Clonidine or Butorphanol as an Adjuvant to Epidural Bupivacaine in Orthopaedic Surgery – A Comparative Analysis of the Quality & Duration of Anaesthesia.

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ABSTRACT

Background: The study was conducted to compare the quality and duration of block by addition of either clonidine or Butorphanol as an adjuvant/additive to epidural bupivacaine in orthopaedic surgical patients. **Methods:** 75 patients of either sex of ASA status I &II, between 20-60 years of age undergoing orthopaedic surgery were selected for the study. Patients were randomly divided into three groups of 25 each. Group I received 0.5% Bupivacaine (15ml) with 50 µg Clonidine in (1ml), Group II patients, received 0.5%Bupivacaine (15ml) with 1 mg Butorphanol (1ml) and Group III patients received 0.5% Bupivacaine (15ml) with Normal Saline (1ml). The hemodynamic parameters as well as quality of block including onset, completion and regression of motor block were observed. Parametric data were compared using analysis of variance (ANOVA). Inter group comparison was done using unpaired t-test, and chi square test. **Results** were expressed as mean ± SD and p< 0.05 was considered statistically significant. Result: The demographic profile was comparable among the three groups. Onset of analgesia was significantly early in butorphanol (9.08±2.58 min) group, followed by clonidine (10.6±2.5min) and control group. Duration of analgesia was longest in butorphanol group, followed by clonidine and control group. Height of sensory block achieved was comparable in the three groups (p>.05). Four hour postoperative pain score was significantly lower in butorphanol group as compared to clonidine and control group<0.05.**Conclusion:** The quality as well as block duration can be enhanced safely by addition of butorphanol as an additive to bupivacaine; butorphanol having an edge over clonidine for the same.

Keywords: Bupivacaine, Clonidine, Epidural, Orthopaedic Surgery.

INTRODUCTION

Prolonged effective pain control is an essential component of optimal care of surgical patients during perioperative period. The primary goal of pain management is to provide the patient with an adequate comfort level. Epidural anaesthesia is a safe and popular technique for providing surgical anaesthesia and prolonged postoperative pain relief. Local anaesthetic solutions have remained the primary drug administered for Epidural anaesthesia but side effects are frequently observed, especially when used in full doses necessary for total pain relief. Bupivacaine or lignocaine is still the most commonly used drug for regional anaesthesia.[1] The advancement in the field of regional anaesthesia with the surge of newer local anaesthetic has not yet revolutionised the current clinical practice of regional anaesthesia.[2]

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Use of adjuvants with local anaesthetics has gained widespread popularity due to the belief that the addition of opioids or other additives allows the reduction of the amount of local anaesthetic and thus the incidence of side effects. A whole range of them have been used, refined and debated. The primary adjuvants, especially to improve analgesia, have been the opioids.[3] However, the availability of most potent opioids has been limited by the Narcotic Drugs and Psychotropic Substances Act 1985. Unlike other potent opioids, butorphanol is not a controlled substance which makes it a drug of special value in long-term management of chronic pain. Its high lipid solubility and high affinity for opioid (κ) receptors contribute to the paucity of side effects with its use like nausea, vomiting, pruritus and urinary retention.[4] Among the approved non-opioids in the epidural space, the selective α2 agonist clonidine stands out as an effective adjuvant for epidural anaesthesia[5,6] with reduced side effects as compared to epidural opioids. Clonidine, however, has its own set of side effects namely hypotension, bradycardia, sedation etc.[7] This prospective, randomized, controlled, double blind study was undertaken to compare and analyze the quality and duration of block by addition of either Clonidine or Butorpahanol to epidural bupivacaine, as an efficacious alternative in resource deficient situation.

MATERIALS AND METHODS

After obtaining approval from the institutional ethical committee, the study was commenced in Jawaharlal Nehru medical college hospital, Aligarh Muslim University, Aligarh. The period of study was 2010-2012.

Duration of analgesia was taken as the primary outcome measure of interest for the purpose of sample size calculation. It was estimated that 21 subjects would be required per group in order to detect a difference of 20 min in this parameter between the two groups, with 90% power and 5% probability of Type 1 error. Therefore, after written informed consent 75 ASA grade I/II patients undergoing lower limb surgery were included in the study. Exclusion criteria include spinal deformity, coagulopathy, sepsis, and any neurological illness. Tab alprazolam 0.25 mg orally was given to all patients on the night prior to surgery. Patients were familiarised with visual analgesic scale scoring preoperatively. Peripheral venous access with 18G or 20G cannula was secured. Patients were preloaded with ringer lactate 10ml/kg over 15-20min prior to epidural block. With proper positioning, under all aseptic precautions the epidural space was located with 18G Tuohy's needle through loss of resistance technique in L3 –L4 intervertebral space. Epidural catheter was threaded 3-4 cm inside the epidural space and fixed. A test dose containing 3 ml of 2% Lidocaine with 1:200,000 Epinephrine was given after negative aspirate for blood or CSF. 15ml of 0.5%bupivacain alone or along with one of the two study drugs was injected into the epidural space.

Randomization and Blinding: All patients were randomly allocated to one of the study group using a computer generated random number list. The anaesthesiologist administering the injections and observing the effects received sealed envelopes numbered 1 to 75 containing one of the three codes for the anaesthetic mixture to be administered epidurally for surgical anaesthesia. Group I patients received 0.5% Bupivacaine (15ml) with 50 µg Clonidine in (1ml), Group II patients received 0.5% Bupivacaine (15ml) with 1 mg Butorphanol (1ml) and Group III patients received 0.5% Bupivacaine (15ml) with Normal Saline (1ml).The anaesthetic mixtures were loaded with drug by another investigator not involved in administering the injections and in further evaluation of the patients.

The hemodynamic variables, oxygen saturation, time required to achieve surgical block in the operation and the time to rescue analgesic in the postanesthesia care unit were recorded in a blinded manner at every 5 minutes for the first 30 min and then at 15 min intervals throughout the duration of surgery. Block characteristics were assessed by an independent observer who was blinded to the treatment throughout the course of study. Onset of sensory block was tested as the time from injection up to feeling of warmth or loss of pinprick sensation in any dermatome at 0, 2, 5, 10, 20, 30 and 60 minute post drug injection into the epidural space.

Motor blockade was graded using the Modified Bromage scale (Score 0 Able to move hip, knee and ankle, Sore 1 Unable to move hip, able to move knee and ankle, Score 2 Unable to move hip and knee, able to move ankle and Score 3 Unable to move hip, knee and ankle). The duration was recorded as the time from zero (epidural administration of drug) to motor recovery equivalent to Modified Bromage scale 0.

Postoperative pain assessment was done by Verbal Rating Scale (VRS) (Pain score 0 - No pain; Score 1 - Mild/Slight pain; Score 2 - Moderate; Score 3 - Severe; Score 4 - Very severe/Intolerable). Any complication was also noted.

Statistical Analysis: All statistical analyses were performed using SPSS for windows version 17. All parametric data were compared using Analysis of variance (ANOVA) and intergroup comparison was done using unpaired t- test. All the categorical data were compared using Chi- square test. The results were expressed as mean ± S.D. and $p < 0.05$ was considered statistically significant.

RESULTS

The age, sex distribution of patients in the three groups was found to be comparable $p>0.05$. The patients and surgical characteristics did not differ among the groups [Table 1]. The onset of analgesia was significantly earlier in butorphanol group as compared to clonidine and control group [figure1].

The duration of analgesia was significantly longer in butorphanol as compared to clonidine group and control group. In comparison to the control group duration of analgesia was significantly longer in clonidine group [Figure 1]. The duration of motor block was significantly prolonged in butorphanol and clonidine group as compared to control group ($p<0.001$). The maximum height of sensory block attained was found to be comparable among the three groups.

Patients in butorphanol group were found to have a significant reduction in pain score at 4 hr ($p<0.05$) as compared to the clonidine and control group [Figure 2].However, At 12 hrs pain score was comparable among the three groups. The patients in butorphanol and clonidine group required significantly less doses of analgesics in the post-operative period as compared to control group [Figure 3].

Incidence of hypotension was highest significantly in group I (60%) as compared to group II (24%) and group III (20%) with $p < 0.05$ [Table 2].

The Incidence of bradycardia was higher in group I (32%) followed by group II (24%) and group III

(12%), this change was not statistically significant between any of the group [table 2] p>0.05.
The Incidence of nausea was also highest in group I (16%) followed by group II (8%) and group III (8%) which was statistically not significant p>0.05 [Table 2].

The Incidence of shivering was also highest in group I (24%) followed by group III (8%) and group II (4%). Incidence of shivering was significantly higher in group I as compared to group III p < 0.05.The Incidence of respiratory depression was 4% in group II while it was absent in group I and group III [Table 2].

Table 1: Demographic profile of patients among the three groups using ANOVA

Variables	Group I (Mean ± S.D.)	Group II (Mean ± S.D.)	Group III (Mean ± S.D.)	ANOVA p value
Age (yrs)	35.76±12.66	37.4±11.81	36.4±10.64	0.88
Male/Female	15/10	16/9	15/10	p>0.05
Weight of pts (Kg)	57.16±7.19	59.36±7.29	59.2±6.94	0.48
Height of pts (cms)	158.88±7.33	160.6±6.46	163.4±8.87	0.11
BMI (Kg/m^2)	22.57 ± 1.57	23.00 ± 2.49	22.11 ± 1.11	0.23

Table 2: Incidence of side effects among three groups

Side effects	Group I (n = 25)	Group II (n = 25)	Group III (n = 25)
Respiratory depression	-	1	-
Hypotension	15*	6	5
Bradycardia	8	6	3
Nausea	4	2	2
Vomiting	-	-	-
Pruritus	-	-	-
Shivering	6*	1	2
Sedation	-	-	-

DISCUSSION

On considering the demographic data, we found that there were no statistical differences among the three groups with respect to age, sex distribution and mean body mass index (BMI). This comparability reduced the chances of demographic difference as a cause of variability.
The baseline hemodynamic parameters (HR, SBP, DBP and MAP) were comparable in all three groups (p>0.05).Heart rate decreased in each group over time. The decline in heart rate was maximum in clonidine group which can be attributed to the central sympatholytic action of clonidine[6] as well as its direct action on heart.[7] The maximal decrease in the MAP from baseline value was 16.5 % in Clonidine group, 9.7% in Butorphanol and 10.4% in Control group. The average decline in MAP was statistically significant in Clonidine group at 5 min and 10 min as compared to Butorphanol and control group (p<0.05).Similar trends were noted with Systolic and Diastolic blood pressure. These results are in agreement with the majority of previous studies[6-8], in which a significant fall in blood pressure was noted with Clonidine.
No significant change in the haemodynamic parameters was observed in patients receiving Butorphanol, which is consistent with the prior studies.[9-11]

The baseline Respiratory rate was comparable among three groups (16 ± 2.30, 16.08 ± 1.86 & 14.92 ± 1.46 /minute in Group I, II, & III respectively).Butorphanol group observed a Significant decrease in average respiratory rate as compared to clonidine and control group. But none of the patients in any of the groups developed respiratory rate < 8/min [one patient in Butorphanol group developed apnea 15 min after administration of epidural block, which was probably due to profound hypotension in that patient leading to medullary ischemia and depression of medullary respiratory center.[12]
The onset of analgesia was fastest with Butorphanol (9.08 ± 2.58min) followed by Clonidine (10.6 ± 2.5min) and control group (14.16 ± 3.05min).Similar to our study, various authors have found significant reduction in onset of analgesia by using Butorphanol as adjuvant to epidural local anaesthetic.[13] However, there is some disparity in the time of onset of analgesia in clonidine group observed by us with prior studies[14,15] which might be due to the different techniques and ways of assessment of the parameter and different doses of clonidine used. But the early onset of superior analgesia on addition of Clonidine to bupivacaine may be explained by the high solubility of Clonidine, which is likely to diffuse rapidly across the duramater, resulting in quick absorption and action.

Duration of analgesia was longest in Butorphanol group (226.72±37.37min) followed by clonidine (162.16±23.48min) and control group (120.32±14.62min).Prolongation of duration of analgesia by Butorphanol has been demonstrated by the previous studies.[13] Prior studies have also supported observation of prolongation of postoperative analgesia by Clonidine.[15-17] The prolongation of duration of analgesia by Butorphanol can be explained by its lipid solubility and greater affinity for opioid receptors.

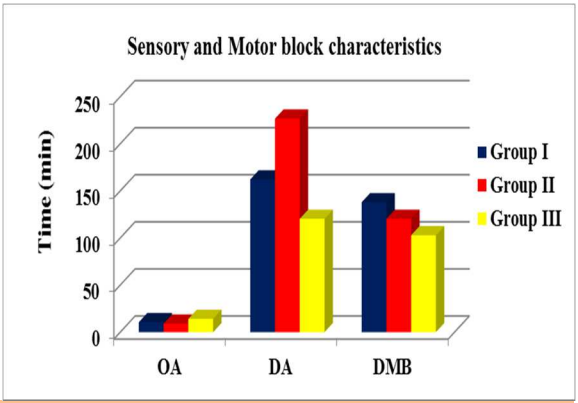

Figure 1: Comparison of sensory and motor block characteristics at 4 hr. OA–Onset of Analgesia; DA–Duration of analgesia; DMB–Duration of motor block

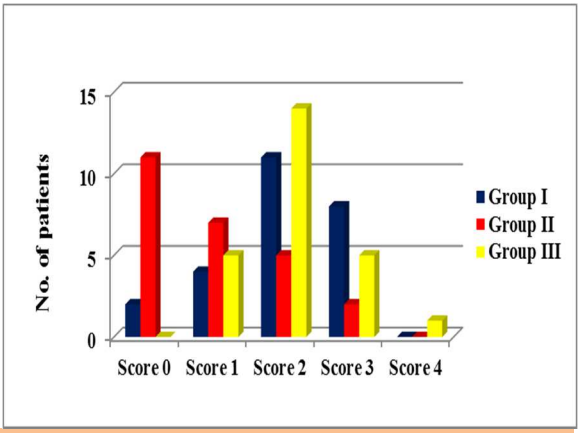

Figure 2: Comparison of pain score (VRS) at 4 hrs.

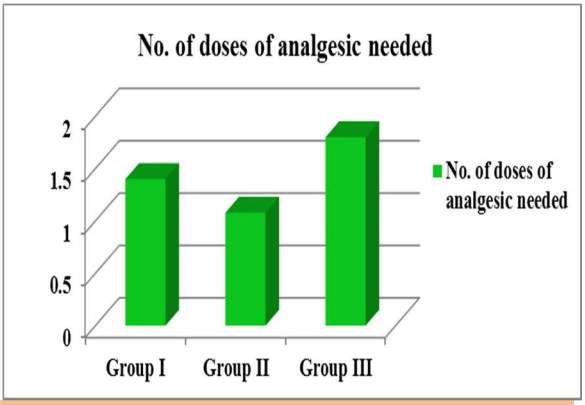

Figure 3: No. of doses of analgesic needed in three groups

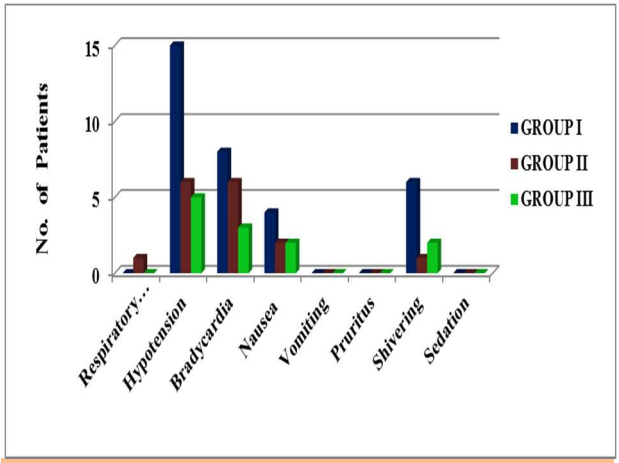

Figure 4: The incidence of side effects in three groups

The height of Sensory Block achieved was comparable in the three groups (p>0.05). Our observation is supported by previous studies, which showed that neither Clonidine nor Butorphanol increases the maximal height of block produced by local anaesthetic.

The mean duration of motor block was longest in clonidine group followed by butorphanol and control group. Similar to our study, prolongation of motor blockade was demonstrated with clonidine as an adjuvant to local anaesthetic in spinal, epidural blocks and peripheral nerve block.[18,19,8] However our observation of prolongation of motor block by butorphanol is not supported by previous studies.[4,20] But this finding might be due to the higher concentration and larger volume of local anesthetic used in our study. Significant prolongation of motor block in clonidine group as compared to butorphanol group can be explained by the vaso-constrictive property of clonidine leading to reduced systemic absorption and hence increased availability of local anesthetic at the site of action resulting in prolonged motor block, in fact there are no studies till date which can either support or refute this observation.

At 4 hour the post operative pain score by Verbal Rating Scale (VRS) was significantly lower in Butorphanol group as compared to clonidine and control group (p<0.05). However, the pain score was comparable between clonidine and control group at 4 hour. In contrast to our study.[14,16,21] found a significant difference in the pain score of patients receiving clonidine from control group, this disparity may be due to the lower doses of clonidine used in our study (50µg) as compared to Forsters et al[21] used infusion of 2µg/ml an Chassard et al[16] used infusion of 100µg & 150 µg and Parker et al[22] used the infusion of 5µg/ml. However, similar to our study a significant decrease in requirement of postoperative analgesics was noted in each of the above studies.Our findings are also supported by the observations of previous studies that administration of Butorphanol is

associated with better pain control in postoperative period along with the overall reduction in requirement of additional analgesics.

CONCLUSION

To conclude, butorphanol and clonidine are effective adjuvants to epidural bupivacaine for prolongation of duration of analgesia. Epidural butorphanol combined with bupivacaine produces significantly earlier onset of pain relief, longer duration of analgesia and less incidence of side effects. Hence, butorphanol was found to be superior to clonidine as an adjuvant to epidural bupivacaine. However respiratory rate of patient should be monitored while using butorphanol during the anaesthesia.

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