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Original Article

Comparative Study of the Effect of Buprenorphine and Fentanyl as an Adjunct to Bupivacaine in Epidural Anesthesia for Lower Abdominal and Lower Limb Surgeries

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Abstract

Introduction: Central neuraxial opioids' administration has opened a new horizon in pain management in perioperative period. Buprenorphine, an agonist - antagonist is thirty times more potent than morphine and with lipid solubility about 5 times greater than that of morphine. Fentanyl, a short-acting agonist, acts at μ receptor which is 100 times more potent than morphine.

Aim: The aim of this study was to compare the effect of buprenorphine and fentanyl as an adjunct to 0.5% bupivacaine in epidural anesthesia for lower abdominal surgeries and lower limb surgeries.

Materials and Methods: This is a randomized clinical study conducted at a tertiary care center. A total of 60 patients posted for elective lower abdominal surgeries were divided into two groups of 30 each. Group A received 0.5% bupivacaine 14-20 ml in the doses of 1.5 mg/kg with 300 μg buprenorphine and Group B received 0.5% bupivacaine 14-20 ml in the doses of 1.5 mg/kg with 50 μg fentanyl.

Results: Both the groups maintained hemodynamic stability which was statistically insignificant. Onset of sensory block and mean time to achieve motor blockade were same in both groups. Duration of analgesia was significantly prolonged in Group A (766.6 min) when compared to Group B (471 min) with significant ($P < 0.05$).

Conclusion: We observed that the postoperative analgesia was definitely of a longer duration with the buprenorphine group when compared to fentanyl group. Hence, it is concluded that epidural buprenorphine is better in providing prolonged satisfactory postoperative analgesia as compared to fentanyl when it is used as adjuncts with bupivacaine.

Key words: Epidural anesthesia, Fentanyl, Buprenorphine, Post-operative analgesia

INTRODUCTION

Epidural anesthesia is one of the best accepted techniques for lower abdominal surgeries as it provides good sensory and motor block with contracted bowels, retaining spontaneous respiration, hemodynamic stability, and also an indwelling catheter which facilitates further administration of analgesic drugs for the postoperative period. Epidural and intrathecal opioids have gained significance in the past three decades. The side effects of opioids were mostly seen with morphine due to its hydrophilic nature and its rostral spread.

Buprenorphine is semisynthetic, highly lipophilic opioids derived from the Baine in 1966 and is 33 times more potent than morphine. It acts as narcotic agonist (at lower doses) and antagonist (at higher doses) in doses varying from 60 to 300 μg have been used for epidural administration for postoperative pain relief.

Fentanyl, a synthetic opioid, a tertiary amine, and a phenyl piperedine derivative, was first synthesized by Dr. Paul

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Jannsen in 1960. It is available as an injection, transdermal patches, and lollipop.

Aim

In this context, the present study was undertaken to compare the effect of buprenorphine and fentanyl as an adjuncts to 0.5% bupivacaine for epidural anesthesia in lower abdominal surgeries and lower limb surgeries in providing, (1) Intraoperative good sensory and motor blockade, (2) quality and duration of postoperative analgesia, (3) changes in hemodynamic and respiratory parameters, and (4) to study the side effects such as nausea, vomiting, respiratory depression, urinary retention, pruritus, and others if any.

MATERIALS AND METHODS

This is a randomized clinical study conducted in the Department of Anesthesiology, Rajah Muthiah Medical College and Hospital, Chidambaram, during 2015-2016, after getting approval from the Institutional Ethical Committee. The study was conducted on a total of 60 adult patients of either sex, aged between 20 and 60 years, belonging to either ASA Class I or II, posted for elective surgery. Patients were excluded when they refused or if they had any spinal deformity, neurological deficit, or local sepsis in the site of needle insertion. A detailed preanesthetic checkup was done for all patients and informed consent with prior explanation of the procedure to them was taken.

Patients were randomly assigned to any one of the groups with 30 patients each in each group.

In the operating room, an intravenous (IV) line was secured with and IV fluid connected. Monitors including noninvasive blood pressure, electrocardiogram, and pulse oximeter were connected and pre-operative baseline blood pressure, heart rate, and oxygen saturation were recorded.

Patients in lateral position with a small pillow under the head, local infiltration was done after thorough aseptic preparation of needle insertion site. Epidural space was found using a 16 G Tuohy needle at L2-L3 interspaces using loss of resistance technique. Epidural catheter was then threaded through this needle for 5-6 cm in the cephalad direction and was properly fixed after removing the needle. After giving the epidural test dose with negative signs of intravascular or subarachnoid injection, the full test drug was given through the epidural catheter.

Group A	30 patients	0.5% bupivacaine 14-20 ml in the doses of 1.5 mg/kg with 300 μg buprenorphine
Group B	30 patients	0.5% bupivacaine 14-20 ml in the doses of 1.5 mg/kg with 50 μg fentanyl

The drug was injected approximately at the rate of 1 ml/s and level of the block was determined by loss of sensation to pin prick. The spread was considered to be complete when two identical dermatomes on both sides were insensitive. Heart rate, blood pressure, oxygen saturation, and respiratory rate were recorded for every 5 min for the first 15 min and every 15 min thereafter for the first 3 h.

After the completion of surgery, the patients were observed in the recovery room. The duration of analgesia was measured from time of first administration of the epidural drug till the time when the patient complaint of pain of more than 5 cm on the visual analog scale and the rescue analgesic was administered.

The onset of surgical analgesia to achieve the highest grade of motor block was recorded and was graded according to modified Bromage scale.

Scale	Criteria
0	Free movements of legs and feet with ability to raise extended leg
1	Decreased knee flexion, inability to raise extended leg with full flexion of feet and ankles
2	Inability to raise legs or flex knees but with flexion of ankles and feet
3	Inability to raise legs, flex knees or ankle or move toes

Side effects such as nausea, vomiting, hypotension, respiratory depression, pruritus, and allergic reaction were looked and were recorded if any.

OBSERVATIONS AND RESULTS

A total of 60 patients of either sex participated in the study. Statistical data were analyzed using

- Chi-square-test
- Student *t*-test (paired and unpaired *t*-test)
- $P < 0.05$ - significant, <0.01 - highly significant, <0.001 - very highly significant, and >0.05 not significant.

Demographic Data Analysis

Table 1 shows Group A: 0.5% bupivacaine with 300 μg of buprenorphine.

Table 2 shows Group B: 0.5% bupivacaine with 50 μg of fentanyl.

Sensory Block

It was observed that the onset of analgesia in Group A was 7.56 min when compared to Group B which was 6.6 min, which is statistically significant ($P > 0.05$). It shows that there was no difference in the onset of action (Table 3 and Graph 1).

Table 1: Group A - 0.5% bupivacaine with 300 µg of buprenorphine

Number of patients	Age (years)	Weight (kg)	Number of male patients	Number of female patients
30	22-58	46-72	11	19
Mean	43.77	57.90	36.7	63.3

Table 2: Group B - 0.5% bupivacaine with 50 µg of fentanyl

Number of patients	Age (years)	Weight (kg)	Number of male patients	Number of female patients
30	26-59	45-74	19	13
Mean	39.43	56.56	56.7	43.3

Table 3: Sensory block

	Mean duration of onset					Significance
Dermatome level	Group A (min)	SD	Group B (min)	SD	*t*	
T_{12}	7.56	3.11	6.66	2.44	1.246	
T_{10}	11.06	3.08	10.20	2.80	1.138	*P*>0.05 (Not significant)
T_{8}	15.51	3.14	13.88	3.20	1.940	
T_{6}	18.54	2.76	17.00	3.19	1.101	

SD: Standard deviation

Motor Block

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. The mean time to achieve complete motor blockade was 18.9 min in Group A and 18.63 in Group B, which was statistically insignificant in both the groups (Table 4 and Graph 2).

There were no significant changes in other parameters such as mean pulse rate, mean arterial pressure, and respiratory rate.

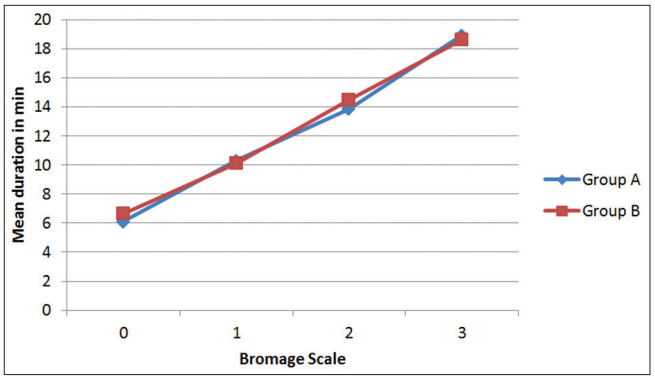
Graph 1: Onset of sensory block

Mean Duration of Analgesia

Duration of analgesia in Group A was 766.6 min compared to Group B which is 471 min. This was statistically significant ($P < 0.05$) (Table 5 and Graph 3).

Side Effects

Incidence of nausea and vomiting was noted in 12 patients in Group A (40%) and 2 patients in Group B (10%). However, it was treatable with single dose of antiemetic without deleterious effects on the patients. 10 patients (33%) in Group B developed pruritus which was mild in nature and did not require any intervention (Table 6).



Graph 2: Onset of complete motor block

DISCUSSION

Pain includes not only the perception of an uncomfortable stimulus but also the response to that perception. Localised sensation of discomfort felt immediately after noxious stimulus which disappears when the stimulus ceases is called fast pain. Pain that is perceived later by the patient for longer duration as burning, dull or warm is called slow pain.[1] Satisfactory pain relief has always been a difficult problem in clinical practice. Epidural anesthesia using a single injection of 0.5% bupivacaine will provide good

Table 4: Motor block

	Mean duration of onset					Significance
Grade	Group A (min)	SD	Group B (min)	SD	*t*	
0	6.1	2.6	6.66	2.02	0.204	*P*>0.05 (Not significant)
1	10.3	2.84	10.13	2.35		
2	13.83	2.78	14.46	3.08		
3	18.9	3.55	18.63	3.25		

SD: Standard deviation

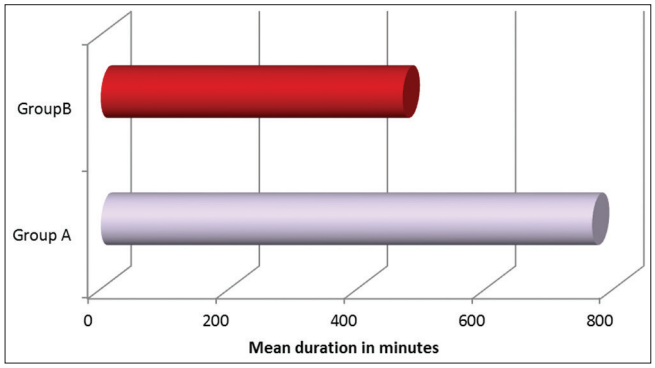
Table 5: Mean duration of analgesia

Groups	Number of patients	Mean±SD	*t*	Significance
Group A	30	766.6±169.67	7.178	*P*<0.05 S
Group B	30	471±148.68		

SD: Standard deviation

Table 6: Side effects

Side effects	Patients (%)	
	Group A	Group B
Nausea	9 (30)	2 (10)
Vomiting	3 (10)	
Urinary retention	-	-
Pruritus	-	10 (33.3)
Hypotension	-	-



Graph 3: Mean duration of analgesia

perioperative analgesia and muscular relaxation with graded hypotension and decreased blood loss by causing motor, sensory, and sympathetic blockade, hence gaining popularity ever since its introduction.

Epidural administration of various analgesics gained increasing popularity following the discovery of opioid receptors in the spinal cord capable of producing potent analgesia as reported by Taksh and Rudy in 1976. Opioid receptors in the dorsal horn have pre- and post-synaptic effects and affect the modulation of nocioceptive input but does not cause sympathetic or motor blockade. It is now clear that epidural administration of opioid is superior to traditional intravascular and intramuscular injection of opioids.[2] Morphine and pethidine remain the standard drugs used for postoperative pain,[3] but they are associated with delayed respiratory depression and abuse potential.[4]

Buprenorphine which was introduced in 1966, when given epidurally acts on supraspinal region and produces spinal segmental analgesia in a dose-related manner.[5] The diffusion of buprenorphine from the spinal cord in the blood stream is slow and does not reach the bulbar centers with bulk of cerebrospinal fluid due to its lipophillic nature.[6]

Fentanyl when administered through epidural crosses dura and binds to spinal opioid receptors. It is absorbed systemically, binds to supraspinal opioid receptors to produce analgesia.[7]

The aim of this study is comparison of efficacy of buprenorphine and fentanyl when used as adjuncts to bupivacaine epidurally for perioperative analgesia in lower abdominal and lower limb surgeries. Sixty patients were selected into two groups: A and B as discussed earlier.

Mean time for onset of analgesia is noted as 7.53 min in Group A and 6.60 min in Group B, which was statistically insignificant. Zenz *et al.*[8] compared epidural buprenorphine and epidural morphine and concluded that buprenorphine-produced analgesia with short latency 6.8 min which is closer to our observation of 7.53 min. High lipid solubility of buprenorphine results in fast distribution to opioid receptors present in spinal cord and central nervous system and increases its concentration there.[9] Dhale *et al.*[10] in 2000 studied different doses of epidural fentanyl (25, 50, 75 μg) with 0.5% bupivacaine for perioperative analgesia found that 50 μg had a quicker onset of analgesia within 9.53 min which is closer to our observation. The mean time to achieve complete motor blockade was 18.9 min in Group A and 18.63 min in Group B which was statistically insignificant when compared.

Both the groups maintained hemodynamic stability which was statistically insignificant and there were no significant changes with respiratory parameters in either of the groups during both peri- and post-operative period. Rathi and Singh[11] in 1993 studied postoperative analgesic efficacy with different doses of extradural buprenorphine for herniorrhaphy and found that buprenorphine in 0.3 mg is

suitable for single-shot epidural injection which provides both intra- and post-operative analgesia with hemodynamic stability. Ozalp *et al.*[12] concluded that epidural fentanyl was hemodynamically stable with fewer side effects and excellent in providing postoperative analgesia when compared to epidural morphine.

Ichiishi *et al.*[13] found that 0.2 mg of epidural buprenorphine gave a satisfactory postoperative pain relief and less respiratory depression and respiratory inductive plethysmography is a useful method for the measurement of postoperative respiratory function.

Incidence of nausea and vomiting was more in Group A (40%) compared to Group B (10%). 33% of patients in Group B developed pruritus which was mild in nature and did not require any intervention. Observations of the study done by Kumar and Gupta[14] and and Hayashi *et al.*[15] also correlate with our study.

Duration of analgesia was significantly longer in Group A (766 min) when compared to Group B (471 min). Hence, buprenorphine scored over fentanyl in offering longer duration of analgesia. High lipid soluble, strong opiate receptor binding, and intense and prolonged activity of epidural buprenorphine were responsible for longer duration of action.[6]

CONCLUSION

The postoperative analgesia was definitely of a longer duration with the buprenorphine group when compared to fentanyl group. Hence, it is concluded that epidural buprenorphine is better in providing prolonged satisfactory postoperative analgesia as compared to fentanyl when it is used as adjuncts with bupivacaine. There were no significant hemodynamic changes in either of the groups. Regarding the side effects, although the incidence of nausea and vomiting was more in buprenorphine as compared to fentanyl group, it was treatable with single dose of antiemetic without deleterious effects on the patients.

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