Original Article

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Comparative Study of Post Operative Analgesia with Epidural Clonidine and Epidural Normal Saline Using Combined Spinal Epidural Technique

Kamalakar Karampudi*, Saketh K.V., Naga Ramya****

Abstract

Introduction: Epidural anaesthesia/analgesia with adjuvant is the preferred method for intra and postoperative pain relief in lower abdominal and lower limb surgeries but search for ideal adjuvant without any side effect goes on. Alpha (α_2) adrenergic agonists have both analgesic and sedative properties when used as an adjuvant in regional anesthesia.

Aim: It is a comparative study of post operative analgesia with epidural Clonidine and epidural normal saline in patients undergoing lower abdominal and lower limb surgeries using combined spinal epidural technique.

Materials and Methods: The present study was undertaken during the period of May 2015 to October 2016. 100 patients posted for elective major lower abdominal and lower limb surgeries were selected and allocated randomly into two groups. Each group has 50 patients. Group 1:-Patients received intrathecal 0.5% Hyperbaric Bupivacaine + epidural Clonidine 1µg/kg or 50µg whichever is lower, diluted to 10ml with normal saline. Group 2:- Patients received intrathecal 0.5% Hyperbaric Bupivacaine + epidural 10ml normal saline. Quality of analgesia, duration of analgesia and duration of motor blockade between the two groups were compared. Patient vitals like pulse rate, blood pressure, respiratory rate, SPO_2 and ECG were monitored during the study. During the study patients were observed for the side effects like nausea, vomiting, hypotension, bradycardia and dryness of mouth.

Results: In present study majority of patients were in the age group between 31-50 yrs in both the groups and most of them weigh between 61-70 kgs. Total abdominal hysterectomy cases were majority cases observed in both groups. Quality of analgesia is excellent in both the groups and none of the patients complained of severe pain. Mild pain was observed in most of the cases in both the groups. The average time taken for 2 segment regression is more in Clonidine group compared to control group. The total duration of analgesia is more in Clonidine group compared to control group. The time taken for 1st movement i.e. beginning of motor recovery is more in Clonidine group compared to control group. Mean pulse rate, systolic BP and diastolic BP changes are statistically significant in Group 1. Complications observed in Group 1 were nausea & vomiting in 7 patients, hypotension in 7 patients, bradycardia in 1 patient, sedation in 1 patient, dry mouth in 2 patients. Hypoxia and bleeding were not reported.

Conclusion: Quality of analgesia is excellent in patients receiving Clonidine when compared to placebo group. Total duration of analgesia and motor blockade is significantly prolonged in Clonidine group compared to placebo group. Minimal side effects like mild hypotension, mild sedation and dryness of mouth were seen in Clonidine group which does not require any active intervention.

Keywords: Epidural Analgesia; Bupivacaine; Clonidine.

Introduction

Epidural anaesthesia provides both intra and post operative pain relief in various lower abdominal and lower limb surgeries. Epidural Bupivacaine has been used extensively for providing adequate postoperative pain relief in patients undergoing lower abdominal surgeries [1]. Many techniques and drug regimens,

Author's Affiliation:
*Associate Professor, **Post Graduate, Department of Anesthesiology, Prathima Institute of Medical Sciences, Karimnagar, Nagunur, Telangana 505417.

Corresponding Author:
Kamalakar Karampudi, Associate Professor, Department of Anesthesiology, Prathima Institute of Medical Sciences, Karimnagar, Nagunur, Telangana 505417.
Email: drkamalkarampudi@yahoo.com

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with partial or greater success, have been tried from time to time to calm the patients and to eliminate the anxiety component during regional anesthesia [2-4]. Neuraxial anaesthesia and analgesia provide solid analgesic effect by inhibiting nociceptive transmission from peripheral to central nervous system, but their analgesic advantages might be limited by the short half life of current local anaesthetics. The analgesic duration can be prolonged by increasing the dose of local anaesthetics; however the risk of accompanied systemic neurotoxicity can be increased [5]. Therefore, adjuvant can be added to local anaesthetics to prolong the analgesic duration and to limit the dose requirement of local anaesthetics. Recently, several neuraxial adjuvants, including Clonidine, opioids, dexamethasone, ketamine, magnesium sulphate and midazolam have demonstrated the synergistic analgesic effect with local anaesthetics with varying degrees of success. But the search for ideal adjuvant for a particular local anaesthetic goes on [6]. Alpha 2-adrenergic receptor agonists have been the focus of interest for their sedative, analgesic, perioperative sympatholytic, anesthetic sparing and hemodynamic stabilizing properties [7]. Clonidine, an α_2-adrenergic agonist added to a solution of bupivacaine and morphine has analgesic properties [8]. It also has a synergistic effect on local anesthetics and has been effectively used for postoperative analgesia. It has been used epidurally in different doses 18.75 mcg/h, 10, 15, and 20 mcg/h (Peach) and 6 mcg/kg/h (De Koch) [9]. The objective of present study is to evaluate the effect of spinal bupivacaine in combination with either epidural Clonidine or epidural normal saline administered by combined spinal epidural technique on postoperative outcome in patients undergoing lower abdominal or lower limb surgeries.

Material and Methods

This is "A Comparative study of Post operative analgesia with epidural Clonidine and epidural normal saline in patients undergoing lower limb and lower abdominal surgeries using combined spinal epidural technique". The study was undertaken at Prathima Institute of Medical Sciences, Karimnagar during the period of May 2015 to October 2016.

Patients selected for the study were between age groups 25 to 60 years, who had no complicating systemic disorders {ASA I and II}. 100 patients were divided into two groups of 50 each according to the drug they received. In Group 1 patients received epidural Clonidine 1μg/kg or 50μg whichever is lower, diluted in normal saline, the total volume injected was 10ml and in Group 2 the patients received 10ml of normal saline epidurally; in both the groups 0.5% Hyperbaric Bupivacaine was injected into subarachnoid space; the volume was determined by the type of surgery. Epidural drug was given after 15min after positioning the patient supine.

All the selected patients were thoroughly examined and investigated to rule out any systemic disorders. All patients were explained about the procedure and informed consent was taken.

Equipment used: Sterile gown and gloves, Sterile drape, Syringes: 2cc, 5cc, 10cc, insulin syringe {for Clonidine}, Loss of resistance syringe, Combined spinal epidural needle {18G Touhy combined spinal epidural needle and 27G sprotte spinal needle}, 18G epidural catheter with filter and sterile steel bowl.

Monitors used: Pulse oximeter, NIBP monitor, ECG, visual analogue scale for pain assessment.

Drugs used: Bupivacaine hydrochloride- 0.5% hyperbaric solution sterile ampoule, Clonidine hydrochloride 150μg ampoule {Cloneon by Neon labs} and 0.9%Normal saline.

Anaesthesia machine, resuscitation equipment and drugs were checked and kept ready, before undertaking the procedure.

Procedure

Preoperative vital data such as pulse rate, SPO_2 and blood pressure were noted. Heart and lungs were examined. An intravenous line established with 18G IV cannula and Ringer lactate drip started before the procedure.

With the patient in sitting position, under aseptic precautions L2-L3 / L3-L4 interspace was identified with highest point of iliac crest as the anatomical landmark. Local infiltration of 2ml 1% lignocaine was given to facilitate introduction of epidural needle. Then 18G CSE needle was introduced and advanced gradually connecting it to Loss of resistance syringe and epidural space identified by loss of resistance to air. 27G sprotte spinal needle was inserted and after obtaining clear CSF 0.5% Hyperbaric Bupivacaine 3-4ml was injected. Spinal needle was removed and an 18G epidural catheter was inserted so that 3-4cm of catheter is inside the epidural space. Patient was made to lie in supine position and level of sensory and motor block was checked.

Intraoperatively, patient was monitored for pulse rate, SPO_2, blood pressure, ECG changes, blood loss,

urine output and adverse reactions. Any side effect due to the drugs administered was documented.

Patient was shifted to postoperative ward in a hemodynamically stable state and after 2 segment regression of sensory blockade was confirmed. In postoperative period all the vital parameters were monitored and regression of motor blockade and sensory blockade, duration of analgesia and side effects were noted. Duration of analgesia was calculated from the time of injection of intrathecal bupivacaine to first complaint of pain. Pain was treated with epidural tramadol injections. Analgesia is scored by visual analogue scale ranging from 0 to10.

Visual Analogue Scale scoring as follows 0- No pain; 1, 2, 3- mild pain; 4, 5, 6- moderate pain; 7, 8, 9- severe pain and 10- Worst ever felt pain.

Quality of Analgesia: Assessed as No analgesia/ complaints of severe pain; Minimal analgesia/patient uncomfortable with pain; Good analgesia/patient comfortable, but complains of mild pain and Excellent analgesia/no pain.

All the patients were observed for the following side effects like nausea & vomiting, hypotension, ECG rhythm changes, sedation, dry mouth, bleeding, hypoxia, giddiness and voiding difficulty throughout the study period and rescue medications given.

Results

This study includes 100 patients posted for elective lower limb or lower abdominal surgeries divided into 2 groups of 50 each. Group 1 received intrathecal Hyperbaric Bupivacaine and epidural Clonidine and Group 2 received intrathecal Hyperbaric Bupivacaine and epidural normal saline. The effect of recovery from neuraxial blockade and duration of analgesia was compared and contrasted.

Table 1: Comparasion of surgeries undertaken in both groups

Name of Surgery	Group 1	Group 2
Surgeries on hip joint	5	3
Surgeries on femur	12	13
Surgeries on leg	10	12
Total abdominal hysterectomy	15	16
Vaginal hysterectomy	4	2
Incisional hernia below umbilicus	2	3
Ovarian cystectomy	2	1

Table 2: Age and weight distribution among 2 groups

Age distribution in years	Group 1	Group 2
20-30	9	11
31-40	18	14
41-50	13	15
51-60	10	10
Weight in kgs		
40-50	11	8
51-60	1	14
61-70	18	19
71-80	9	9

In the present study, cases observed in Group 1 was 5 cases were hip joint surgeries, 12 cases were femur surgeries, 10 cases were surgeries on leg, 15 cases were total abdominal hysterectomy, 4 cases were vaginal hysterectomy, 2 cases were Incisional hernia below umbilicus and 2 cases were ovarian cystectomy where as in Group 2 was 3 cases were hip joint surgeries, 13 cases were femur surgeries, 12 cases were surgeries on leg, 16 cases were total abdominal hysterectomy, 2 cases were vaginal hysterectomy, 3 cases were Incisional hernia below umbilicus and 1 case was ovarian cystectomy.

In the present study age distribution in Group 1 was 9 patients were in 20-30 yr age group, 18 patients in 31-40 yr age group, 13 patients in 41-50 yr age group and 10 patients in 51-60 age group where as in Group 2 was 11 patients were in 20-30 yr age group, 14 patients in 31-40 yr age group, 15 patients in 41-50 yr age group and 10 patients in 51-60 age group.

The P value calculated by unpaired student t test is 0.765 {t value 0.29, df 98%}, which is more than 0.05, so it is not statistically significant. Age distribution in both the groups is comparable.

Weight distribution in Group 1 was 11 patients were between 40-50 kgs, 12 patients were in 51-60 kgs, 18 patients were in 61-70 kgs and 9 patients were in 71-80 kgs where as in Group 2 was 8 patients were between 40-50 kgs , 14 patients were in 51-60 kgs, 19 patients were in 61-70 kgs and 9 patients were in 71-80 kgs. The P value calculated by unpaired student t test is 0.707 {t value 0.376, df 98}, which is more than 0.05, so it is not statistically significant. Weight distribution in both the groups is comparable. (Table 2).

Table 3: Comparasion of quality, duration of analgesia, 2 segment regression and motor movement in both groups

Variable	Group 1	Group 2
	Quality of analgesia	
Mild pain	44	42
Moderate pain	6	8
Severe pain	0	0
2 Segment regression (in hrs)	1.45	1.3
Duration of analgesia	3.32	2.23
Time of first movement	2.54	2.43

Quality of analgesia is excellent in both the groups and none of the patients complained of severe pain. Complaints of mild pain in Group 1 was in 44 cases, Group 2 was in 42 cases while moderate pain in Group 1 was in 6 cases and in Group 2 was 8 cases. The calculated P value is > 0.05 and it is statistically insignificant.

The average time taken for 2 segment regression is more in Clonidine group compared to control group i.e., Mean Group1=1.45{0.3}, Group 2=1.30{0.03}. The calculated P value is <0.001 which is less than 0.05, so this is statistically significant.

The total duration of analgesia is more in Clonidine group compared to control group. So patients in Group1 are pain free for a longer time. The calculated P value is <0.0001 which is less than 0.05, which is highly statistically significant.

The time taken for 1st movement i.e. beginning of motor recovery is more in Clonidine group compared to control group. The calculated P value is <0.001 which is less than 0.05, and is statistically significant (Table 3).

Table 4: mean pulse rate, systolic and diastolic BP changes

Mean Values	Group 1	Group 2
Mean pulse rate changes	83.6{2.88}	85.76{3.81}
Mean systolic BP changes	108.2{5.87}	111.87{4.91}
Mean diastolic BP changes	71.25{3.96}	73.4{2.89}

Mean pulse rate, systolic BP and diastolic BP changes are statistically significant in both groups.

The calculated P value for mean pulse rate changes is 0.042 which is less than 0.05, and is statistically significant. The calculated P value for systolic BP changes is 0.028 which is less than 0.05, hence statistically significant. The calculated P value for diastolic BP changes is 0.019 which is less than 0.05, therefore statistically significant (Table 4).

Complications observed in Group 1 were nausea & vomiting in 7 patients, hypotension in 7 patients, bradycardia in 1 patient, sedation in 1 patient, dry mouth in 2 patients where as in Group 2 nausea &

Table 6: Comparasion of complications in both groups

Complication	Group 1	Group 2
Nausea &vomiting	7	8
Hypotension	7	5
Bradycardia	1	0
Sedation	1	0
Dry mouth	2	0
Hypoxia	0	0
Bleeding	0	0

vomiting in 8 patients, hypotension in 5 patients observed and bradycardia , sedation, dry mouth. Hypoxia and bleeding were not reported in either group (Table 5).

Discussion

This study is conducted to observe the effects of a combination of Bupivacaine spinal technique with epidural Clonidine in patients undergoing lower limb and lower abdominal surgeries comparing it with spinal Bupivacaine and epidural normal saline.

Clonidine is a selective partial agonist for α_2 adrenoreceptors. It is known to increase both sensory and motor block of local anaesthetics. It produces analgesia by mimicking the activation of descending noradrenergic pathways. Sympathetic hyperactivity may be reduced by the administration of epidural Clonidine through three mechanisms of action. First mechanism proposed is Clonidine may inhibit nociceptive neurotransmitter release in the dorsal horn and sympathetic outflow in the spinal cord intermediolateral column. Second is it may inhibit norepinephrine release from sympathetic terminals in the periphery. Third one is epidural Clonidine may also be reabsorbed into the systemic circulation where it reaches the α_2 adrenoreceptors of the dorsal horn and provides analgesia by increasing the antinociceptive threshold of the spinal cord which activates the descending noradrenergic pathway to inhibit small-diameter afferent-induced substance P release.

Clonidine blocks conduction of C and Aδ fibers and increases potassium conductance, intensifying the neural block of local anesthetics. It may also cause local vasoconstriction reducing removal of local anesthetic. Clonidine reduces blood pressure by inhibiting preganglionic sympathetic neural activity in the spinal cord. It can also reach the brainstem via systemic redistribution or cephalad spread in the cerebrospinal fluid, further contributing to decreased blood pressure. These same mechanisms may also be responsible for the noted decreases in HR after the administration of epidural Clonidine.

The present study was undertaken to evaluate the addition of Clonidine in epidural space to surgeries in which intrathecal bupivacaine is given. 100 patients were randomly allocated to two groups, 50 patients received 1μ/kg or 50μg Clonidine epidurally while others received same volume of normal saline. All the patients received intrathecal bupivacaine heavy. The effect on analgesia, sensory and motor blockade and duration was studied.

W.Scott Jellish et.al [10] in 2003 studied the effect of epidural Clonidine in combination with spinal bupivacaine in patients undergoing lumbar laminectomy procedures. They concluded that epidural Clonidine prolongs the time of sensory analgesia and motor blockade. Our study is in agreement with the former study. The duration of analgesia is 3.33 {S.D0.181} in Clonidine group compared to 2.29 {S.D 0.075} in control group.

M J Paech et.al [11] 1997 in their study on Epidural Clonidine infused 20 μg/hour improves analgesia during coughing when combined with epidural bupivacaine-fentanyl in patients undergoing lower abdominal surgery but is associated with hemodynamic changes and increased vasopressor requirement. Our study is in agreement with them that there is better postoperative outcome and decreased requirement of analgesics after Clonidine. But the hypotension incidence and requirement of vasopressors in our study was similar in both the groups.

Dobrydnjov et. al [12] in 2005 concluded low-dose intrathecal Clonidine provided a better quality of anesthesia and longer-lasting analgesia. Epidural Clonidine-ropivacaine infusion resulted in improved postoperative analgesia but was associated with a moderate decrease in blood pressure. The same result has been seen in our study and the hypotension was not alarming and required treatment with fluids and smaller doses of mephentermine only. Although Clonidine prolonged motor block in our patients, this increase was not clinically significant and did not require a prolonged PACU admission.

Andrew D. Farmery [13] in 2009 proved in his study that Low-dose epidural Clonidine significantly reduced the demand for morphine and reduced postoperative nausea with few side effects in patients undergoing decompressive spine surgeries. This is in agreement with our study where the incidence of nausea is similar in both test and control groups.

Bonhomme et al [14]. recently evaluated the effect of epidural small-dose morphine in combination with Clonidine for postoperative analgesia after lumbar disc surgery. They reported reduced pain with movement after surgery using small-dose Clonidine and morphine, which was not manifested when a combination of bupivacaine and Clonidine was used. Their patients experienced a frequent incidence of difficulty in initiating micturition (30%–45%) not seen in our population. This may be related to the fact that their patients received a general anesthetic in which both IV and epidural narcotics were given. Our patients received a spinal anesthetic with no

intraoperative narcotics. Urinary retention has not been noted with neuroaxial Clonidine administration and, in fact, it may actually hasten the time to first micturition after spinal anesthesia.

There were no statistical differences in the number of patients experiencing nausea or vomiting in either the PACU or during the 24-hour postsurgical period. In addition, there seemed to be no sedative effect of epidural Clonidine as demonstrated by no difference in Steward Recovery scores among the groups. This is one of the noted advantages of administering epidural Clonidine compared with other forms of analgesia.

Many previous studies have used intrathecal Clonidine combined with opioids and local anaesthetics for labor analgesia and orthopedic surgery. The combination of Clonidine with opioids developed problems like respiratory depression, pruritis, urinary retention and abuse liability. In our study sedation was seen in the Clonidine group but the respiratory depression and opioid related complications were not seen.

Conclusion

Quality of analgesia is excellent in patients receiving epidural Clonidine when compared to placebo group.

Total duration of analgesia and motor blockade is significantly prolonged in Clonidine group compared to placebo group. Minimal side effects like mild hypotension, mild sedation and dryness of mouth were seen in Clonidine group which does not require any active intervention.

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