

A Comparative Study of Cardiovascular Response and Analgesic Effects of Bupivacaine and Butorphanol

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Abstract

Background: Several methods have been used to relieve post-operative pain, among which epidural administration of local anaesthetic and opioids gained popularity. While proving analgesia through epidural route, cardiovascular response of epidural administered 0.25% bupivacaine with 2mg butorphanol. **Subjects and Methods:** 50 patients between 40-50 years of age undergoing hysterectomy randomly allotted to 2 groups of 25 patients in each group. Group I received 10ml of 0.25% Bupivacaine and Group II received 2 mg Butorphanol diluted in 18ml of normal saline via epidural placed catheter before giving General Anaesthesia for performing hysterectomy. The general anaesthesia technique was the same in both groups of patients. Cardiovascular responses like heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were monitored post-operatively for 10 hrs. Onset of analgesia, duration of analgesia and side effects like nausea, vomiting and sedation were also noted. **Results:** Heart rate were similar between 2 groups before and after injection of drugs into the epidural space ($P>0.05$). There was decrease in the mean systolic blood pressure ($P<0.05$), mean diastolic blood pressure ($P<0.001$) and mean arterial pressure ($P<0.001$) in group I. Onset of analgesia was faster with butorphanol(11.76 minutes) when compared to Bupivacaine(14.38 minutes) and duration of analgesia was longer with butorphanol(7.48 minutes) when compared with Bupivacaine(6.67 minutes). Side effects like nausea, vomiting were more with Bupivacaine (20%) and sedation was the main side effect with butorphanol (40%). **Conclusion:** Our study concludes that epidural administration 10ml of 0.25% Bupivacaine causes significant hypotension when compared to 2mg Butorphanol with 8ml of normal saline given epidural. Butorphanol in epidural space has quicker and longer analgesic action than 0.25% bupivacaine.

Keywords: Cardiovascular Response, Epidural Analgesia, Bupivacaine and Butorphanol

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Introduction

Post-operative pain is an acute form of pain which start with surgical trauma and ends with surgical healing. Despite advances in the knowledge, skill and understanding of pain process there appears to be little improvement in the management of postoperative pain. Anaesthesiologists occupy a unique position to co-operative multi-disciplinary pain management.

Pain is not just a sensory modality but an experience. The International Association for the Study of pain defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage'.^[1] The response to pain is highly variable between persons as well as in the same person at different times.^[2] The relation between quality of analgesia and post-operative outcome remains ill defined. In numerous studies have perioperative physiologic responses in addition to pain relief.

In controlling post-operative pain several methods are adopted of which epidural analgesia gained much popularity because it improves the cardio respiratory function. Several drugs are used in the epidural space.

Use of local anaesthetics like Bupivacaine & opioids like Butorphanol are established for its analgesic property. In the enthusiasm of providing good analgesia in a postoperative patient, sometimes it can result in Cardiovascular collapse if the volume status of the patient is compromised. Central neuraxial blockade is associated with physiological reposes mainly variation in heart rate and cardiac contractility which results from decreased sympathetic tone and unopposed parasympathetic tone.^[3] These physiological responses are more pronounced when bupivacaine was used. Bupivacaine has acquired a reputation for slower onset and hence it would seem attractive to use an agent having the characteristics of faster onset while still retaining the desirable long duration of action of bupivacaine.^[4,5]

Butorphanol, a synthetic agonist-antagonist analgesic is effective in relieving pain when used epidural. Butorphanol is considered for its excellent analgesia and cardiovascular stability.^[4,5]

Aims and Objectives

1. To study the cardiovascular response of epidurally administered 10 ml of 0.25% bupivacaine or 2mg butorphanol in providing postoperative analgesia in

- patients for hysterectomies under the same technique of general anaesthesia.
- To compare the onset, duration and quality of pain relief among patients who received epidural 10ml of 0.25% bupivacaine or 2mg of butorphanol as method of postoperative pain therapy.
 - To find out this of these drug causes significant hypotension following administration into the epidural space

Subjects and Methods

Fifty patients of ASA class 1 and 2, posts for Hysterectomy selected for the study after obtaining ethical committee clearance, institutional approval and informed consent from the patients. Patients were randomly divided into two groups of 25 each.

Group I- Receiving 10ml of 0.25% of Bupivacaine.

Group II- Receiving 2mg Butorphanol diluted with 8ml saline.

Inclusion criteria:

- ASA physical status class 1 and 2
- Both abdominal & vaginal Hysterectomies
- Age between 40 and 50 Years

Exclusion criteria:

- Emergency surgeries
- Severe anaemia, coagulation abnormalities and bleeding disorders.
- Patients with previous history of spine surgeries
- Patients with spinal deformity
- Patients with history of chronic backache
- Patients with active skin lesions over the lumbosacral area.
- Patients with IHD, valvular diseases, COPD, bronchial asthma.

A thorough pre-anaesthetic evaluation was done Tab Diazepam 5-10mg orally was given on the previous night. Patients were kept nil orally for 8 hrs before surgery.

On the day of surgery premedication was given using inj. Pethidine 1.5 mg/kg & inj. Promethazine 0.5 mg/kg intramuscularly 90 minutes before induction of Anaesthesia.

After shifting the patient to the operation table, monitors were connected and patient was positioned in right or left lateral or sitting position. Under aseptic precautions, L2-L3 or L3-L4 interspace was identified and skin was infiltrated with injection of local anaesthetics.

Epidural space approached with 16G or 18G Tuohy needle using loss of resistance technique with air. Then 16G or 18G epidural catheter was passed through the needle till about 4-6 cms of the catheter is in the space. The needle was withdrawn and catheter fixed to the back.

3ml of 2% lignocaine with adrenaline 1:2,00,000 was injected through the catheter as a test dose to rule out intravascular / intrathecal placement of the catheter.

General Anaesthesia was administered to all patients using same kind of drugs and techniques to perform hysterectomy. After the surgery patients were shifted to postoperative care area and monitoring was done. Those patients who had

variable cardiovascular parameters were corrected by oxygen & fluid therapy. When the patients first complained of pain, they were shown Visual Analogue Scale (VAS) to express the intensity of pain on the scale. When it reached 6 mark on the scale, patients were given the following drugs through the epidural catheter according to their group.

Group 1- 10 ml of 0.25% of Bupivacaine.

Group 2- 2mg Butorphanol diluted with 8 ml saline.

Visual Analogue Scale (VAS) was used to assess the intensity of pain and pain relief at regular intervals. Onset of analgesia is time interval from drug administration till VAS score come down to 2. Duration of analgesia is time interval between the onset, till patient complaints of pain (VAS \geq 6) when rescue analgesia was given – the end point of her participation in the study. The following parameters were recorded hourly till 12 hrs Onset of analgesia. Duration of analgesia Cardio vascular monitoring: Pulse rate, systolic, diastolic and mean arterial pressure. Side effects: Nausea/vomiting, pruritus, sedation, shivering, seizures. All the observations and particulars of each patient were recorded

Statistical Methods:

Student t test/ Chi-square test have been used to find the significance of homogeneity of study characteristics between two groups of patients.

Student t test (Unpaired, two tailed) has been used to find the significance of hemodynamic between two groups.

Chi-square / Fisher Exact test has been used to find out the significance of incidence of nausea and vomiting between two group of patients.

Significant figures

P > 0.05 statistically insignificant

P < 0.05 statistically significant

P < 0.01 statistically highly significant

P < 0.001 statistically very highly significant.

Results

Present study was conducted on fifty adult patients in ASA class 1 & 2 aged between 40-50 years, weighing 40 to 60kgs. A prospective randomized comparative study was undertaken to evaluate and compare the cardiovascular response in patients divided into 2 groups of 25 each. Group I received 10ml of 0.25% bupivacaine epidurally and Group II received 2 mg of butorphanol diluted with 8 ml of normal scale epidurally.

Table 1: Demographic Data

	Group I	Group II	P value
Age in years	44.32 ± 2.04	43.92±2.53	0.541
Weight in kg	51.67	51-60	0.747

Table 2: Type of Surgery

Type of surgery	Group I	Group II	P value
TAH	15 (60.0%)	17(68.0%)	0.558
VH	10(40.0%)	8 (32.0%)	

The two groups were comparable with respect to age, weight, and Type of surgery

Table 3: Comparison of Mean Heart Rate [Bpm]

Study period	Group I		Group II		P value
	Mean	SD(±)	Mean	SD(±)	
Pre-injection	79.92	3.43	81.48	3.71	0.129
Post – Injection period					
5 minute	80.40	3.97	80.68	3.69	0.797
10 minute	81.36	4.63	80.60	3.82	0.529
15 minute	83.16	3.47	81.92	3.23	0.197
30 minute	82.56	3.81	82.60	3.01	0.967
1 hour	80.68	3.59	82.12	3.27	0.145
2 hour	80.72	3.48	81.68	3.22	0.317
4 hour	80.72	3.68	81.68	3.75	0.365
6 hour	78.92	3.05	80.48	3.00	0.075+
8 hour	81.64	3.53	80.84	3.33	0.414
10 hour	79.92	3.43	81.48	3.71	0.129

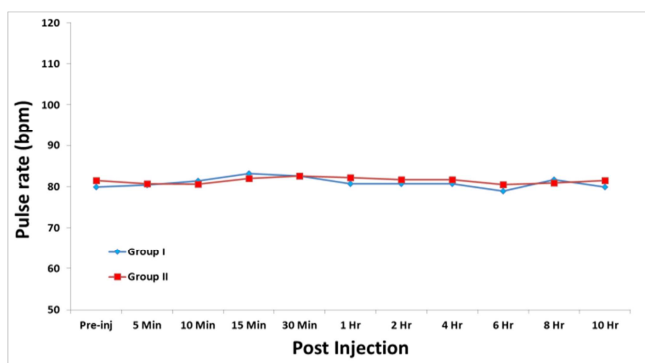


Figure 1: Comparison of Mean Heart Rate [bpm]

Heart rate was similar between two groups before & after injection of drugs into the epidural space. The groups were comparable as $P \geq 0.05$

Table 4: Comparison of Mean Systolic Blood pressure [mm Hg]

Study period	Group I		Group II		P value
	Mean	SD(±)	Mean	SD(±)	
Pre-injection	136.84	3.52	136.52	4.51	0.781
Post – Injection period					
5 minute	130.48	3.83	135.64	4.17	<0.001**
10 minute	118.52	17.34	135.16	4.34	<0.001**
15 minute	120.56	16.85	134.68	4.42	<0.001**
30 minute	128.52	5.67	135.16	4.76	<0.001**
1 hour	129.72	4.84	136.24	3.79	<0.001**
2 hour	131.84	4.74	135.56	3.65	0.003**
4 hour	131.76	3.46	134.80	3.61	0.004**
6 hour	132.60	3.42	132.08	3.50	0.597
8 hour	133.56	3.03	132.72	2.57	0.296
10 hour	136.84	3.52	136.52	4.51	0.781

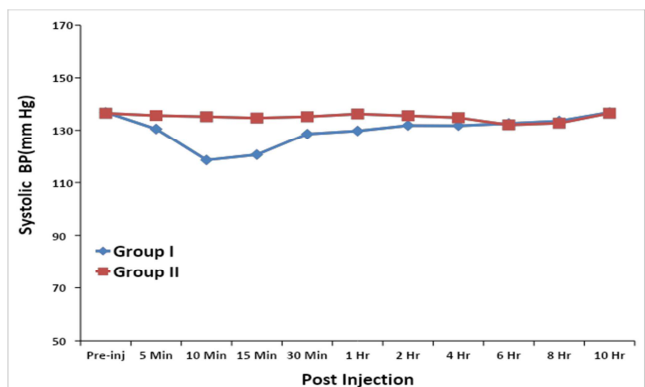


Figure 2: Comparison of Mean Systolic Blood Pressure [mm Hg]

The mean systolic BP decreased after epidural injection of bupivacaine and there was no significant change in butorphanol group. A significant decrease in mean systolic BP occurred between 5 to 15 minutes and persisted up to 4 hrs. $P < 0.05$ highly significant.

Table 5: Comparison of Mean Diastolic Blood pressure [mm Hg]

Study period	Group I		Group II		P value
	Mean	SD(±)	Mean	SD(±)	
Pre-injection	81.84	3.45	83.16	3.01	0.156
Post – Injection period					
5 minute	80.16	4.33	82.76	2.52	0.012*
10 minute	67.92	14.73	83.56	3.66	<0.001**
15 minute	69.04	13.60	83.20	3.88	<0.001**
30 minute	76.28	4.95	82.92	3.44	<0.001**
1 hour	78.12	3.77	82.64	3.11	<0.001**
2 hour	77.60	4.45	83.48	2.84	<0.001**
4 hour	77.24	3.74	83.48	2.43	0.058+
6 hour	79.24	3.07	79.16	4.51	0.942
8 hour	80.44	2.45	80.92	2.00	0.452
10 hour	81.84	3.45	83.16	3.01	0.156

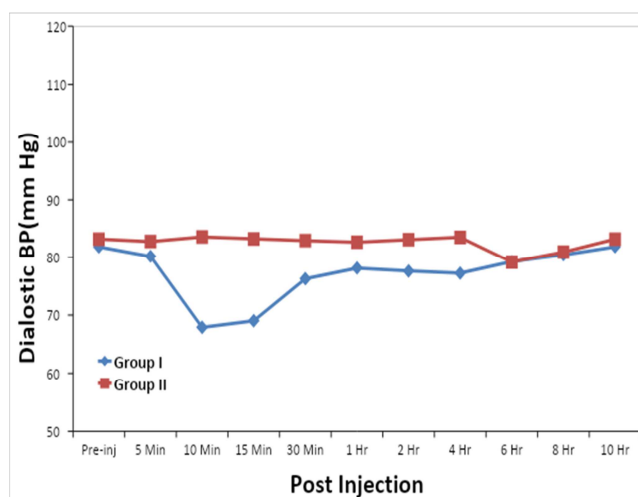


Figure 3: Comparison of Mean Diastolic Blood Pressure [mm Hg]

The mean decrease in diastolic BP seen in bupivacaine group between 5 and 15 minutes and persisted up to 2 hrs. $P < 0.001$ highly significant.

Table 6: Comparison of Mean arterial pressure [mm Hg]

Study period	Group I		Group II		P value
	Mean	SD(±)	Mean	SD(±)	
Pre-injection	99.77	2.95	100.95	3.24	0.187
Post – Injection period					
5 minute	96.93	3.08	100.39	2.39	<0.001**
10 minute	84.79	15.44	100.76	2.83	<0.001**
15 minute	86.21	14.55	100.36	3.43	<0.001**
30 minute	93.69	4.12	100.33	2.88	<0.001**
1 hour	95.32	2.84	100.51	2.29	<0.001**
2 hour	95.68	2.83	100.57	2.24	<0.001**
4 hour	95.41	2.84	100.59	2.47	<0.001**
6 hour	97.03	2.62	96.80	2.74	0.766
8 hour	98.15	1.75	98.19	1.39	0.929
10 hour	99.77	2.95	100.95	3.24	0.187

There was fall in mean arterial pressure in bupivacaine group between 5 to 15 minute after epidural injection and persisted up to 4 hrs $P < .001$ highly significant.

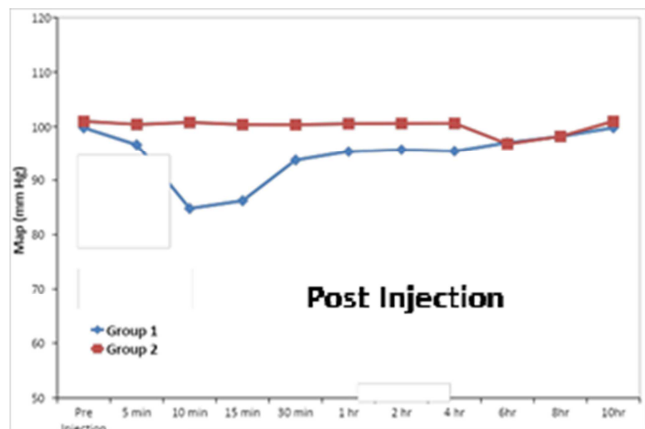


Figure 4: Comparison of Mean arterial pressure [mm Hg]

Table 7: Comparison of onset of analgesia and duration of analgesia

Onset of analgesia / Duration of Analgesia	Group I	Group II	P Value
Onset of analgesia (min)	14.38±3.75 (10-24)	11.76±3.54 (16-20)	0.016*
Duration of Analgesia (hrs)	6.67±1.05 (5-8)	7.48±1.05 (6-9)	0.009**

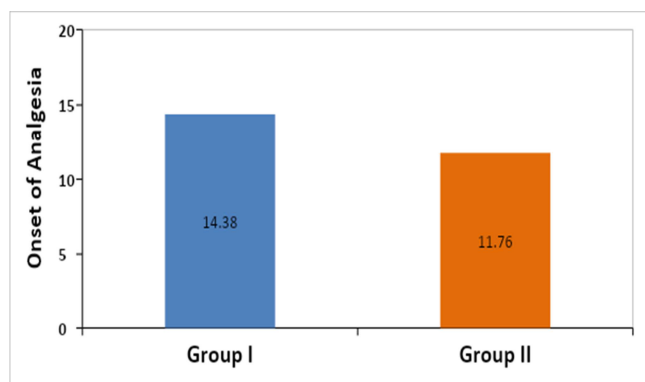


Figure 5: Onset of analgesia

Onset of analgesia with bupivacaine group occurred at 14.38 minute and with butorphanol at 11.76 minute ($P < 0.05$).

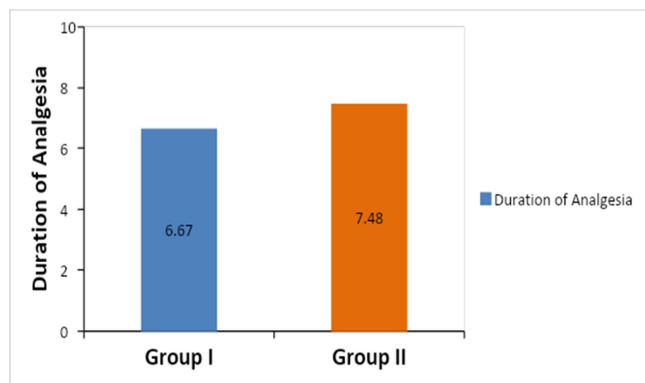


Figure 6: Duration of analgesia

Duration of analgesia with bupivacaine was 6.57 Hours and with Butorphanol for 7.48 hours ($P < 0.01$).

Figure 8: Comparison of side effects

Side effects	Group I	Group II	P Value
Nausea / Vomiting	5 (20.0%)	1 (4.0%)	0.189
Sedation	11 (44.0%)	-	<0.001**

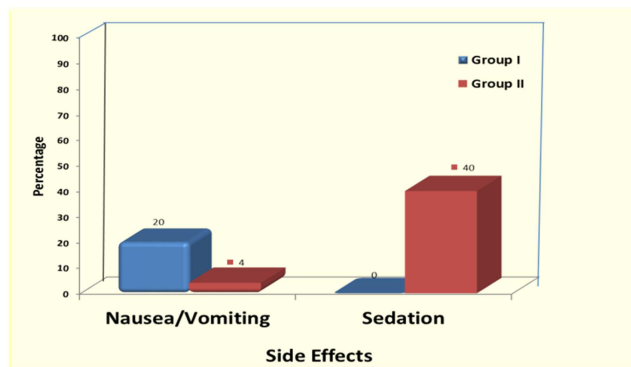


Figure 7: Comparison of side effects

Nausea/vomiting was seen in 20% of patients in bupivacaine group and 4% of Patients in butorphanol group. $P > 0.5$ is significant.

Sedation was seen in 40% of patients in butorphanol Group and no reported case in bupivacaine group. $P < 0.01$ highly significant.

Discussion

Epidural administration of local anaesthetic and opioids are practised for post-operative analgesia. The haemodynamic reposes like Hypotension & bradycardia is known for local anaesthetics like lignocaine and bupivacaine. It is believed that opioids do not cause side effects like motor block, hypotension and bradycardia when used in the epidural space for providing analgesia. Butorphanol a new synthetic agonist - antagonist opioid drug can be used in the epidural space for providing postoperative analgesia. Only a few reports are there to highlight its advantages to use it alone or combined with local anaesthetics.

We conducted a study on 50 patients with demographic data in terms of age, weight, similar in both group. In group I we administered 10 ml of 0.25% bupivacaine and in group II we administered 2 mg butorphanol with 8 ml of normal saline. There was no difference in the base line values of haemodynamic variables between the two groups.

In our study there was no difference in the mean heart rate between two groups ($P > 0.05$). But when mean systolic blood pressure, mean diastolic blood pressure and mean arterial pressure were taken in to account there was a significant fall in blood pressure 5 minutes after post-operative epidural injection lasting up to 4 hours, but value assumed significance with fall of more than 20% blood pressure in bupivacaine group between 5th minute and up to 4 hrs. When compared with butorphanol. ($P < 0.01$) highly significant. Similar studies done by WD Nagan et al⁶, found a fall in BP in 17% of their patients. Hergert,⁷ and his colleagues also experienced hypotension in their subjects who were given epidural bupivacaine. There was no case of hypotension in group II of our study. Studies

conducted by Abboud et al,^[8] also found no episode of hypotension when butorphanol was given epidurally. Similarly there was no clinically important change in either heart rate or blood pressure when epidural butorphanol was given by Palacios and associated in their study.^[9]

In our study the onset of pain relief with epidural Bupivacaine began at 14.38 minutes and action lasted for 6.67 hours. When this was compared with epidural butorphanol the action was relatively earlier which began at 11.76 minutes and lasted for 7.48 hours $P < 0.001$. Studies done by Zand,^[10] and colleagues using 0.5% bupivacaine epidurally had a similar onset of action which began at 17.12 minutes but duration of action terminated earlier at 116.37 minutes, the discrepancy in duration of action when compared to our study is probably because this study used pin prick test to measure the maximum sensory level which is more sensitive when compared to VAS which was used in our study as it is subjective. In a study done by Mok,^[11] and his associates found that onset of pain relief with epidural butorphanol was at 15th minute lasting for 5.4 hours. The results of this study can be compared with our study. In our study the main side effect in bupivacaine group was nausea/vomiting (20%) but in Butorphanol group majority of patients had sedation as the main side effect. Studies done by Adooud⁶ and colleagues found that somnolence was predominant side effect which can be compared to our study. Our study suggests that Butorphanol can be used as an alternative to Bupivacaine with faster and longer duration of action except sedation as it predominant side effect.

Conclusion

Our study concludes that epidural administration of 10 ml of 0.25% Bupivacaine causes significant hypotension when

compared to 2 mg of epidural Butorphanol. 2mg of Butorphanol in the epidural space has quicker and longer analgesic action than 10ml of 0.25% Bupivacaine except sedation as it main side effect.

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