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ORIGINAL ARTICLE

A COMPARATIVE STUDY OF THE EFFECT OF EPIDURAL BUPIVACAINE (0.125%) VERSUS EPIDURAL BUPIVACAINE (0.125%) AND BUTORPHANOL (2mg) FOR POST-OPERATIVE PAIN RELIEF IN LOWER ABDOMINAL AND LOWER LIMB SURGERIES

Krishna Chaithanya[1], Narasimha Reddy[2], Sangamitra Gandra[3], Sujith T. R[4], Venkateswar Rao[5]

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ABSTRACT: BACKGROUND: Postoperative pain gives rise to various physiological and psychological phenomenons. Epidural analgesia with combination of local anesthetics and opioids provides better pain relief than local anesthetics alone in the postoperative period. Epidural opioids acting through the spinal cord receptors improve the quality and duration of analgesia along with dose-sparing effect with the local anesthetics. **AIMS:** The study was conducted to evaluate the efficacy of addition of opioids to local anesthetics for postoperative pain relief. **METHODS:** Fifty patients of American society of anesthesiology grade I and II physical status undergoing lower abdominal surgeries & lower limb surgeries in narayana general hospital, Nellore, were divided into two groups B and BB. Group B was given 0.125% bupivacaine alone and Group BB was given 0.125% bupivacaine plus 2mg of butorphanol postoperatively when the patients first complained of pain. Onset of Analgesia, duration of analgesia, visual analog scores and side effects were compared. **RESULTS:** The onset of analgesia in group B patients (10ml of 0.125% Bupivacaine) was varied from 4-8 minutes (mean 5.2 minutes) and duration of analgesia lasted for 2-4 hours (mean 2.98)($p<0.0001$) where as in group BB patients (2mg butorphanol + 0.125% bupivacaine) the onset was 2-4 minutes (mean 2.69) and duration of analgesia lasted for 6-8 hours (mean 6.98) ($p<0.0001$).The Visual Analog Scores of Group B were in the range of 7 to 9 and Group BB were in the range of 5 to 6 ($P<0.0001$). **CONCLUSION:** This study concludes that addition of butorphanol (2mg) to bupivacaine (0.125%) gives more effective and prolonged duration of postoperative pain relief when administered epidurally, without significant side effects.

KEYWORDS: Postoperative pain, pain management, bupivacaine, butorphanol, epidural anesthesia.

INTRODUCTION: Effective postoperative pain relief is vital for early mobilization and discharge as postoperative pain gives rise to various physiological and psychological phenomenon.[1] Epidural analgesia using local anesthetic agent is effective and economical way of providing postoperative analgesia. Narcotic analgesics are commonly used as adjuncts to local anesthetics (LA) in epidural anesthesia. They hasten the onset, improve the quality of the block as well as prolong the duration of analgesia.

However, the parent drug (morphine) that was initially employed for epidural analgesia had low lipid solubility and a long latency. Its use has been associated with the occurrence of undesirable side effects as pruritus, nausea, vomiting, urinary retention and respiratory depression.[2] The search for a better molecule is still going on. Butorphanol is a lipid-soluble narcotic with weak μ-receptor agonist and antagonist activity and strong k-receptor agonism.[3]

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It has strong analgesic and sedative properties without respiratory depression. Butorphanol has been frequently used for post-operative analgesia and labor analgesia.[4, 5] We conducted this study to evaluate the efficacy of addition of butorphanol which is an opioid to local anesthetic bupivacaine for postoperative prolongation of epidural analgesia.

MATERIALS AND METHODS: Fifty patients of American Society of Anesthesiology (ASA) grade I and II physical status undergoing lower abdominal & lower limb surgeries in narayana general hospital, nellore, were selected for this study. The study was approved by the hospital ethics committee. Informed consent was obtained from all the patients, after a detailed explanation of the procedure.

Exclusion criteria included patient's refusal, spinal deformity, bleeding diathesis, sepsis, significant cardio respiratory and hepatic, renal and neurological disease.

Patients were familiarized with visual analgesia scale (VAS) scoring pre-operatively and taught to grade their pain on the scale. The patients were randomly allocated into two groups, 25 patients each in Group B and BB. Group B (n=25) received 10ml of 0.125% bupivacaine. Group BB (n=25) received 10ml of 0.125% bupivacaine along with 2mg of butorphanol.

Ranitidine 150 mg and alprazolam 0.5 mg orally were given as premedicants on the night before the surgery. In the operating room, the patient was connected to a multichannel monitor showing electrocardiography, heart rate, non-invasive blood pressure, pulse oximetry and respiratory rate. A peripheral venous access with 18G cannula was secured.

The patients were pre-loaded with ringer's lactate 10 ml/kg over 15-20 min prior to the procedure. With proper positioning and under all aseptic precautions epidural space was identified in L_{3-4} intervertebral space using 18G Tuohy's needle with the loss of resistance to air technique. Epidural catheter was threaded 4 cm inside the epidural space and fixed.

A test dose of 3 ml of 1.5% lignocaine with adrenaline was given after initial negative aspiration for blood and cerebrospinal fluid. After 3 minutes, spinal anesthesia was achieved with 25G quincke- Babcock's needle with 0.5% bupivacaine. Patient was turned to supine posture. Intraoperatively no narcotics were administered. The surgeries were completed within 1 to 1½ hour. Postoperatively when the patients complained of pain and requested for relief, group B (n=25) received 10ml of 0.125% bupivacaine. Group BB (n=25) received 10ml of 0.125% bupivacaine along with 1ml of 2mg of butorphanol.

The time of injection was recorded as zero hour and vital parameters were noted. Then the patient was monitored for the vital parameters like blood pressure, pulse rate, respiratory rate, SpO2, visual analog score (VAS) every 5 mins for the first 15mins and every 15 mins for the first hour and every two hours thereafter. Duration of analgesia was taken as the time from the onset of analgesia up to the time when the VAS reached.[5]

Any untoward side effects like nausea, vomiting, urinary retention, respiratory depression, pruritus, paradoxical excitement were noted. If there was any fall in blood pressure, intravenous fluids (ringer lactate/normal saline 500ml to 1Ltr.) were administered and if the fall was more than 30% below the base line value, fluid administration was supported by inj. mephenteramine sulphate in titrated doses.

In the postoperative ward no narcotics or analgesics were given. The duration of analgesia was calculated till the visual analogue score reaches 5 or more i.e. moderate to severe pain. The time

of onset of analgesia and duration of analgesia were noted, compounded and the results were analyzed.

STATISTICAL ANALYSIS: The statistical analysis was performed using IBM SPSS Version-20. Categorical data was presented as actual numbers and percentages. Continuous data were expressed as Mean (SD). For normally distributed data, between group analyses was performed using unpaired t test. Categorical variables were analyzed with "Fischer's exact test". VAS was expressed as median, and between groups analysis was done using Mann Whitney U test. For statistical significance, a two tailed probability value of less than 0.05 was considered.

RESULTS: On evaluation, there was no statistical difference in mean age, height and weight between two groups and groups were comparable at baseline demographic characters. (P= 0.38, P=0.97 & P=0.9 respectively). However, the mean onset of analgesia was significantly high in bupivacaine group as compared to bupi+butorphanol group (5.27±1.06 min vs. 2.69±0.59 min, P=<0.0001). Mean duration of analgesia was significantly less in bupivacaine group as compared to bupi+butorphanol group (2.98±0.46 hrs. vs. 6.98±0.52 hrs. P=<0.0001. ((Table 1, Fig 1)

Two patients in bupivacaine group and four patients in bupi+butorphanol group had nausea, one patient in bupivacaine group had shivering and two patients in bupi+butorphanol group had pruritus. Median VAS significantly differed between two groups at 5, 10, 15, 30, 45 and 60 min (P=<0.0001) as shown in Table 2; Fig 2.

DISCUSSION: The traditional old time management of post-operative pain by intramuscular administration of narcotics has been limited by elaborate array of checks and counter checks. The administered dose has its inherent delayed onset and erratic absorption pattern resulting in under treatment of discomfort and frequent over sedation of the patient.

Effective pain management is essential and has been recognized as a prime concern for anesthesiologists. Post-operative analgesic techniques have evolved over a period of time starting from parenteral administration of various analgesics to injection of local anesthetics solutions with or without adjuvants into the subarachnoid space, epidural or nerve plexus. Opioids as epidural adjuvants to local anesthetics improve the quality of the block and provide a dose-sparing effect.[6, 7] Combination of local anesthetics and opioids enable to get effective early onset and increased duration of analgesia and better quality of pain relief.

Butorphanol, a synthetic compound of opioid agonist-antagonist drug which was introduced in west in 1978 was available in our country since 2001.It is a nitrogen-substituted 3, 14-dihydroxymorphinan. This synthetic member of the benzomorphan series is structurally similar to other drugs having the various degrees of narcotic agonist and antagonist properties at room temperature. Butorphanol is a potent analgesic with both opioid agonist and antagonist effect. Butorphanol and its major metabolites are agonist at kappa-opioid receptors and mixed agonist-antagonists at mu opioid receptors.

The side effects of butorphanol when compared with morphine were less since the dose response curve for butorphanol is bell shaped i.e. higher doses producing lesser effects than lower doses.[8] The butorphanol induced respiratory depression was minimal and was reversible with moderate doses of (<0.8mg) naloxone. It has less additive potential than morphine.

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Because of no dependency, better analgesia, less respiratory depression and cost effectiveness, we preferred small dose of butorphanol as an adjuvant to bupivacaine for post-operative analgesia study by epidural route to improve the onset, intensity and duration of analgesia postoperatively with minimal side effects.

Placement of opioids in epidural space is based on opioid receptors (mu) in the substantia gelatinosa of spinal cord. Advantages of epidural opioids prolonged duration of action**,** early ambulation, and lower risk of postoperative venous thrombosis.[9] Narcotic analgesics are well-known for the potential side effects such as pruritus, nausea, vomiting, urinary retention and respiratory depression.[10] Delayed respiratory depression is the most troublesome of these side effects and appears to be largely responsible for the reluctance of anesthesiologists to use intrathecal or epidural narcotics.

This phenomenon is thought to be due to transport of drug in cerebrospinal fluid from the lumbar region to the fourth ventricle, with consequent depression of the medullary respiratory centers. The incidence of delayed respiratory depression appears to be greatest with poorly lipid-soluble narcotic drugs, like morphine.[11] Bromage suggested that lipid-soluble, highly protein bound narcotic analgesics might be less likely to exhibit this phenomenon and this appears to be true for both butorphanol and fentanyl.

In our study, the onset of epidural analgesia in group B (10ml of 0.125% Bupivacaine) was varied from 4-8 minutes (mean 5.27 minutes) whereas in group BB (2mg Butorphanol + 0.125% Bupivacaine) the onset was 2-4 minutes (mean 2.69, $p < 0.0001$) which is statistically significant. The duration of analgesia in group B lasted for 2-4 hours (mean 2.98) where as in group BB patients duration of analgesia lasted for 6-8 hours (mean 6.98 $p<0.0001$) which is also statistically significant.

Our findings were consistent with Modig and Paalzov.[12] Various studies using epidural butorphanol for post-operative analgesia have reported the duration of analgesia to be 4-6 h, 5 h and 5.35 h with 0.5 mg, 1 mg, 2 mg and respectively.[13-15] Malik et al. [16] have also reported in their study that butorphanol provides a longer duration of analgesia than fentanyl.

The Visual analog scores of patients in group B at the time of recovery, were in the range of 7 to 9 with a mean of 7.84, whereas in Group BB patients the visual analog scores at the time of recovery were in the range of 5 to 6 with a mean value of 5.44 ($p<0.0001$) .

The “p”value signifies that group BB patients are having higher intensity of block and pain relief which is reflected in the low Visual Analog Scores. The patients were continuously observed for respiratory depression with SpO_2 (< 90%) and RR (< 10). No case of respiratory depression was observed in butorphanol group.

CONCLUSION: Addition of the opioids like butorphanol to bupivacaine for postoperative analgesia in epidural space significantly quickens the onset and provides more effective and longer duration of analgesia as compared with bupivacaine alone.

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Parameters	Bupivacaine (n=25)		Bupi + Butorphanol (n=25)		P value
	Mean	SD	Mean	SD	
Age (yrs)	40.00	11.79	42.92	11.57	0.38
Height (cm)	156.76	4.13	156.72	4.75	0.97
Weight (kg)	57.40	5.97	57.20	5.21	0.90
Onset of analgesia (min)	5.27	1.06	2.69	0.59	<0.0001
Duration Of Analgesia / Recovery Time (hours)	2.98	0.46	6.98	0.52	<0.0001
Nausea	2(8%)		4(16%)		0.3
Shivering	1(4%)		0		0.2
Pruritus	0		2(8%)		0.5

Table 1: comparison of demographic and clinical parameters between groups.

Group	0 min	5 min	10 min	15 min	30 min	45 min	60 min	120 min	240 min	360 min	Recovery From Analgesia (VAS > 5)
Bupivacaine	9	6	4	3	2	2	2	4	-	-	8.00
Bupi+Butorphanol	8	4	3	0	0	0	0	0	0	2	5.00
P value	0.6	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	-	-	<0.0001

Table 2: Median VAS

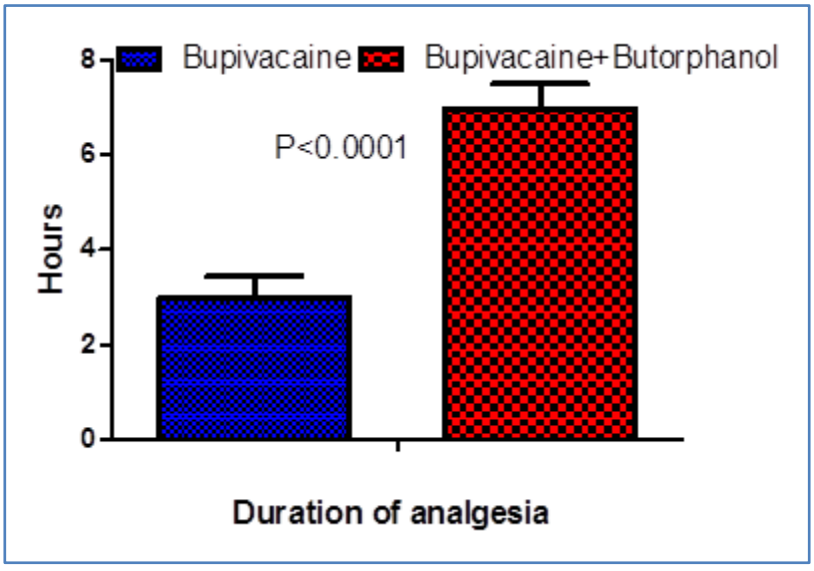

Figure 1: Comparison of duration of analgesia between groups

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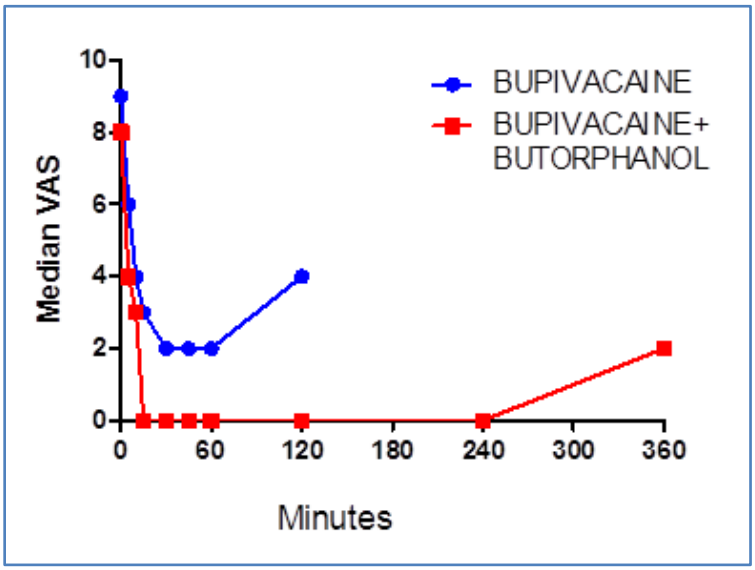

Figure 2: Comparison of median VAS at regular intervals between groups

AUTHORS:

1. Krishna Chaithanya
2. Narasimha Reddy
3. Sangamitra Gandra
4. Sujith T. R.
5. Venkateswar Rao

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Anaesthesiology, Narayana Medical College, Nellore, Andhra Pradesh.
2. Professor, Department of Anaesthesiology, Narayana Medical College, Nellore, Andhra Pradesh.
3. Assistant Professor, Department of General Medicine, Narayana Medical College, Nellore, Andhra Pradesh.
4. Senior Resident, Department of Pharmacology, Narayana Medical College, Nellore, Andhra Pradesh.
5. Senior Resident, Department of Anaesthesiology, Narayana Medical College, Nellore, Andhra Pradesh.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Krishna Chaithanya,
Flat No. 3A,
Krishna Sanjeeva Homes,
MK Apartments, Gomathy Nagar,
Nellore-524003, Andhra Pradesh.
Email: chaithu8@gmail.com

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