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COMPARISION OF ANALGESIC EFFECTS OF EPIDURAL BUTORPHANOL VERSUS EPIDURAL BUPRENORPHINE IN POST OPERATIVE PATIENTS AFTER LOWER LIMB ORTHOPAEDIC SURGERIES

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ABSTRACT

Background : Central neuraxial blockade is an important tool in the armamentarium of the anaesthesiologist. It is one of the safest and efficacious methods of anesthesia and analgesia; it is cost effective and has the added advantage of prolonged pain relief into the postoperative period.

Objective :Comparision of analgesic effects of epidural Butorphanol versus epidural Buprenorphine in post operative patients after lower limb orthopaedic surgeries.

Methodology : After institutional ethical committee approval, 50 patients were enrolled for the study. Base line heart rate, systolic and diastolic blood pressure was recorded. Combined spinal-epidural anaesthesia was administered for all the patients. Postoperatively when ever patient complained of pain, epidural test drug was given. All continuous variables were analysed using the two-sample 't' test and all discrete & qualitative variables were analysed using the Kruskal-Wallis one-way ANOVA.

KEYWORDS :

INTRODUCTION

Central neuraxial blockade is an important tool in the armamentarium of the anaesthesiologist. It is one of the safest and efficacious methods of anesthesia and analgesia; it is cost effective and has the added advantage of prolonged pain relief into the postoperative period.

Epidural Anaesthesia is a central neuraxial technique offering a wide range of applications in the context of providing analgesia to the patient. Epidural analgesia has increased steadily in its popularity in the second half of the twentieth century, firstly with the decline of spinals owing to their serious neurological sequences and secondly with the advent of improved post operative analgesia with epidural Opioids and as a consequence decreased side effects and prolonged duration of analgesia.[1,2]

The epidural administration of Opioids has been used increasingly in the management of postoperative pain, since Behar & colleagues first used epidural morphine, (2mg) in the management of chronic pain. [3]Unfortunately these were associated with side effects including pruritus (20-93%) nausea (17-60%), vomiting, urinary retention, somnolence and respiratory depression. Stimulation of Opioid receptors, specifically μ-receptors, appears to be the cause of pruritus and nausea.In an attempt to reduce the severity of pruritus & nausea, Opioids with agonist-antagonist profile have been administered epidurally for post-operative pain relief.[4,5]

The purpose of a medicine in general and in anaesthesiology in particular is to preserve and restore health by relieving pain and suffering. Therefore understanding of pain is essential to achieve these goals. Therefore the aim of the study was comparision of analgesic effects of epidural Butorphanol versus epidural Buprenorphine in post operative patients after lower limb orthopaedic surgeries.

MATERIALS AND METHODS

After institutional ethical committee approval, 50 patients were enrolled for the study, in this prospective randomized double blind study, patients were randomly allocated into two equal groups (Bt&Bp). Group Bt patients received epidural Butorphanol and group Bp patients received epidural Burprenorphine for post-operative analgesia. Written informed consent was obtained from all patients for participation in the study. The study was carried out over a 3 month period from september 2018 to December 2018.

Inclusion criteria : Patients of either gender, age between 18-50 years, ASA physical status I & II, Patients undergoing lower limb orthopaedic surgeries under combined spinal epidural anaesthesia.

Exclusion Criteria: Patients who are uncooperative, patients with moderate to severe cardiovascular, renal, pulmonary and neurological disorders, ASA grade 3 or more, Distorted anatomy of spine, Morbidly obese patients, Pregnant patients, Patients with coagulopathy; Routine pre-operative haematological & biochemical test were performed. Weight of the patient was recorded. Premedication with Diazepam 5 mg and Ranitidine 150 mg administered orally an hour before surgery. Those patients who would require subsequent general anesthesia or intraoperative sedation during the surgery were excluded from the study. Patients who required antiemetic treatment, antihistaminics intraoperatively and postoperatively were excluded from the study.

Base line heart rate, systolic and diastolic blood pressure was recorded. Venous access was secured using a 16G or 18G cannula after infiltrating with 2% lignocaine. Preloading was done using 500 ml Ringer Lactate. Patients were positioned in sitting posture for the block.

Combined spinal-epidural anaesthesia was administered for all the patients. The epidural space was identified using loss of resistance to air with 18G tuohys epidural needle in the L2 – L3 intervertebral space. Then the epidural catheter was threaded and fixed by using the epidural catheter fixator. 5 cms of the catheter was inside the epidural space. Afterwards using a 25G spinal needle lumbar puncture was done in the L3-L4 intervertebral space. After the appearance of the CSF at the hub of the spinal needle , 3cc of 0.5% Bupivacaine (heavy) was deposited in the subarachnoid space, the spinal needle removed. Monitoring included ECG, Non-invasive blood pressure every 5 minutes and pulse oximetry. Decrease in heart rate below 20% and blood pressure below 30% from the base line respectively was considered significant and treated with intravenous fluids and inj.Mephenteramine 6 mg I.V. boluses. In case of prolongation of surgery; anaesthesia was maintained by administering 5cc of 0.5% bupivacaine epidurally after negative aspiration.[6]

Postoperatively when ever patient complained of pain, epidural test drug was given. The drug randomization sequence was selected according to a random number table and written on a paper enclosed in sealed envelope. Anaesthesia personnel not involved in the study prepared the drug and randomly allocated coded syringes.

Btgroup : 25 patients3 mics/kg Butorphanol in 8ml of normal saline, Bp group: 25 patients, ug/kg Buprenorphine in 8ml of normal saline. The test drug was given for postoperative analgesia as a single dose, whenever the patient complained of pain, the VAS score considered as 10 at that time.

Onset of analgesia, duration of analgesia, vital signs – heart rate, systolic blood pressure, diastolic blood pressure, respiratory rate, VAS, pruritus score, sedation score, nausea and vomiting, urinary retention were monitored and noted.

Pain complained by the patient after the study drug was considered as the end point of the study. VAS score 0-3 is considered as good pain relief, VAS score of 4-5 with no discomfort considered as adequate pain relief. VAS score >5 was considered as the end point of the study and rescue analgesia administered on demand by the patient, this was Tramadol 2 mg/kg by the intravenous route. Post dural puncture headache and neurological deficits were monitored for next 48 hours.

After doing a pilot study of 12 cases, POWER analysis was done to determine the N-number with NCSS & PASS 2004 trail version software for the present study; and it was found to be 23 in each group. We have done 25 cases in each group. Continuous variables including Visual Analogue Scale (VAS) data were analyzed using parametric tests. After completion of the clinical study the results were tabulated in Microsoft excel sheet, and the statistical analysis was done using the NCSS trial version. All continuous variables were analysed using the two-sample 't' test and all discrete & qualitative variables were analysed using the Kruskal-Wallis one-way ANOVA.

RESULTS

Total number of cases enrolled was 57, of which 7 cases were excluded from the study. Of these, two cases were due to dural puncture, one case due to catheter blockade, one case due to catheter displacement during shifting, one case because Midazolam was administered to the patient to relieve anxiety intraoperatively and one more patient due to inadvertent intramuscular injection of Tramadol in the post operative ward.

From the study, the parameters observed were onset of analgesia, duration of analgesia, effectiveness of analgesia in terms of VAS score, vomiting score, pruritus score, sedation score and urinary retention.

OBSERVATIONS AND RESULTS:

The mean age in Bt group was 33.08 years (95% CI – 28.9-37.26), and in the Bp group was 31.2 years (CI – 27.75 – 34.75). There was no statistically significant difference between the groups.The mean weight in the Bt group was 62.28 kilograms (CI – 58.35 – 66.21) and in the Bp group was 61.08 kilograms (CI – 55.85-66.31). There was no statistically significant difference between the groups. There were 21 male and 4 females in the Bt group and 18 males and 7 females in the Bp group, there were 23 ASA I and 2 ASA II patients in the Bt group, 23 ASA I and 2 ASA II patients in the Bp group.

Preoperative vitals

Factors	Bt group Mean (95% CI)	Bp group Mean (95% CI)	Statistical significance
HR (Bpm)	85.76(80.2 – 91.32)	87.12(79.49-94.75)	NS
SBP (mmHg)	120.48 (116.18 – 124.78)	118.56(113.47-123.65)	NS
DBP (mmHg)	80.24 (77.24 – 83.24)	74.48(68.57 - 80.39)	NS
RR (/min)	17.68 (16.83 – 18.53)	16.4 (15.03 - 17.77)	NS

There was no statistically significant difference between the groups in vital signs in the preoperative period.

TEST DRUG ONSET AND DURATION (MIN):

Factor	Bt group Mean (95% CI)	Bp group Mean (95% CI)	Statistical significance
Onset (min)	10.76(9.17-12.35)	14.72(12.89-16.55)	Significant* (0.0015)
Duration (min)	270.16(160.8-379.52)	386.88 (268.79-504.97)	NS

The onset of action in Bt group was 10.76 (9.17-12.35) min, in Bp group was 14.72 (12.89-16.55) min, there is significant difference in onset of analgesia between the two groups (P Value – 0.0015). Duration of analgesia in Bt group was 270.16 (160.8-379.52) min, in Bp group it was 386.88 (268.79-504.97) min, there was no statistically significant difference between the groups.

There was no statistically significant difference between the two groups in the heart rates at any point of time during the study period.There was no statistically significant difference between the two groups in systolic blood pressures (mmHg) at any point of time during the study period.There was statistically significant difference between the two groups in diastolic blood pressures (mmHg) at 8th hour adn at >10 hours, but there is no clinical correlation between the groups.There was no statistically significant difference between the two groups in respiratory rate (/min) at any point of time during the study period.

There was a statistically significant difference in between the two groups in VAS score at 15 min (P value 0.006), demonstrating early onset of analgesia in Bt group. At 15 min the mean VAS score in Bt group was 0.8, in Bp group it was 2.6.

Sedation Score (S.S):

Time	Bt group mean (95% CI)	Bp group mean (95% CI)	p value
0 min	1	1	NS
15 min	1.6(1.35-1.77)	1.2(1.03-1.4)	S (0.02)
30 min	1.8(1.63-1.97)	1.36(1.16-1.56)	S (0.007)
1 hr	1.44(1.23-1.65)	1.44(1.23-1.65)	NS
2ndhr	1.19(1.01-1.37)	1.35(1.14-1.56)	NS
3rdhr	1.21(0.97-1.46)	1.32(1.09-1.55)	NS
4thhr	1.63(1.19-2.06)	1.63(1.19-2.06)	NS
5thhr	1.38(0.94-1.81)	1.33(1.06-1.6)	NS
6thhr	1.13(0.83-1.42)	1.36(1.02-1.7)	NS
7thhr	1.0(1-1)	1.36(1.02-1.7)	NS
8thhr	1.67(0.23-3.1)	1.38(0.94-1.81)	NS
9thhr	1.67(0.23-3.1)	1.5(0.93-2.07)	NS
10thhr	1.67(0.23-3.1)	1.33(0.79-1.88)	NS
>10 hrs	1.67(0.23-3.1)	1.2(0.64-1.76)	NS

There was a statistically significant difference in between the two groups in sedation score at 15 min and at 30 min (P Value 0.02, 0.007 respectively). Sedation score was more in Bt group than Bp group.

DISCUSSION:

Pain is defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”. The goals of postoperative pain therapy must be to optimize pain control, minimize side effects and adverse outcomes and enhances the functional status of patients. Despite the availability of advanced techniques in pain management, more than 50% patients do not receive adequate pain relief following surgical procedures. Postoperative care personnel frequently under treat pain for fear of Opioid-related side effects.

Untreated pain itself has shown to produce adverse effects including the impairment of pulmonary function, increased cardiac work and vascular resistance, and may lead to gastrointestinal compli cations.Some reasons for under treatment of postoperative pain include a lack of knowledge of effective dosing regimens, fear of Opioid addiction in hospitalized patients and patient acceptance of pain as a consequence of surgery. Proper pain management can allow patients to return to normal function quickly and can reduce the postoperative side effects.

There is a need for a safe and effective agent that provides satisfactory analgesia with quick onset and long duration of action and with least side effects. Central neuraxial blockade is an important tool in the armamentarium of the anaesthesiologist; epidural narcotics in adequate dosage are an effective means for production of prolonged and segmental postoperative analgesia. There is no sensory loss, no muscle paresis and autonomic blockade with Opioid administered by these route.

In this present study, post operative analgesia of Butorphanol, a recently introduced drug in India is compared with postoperative epidural analgesia of Buprenorphine. Butorphanol is a synthetic Opioid with both agonist-antagonist activity and Buprenorphine is a semi synthetic Opioid with agonist-angtagonist activity. These drugs were compared in terms of onset of analgesia duration of analgesia and profile of their side effects.

The present comparative study showed that epidural Butorphanol has early onset of action for postoperative analgesia when compared with epidural Buprenorphine. A comparative study of epidural Butorphanol with epidural Morphine by various studies et al.[7,8,9] showed that oneset of analgesia with epidural Butorphanol was 22 min. In the present

study onset of analgesia in Butorphanol group was 10.76 (CI 9.17-12.35) min. In the present study, when the patient complained of pain, the test drug was given epidurally. VAS scale was taken that time as 10, we took the onset of analgesia as the time taken to reach the VAS score zero to maintain the uniformity for comparison. The reason for early onset in our study may be related to early intervention.

One study[10]et al., on mode and site of analgesic action of epidural Buprenorphine in humans, the onset of analgesia with 2 μ g/kg Buprenorphine ws at 33.0±9.5 minutes. In the present study the onset of analgesia in Bp group was 14.72 (12.89-16.55) min. The reason for early onset in our study may be related to early intervention.

A comparatively study on epidural Butorphanol versus epidural morphine by one study [11]has shown that duration of action with epidural Butorphanol was 330±52 min, which is comparable with the present study in which the duration of analgesia in Bt group was 270.16 (160.8-379.52) min.

In a study [12]on mode and site of analgesic action of epidural Buprenorphine in humans, the duration of analgesia with epidural Buprenorphine ws 769±151. In the present study, the duration of analgesia was 386.88 (268.79-504.97) min. The duration of analgesia in Bp group, which was lesser when compared to a previous study, might be related to the type of surgery (orthopaedic surgery).

The present study of comparison of epidural Butorphanol versus Buprenorphine in postoperative analgesia showed a statistically significant difference in the VAS scores between the groups at 15 min. Patients in Bt group had low VAS scores than Bp group at 15 mins. This may be related to early onset of analgesia with Butorphanol than Buprenorphine (Pvalue-0.0015). But, there is no significant difference between the two groups in relation to overall pain relief scores. There are no previous studies to date comparing Butorphanol with Buprenorphine in epidural postoperative analgesia.

In the present study patients in both Bt group and Bp group showed a fall in heart rate from the base line value by 6%. There is fall in both systolic and diastolic blood pressures from the base line value by 4% approximately.In both the group there is no fall in respiratory rate significantly and none of the patients in the present study had life threatening respiratory depression. This is comparable to studies by Palacios, Quisqueya T et al;[9] and Yoshimi Inagaki et al., who showed that none of the patients who received epidural Butorphanol and Buprenorphine respectively had respiratory depression (respiratory rate<12).

We conclude that from the present study, the onset of analgesia following epidural Butorphanol was more rapid, this suggests that Butorphanol may be useful in clinical situations where prompt onset of analgesia is required. The duration of analgesia was longer in Buprenorphine group (almost two hours clinically), therefore Buprenorphine might be a useful drug for providing long duration of analgesia with minimal side effects.

Subjective bias in VAS and pain relief scores.Oxygen saturation is not observed in the postoperative period. Drug trails need a meta analysis with same **objectives** to draw a conclusion.

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