

Randomized Prospective Double-Blind Comparative Assessment of the Effect of 0.0625% Bupivacaine with 2% Fentanyl and 0.125% Bupivacaine with 2% Fentanyl Epidural Infusion on Haemodynamic Parameters in Infraumbilical Surgeries

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Abstract

Aim: The aim of the study was to compare effect of 0.0625% bupivacaine with 2% fentanyl and 0.125% bupivacaine with 2% fentanyl epidural infusion on haemodynamic parameters for 48 hrs in infraumbilical surgeries and VAS as the secondary objective with preserved hemodynamic parameters.

Methods: The proposed study was conducted at Department of Anaesthesia, Darbhanga Medical College and Hospital, Darbhanga, Bihar, India for one year. A total of 50 patients with consenting candidates who satisfy necessary inclusion/exclusion criteria during the 18 months period were included. Patients accepted in ASA I and II in whom surgeries were performed by infra umbilical incision and required epidural infusion were included. Valid Written Informed Written Consent of patient was taken.

Results: Among study population, 21 (42%) of them had diagnosis of Carcinoma Ovary and 20 (40%) had diagnosis of Fibroid Uterus followed by 3 (6%) had diagnosis of Carcinoma Endometrium. There was no statistically significant difference between two groups in parameter Pulse Rate, Respiration rate, Diastolic Blood Pressure ($P>0.05$). There was no statistical difference of mean systolic pressure between two groups at starting period, 3 hrs, 6 hrs, 9 hrs, 12 hrs, 15 hrs, 18 hrs, 21 hrs, 24 hrs and 48 hrs ($p>0.05$) of infusion. There was no statistical difference of mean diastolic pressure between two groups at starting period, 3 hrs, 9 hrs, 12 hrs, 15 hrs, 21 hrs, 24 hrs and 48 hrs ($p>0.05$). There is statistical difference between two groups at 6 hrs and 18 hrs.

Conclusion: The study showed that the infusion of 0.125% bupivacaine with 2 μ g fentanyl lead to stoppage of infusion in 12 patients in view of Hypotension and no significant changes in VAS score was noted in two groups of patients.

Keywords: Epidural; Bupivacaine; Abdominal Surgery.

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Introduction

The most common type of acute pain that the anesthesiologists deal with is postoperative pain with resultant

neuroendocrine stress response causing protein catabolism, hyperglycemia, poor wound healing, decreased respiratory

function, and increase in myocardial oxygen demand. [1] Epidural analgesia has been extensively used to provide pain relief. Epidural bupivacaine is still the most widely used local anesthetic. [2] However, it's potential for motor blockade and central nervous system and cardiac toxicity by accidental intravenous injection of high dose is clinically undesirable. [3] In addition, to minimize unwanted motor block, a trend toward the use of lower concentrations of local anesthetics combined with opioids has been used in many clinical trials with good results. [4-6]

Opioids like fentanyl have been used traditionally as an adjunct for epidural administration in combination with a lower dose of local anesthetic to achieve the desired anesthetic effect. [7] The addition of opioid does provide a dose sparing effect of local anesthetic and superior analgesia [8] and there is improved dynamic pain relief, limited regression of sensory blockade, and decreased dose of local anesthetic. Use of lipophilic opioid (fentanyl) is preferred to hydrophilic as it provides rapid onset of action, rapid clearance, and prevents delayed respiratory depression. [9] It was found out by preliminary study that in most of the patients in whom 0.125% bupivacaine with 2% fentanyl infusion was started had to be stopped because of haemodynamic instability. [10]

Patients receiving epidural injections of local anaesthetics combined with opioids report a more rapid onset of analgesia, more profound and long lasting pain relief and less motor blockade than do in the patients receiving either of the drugs alone. Therefore the opioid and local anaesthetic combination is considered highly effective in reducing movement associated pain. [11] Previously, the efficacies of epidural analgesia for labor with bupivacaine and ropivacaine have been reviewed, and the outcomes were found similar for both the drugs except for a statistically untested (because of higher heterogeneity) evidence

of higher incidence of motor blocks in bupivacaine-treated women. [12] Recently, the efficacy and safety of bupivacaine in combination with sufentanil have been reviewed against levobupivacaine and ropivacaine both in combination with sufentanil where it has been observed that the incidence of motor blocks was nonsignificantly higher in the bupivacaine-sufentanil combination. [13]

The aim of the study was to compare effect of 0.0625% bupivacaine with 2% fentanyl and 0.125% bupivacaine with 2% fentanyl epidural infusion on haemodynamic parameters for 48 hrs in infraumbilical surgeries and VAS as the secondary objective with preserved hemodynamic parameters.

Materials and Methods

The proposed study was conducted at Department of Anaesthesia, Darbhanga medical College and Hospital, Darbhanga, Bihar, India for one year. A total of 50 patients with consenting candidates who satisfy necessary inclusion/exclusion criteria during the 18 months period were included. Patients accepted in ASA I and II in whom surgeries were performed by infra umbilical incision and required epidural infusion were included. Valid Written Informed Written Consent of patient was taken.

Following were excluded from study: who were not willing for valid written informed consent and patients of ASA III or more, contraindications for epidural placement like coagulopathy, bleeding disorders. After Institutional Ethics Committee approval, a randomized, prospective, double-blind study was carried out in seventy ASA (American Society of Anesthesiologists) I and II consenting adult patients of either sex between the ages of 18-65 years undergoing infraumbilical surgery. Patients with ASA III and IV, those with infection at the site of epidural injection, coagulopathy or bleeding disorders,

severely hypovolemic patients, those with raised intracranial pressure, sepsis, preexisting neurological deficit, demyelinating disorder, or severe spinal deformities were excluded from this study. Sample size of 25 in each group was calculated based on available reference studies.

Patients were randomized by computer generated randomization charts into two study groups, Group 1 (n=25) received 0.0625% bupivacaine with 2 ug/ml fentanyl and Group 2 (n=25) received 0.125% bupivacaine with 2 ug/ml fentanyl postoperatively. Both groups were comparable with respect to their demographic data. Baseline blood pressure, pulse rate, and SpO₂ were recorded. Adequate preloading (500 ml) was done with 18-gauge intravenous cannula. Patients received injection glycopyrrolate (0.002 mg/kg) and injection ranitidine (1 mg/kg) intravenously as premedication. Thereafter, an epidural catheter was inserted at the lumbar level (L1-L2 or L2- L3). The space was checked by loss of resistance technique and confirmed by the meniscus sign. Epidural test dose was given with 3 ml 2% adrenalized lignocaine. The absence of tingling numbness in the lower limbs and tachycardia was confirmed after 4-6 cm of catheter was placed in the epidural space. After fixation of catheter, patients were made supine and free injection of saline through the catheter was checked. Patients were premedicated with injection fentanyl 2 ug/kg and injection midazolam 0.02 mg/kg. Patients were preoxygenated with 100% O₂ for 3 min. General anesthesia was given with injection propofol 2 mg/kg mixed with injection xylocard 20 mg intravenously. Suitable relaxant was given to facilitate tracheal intubation after confirming ventilation. Anesthesia was maintained with oxygen, air and sevoflurane. Muscle paralysis was maintained with injection vecuronium bromide intravenously.

Group 1 patients received continuous epidural infusion of 0.125% bupivacaine with 2 ug/ml fentanyl after induction of general anesthesia at the rate 7 ml/h intraoperatively. The rate of infusion was adjusted as per the hemodynamic parameters of the patient. Group 2 patients received continuous epidural infusion of 0.0625% bupivacaine with 2 ug/ml fentanyl at the rate 7 ml/h intraoperatively. The pulse rate, blood pressure, SpO₂, and EtCO₂ were monitored intraoperatively. Infusion was stopped at closure which was approximately 30-45 min before reversal. All patients were reversed with 0.01 mg/kg glycopyrrolate and 0.06 mg/kg neostigmine. The infusion again was started after 30 min of extubation once patient reached the ward. The baxter elastomeric infusion pump had 5 ml/hr, 7 ml/hr and 12 ml/hr rates of infusion. The hemodynamic parameters like SpO₂, heart rate, systolic blood pressure, diastolic blood pressure, MAP, VAS was recorded at interval of 3 hrs till 48 hrs. Initially the rate was set to 7 ml/hr and adjusted based on hemodynamic parameters and VAS. The infusion was stopped if there was hypotension even with lowest infusion rate (5 ml/hr) and bolus of 500 ml crystalloid was given and other modalities of analgesia like paracetamol and tramadol were given intermittently.

Statistical Methods

Hemodynamic parameters at different time periods and VAS were considered as primary and secondary outcome variables. Study group was considered as primary explanatory variable. All Quantitative variables were checked for normal distribution within each category of explanatory variable by using visual inspection of histograms and normality Q-Q plots. Shapiro-wilk test was also conducted to assess normal distribution. Shapiro wilk test p value of >0.05 was considered as normal distribution.

Results

Table 1: Descriptive analysis of study and diagnosis

Study group	N	%
Group 1 (0.0625% bupivacaine with 2 mcg fentanyl)	25	50
Group 2 (0.125% bupivacaine with 2 mcg fentanyl)	25	50
Diagnosis		
Ano-rectal carcinoma	2	4
Carcinoma-descending colon	1	2
Carcinoma ovary	21	42
Carcinoma-vulva	1	2
Fibroid uterus	20	40
Vault prolapse	2	4
Carcinoma endometrium	3	6

A total of 50 people included in the final analysis. Among the study population, 25 (50.00%) had 0.0625% bupivacaine with 2 µg fentanyl and remaining 25 (50.00%) participants had 0.125% bupivacaine with

2 µg fentanyl. Among study population, 21 (42%) of them had diagnosis of Carcinoma Ovary and 20 (40%) had diagnosis of Fibroid Uterus followed by 3 (6%) had diagnosis of Carcinoma Endometrium.

Table 2: Comparison of mean of baseline parameter between study groups

Baseline parameter	Group 1 (N=25) (Mean ± SD)	Study group	Group 2 (N=25) (Mean ± SD)	P-value
Pulse rate	86.50 ± 12.48		86.24 ± 9.91	0.7
SPO ₂	98.2 ± 2.08		96.4 ± 2.58	0.08
Respiration rate	12.88 ± 1.35		14.06 ± 1.60	0.5
Systolic blood pressure	128.02 ± 14.6		127.40 ± 14.8	0.3
Diastolic blood pressure	86.00 ± 7.4		83.97 ± 10.6	0.58

There was no statistically significant difference between two groups in parameter Pulse Rate, Respiration rate, Diastolic Blood Pressure (P>0.05).

Table 3: Comparison of mean systolic blood pressure between study groups at different time period

Time period	Study group		P-value
	Group 1	Group 2	
	(Mean ± SD)	(Mean ± SD)	
Starting	128.62 ± 14.07	136.54 ± 14.76	0.2
3 hours	124.16 ± 14.46	128.81 ± 17.03	0.25
6 hours	119.31 ± 14.96	122.88 ± 18.92	0.40
9 hours	116.24 ± 14.86	114.76 ± 16.74	0.45
12 hours	113.47 ± 14.46	109.82 ± 20.40	0.29
15 hours	111.69 ± 12.88	105.90 ± 18.20	0.8
18 hours	113.37 ± 14.76	107.23 ± 18.02	0.26
21 hours	112.8 ± 16.08	112.42 ± 18.96	0.49
24 hours	117.17 ± 15.45	118.62 ± 18.16	0.87
48 hours	119.81 ± 17.03	117.23 ± 18.45	0.50

There was no statistical difference of mean systolic pressure between two groups at starting period, 3 hrs, 6 hrs, 9 hrs, 12 hrs, 15 hrs, 18 hrs, 21 hrs, 24 hrs and 48 hrs ($p>0.05$) of infusion.

Table 4: Comparison of mean diastolic blood pressure between study groups at different time period

Time period	Study group		P-value
	Group 1 (Mean \pm SD)	Group 2 (Mean \pm SD)	
Starting	86.09 \pm 8.40	83.87 \pm 10.20	0.9
3 hours	76.14 \pm 7.45	77.23 \pm 7.43	0.2
6 hours	74.26 \pm 4.67	78.62 \pm 8.32	0.01
9 hours	75.35 \pm 6.36	72.32 \pm 7.93	0.06
12 hours	69.71 \pm 7.63	71.59 \pm 8.32	0.36
15 hours	74.4 \pm 6.34	72.48 \pm 8.40	0.5
18 hours	76.66 \pm 11.56	68.72 \pm 7.53	0.01
21 hours	72.8 \pm 6.67	72.8 \pm 7.63	0.10
24 hours	71.89 \pm 6.55	74.16 \pm 8.12	0.26
48 hours	72.18 \pm 4.96	71.89 \pm 6.84	0.45

There was no statistical difference of mean diastolic pressure between two groups at starting period, 3 hrs, 9 hrs, 12 hrs, 15 hrs, 21 hrs, 24 hrs and 48 hrs ($p>0.05$). There is statistical difference between two groups at 6 hrs and 18 hrs.

Table 5: Comparison of VAS between study groups at different time period

VAS @ time period	Group 1 (N=30) Median (IQR)	Group 2 (N=30) Median (IQR)	Man Whitney U test P-value
Starting	4 (4 to 4)	4 (4 to 5)	0.069
3 hours	4 (3 to 4)	4 (3 to 4)	0.782
6 hours	4 (3 to 4)	3 (3 to 3)	0.237
9 hours	3 (3 to 3)	3 (3 to 3)	0.317
12 hours	3 (3 to 3)	3 (3 to 3)	0.655
15 hours	3 (3 to 3)	3 (3 to 3)	0.655

Discussion

Analgesic adequacy during labor along with the avoidance of adverse effects is vital for obstetric conditions. Painful labor can have negative impacts on maternal and fetal physiology. In neuraxial analgesia, the analgesics are injected or infused in close proximity to the spinal cord by using catheter, usually either intrathecally into the cerebrospinal fluid or epidurally into the fatty tissues around the dura, to block nerves that transmits pain signals to the brain. [14,15] Much lower pain scores with least adverse effects on maternal cardiovascular or pulmonary functions and fetal physiology with higher maternal

satisfaction are reported with the use of neuraxial analgesic techniques during labor and delivery. [16] The rationale for the combination of opioid and local anaesthetic is that these two types of drugs eliminate pain by acting at two distinct sites, the local anaesthetic at nerve axons while the opioid at the receptor site in the spinal cord. Local anaesthetic and opioid combination techniques have been studied extensively in the obstetric population. Even if, an extremely low concentration of local anaesthetic is added to the opioid, the quality of analgesia is far superior. [17] Spinal opioids alone provide a good pain relief at rest but may not be adequate

during physiotherapy and or mobilization. [18]

The volume and concentration of anesthetic solution probably influences the spread of anesthesia. 0.125% bupivacaine produce adequate postoperative analgesia in many clinical settings with only mild motor deficits. [19] Continuous epidural infusions of bupivacaine as dilute as 0.0625% to 0.1% are useful for labor epidural analgesia, especially when administered in combination with opioids and epinephrine. [20] Bupivacaine 0.25% may be used for more intense analgesia (particularly during combined epidural-general anesthesia cases) with moderate degrees of motor block. When taken into consideration of whole 50 patients there was no statistically significant difference between two groups in parameters of Pulse Rate, Respiration rate, Systolic Blood Pressure ($P>0.05$). However the Diastolic Blood pressure was statistically significant after 6 hrs, 9 hrs and 18 hrs. [21] The study by Duncan et al. [22] also showed that significant quantity of 62% within 24 hrs had hypotension. But this study mentioned significant difference in VAS of 3.8 against 2.5 in 0.0625% bupivacaine against 0.125% respectively.

However there was no statistically significant difference in VAS. The study also followed the same concentration as in our study and found no significant change in VAS. There were no other side effects like lower limb weakness, nausea vomiting as studied in other studies. [19] That continuous infusion as compared to intermittent boluses provided better pain relief at rest, on movement and provided sustained degree of analgesia. The motor block was more pronounced in higher concentration of bupivacaine like 0.125% and this was also one of the causes for stoppage of infusion of 0.125% Bupivacaine. [23] Bupivacaine at concentrations of 0.5% to 0.75% is associated with a more profound degree of motor block, and surgical anesthesia. [24]

It should be emphasized that although high concentrations of local anesthetics may be appropriate for episodic bolus dosing for surgery, these concentrations (i.e., 0.25% for bupivacaine) should not be first choice for continuous epidural infusions. [27,28] In some patients, increasing the local anesthetic dose or addition of adjuvants such as epinephrine and lipophilic opioids is necessary to achieve adequate block intensity. [25] Bolus injections produce much more cephalocaudad spread than continuous infusions do. [1] When concentrated bupivacaine solutions are used for infusions, they have the potential for excessive local effect with an associated risk for unwanted and very prolonged motor blockade and hemodynamic changes. The common side effects of neuraxial blockade or epidural in this case are Hypotension, Bradycardia. [26] Study also raised concerns of hypotension. [22]

Conclusion

The study showed that the infusion of 0.125% bupivacaine with 2 μ g fentanyl lead to stoppage of infusion in 12 patients in view of Hypotension and no significant changes in VAS score was noted in two groups of patients. However there was significant change in VAS noted when compared among the patients in whom 0.125% bupivacaine with 2% fentanyl infusion was stopped against the patients in whom it was continued.

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