Original Research Paper

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Anesthesiology

COMPARATIVE ANALYSIS OF EPIDURAL ISOBARIC 0.5% LEVOBUPIVACAINE AND ISOBARIC 0.5% LEVOBUPIVACAINE WITH CLONIDINE IN INFRAUMBILICAL SURGERIES

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ABSTRACT

Background- Regional anaesthesia is usually preferred when treatment site is on infraumblical region.Levobupivacaine has been used as an alternative to bupivacaine because of its lower risk of cardiotoxicity. Its higher lipid solubility makes it more potent and prolong duration of action than ropivacaine. The addition of clonidine to the levobupivacaine during epidural block can improve the quality of anesthesia while providing adequate and prolonged intra and postoperative analgesia.

Method- 76 patients scheduled to undergo lower abdominal and lower limb surgery were divided randomly into two groups by chit box method:
Group L: receiving epidural 0.5% levobupivacaine (1.5 mg/kg) and NS
Group LC: receiving epidural 0.5% levobupivacaine and inj. Clonidine 3 micro gram/kg

Results- The patients in group LC had a lesser need for analgesics than group L. Even the VAS scores were significantly low in group LC when compared to group L.

KEYWORDS : Epidural, clonidine, levobupivacaine

INTRODUCTION

Regional anesthesia is an excellent option when the surgical site is located on the lower extremities, perineum or lower abdomen.

The sensorimotor block by regional anesthesia requires low dose of local anesthetics (hence local anesthetic toxicity is rarely a concern). It's often more dense in character[1] and also has advantages of having rapid onset, less failure rates and cost-effectiveness. Single shot epidural anaesthesia has the drawbacks of shorter duration of block and less postoperative analgesia.[2] even with use of long acting local anaesthetic agent such as bupivacaine[3] or ropivacaine[4].

Epidural anaesthesia by placing a continuous catheter provide not only peri-operative surgical anaesthesia but can also be used for postoperative analgesia. Prolongation of epidural analgesia has been achieved by the addition of various adjuvant such as opioids, ketamine, ephedrine and α2-agonist[5,6]

However with opioid adjuvant ,the side effects such as pruritus, nausea, vomiting, urinary retention and delayed respiratory depression have prompted further research toward non-opioid analgesics with less serious side effects.[7]

Clonidine possesses anxiolytic, sedative, sympatholytic and analgesic properties with less respiratory depressant effect.[8]

The addition of clonidine to the local anesthetics during epidural block can improve the quality of anesthesia while providing adequate and prolonged intra and postoperative analgesia. It reduces requirements of anesthetic agent intraoperatively thus avoiding excessive sedation.[9]

Levobupivacaine has been recently widely used as an alternative to bupivacaine to achieve a lower risk of cardiotoxicity than bupivacaine.[10] Its higher lipid solubility makes it more potent than ropivacaine and results in a longer duration of action[11]

MATERIAL AND METHODS

This prospective randomized double blinded study was conducted in Department of Anaesthesia and Critical Care, Dr. S. N. Medical College, Jodhpur after getting approval from Ethical Committee and informed and written consent. In this study 76 patients scheduled to undergo lower abdominal and lower limb surgery and randomly divided into two groups by chit in box method:-

Group L (38 each): Patients received epidural 0.5% levobupivacaine (1.5 mg/kg) and normal saline

Group LC (38 each): Patients received epidural 0.5% levobupivacaine (1.5 mg/kg) and injection clonidine 3mcg/kg dissolved in NS up to 1ml (Max.150 mcg).

Patients aged between 20-60 years, weight 50-75kgs and ASA Grade 1st &2nd are included in the study.

Patient having compromised renal, pulmonary and cardiac status and contra indications to the epidural block like coagulation disorders, pre-existing neurological disease, anatomical abnormalities of spine, infection at the local site and known allergy to local anesthetics are the exclusion criteria of the study.

To reduce subjective and objective bias, anesthesiologist preparing drugs and anesthesiologist doing procedure and monitoring were not aware of group allocation.

All patients were evaluated thoroughly in pre-anaesthetic clinic. On arrival of patient to the operating room (OR), all standard monitoring like pulse oximetry, continuous electrocardiogram and non- invasive blood pressure were attached and baseline parameter were recorded. Intravenous access was secured with wide bore (18G) cannula and lactated Ringer's solution infused during the operation. Under aseptic precaution, epidural anesthesia with the loss of resistance technique were employed at L3-4 level with the patient in sitting position, after skin infiltration with 1% lidocaine 3ml, using an 18G Tuohy epidural needle.

A test dose of 3ml normal saline with adrenaline 1:200,000 was used to exclude both subarachnoid and intravascular injection. After confirming negative subarachnoid and intravascular injection a 20G multi-hole epidural catheter was threaded and secured in place. Epidural activation was done by injecting the drugs according to the group allocated.

Sensory block was assessed by loss of sensation to pin prick test method in the midline using a 23G blunt hypodermic needle every 5 min interval until T_{10} dermatome was reached and then every 15 min interval until no change in level occurred. Onset and duration of sensory block (interval from epidural administration of drug until the regression of sensory block to S_1 dermatome) was noted. The sensory block was assessed by pin prick test.[14,15]

0= no sensation, 1= analgesia (touch sensation) and 2= anaesthesia (no sensation).

The onset and duration of motor block was assessed by Modified Bromage scale every 5 min for first 30 min and then every 15 min till Modified Bromage 3 score achieved.

Mean arterial pressure (MAP), systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), oxygen saturation (SpO2) and respiratory rate (RR) were measured and recorded before and after epidural drug injection, every 5 min till 30 min and thereafter every 15 min till the end of surgery.

In the PACU, quality of analgesia was assessed by using visual analog score (VAS)[12] on a 0-10 scale, where a score of 0 represents no pain and 10 is the worst pain imaginable. VAS was measured every hour till 6 hour post-operative and then at 6 hour intervals for 24 hour either by an observing nurse in the recovery room or the trained ward nurse. On observation, whenever VAS score was ≥ 4 or the patient request pain medication, rescue analgesia given with 10ml levobupivacaine (0.20%) via epidural catheter.[13]

Duration of analgesia defined as interval between activation of epidural block and time to first analgesic requirement. Total dose of rescue analgesic consumed during the observation period was also recorded. Quality of sedation assessed using Ramsay sedation scale every hour till 6 hour post-operative.

Any adverse effects, e.g. nausea, vomiting, itching, bradycardia, hypotension excessive sedation, retention of urine or respiratory depression (respiratory rate < 10/min or $SpO_{2<}$ 90%) were recorded.

The sample size calculation is based on the previous study, using a SPSS software version 22.0, (SPSS Inc., Chicago, IL, USA). *T* test for independent samples was used to compare two groups for data with normal distribution and Mann---Whitney *U* test was used for comparing data with non-normal distribution. Yates continuity correction test (Chi square test), Fisher's exact test and Fisher---Freeman---Hilton test were used for comparison of qualitative data.

RESULTS

All quantitative data were summarized in the form of mean ±SD. Two groups were compared in accordance with patient's age, weight and height. Baseline and intraoperative hemodynamic parameter (SBP, DBP, MAP, HR, SPO2 and RR) are comparable between both groups as p value more than 0.05.

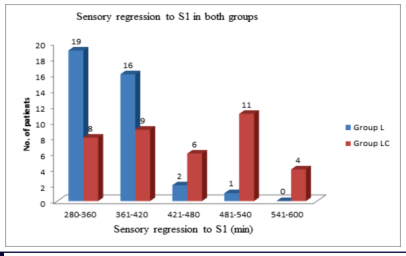
Table 1: Demographic variable are comparable between both groups.

Parameters	Group L (Mean±SD)	Group LC (Mean±SD)	P value
Age	43.89±12.01	43.89±12.01	0.415
Weight (kg)	66.02±6.96	67.97±11.19	0.365
Height (cm)	161.92±6.87	162.65±6.61	0.635

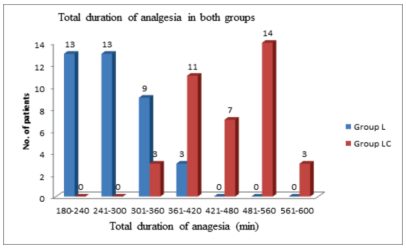
TABLE 2: study results

Parameter	Group L	Group LC	P value
Sensory onset (Time to achieve T10 dermatome)	15.76±2.22 min	7.71±1.76 min	<0.0001
Motor onset (Time to achieve bromage 3)	18.81±2.47 min	10.00±1.64 min	<0.0001
Total duration of analgesia	278.13±59.79 min	465.78±75.96 min	<0.0001
Duration of motor block(Motor regression bromage3 TO 1)	303.68±44.92 min	350.52±73.52 min	<0.0001
Duration of sensory block (Sensory regression T10 to S1)	358.94±47.97 min	450.52±77.49min	<0.0001

Graph 1: comparison of duration of sensory block



Graph2: comparison of total duration of analgesia.



Shows distribution of patients according to the number of rescue analgesia given in first 24 hours. In our study, the number of rescue analgesia required by group L was significantly higher as compared to group LC (p value < 0.0001).

Graph 3: comparison of total number of rescue analgesic requirement

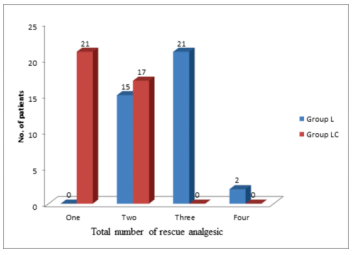


Table 3: comparison of side effects between groups

SIDE EFFECTS	GROUP L	GROUP LC
Hypotension	3	2
Bradycardia	3	3
Nausea	3	-
Shivering	3	1

DISCUSSION

Epidural analgesia offers superior pain relief and early mobilization especially when local anesthetic dose is combined with an adjuvant.[14] Epidural anesthesia is popular and offers several benefits to the patients but also linked with drawbacks like pain at the puncture site, fear of needles, and recall of the procedure.[15] These factors stress the importance of sedation that offers analgesia, anxiolysis and amnesia as sedation increase patient's acceptance of regional anesthesia and it greatly improves patient wellbeing during the surgical procedure.[16]

It blocks nerve conduction in sensory and motor nerves mainly by interacting with voltage sensitive sodium channels on the cell membrane. It also interferes with impulse transmission and conduction in other tissues.[17]

Now a days, lot of adjuvants are used with local anesthetics in epidural anaesthesia with the aim to fasten and prolong the sensory and motor block and produce more sedation and analgesia.[18]

The high cephalic spread of analgesia with local anesthetics may be significant but still its quality sometimes may not correlate with the level of sensory analgesia.[19] At this stage, the impulsive use of large dose of sedation or even general anaesthesia with mask defeat the novel purpose of regional anaesthesia whereby a continuous verbal contact with the patient is lost. Sedation, stable hemodynamics and an ability to provide smooth and prolonged postoperative analgesia are the main desirable qualities of an adjuvant in neuraxial anaesthesia.

Clonidine acts by binding to the presynaptic C-fibers and post synaptic dorsal horn neurons. They produce analgesia by depressing the release of C-fiber transmitters and by hyperpolarization of post synaptic dorsal horn neurons.[20,21].

Clonidine being a lipophilic drug is rapidly absorbed into the spinal compartment and blocks the conduction of C and Aδ fibers.[22]

Clinical studies exhibit the potentiation of neuraxial local anaesthetics as they decrease the intraoperative awareness, anaesthetic requirements and post-operative analgesia when epidural or caudal clonidine was used in conjunction with general anaesthesia.[23,24]

Clonidine has been used successfully over the last decade for the said

purpose. The introduction of dexmedetomidine has further widened the scope of α-2 agonists in regional anaesthesia. [25]

The faster onset of action of local anaesthetics, rapid establishment of both sensory and motor blockade, prolonged duration of analgesia into the post-operative period, dose-sparing action of local anaesthetics and stable cardiovascular parameters makes these agents a very effective adjuvant in regional anaesthesia.

Sensory and motor blockade-

Time of onset of sensory block in Group LC (7.71±1.76 min) was found to be earlier than Group L (15.76±2.22 min). These results were in concordance with the results of A. Arumugham et al,[26] using levobupivacaine and with clonidine onset at T6 dermatome.

Clonidine combined with levobupivacaine had a faster onset of sensory and motor block which was in accordance with Milligan KR et al, Gupta S et al and Jain A et al.[27] Chalkiadis DS et al [28] in their study demonstrated the absorption characteristics of epidural levobupivacaine with clonidine and adrenaline via caudal epidural route and showed that clonidine mixed with levobupivacaine had a faster absorption compared to adrenaline mixed with levobupivacaine.

In our study the mean time of onset of motor blockade in Group LC was 10±1.64 min and in Group L was 18.81±2.47 min, which was significant. A Arumugham et al [29] in their study also observed the same.

Regression of sensory block to S1 dermatome was earlier in Group L (358.94±47.97 min) when compared to Group LC (450.52±77.49 min). These results were in concordance with the results of Agreta Gecaj-Gashi et al[30]

The total duration of motor block (regression to Bromage 1) in Group LC (350.52±73.52) min and L (303.68±44.92 min) which is in concordance with the results of Agreta Gecaj-Gashi et al.[30]

ANALGESIA-

Total duration of analgesia in Group LC (465.78±75.96 min) and L (278.13±59.7 min) which is in concordance with the results of A Arumugham et al[29]. Dr. Satyendra S. Yadav et al[31] also found that addition of clonidine as an adjuvant to levobupivacaine had prolonged duration of analgesia in LC group compared to L group.

The VAS score was lower in group LC compared to the control group L which was statistically significant ($p<0.05$). A Arumugham et al,[29] Alves TCA and Braz JRC et al [32] also showed a significant lower VAS score compared to the control group.

In our study number of rescue analgesic required in group LC was less compared to group L. Milligan KR et al,[33] found in their study that the time to rescue analgesia was significantly delayed in group LC (levobupivacaine with clonidine) compared to group L. Other studies by Gupta S et al , Ghatak T et al,[34] Alves TCA and Braz JRC et al [32] also showed a significant prolongation of duration of analgesia when clonidine was used as an adjuvant to local anaesthetics.

Disma N et al [35] showed that a dose of 2 μg/kg of clonidine increases the duration of post-operative analgesia in caudal anaesthesia for lower abdominal surgery.

Sedation Score-

Throughout surgery, patients were calm and composed in the group L and LC, but sedation score was highly significant (P value < 0.0001) in the group LC as grade 3,4 was seen .These showed that the sedative properties of clonidine was far superior to Levobupivacaine alone. None of the patient in group LC required any other sedative during the peri- operative period.

This was in accordance with the study done by A Arumugham et al [29] . Gupta S et al, Alves TCA and Braz JRC et al [32] which showed significant sedation produced by addition of clonidine to Levobupivacaine. The sedative effect of clonidine can be explained by the agonistic action of clonidine on locus coeruleus. Ghatak T et al [34] also showed that the sedative properties of clonidine are far superior to bupivacaine with magnesium sulphate.

Side effects-

That group LC having lesser side effects than group L, but P value > 0.05 which is not statistically significant, which was also reported by the studies conducted by A Arumugham et al, [29] Gupta S et al, Alves TCA and BrazJRC et al.[32] In our study, most of the patients were catheterized so incidence of urinary retention could not be evaluated.

CONCLUSION

Addition of epidural clonidine with levobupivacaine produces predictable rapid onset of both sensory and motor blockade and prolonged duration of analgesia with negligible side effects.
Hemodynamic and respiratory parameters were comparable in both the groups at all interval of time.

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