were shown a scale of 10 cm length. Zero end of the scale was taken as No pain" and 10 cm marks as Maximum pain". Intensity of pain increases gradually from "0" to "10". Patients were instructed to point the intensity of pain on the scale. All patient were administered Tab. Alprazole 0.5 mg and Tab. Ranitidine 150 mg day prior to surgery at 10 p.m and advised to be nil per oral thereafter. In the operation theatre, all resuscitation equipments, E.T tubes, anesthesia machine, emergency drugs were kept ready to deal with any untoward reactions, and able to administer general anaesthesia if required. On the day of surgery patients were connected to multichannel monitor ECG and baseline heart rate, non-invasive blood pressure, SpO2 and respiratory rate were recorded. After insertion of 18G i.v cannula, patients were preloaded with ringer lactate 500 ml. After taking all aseptic precautions, in sitting position, the lumbar epidural block was induced using 18 gauge touhy needle. After skin infiltration with 2% lignocaine in L2-L3 inter-space, the epidural needle was inserted, and epidural space was identified by loss of resistance to air technique. An epidural catheter was inserted and kept 6 cm in the epidural space and then fixed on the back of the patient. Test dose of 3 ml 2% lignocaine adrenaline was given through the catheter after giving supine position. After ruling out intradural and intravascular placement of the catheter, the study drug was given epidurally, which was prepared by another anesthetist who was unaware of the study design. The anesthetist conducting the study was blinded to the study drug which was prepared by another anesthetist as per instructions. 5 minutes after test dose, in the absence of any adverse sequelae, 16ml of study drug was injected through epidural catheter in incremental boluses. Time of injection was noted as "0" time.

After adequate blockade (T10) patients were repositioned based on surgical requirements. Intraoperatively assessment of sensory and motor blockade was done at the end of each minute till 30 minutes after injecting 16 ml of the study drug.

The onset time and the time for maximum motor and sensory block and the maximum level of sensory and motor block were recorded. Spread was considered to be complete when two identical dermatomes on both sides were insensitive. Time for two segmental dermatomal regression, time when the patient starting moving his limbs independently, time for first rescue analgesic ,number of top up doses of analgesic after giving rescue analgesia were recorded during the study. Sensory blockade was assessed using a short beveled 22 gauge needle. Motor blockade in the lower limbs was assessed using modified Bromage scale.10 Side effects: Like nausea, vomiting, hypotension, respiratory depression and pruritus allergic reaction were looked for. Vital parameters such as the HR, BP, RR and oxygen saturation were continuously monitored for every 5 min for first 15min and every 15min throughout intraoperative period or for first 3 hours. Duration of the surgery was recorded. In the perioperative period, pain scores were assessed on the VAS scale every hour till 6 hours and the every 2 hrs till 20 hrs.

Statistical analysis

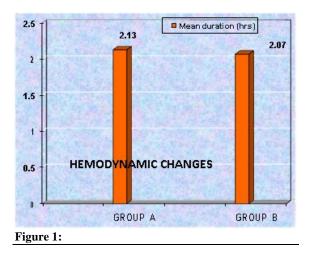
The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). Quantitative variables were described as means and standard deviations or median and interquartile range based on their distribution. Qualitative variables were presented as count and percentages. For all tests, confidence level and level of significance were set at 95% and 5% respectively.

RESULTS

[Table 1] shows Percentage of patients belonging to the age of 21-30years, 31-40 years,41- 50years, >50yrs in Group A and Group B were 12%, 20%, 44%, 24 % and 16%, 42%, 30%, and 12% respectively.

62% of the patients in Group A and 42% of patients in Group B were Males. 38% of the patients in Group A and 58% of the patient in Groups B were females. 60% of the patients belonged to ASA I and 40% to ASA II in group A. 72% of the patients belonged to ASA I and 28% to ASA II in Group B. [Table 2]

Mean baseline data of Pulse rate, systolic pressure, diastolic pressure, MAP, R.R in Group A were 81.4 ± 9.1 /minutes, $126.9\pm7,4$ mmHg, 80.3 ± 7.9 mmHg, 95.6 ± 6.8 mmHg, 17.1 ± 1.3 /minutes respectively. Mean baseline data of Pulse rate, systolic pressure, diastolic pressure, MAP, R.R in Group B were 81.9 ± 9.4 /minutes, 128.4 ± 8.1 mmHg, 83.5 ± 5.2 mmHg, 98.3 ± 5.6 mmHg, 16.6 ± 1.3 /minutes respectively. [Table 3]



Mean duration of surgery in Group A was 2.15 ± 0.7 hours. Mean duration of surgery in Group B was 2.09 ± 0.65 hours.

The difference in heart rate in between the groups is insignificant, there is a significant difference at 135, 150, 165 minutes. Variation of pulse rate in group A and group B was studied at different time intervals up to 3 hrs. There was moderate change in the pulse rate in both the groups at 135, 150, 165 minutes which was statistically significant. There is a significant difference between MAP between the groups at 45, 60, 75, 120 minutes.

In group A, MAP from base line 95.3mmHg fell to 84.8 mmHg at 45min.Then picked up to 87.5 mmHg at 120 min thereafter remained the same throughout the study. In group B, MAP from baseline 98.3 mmHg fell to 87.7 mmHg at 45 min then picked up slowly to 91.3mmHg at 120 min thereafter remained significantly high throughout the study but the difference was not significant in both the groups.

There is a significant difference in respiratory rate between the groups at 120, 135,150 minutes. Mean baseline respiratory rate in group A fell from 17.0/min to around 15.2 in 30 min gradually picking up to16.2/min by 120 minutes and remained almost the same throughout. In group B, mean base line respiratory rate which was 16.4/min which fell to 15.2/min at 30min, picked up to 15.9/min at 90 min which is comparable without any significant difference.

In Group A mean time for onset of sensory blockade at T12, T10, T8, T6 in minutes was 7.6 ± 3.12 , 11.20 ± 3 , 15.30 ± 3.25 , 18.6 ± 2.7 respectively. In Group B mean time for onset of sensory blockade at

T12, T10.T8, T6 in minutes was 6.7±2.5, 10.5±2.8, 13.90±3.11, 17.5±3.6 respectively. [Table 4]

The mean time to achieve complete motor blockade was 18.9 min in group A and 18.7 in group B which is statistically insignificant in between both the groups. [Table 5]

[Table 6] shows the mean VAS Scores between the 2 groups. At 2 hours there was no significant difference in VAS scores but difference was seen from 3rd hour onwards. Data after 6th hour is not representative as most patients in Group B started getting rescue analgesia

Proportion of patients having better quality of analgesia at 2 hours measured in VAS Score (VAS = 0). Hypothesis test of significance Chi-squared 0.00, significance P=0.9880. There was no significant difference in the proportion of patients having good analgesia (VAS Score "zero") at 2 hours.

The mean duration for rescue analgesia in group A was 12.80 ± 2.78 hrs compared to group B of 7.80 ±2.32 hrs which is statistically significant. The mean duration of analgesia in group A is 760.2 minutes compared to 466 minutes in group B which is statistically significant.

Mean duration of sensory blockade is 199.5±22.5 minutes in group A and 147.2±15.2 minutes in Group B which is statistically significant. Mean duration of motor blockade 221±20.4 minutes in Group A and 202±19.9 minutes in group B which is statistically significant. In Group A 30% of patients experienced nausea compared to 7% of patients in group B which is statistically significant.32% of the patients in group B had pruritus, while none in group A.

| Table 1: Age Distribution | n (in years) | | | | |
|---------------------------|---------------|---------|----------|-------|--|
| Age Group | Group A | | Group | В | |
| | No. | % | No. | % | |
| 21 - 30 yrs | 6 | 12 0 | 8 | 16 | |
| 31 – 40 yrs | 10 | 20 0 | 21 | 42 | |
| 41 – 50 yrs | 22 | 44 | 15 | 30.0 | |
| Above 50 yrs | 12 | 24 | 6 | 12.0 | |
| Total | 50 | 100.0 | 50 | 100.0 | |
| Mean | 44.5 yrs | | 38.9 yrs | | |
| SD | 8.2 yrs | | 8.5 yrs | | |
| ʻp' | 0.09 Not Sign | ificant | | | |

| Fable 2: Gender Distribution | | | | | | | | |
|------------------------------|---------------|--------|---------|----|--|--|--|--|
| Sex | Group A | | Group B | | | | | |
| | No. | % | No. | % | | | | |
| Male | 31 | 62 | 21 | 42 | | | | |
| Female | 19 | 38 | 29 | 58 | | | | |
| ʻp' | 0.1 Not Signi | ficant | | | | | | |

Table 3: Baseline Data

| Parameter | Pulse rate beats per min | | Systolic p in mmHg | | Diastolic in mmHg | 1 | MAP in 1 | nmHg | RR per n | nin |
|-----------|--------------------------|------------|-----------------------|------------|----------------------|-------------|------------|-------------|------------|------------|
| | Group A | Group B | Group A | Group B | Group A | Group B | Group A | Group B | Group A | Group B |
| Mean | 81.4 | 81.9 | 126.9 | 128.4 | 80.3 | 83.5 | 95.6 | 98.3 | 17.1 | 16.6 |
| SD | 9.1 | 9.4 | 7.4 | 8.1 | 7.9 | 5.2 | 6.8 | 5.6 | 1.3 | 1.3 |
| ʻp' | 0.9 Not Si | gnificant | 0.4 Not Si | gnificant | 0.09 Not S | Significant | 0.07 Not S | lignificant | 0.08 Not s | ignificant |

| Table 4: Onset of sensory block (minutes) | | | | | | | | | |
|---|----------------------------------|---------------|------------|-----------|------------|-----------|-----------|------------|--|
| Group | Onset of sensory block (minutes) | | | | | | | | |
| | T12 | T12 T10 T8 T6 | | | | | | | |
| | Mean | SD | Mean | SD | Mean | SD | Mean | SD | |
| Group A | 7.6 | 3.1 | 11.20 | 3.0 | 15.30 | 3.25 | 18.6 | 2.7 | |
| Group B | 6.7 | 2.5 | 10.5 | 2.80 | 13.90 | 3.11 | 17.5 | 3.6 | |
| ʻp' | 0.3 Not Sig | nificant | 0.1 Not Si | gnificant | 0.9 Not Si | gnificant | 0.4 Not S | ignificant | |

| Table 5: Onset of | of motor blockade | e in bromag | e scale | | | | | | | |
|-------------------|-------------------|--|---------|---------------------|------|---------------------|------|---------------------|--|--|
| Group | Onset of M | Onset of Motor Blockade in Bromage scale (minutes) | | | | | | | | |
| | 0 | 0 1 2 3 | | | | | | | | |
| | Mean | SD | Mean | SD | Mean | SD | Mean | SD | | |
| Group A | 6.10 | 2.5 | 9.8 | 3.1 | 13.5 | 2.54 | 18.9 | 3.50 | | |
| Group B | 6.70 | 2.01 | 9.9 | 2.8 | 14.4 | 3.1 | 18.7 | 3.40 | | |
| ʻp' | 0.4 Not Sig | 0.4 Not Significant | | 0.9 Not Significant | | 0.3 Not Significant | | 0.9 Not Significant | | |

| Perioperative VAS at | Periopera | tive VAS in | 'p' | Significance | | |
|----------------------|-----------|-------------|---------|--------------|-------|-----------------|
| | Group A | | Group B | | | |
| | Mean | SD | Mean | SD | | |
| 0 hour | 2.5 | 0.5 | 2.41 | 0.7 | 0.7 | Not Significant |
| 1 hour | 0.12 | 0.32 | 0.12 | 0.09 | 0.1 | Not Significant |
| 2 hours | 0.35 | 0.22 | 0.4 | 0.59 | 0.9 | Not Significant |
| 3 hours | 0.69 | 0.51 | 1.15 | 0.89 | 0.008 | Significant |
| 4 hours | 0.90 | 0.49 | 1.29 | 0.6 | 0.02 | Significant |
| 5 hours | 1.2 | 0.7 | 2.21 | 0.9 | 0.05 | Significant |
| 6 hours | 1.90 | 0.6 | 2.70 | 1.15 | 0.001 | Significant |
| 8 hours | 2.50 | 0.81 | 2.24 | 1.22 | 0.3 | Not Significant |
| 10 hours | 2.60 | 1.1 | 1.85 | 1.2 | 0.006 | Significant |
| 12 hours | 2.50 | 1.21 | 1.68 | 0.90 | 0.005 | Significant |
| 14 hours | 2.10 | 1.19 | 2.15 | 1.05 | 0.9 | Not Significant |
| 16 hours | 2.05 | 0.87 | 2.02 | 0.85 | 0.8 | Not Significant |
| 18 hours | 2.2 | 0.6 | 2.35 | 1.06 | 0.2 | Not Significant |
| 20 hours | 2.45 | 0.50 | 2.78 | 0.9 | 0.2 | Not Significant |

| Table 7: Time for rescue analgesia (hrs) | | | | | | | | |
|--|--------------------|---------------------------------|--|--|--|--|--|--|
| Group | Time for rescue | Time for rescue analgesia (hrs) | | | | | | |
| _ | Mean | SD | | | | | | |
| Group A | 12.80 | 2.78 | | | | | | |
| Group B | 7.80 | 2.32 | | | | | | |
| ʻp' | < 0.001 Significan | t | | | | | | |

DISCUSSION

Exclusive epidural route during the study was selected deliberately to avoid the spinal anaesthesia induced sudden hypotension, to avoid invasive dural penetration technique with spinal needle, to provide postoperative pain relief and to study analgesic efficacy and safety of the drugs.

This study directly shows the effects of epidural buprenorphine and epidural fentanyl with 0.5% bupivacaine. Stable hemodynamics and prolonged postoperative analgesia are the main desirable qualities of an adjuvant used in epidural anaesthesia. Surgical trauma and subsequent postoperative pain result in a broad range of endocrinologic, immunologic and inflammatory responses, including increased release of catabolic hormones and inhibited secretion of anabolic mediators. To minimize or overcome these adverse effects, the postoperative pain should be optimally treated. Chemical, mechanical or thermal stimuli of sufficient quantity or intensity to threaten or destroy tissue or to disrupt vascular integrity typically lead to autonomic (changes in heart rate or blood pressure) or hormonal (adrenal and pituitary secretion) responses as well as to the subjective sensation of pain.^[10]

Postoperative pain relief is achieved by various means analgesics like Diclofenac, Ketoralac and Piroxicam. Nerve blocks and neurolysis, Transcutaneous electrical nerve stimulation (TENS) etc. Advantages of epidural anesthesia where feasible, is that a single injection will provide perioperative analgesia, muscular relaxation, graded hypotension and decreased blood loss, hence gaining popularity ever since its introduction. Numerous studies have demonstrated that epidural analgesia does inhibit the stress response. Epidural analgesia provides effective pain relief with minimal side effects and high level of patient satisfaction. Traditionally epidural bupivacaine was used for postoperative analgesia. The epidural bupivacaine 0.5% causes motor, sensory and sympathetic blockade, 0.25% causes sensory and autonomic blockade and 0.125% causes autonomic blockade only. Epidural and intrathecal opioids are today being used for intraoperative and postoperative analgesia. In recent times many opioids have been used for postoperative analgesia as these drugs increase the

duration of analgesia with minimum side effects. Spinal opioids are proved to be reliable. Morphine and pethidine remain the standard drugs used for postoperative pain.12 But they are associated with delayed respiratory depression and abuse potential.^[13]

In the present study all patients belonging to ASA I and ASA II were selected randomly in to two groups - A and B of 50 patients each in the OT. The demographic profile in the present study is comparable to other studies and did not show any statistical difference. There is no significant difference in the onset of analgesia between the Group A and Group B. Zenz M, Pipenbrocks S,^[14] did a double blind comparison of epidural buprenorphine and epidural morphine for postoperative pain relief. Morphine 4 mg and buprenorphine 0.15 mg were given through epidural route. Buprenorphine produced analgesia with short latency 6.8 minutes which is close to our observation of 7.57 minutes. High lipid solubility and high potency may explain the faster onset of pain relief in buprenorphine group. High lipid solubility results in fast distribution to opioid receptors present in spinal cord and CNS and increases its final concentration there.^[15]

Mean duration of sensory blockade is 199.5±22.5 minutes in group A and 147.2±15.2 minutes in Group B which is statistically significant. Mean duration of motor blockade 221±20.4 minutes in Group A and 202±19.9 minutes in group B which is statistically significant. Buprenorphine prolonged the duration of sensory blockade compared to fentanyl. Ipe S, Koshy L et al,^[17] conducted a study on extradural anesthesia using 0.75% ropivacaine, 0.75% ropivacaine with fentanyl and 0.75% ropivacaine with buprenorphine for caesarean section. They found that mean duration of sensory block in buprenorphine group was 120.41 min and fentanyl group was 95.68 min and the difference was statistically significant, which correlates with our study, as we have statistically significant difference in the duration of sensory blockade between the groups.

The onset of motor blockade, degree and time required to achieve complete blockade were recorded. The degree of motor blockade was graded according to modified Bromage scale. Dhale S and Shelgaonkar V17 studied different doses of epidural fentanyl ($25\mu g$, $50\mu g$, $75\mu g$) with 0.5% bupivacaine for perioperative analgesia where mean onset of motor blockade was 26.13 ± 1.80 minutes. In our study, duration of motor blockade was significant between group A and group B. Buprenorphine prolonged the duration of motor blockade compared to fentanyl. Previous studies on addition of buprenorphine 150 μg epidurally provided good postoperative analgesia without prolonged motor blockade.^[18-20]

In group A, MAP from base line 95.3mmHg fell to 84.8 mmHg at 45min.Then picked up to 87.5 mmHg at 120 min thereafter remained the same throughout the study. In group B, MAP from baseline 98.3 mmHg fell to 87.7 mmHg at 45 min then picked up slowly to 91.3mmHg at 120 min thereafter remained significantly high throughout the study but the difference was not significant in both the groups. In another study, Ozalp G, Guner F, Kuru N51 did a study on postoperative patient controlled epidural analgesia with opioid bupivacaine mixtures. After surgery, patients complaining pain received a loading dose of morphine 2mg (Group A) or fentanyl 50 µg (Group B). For continuing pain, 1mg morphine in 4 ml bupivacaine 0.125% (0.25 mg /ml morphine and 1mg/ml bupivacaine, Group A) or 20 micrograms fentanyl in 4 ml bupivacaine 0.125% (5 µg/ml bupivacaine Group B). They concluded that fentanyl was hemodynamically stable with fewer side effects and excellent in providing postoperative analgesia which is close to our observation.

There is a significant difference in respiratory rate between the groups at 120, 135,150 minutes. Mean baseline respiratory rate in group A fell from 17.0/min to around 15.2 in 30 min gradually picking up to16.2/min by 120 minutes and remained almost the same throughout. In group B, mean base line respiratory rate which was 16.4/min which fell to 15.2/min at 30min, picked up to 15.9/min at 90 min which is comparable without any significant difference. There is a significant difference in between the groups at 120,135,150 minutes. In the other study, Ichiishi N, Hiraishi T et al, studied effects of epidural buprenorphine on postoperative respiratory function, using respiratory inductive plethysmography in two groups of patients [(1) 0.1 mg (2) 0.2 mg] after upper abdominal surgery. Buprenorphine 0.1 mg group showed decreased respiratory rate and increased tidal volume. Decrease in the respiratory rate and tidal volume were seen in buprenorphine 0.2 mg group and continued for 3-4 hrs after epidural administration. However, there was no severe respiratory depression in either group. They found that 0.2 mg of epidural buprenorphine may give a satisfactory postoperative pain relief and less respiratory depression and RIP is a useful method for the measurement of postoperative respiratory function.

The pain scores as assessed on the VAS were low and remained low for a significant time in the postoperative period with addition of buprenorphine or fentanyl to bupivacaine.

The duration of analgesia was also significantly prolonged with addition of either of the narcotics to local anesthetics. In our study, mean duration of analgesia in group A was significantly higher compared to group B, of mean duration of analgesia. Following studies make a similar observation. Wolff J, Carl P et al. In their study on epidural buprenorphine 0.3mg for postoperative analgesia in comparison with morphine 4 mg after major orthopedic surgery found that duration of action was 620 minutes with buprenorphine group which is similar to our study. Abboud TK et al. used higher doses of buprenorphine alone, epidurally, and observed a remarkably longer duration of postoperative analgesia. Furthermore, investigators

have also found that analgesia provided by buprenorphine has a significant correlation with the affective domain, with greater reduction in affective magnitude than in pain intensity. Dhale S and Shelgaonkar V studied different doses of epidural fentanyl with 0.5% bupivacaine for perioperative analgesia found that 50µg had mean duration of analgesia 256.66±6.17 minutes. In our study mean duration of action was 461.00 minutes.

Patients in our study received analgesia at anesthetic doses prior to beginning of surgery. We recorded the VAS Score through the perioperative period. The average duration of surgery was not significantly different between the two groups. The quality of analgesia at 2 hrs from the time of administration of drug was not different between the groups. There was no difference in VAS Scores or proportion of patients with VAS of 0. However, from 3 hours but in an average 1 hour post operation, there was significant difference in VAS Scores till about 6 hours. Hence, we conclude that the quality and duration of analgesia were superior in group A compared to group B in the perioperative period.

The commonly seen adverse effects with epidural opioid administration include nausea, vomiting, retention of urine and pruritus and hypotension. Limited sample size and single center were our major limitations. However VAS score is dependent on the patients response and they were blinded to the medication being received. Another limitation could be with the use of 0.5% bupivacaine in both groups. This dose did give sufficient motor and sensory blockade but could have limited the observed analgesic effect seen between the 2 groups perioperatively.

CONCLUSION

The perioperative analgesia was of better quality and of a longer duration in the buprenorphine group compared to fentanyl group. There were no hemodynamic significant and respiratory abnormalities in either of the groups. So it is concluded that epidural buprenorphine in a dose of 150µg given with 15ml of 0.5% bupivacaine is better in providing prolonged satisfactory perioperative analgesia as compared to epidural fentanyl in a dose of 50µg with 15ml of 0.5% bupivacaine. There was faster onset of sensory and motor blockade in both the groups. Buprenorphine prolonged the duration of motor and sensory blockade compared to fentanyl. Regarding the side effects, the incidence of nausea and vomiting was more in buprenorphine as compared to fentanyl group.

REFERENCES

1. Pal N, Malhotra K, Chitra et al. Effect of morphine on postoperative respiratory functions: Comparison between

systemic and epidural routes. Indian J Anaesth .2004;48(3):204-207.

- Nagesh KS, Sathesha M, Prasad RS. Comparative study 2 between epidural bupivacaine with buprenorphine and epidural bupivacaine for postoperative analgesia in abdominal and lower limb surgery. Journal of Evolution of Medical and Dental Sciences.2015 March 02;4(18):3057-3064.
- 3. Simpson BP, Park House J. The problems of postoperative pain. Br J Anaesthesia. 1961; 33:36. Kehlet H. Acute pain control and accelerated postoperative
- 4 surgical recovery. Surg Clin North Am.1999;79:431-43.
- 5 Bradshaw BG, Liu SS, Thirlby RC. Standardized perioperative care protocols and reduced length of stay after colon surgery. J Am Coll Surg.1998;186:501-6.
- 6. Kehlet H, Mogensen T. Hospital stay of 2 days after open sigmoidectomy with a multimodal rehabilitation programme. Br J Surg. 1999;86:227-30.
- 7. Zaric D, Nydahl PA, Philipson L, Samuelsson L, Heierson A, Axelsson K. The effect of continuous lumbar epidural infusion of ropivacaine (0.1%, 0.2%, and 0.3%) and 0.25% bupivacaine on sensory and motor block in volunteers: A double-blind study. Reg Anesth.1996;21:14-25.
- McClellan KJ, Faulds D. Ropivacaine: An update of its use in regional anaesthesia. Drugs.2000;60:1065-93.
- 9 Vallem B, Juvvala R, Ravanam A, et al. Evaluation of effect of epidural administration of fentanyl added to bupivacaine, on postoperative analgesia, in gynaecological surgical patients. Journal of Evidence Based Medicine and Healthcare.2015;2(17):2539-2544.
- 10. Bromage PR. The price of intraspinal narcotic analgesia: Basic constraints. Anaesth Analg.1981;60:461-3.
- 11. Radha J, Jamuna T, Raghuveer J. A comparative study of postoperative analgesia using bupivacaine with fentanyl and bupivacaine with buprenorphine in gynaecological surgeries using combined spinal epidural technique. Journal of Evidence Based Medicine and Healthcare.2015;2(24):3601-3610.
- 12. Graham JK, King R, McCaughey W. Postoperative pain relief using epidural morphine. Anaesthesia. 1980. Feb 1;35(2):158-160.
- 13. Stenseth K, Sellevold O, Breivik H. Epidural morphine for postoperative pain experience in 1085 patients. Acta Anaesthesiol Scand. 1985. January; 29(1): 148-156.
- 14. Zenz M, Pipen brock S, Hubner B, Glocke M. A double blind comparison of epidural Buprenorphine and epidural morphine in postoperative pain. Anaesth Intensivether Notfallmed. 1981;16(6):333-9.
- 15. Tuohy EB.Continuous spinal anaesthesia. A method utilising a urethral catheter. Surg Clin. N Am.1945;25:834.
- 16. Ipe S, Koshy L, Rakhee S et al. A comparative study of extradural anaesthesia using 0.75% ropivacaine, 0.75% ropivacaine with fentanyl and 0.75% ropivacaine with buprenorphine for caesarean section from a rural teaching hospital in India. J Obstet Anaesth Crit Care.2014;4 (1):29.
- 17. Dhale S, Shelgaonkar V, Akulwar VV. A comparative study of epidural bupivacaine and epidural bupivacaine with for perioperative fentanvl analgesia. Indian J Anaesth.2000;44:35.
- 18. Govindarajan R, Bakalova T, Michael R, Abadir AR. Epidural buprenorphine in management of pain in multiple rib fractures. Acta Anaesthesiol Scand. 2002;46:660-5.
- 19. Goodman SR, Drachenberg AM, Johnson SA, Negron MA, Kim-Lo SH, Smiley RM. Decreased postpartum use of oral pain medication after a single dose of epidural morphine. Reg Anesth Pain Med.2005;30:134-9.
- 20. Korula S, Varma S, George G, Abraham S, Koshy L, Ipe S. A comparative study of intrathecal and epidural buprenorphine using combined spinal-epidural technique for caesarean section. Indian Journal of Anaesthesia. 2010;54(3):205.