Original Article

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Prospective Randomized Control Study of Postoperative Epidural Analgesia of Intermittent Dosing of Bupivacaine and Clonidine vs Bupivacaine and Fentanyl

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Abstract

The aim of the study was to compare the relative potencies and clinical characteristics of epidural Clonidine and Fentanyl with Bupivacaine in lower limb and lower abdominal surgeries using patient-controlled analgesia. In a randomised double-blinded study, 60 ASA I or II patients requiring epidural analgesia for post operative pain relief were allocated to receive either 0.125% Bupivacaine with Clonidine 1µg/kg or 0.125% Bupivacaine with Fentanyl 1µg/kg via a sterile syringe by trained anaesthesiologists. Analgesia was established with 10-15 ml bolus of study solution. There were significant differences in onset time, duration and quality of analgesia, local anaesthetic consumption, between the two groups. We conclude that 0.125% Bupivacaine with Clonidine 1µg/kg group of patients clinically had better quality of analgesia and for a longer duration in comparison with patients receiving 0.125% Bupivacaine with Fentanyl 1µg/kg.

Keywords: Patient-controlled analgesia; Epidural anaesthesia; Post operative pain.

Introduction

Pain after surgery is inevitable, yet it is often underestimated and undertreated. Besides the distress, pain is also associated with psychosocial effects. The effective relief of pain is of paramount importance to anyone treating patients undergoing surgery. This has a smoother postoperative course with early discharge and also reduces the chronic pain syndromes.[1]

In our setup, epidural Bupivacaine is the most widely used local anaesthetic agent for post operative epidural analgesia. Fentanyl is frequently used in combination with Bupivacaine, as its use permits effective analgesia using concentrations of Bupivacaine that would otherwise be sub-therapeutic. In the last decade, so many other drugs have been used as an adjuvant to local anaesthetic agents, to improve the efficacy and potency of local anaesthetic agents and to provide good analgesia.

Epidural technique has been found to provide better pain relief than systemic opioids and also decreased incidence of postoperative complications. Lumbar epidural catheters can be kept in place for prolonged periods. Epidural administration of various analgesics gained increasing popularity following the discovery of opioids receptors in the spinal cord capable of producing potent analgesia as reported by Taksh and Rudy in 1976.[2] The epidural analgesia does inhibit the stress response. This effect seems to be greatest when epidural anaesthesia is continued in the post operative

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period as epidural analgesia.

The current trend in postoperative pain management is multimodal analgesia. Experimentally, Clonidine, local anesthetics, and opioids interact synergistically and clinically, are at least additive. The analgesic neuraxial effect of the á2-adrenergic agonist Clonidine is well described [3] Epidural Clonidine improved analgesia when combined with epidural Bupivacaine- Fentanyl in patients after lower abdominal surgery.[4] The á2-adrenergic agonist Clonidine produces analgesia by different mechanism that mimics the effect of endogenously released Nor-Epinephrine to stimulate postsynaptic á2 receptors in the spinal cord. Widespread application of opioids in spinal analgesia has been limited by side effects such as life threatening and unpredictable respiratory depression. Hence á2 adrenergic agonist, Clonidine is being used as an alternative drug for postoperative analgesia which is free of some opioids related but not all side effects.

Methods

Following Local Research Ethics Committee approval and written informed consent, 60 ASA I or II patients aged 18-75 yrs who were undergoing lower abdominal and lower limb surgeries were included in our study. Exclusion criteria included: contraindication to epidural anesthesia; sensitivity or allergy to amide local anesthetics; coexisting disease which could affect the reliability of clinical assessments;known or suspected drug abuse; and pregnancy,proven or possible. Preoperatively, each patient provided a medical history and underwent routine physical examination. The investigator or research assistant instructed patients in the use of epidural analgesia and the visual analog scale (VAS) pain score.

Oral or parenteral benzodiazepines could be administered preoperatively at the discretion of the investigator. After surgery patients were randomised to one of the study groups.

Prior to surgery an epidural catheter was inserted in a lower thoracic or upper lumbar intervertebral space and threaded cephalad 4 to 5 cm. Patients received

lidocaine 2% 3 mL with added epinephrine 5 pg/mL as a catheter test dose, followed by study drugs l0-20 mL over 5 min.

In the post anesthesia recovery room, when fully awake, patient was asked to score the pain on the basis of VAS. The post operative epidural bolus was given when the patients complains of moderate pain. In group-A patients, epidural bolus of 0.125% Bupivacaine (10-15ml) + Clonidine (1ìg/kg) will be delivered whenever patient complains of pain at a minimum interval of 4 hours. In group-B patients, a combination of 0.125% Bupivacaine (10-15ml) + Fentanyl (1ìg/kg) will be given at similar interval. Other analgesics given during the study period were noted.

In the post-operative period the following parameters were studied: Vital parameters such as the heart rate, blood pressure, respiratory rate, sedation score and visual analogue score were recorded. Duration of analgesia: This was calculated from the time when the first dose of analgesia was given, postoperatively and followed up till the patient complained of pain. Patients were asked to point out the intensity of their pain on the visual analogue scale. Time at which patients complained of pain more than 4 on the scale was noted. That point was taken as the end of fair analgesia and at that point, top up doses of same drug with same dosage given. And the number of additional doses (top

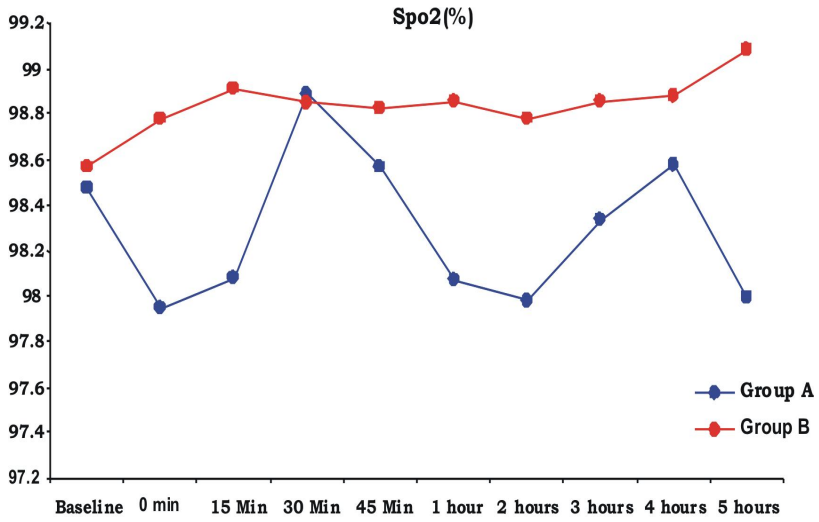
up doses) required in first 24 hrs were noted in both the groups. Side effects: Like nausea, vomiting, hypotension, respiratory depression and pruritus allergic reaction were looked for. Motor blockade assessed according to a four-point modified Bromage scale (0 = no motor block, 1 = inability to raise extended leg, 2 = inability to flex knee, and 3 =inability to flex ankle joint). Sedation was assessed as Score: 0= alert; 1=drowsy; 2=sleeps, easy to arouse verbally, does not fall asleep during or immediately after conversation, can stand up; 3= sleeps, opens the eyes to verbal command, falls asleep during or immediately after conversation, cannot stand up;4= does not open the eyes to verbal command. Patients were instructed to inform when pain of any intensity occurred and pain scoring was done according to Visual Analogue Scale. Epidural bolus as mentioned above will be administered at VAS of 4 or more. Each time the bolus was given parameters mentioned above were recorded every 15 minutes initially for first hour then afterwards hourly till the next bolus was given for 24 hours postoperatively.

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data are made, Assumptions: 1.Dependent variables should be normally distributed, 2.Samples drawn from the population should be random, and Cases of the samples should be independent. Student's T test was used to find the significance of the study parameters on the continuous scale, Inter group analysis on metric parameters and chi square test to find the significance of parameters on categorical scale between two or more groups.

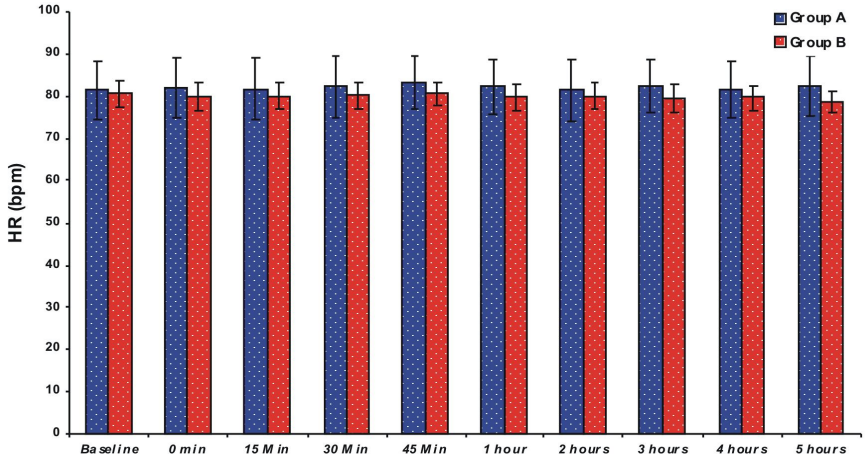
Results

In our study 60 patients of ASA I and II were included in the study and were allocated to the study groups randomly. In our study patients in both the groups

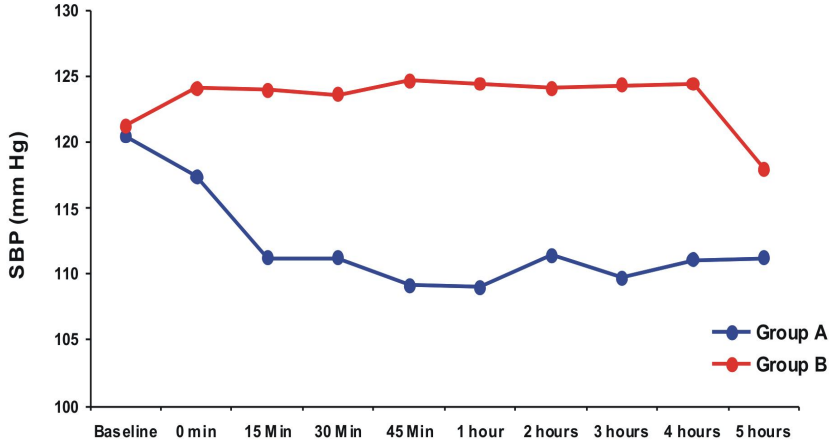
Graph 1: Comparison of SPO2 between two groups of patients studied which shows that group A (Clonidine) patients had no significant drop in saturations when compared to group B (Fentanyl) patients



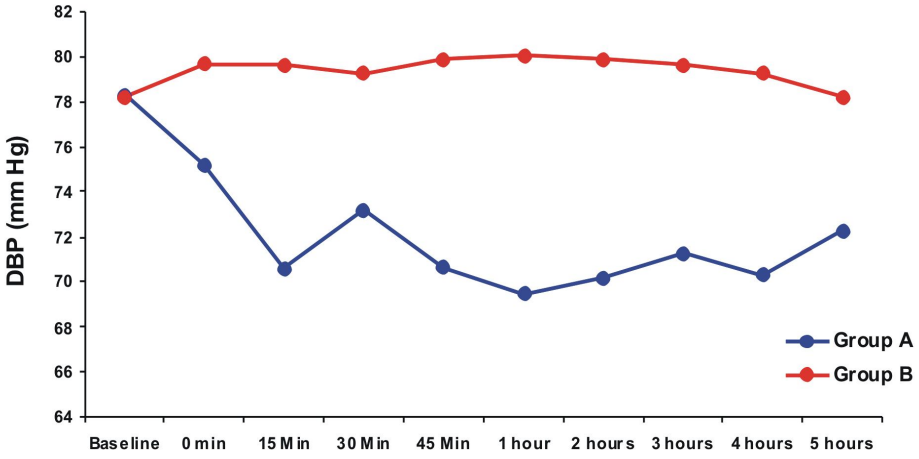
Graph 2: Comparison of Heart rate (bpm) between two groups of patients studied showed that group A patients had bradycardia in comparison to group B patients at various time intervals



Graph 3: A: Comparison of SBP (mm Hg) between two groups of patients studied



Graph 3:B: Comparison of DBP (mm Hg) between two groups of patients studied showed that drop in blood pressures both SBP and DBP noticed with Group A patients



Graph 4: Comparison of Pain Score between two groups of patients studied that group A patients had better quality of analgesia assessed according to pain scores and analgesia lasted for slightly prolonged duration in comparison to group B patients

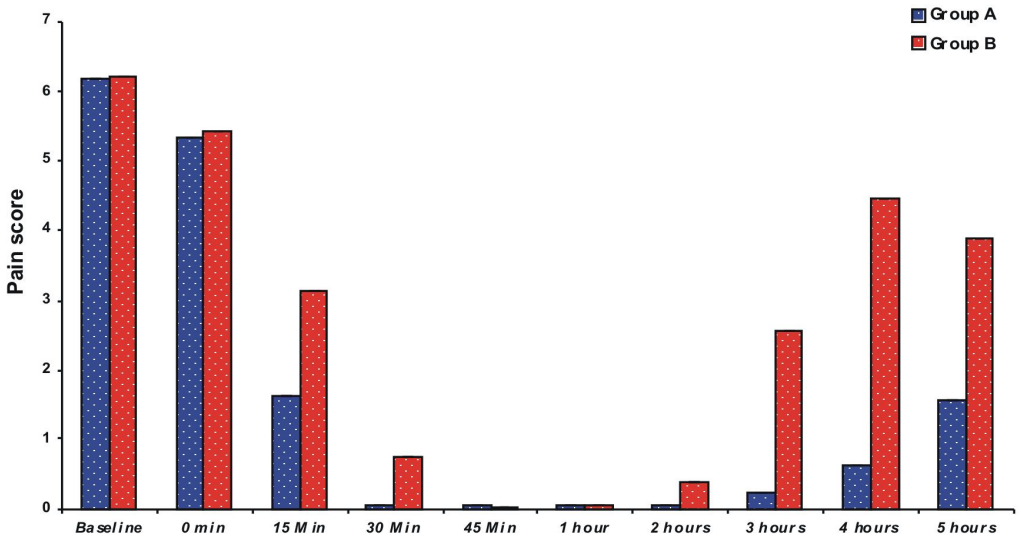


Table 1: Comparison of rescue analgesia- Group B patients needed rescue analgesics more often than Group A.

Rescue analgesia	Group A (n=30)	Group B (n=30)
No	28(93.3%)	28(93.3%)
Yes	2(6.7%)	2(6.7%)

belonged to age group between 31-40 years and there was no significant difference in the sex distribution and anthropometry. In our study we found that SPo2 was significantly stable in group A (99.45—99.20) patients compared to group B (98.78 – 99.08) patients (Graph 1). Group A patients had statistically significant bradycardia with P<0.001 (Graph 2). Group A patients had significant hypotension P<0.001 (Graph 3A and 3B).

Analysis of severity of pain was assessed based on VAS scores and quality of analgesia (Graph 4) Group A patients had better quality of analgesia with faster onset and analgesia lasting for 6-8 hours with less number of bolus doses, Group A patients needed less number of bolus doses (4 Doses) than the group B patients (6 doses). The Need for rescue analgesics was less in group-A patients (93.3% needed no rescue

Table 2: Comparison of Complications /Side effects between two groups of patients studied

Complications	Group A (n=30)	Group B (n=30)	P value
Nausea/Vomiting	0	4(13.3%)	0.112
Hypotension	9(30.0%)	0	0.002**
Purities	0	5(16.7%)	0.052+
Resp Depression	0	0	-
Sedation	12(40.0%)	0	<0.001**
Bradycardia	0	0	-
Motor Blockade	5(16.7%)	1(3.3%)	0.195

analgesics) P=0.254 which again shows that quality of analgesia was better in group A patients. (Table 1) The adverse effects were also noted in the patients during our study. We found that Group A patients had hypotension (12%), sedation(20%), and transient motor blockade (12%), while nausea(33%) and pruritus (16.7%) were most common with group B patients.(Table 2)

Discussion

In the postoperative period when the effect of the anaesthetic disappears, the tissue injury persists and pain producing substances which are liberated during the operation greatly reduce the normally high threshold of the nociceptors, so that innocuous stimulation produces pain. Moreover the cut ends of axons further contribute to nociception. Surgical trauma and subsequent postoperative pain result in a broad range of endocrinologic, immunologic and inflammatory responses, including increased release of catabolic hormones and inhibited secretion of anabolic mediators. To minimize or overcome these adverse effects, the postoperative pain should be optimally treated.

In this study, group-A patients received a combination of 0.125% Bupivicaine (10-15ml) +Clonidine (1ìg/kg) and group-B patients received epidural bolus of 0.125% Bupivacaine (10-15ml) +Fentanyl (1ìg/kg).Pain was measured using visual analogue scale. This study clearly demonstrates that combination therapy with epidural Clonidine and Bupivacaine gives superior pain relief than combination of Fentanyl and Bupivacaine. Although several studies have reported the beneficial effect of epidural Clonidine for intra and post operative pain management.[5,6,7] This study is unique in comparing bolus dosing combination of Clonidine and Bupivacaine with Fentanyl and Bupivacaine. The onset of analgesia was faster and duration of analgesia was prolonged significantly in Clonidine group as evidenced by VAS score measurement in comparison with Fentanyl group. Analgesia lasted for 6 hours in group-A where as in group-B it lasted for 4 hours and number of boluses required in first 24 hrs was less in Clonidine group. [5,6,8,9,10,11,12,14,15,16]

In our study it was found that hypotension and bradycardia was seen more commonly with Clonidine group of patients at different time intervals but both hypotension and bradycardia did not require any medical intervention which further proves that Clonidine though causes hypotension and bradycardia there was no hemodynamic instability. In the Fentanyl group, there were no significant hemodynamic changes noted as compared to Clonidine group. [9,17,18,4,7,19,25]

In the current study, drop in the oxygen saturation was very negligible in Clonidine as compared to Fentanyl group at all intervals. Even in Fentanyl group, although there was statistically significant drop in the Spo2, it was maintained at or above 98 % at all intervals. So, there was no significant respiratory depression in both the groups.[20,21]

In our study it was found that rescue analgesics were more needed in Fentanyl (20%) group of patients than compared to Clonidine (6.7%) group of Patients.[5,9]

In our study, Clonidine was found to cause more sedation and alter the heart rate and blood pressure. Excess sedation was noted in 5out of 30 patients in our study.[22,16,19,24,23]

To conclude, In the management of postoperative pain relief for various surgical procedures both Clonidine and Fentanyl can be used safely and effectively as adjuvant to Bupivacaine. It can be concluded from the above study that epidural Clonidine has a better analgesic action and longer duration of analgesia in comparison to Fentanyl and also Clonidine group of patients required less bolus doses. However the side effects such as hypotension, sedation and motor blockade were common in Clonidine whereas nausea vomiting, Pruritus were common in Fentanyl group. The overall side effects were less in Clonidine group as compared to Fentanyl group.

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