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A COMPARATIVE STUDY BETWEEN 0.125% LEVOBUPIVACAINE WITH CLONIDINE AND 0.125% LEVOBUPIVACAINE ALONE IN EPIDURAL ANALGESIA FOR POST OPERATIVE PAIN RELIEF IN PATIENTS UNDERGOING LOWER LIMB SURGERIES

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Abstract

Background: Epidural anaesthesia is a safe alternative for general anaesthesia and can be supplemented with spinal or general anaesthesia for postoperative analgesia in patients undergoing lower limb surgeries. This study was conducted to evaluate the effect of clonidine as an adjuvant to levobupivacaine, an S (-) enantiomer of bupivacaine. **Material And Methods:** Fifty-two patients of ASA grade I and II undergoing lower limb surgeries were randomized in two groups as L and LC. Group L received 0.125% levobupivacaine (10 ml) and group LC received 0.125% levobupivacaine (9 ml) with clonidine 1 ml (2µg/kg). Epidural top up given at the time of skin closure at the end of surgery and duration of postoperative analgesia, VAS score, time of rescue analgesics were observed in both the groups. The haemodynamic variables such as heart rate, systolic and diastolic blood pressure, respiratory rate and SPO_2 at various time intervals were measured. Any untoward side effects were noted in both groups. **Results:** Duration of analgesia was prolonged in group LC [434.61 mins] compared to group L (264.31 mins) which was statistically significant ($p<0.001$). Similarly clonidine group had less VAS score compared to control group. There was no significant change in the haemodynamic variables between the two groups. Hypotension and bradycardia was found in clonidine group compared to the control group, which was not statistically significant. **Conclusion:** Clonidine as an adjuvant to levobupivacaine prolongs the post-operative analgesia and decreases rescue analgesics requirement for lower limb surgeries.

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Key words: levobupivacaine, clonidine, postoperative epidural analgesia, lower limb surgeries

Introduction

Epidural analgesia is commonly supplemented with spinal anaesthesia and general anaesthesia to provide analgesia during intraoperative, postoperative period. Epidural techniques are used as primary anaesthetic for surgeries from mediastinum and lower extremities. Postoperative pain treatment should be integral component of the routine surgical and anaesthetic management not only for humanitarian reasons but also because it can help to reduce morbidity and complications as well as accelerate rehabilitation. Good perioperative analgesia is important to attenuate the surgical stress response. Post-operative pain relief can be provided by pharmacological and non-pharmacological methods. Non pharmacological methods are hypnosis, relaxation therapy, transcutaneous electrical nerve Stimulation and preoperative explanation and education.

The pharmacological methods are simple analgesics, Opioids NSAIDS, Patient Controlled Analgesia, Epidural or intrathecal, Local anaesthetic agents (wound infiltration, nerve blockade, epidural, intrathecal). Epidural anaesthesia is versatile technique used for providing both anaesthesia and analgesia in the postoperative period.

It provides intraoperative hemodynamic stability and it is proven to reduce perioperative stress response, and decreases complications and helps improving patient outcome helps in early mobilization of the patient by providing relief to postoperative pain and decreases the incidence of thromboembolic events. Epidural anaesthesia is a central neuraxial block technique with many applications. Epidural anaesthesia can be used as sole anaesthetic for procedures involving the lower limbs, pelvis, perineum and lower abdomen.

The advantage of epidural over spinal anaesthesia is the ability to maintain continuous anaesthesia after placement of an epidural catheter, thus making it suitable for procedures of long duration. This feature also enables the use of this technique into the postoperative period for analgesia, using lower concentrations of local anaesthetic drugs or in combination with different number of agents such as opioids, ketamine, alpha agonists be used as adjuvant to local anaesthetics that synergistically Act, thereby increasing the efficacy of the local anaesthetic drugs, decreasing the total required dose and toxic side effects of both groups of drugs.

The duration and the quality of analgesia is improved when local anaesthetic is combined with an alpha 2 adrenergic agonist as adjuvant. Both dexmedetomidine and Clonidine alpha 2 adrenergic agonists potentiate local anaesthetic effects and have analgesic properties.

Aims and Objectives

- To determine the safety and analgesic properties of clonidine in epidural anaesthesia for postoperative pain relief.
- To determine the duration of post-operative analgesia.
- Secondary objective to monitor the haemodynamic variability postoperatively

With clonidine as epidural adjuvant.

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Methods and Materials

Source of Data:

Patients undergoing surgeries in the lower limb under combined spinal and epidural block at Govt. Thiruvarur Medical College Hospital between July 2023 and December 2023 will be assessed for inclusion and exclusion criteria, and will be included in study after obtaining written informed consent.

Sample Size:

Calculation was done based on a reference study (reference below). Time to first morphine was taken as the primary outcome. Comparison of Group Levobupivacaine &Clonidine and Group Levobupivacaine needed a sample size of 26 in each group to detect an effect size of0.79 in the time to first morphine at a standard deviation (SD) of 5.6 Group Levobupivacaine and 8.3 in the Group Levobupivacaine& Clonidine with a power of 80% and alpha error of0.05. Hence a total of 52 patients will be recruited in this study

Two Means - Hypothesis testing for two means
Standard deviation in group I 5.6
Standard deviation in group II 8.3
Mean difference 5.5
Effect size 0.791367
Alpha error (%) 5
Power (1- beta) % 80
1 or 2 sided 2
Required sample size per group 26
Total sample size 52

Inclusion Criteria

- Patients undergoing elective lower limb surgeries under combined spinal and epidural Anaesthesia.
- Duration of surgery 1-2.30hrs.
- Age between 18to 60years
- Males and females
- ASA class 1and 2
- Patients who have given valid informed consent

Exclusion Criteria

- Patients not satisfying inclusion criteria.
- Patients with an allergy or sensitivity to local anaesthetics.
- Patients with pre-existing neurological disorders.
- Patients with bleeding disorders.
- Infection at lumbar injection site.
- Patients with diabetic foot.
- Patients who are unconscious or severely ill.
- Pregnant patients.
- Patients with history of severe cardiac, respiratory, hepatic or renal disease.

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Method of Collection of Data

This prospective observational study will be conducted in an orthopaedic theatre of the Government Thiruvarur Medical College Hospital after obtaining institutional ethical committee approval. Written informed consent will be obtained from all participants before enrolment in the study. The study will include patients aged between 18 and 60 yrs. who are to undergo elective lower limb orthopaedic procedures under

Combined spinal and epidural anaesthesia. Exclusion criteria will be diabetes mellitus, pregnancy, sepsis and peripheral vascular disease and bleeding disorders. No premedication will be given. On arrival in the operating room, baseline cardio respiratory parameters viz., Heart Rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP), Respiratory rate (RR) will be recorded.

A good intravenous access will be established using18GIV cannula. Preloading will be done with crystalloids (10ml/kg). A standard anaesthetic technique will be followed in all patients.

With the patient in sitting posture, after informing the procedure to the patient &under strict aseptic precautions, epidural space will beidentifiedatL2-L3interspace using 16G Touchy needle by loss of resistance technique. 18G epidural catheter will be threaded in a cephalad direction &3cmcatheterlength will be kept inside the epidural space. A test dose of 3cc of1.5% lignocaine with adrenaline (5µg/ml) will be given. Spinal anaesthesia will be performed at L3-L4interspace. Epidural catheter will be fixed and secured with tapes. After skin closure of incision, epidural top up with10ml levobupivacaine 0.125% (L), Levobupivacaine 0.125% [9 ml] plus clonidine 2microgram per kg (LC) will be initiated.

Patients with duration of surgery between 1-2:30 hours will only be included in the study. Unanticipated prolonged duration of surgeries will be excluded from the study. Time of incision will be noted. Intra-operatively the patient will be monitored with ECG, BP and SpO2

The following parameters will be monitored postoperatively:

Time of rescue analgesia
Duration of analgesia
Heart rate (HR)
Systolic blood pressure (SBP)
Diastolic blood pressure (DBP)
Mean arterial pressure (MAP)
Respiratory rate (RR)
Oxygen saturation (SpO2)
VAS score
Nausea and vomiting

Results

In both the groups more than half of the participants were males 61.5% and 69.2% in Group L and Group LC. Females were 38.5%% in Group L and 30.08% in Group LC. There was no difference in gender across the study groups with the p value of 0.56.

Mean (SD) age of the study participants was 39.08[6.29] years in Group Land 39.27[6.07] years in Group LC.

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Onset Of Analgesia

Onset of analgesia is faster in group LC 4.38 min SD of 1.10 when compared to group L 7.88min SD of 1.11 which was statistically significant with p value <0.0001

TABLE 1: ONSET OF ANALGESIA

GROUP		Mean	Std. Deviation	P value
ONSET OF ANALGESIA	Group L	7.88	1.11	<0.0001
	Group LC	4.38	1.10	

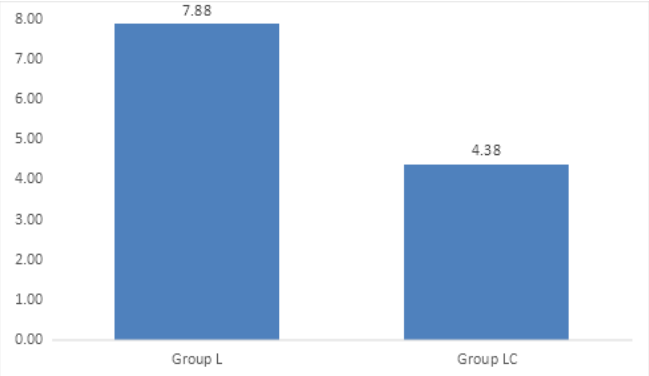

FIGURE 1: ONSET OF ANALGESIA

Mean value of heart rate between group L and group LC showed statistical significant difference at various time from the baseline with p value of <0.0001

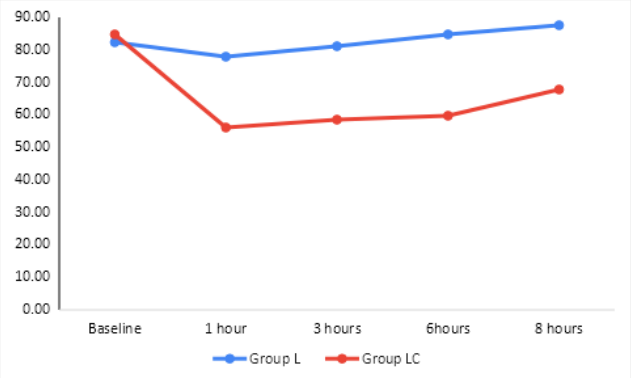

FIGURE 2: HEART RATE

Mean vas score in group L was 4.73[0.45] when compared to group LC 3.19[0.75] which was statistically significant with p value <0.0001

TABLE 2: VAS SCORE

GROUP		Mean	Std. Deviation	P value
VAS	Group L	4.73	0.45	<0.0001
	Group LC	3.19	0.75	

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Mean duration of analgesia in group LC 420.82 min when compared to 264.31 in group L which was statistically significant with p value < 0.0001

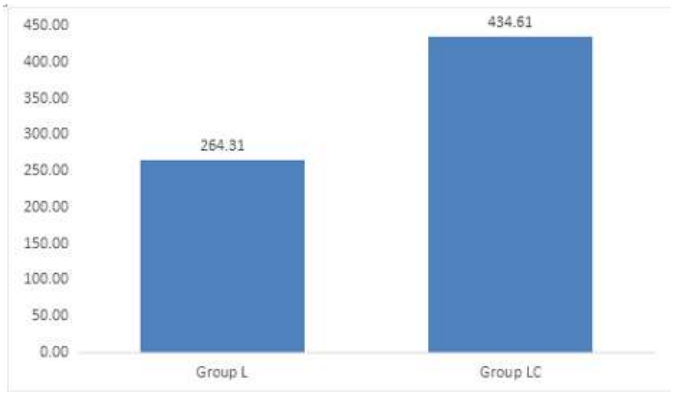

FIGURE 3: DURATION OF ANALGESIA IN MINS

Mean time for rescue analgesic requirement in group LC was 430.64 when compared to group L 276.04. There was statistical significant with p value < 0.0001

TABLE 3: TIME OF RESCUE ANALGESIA BETWEEN TWO GROUPS

GROUP		**Mean**	**Std. Deviation**	**P value**
TIME OF RESCUE ANALGESIA	Group L	276.04	28.53	<0.0001
	Group LC	445.38	38.99	

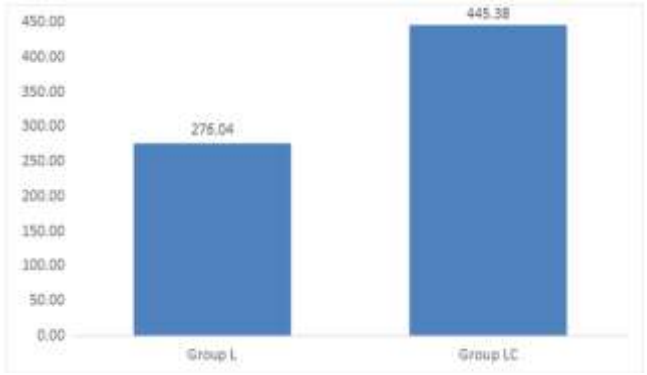

FIGURE 4: TIME OF RESCUE ANALGESIA

Discussion

Bupivacaine possesses an asymmetric carbon atom and can therefore take the form of two enantiomers, levo- and dex-bupivacaine. These have identical physical properties, but Chemical groups occupy different positions and therefore form different three-dimensional Relationships in the asymmetric environment of receptors and enzymes. This can result in differences in both receptor affinity and intrinsic activity of the enantiomers, leading to differences in their toxicities, distribution, protein binding, metabolism, and elimination. so levobupivacaine is preferred because it is associated with less toxicity Clonidine, a partial α2-

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adrenergic agonist, has a variety of different actions, including antihypertensive properties and the ability to potentiate the effects of local anaesthetics. This has been demonstrated in a variety of clinical settings and has been shown to result in the prolongation of the sensory blockade and a reduction in the amount or the concentration of local anesthetic required to produce postoperative analgesia. Previous work with epidural infusions has shown that 150 μg of clonidine, when added to bupivacaine 0.25% approximately doubled the duration of the analgesia produced.

In a study of epidural infusions of levobupivacaine in patients undergoing hip or knee surgery, significantly longer analgesia was achieved with levobupivacaine 0.25% than 0.125% or 0.0625%. The incidence of motor block was similar in the 0.125% and the 0.25% groups, and the latter provided the most effective pain relief as assessed by using VAS. The results of the present study demonstrate that epidural injection of 0.125% levobupivacaine is potentiated by the addition of clonidine. The increase in efficacy of the combination of clonidine and levobupivacaine compared with levobupivacaine alone was demonstrated by the increase in the time to first request for analgesia (from 5 to 13 h) and an accompanying decrease in the total morphine consumption. VAS scores were also lower in the combination group, but all three groups appear to have had reasonable pain relief, might be expected given that they all had free access to a PCA system. The clinical relevance of the small differences in pain scores is therefore open to question, but the improved analgesia may be contributed to the reduction in blood pressure in the clonidine groups. Postoperative nausea was less common in the clonidine groups postoperatively,and this probably reflects the lower consumption of morphine by these patient

Conclusion

Although clonidine lowered blood pressure and HR, the combination of clonidine and levobupivacaine, administered by the epidural route, was well tolerated and produced significantly improved postoperative pain management compared with either drug used alone. There was difference of 3 hours in the duration of analgesia between Group LC and Group L. Patients in Group LC (9 ml of 0.125 % bupivacaine +1ml of 2mcg/kg of clonidine had greater duration of postoperative analgesia when compared to group L (10 ml of 0.125% levobupivacaine] and this difference in duration was statistically significant.

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