# Original Article

# Levobupivacaine versus chloroprocaine with clonidine for early ambulation in short duration surgeries

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**Background:** Spinal anaesthesia is popular and commonly used worldwide. The main aim of anesthesia is to relieve pain during surgery. It has been shown that use of adjunct to spinal anaesthetics significantly improves sensory and motor blockage quality and duration.[1] The aim of the study is to compare Chloroprocaine along with clonidine and Levobupivacaine in their ability to ensure early ambulation in surgeries of short duration. **Material and Methods:** This randomized double blind study was carried out in patients using 1% Isobaric Chloroprocaine with clonidine with 0.5% Isobaric Levobupivacaine in short duration surgeries of lower limb, following approval by the Institutional Thesis committee and written informed consent from study participants. 60 patients was randomly divided in two groups in 1:1 allocation ratio, each comprising 30 patients. In Group 1, patient was given 0.5% of isobaric levobupivacaine 15 mg (3 ml) with 0.2 ml normal saline intrathecally, while, in Group2, 1% Isobaric Chloroprocaine 30 m g(3 ml) with 30 micrograms clonidine (0.2 ml) was given intrathecally. Total volume of 3.2 ml in each group was given intrathecally. Under all strict aseptic precautions, after skin disinfection and infiltrating with 2% lignocaine, lumbar puncture was performed with 25 gauge (Quincke needle) at L2-L3 interspace and drugs was given. The patients were evaluated for sensory (pin prick) and motor block(modified bromage). Hemodynamics was monitored and any side effects was noted. Results: A total of 60 patients were assessed. The Age, Weight, Gender, were comparable in both the groups . The onset of both sensory and motor block was faster is Group 2. The time to peak sensory block was also earlier in Group 2 but it attained a lower dermatomal blockade as compared to Group 1. The duration of both sensory and motor blockade was longer in Group 1. The two-segment regression time was also shorter in Group2 . The differences were statistically significant in all the parameter ($p<0.001$). The difference in hemodynamics was not found to be statistically significant when compared in both the groups. Conclusion: In this study, we found chloroprocaine with clonidine has early onset of both sensory and motor as well as shorter duration of 2 segment regression, sensory and motor effects when used intrathecally as compared to Levobupivacaine; making it suitable for shorter duration surgeries.

**KEY WORDS:** Chloroprocaine, levobupivacaine, spinal anesthesia, clonidine, regional anesthesia

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## INTRODUCTION

Spinal anesthesia is popular and commonly used worldwide. Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. The main aim of anesthesia is to relieve

pain during surgery. It has been shown that the use of adjunct to spinal anesthetics significantly improves quality and duration of sensory and motor blockade.[1]

Chloroprocaine ($C_{13}H_{19}ClN_2O_2$) is an ultra-short-acting, ester derivative of benzoic acid and has been used intrathecally in small doses (30–60 mg) and it was reliable for procedures of short duration. Addition of adjuvants such as clonidine, fentanyl, dexmedetomidine, and midazolam to chloroprocaine has been proved to prolong both motor and sensory effects of sub-arachnoid anesthesia.[2,3]

Levobupivacaine is its S(-)-enantiomer of racemic bupivacaine, has similar onset of sensory and motor block as bupivacaine, with less systemic toxicity, but it has shorter post-operative analgesic duration, compared to bupivacaine.[4]

Clonidine ($C_9H_9C_{l2}N_3$) is an imidazoline derivate and centrally acting alpha2-adrenergic agonist, with antihypertensive activity. Clonidine was first used in 1984 in epidural blocks.[3] Epidural clonidine in doses of 25–50 µg/h has been found to have beneficial effects in various study populations. De Kock *et al*.[5] recommended a dose of 15–45 mg of clonidine as optimal for supplementing spinal anesthesia.[3,5]

The lower doses of long-acting local anesthetic drugs have a variable effect, which is not suitable for surgery. The minimal effective dose of 0.5% levobupivacaine has been shown as 11.7 mg,[4] therefore, a 0.5% 2.5 ml drug was sufficient to conduct surgery. To rule out any discrepancy arising due to variation in the result, the volume of the comparing drugs was made even. Levobupivacaine is also isobaric, similar to that of chloroprocaine, so reducing another factor of discrepancy in the result. Therefore, we conducted the study on comparison of 1% isobaric chloroprocaine with clonidine with 0.5% isobaric levobupivacaine in short duration surgeries of lower limb. The aim of the study is to compare levobupivacaine and chloroprocaine with clonidine in their ability to ensure early ambulation in short duration surgeries. Hence, in this study, we compare onset of sensory and motor block, duration of sensory and motor block, peak height of sensory block, two-segment regression time, hemodynamic changes, and any side effects.

## METHODS AND MATERIALS

This randomized double-blind study was carried out in patients using 1% isobaric chloroprocaine with clonidine with 0.5% isobaric levobupivacaine in short duration surgeries of lower limb. Following approval by the Institutional Thesis committee, Department of Anaesthesiology, and Ethical committee, Rohilkhand Medical College and Hospital, Bareilly, 60 patients were randomly divided in two groups in 1:1 allocation ratio, each comprising 30 patients.

Consent and approval of patient for participation in study was taken. In our study, a total of 60 patients were included as calculated using the software Power and sample size program.[6] The sample size calculated in each group was 30. Patients with contraindication to spinal anesthesia, obesity (body mass index >30 kg/m$^2$), any neuropathy, patients receiving opioids for chronic analgesic therapy, allergy or intolerance to local anesthetics, and patients on beta-blocker or known cardiac dysrhythmia were excluded from the study.

Thorough pre-anesthetic check-up was done 1 day before the surgery and informed written consent for participation in the study was taken. The patients were randomly divided into two groups: Groups 1 and 2. In Group 1, the patient was given 0.5% of isobaric levobupivacaine 15 mg (3 ml) with 0.2 ml normal saline intrathecally, while, in Group 2, 1% isobaric chloroprocaine 30 mg (3 ml) with 30 micrograms clonidine (0.2 ml) was given intrathecally. Total volume of 3.2 ml in each group was given intrathecally. Drugs were prepared by anesthetist who was not being involved in observation. Patients were explained about the procedure of spinal anesthesia. They were kept nil per oral for 6 h and tablet ranitidine 1 mg/kg and tablet alprazolam 0.25 mg was given orally, the night before surgery.

On arrival in the operating room, after application of routine monitors (non-invasive blood pressure measurement, electrocardiography, and pulse oximetry), a peripheral 20 gauge intravenous cannula) was secured, the patient was preloaded with ringer lactate solution 15 ml/kg. Antiemetic prophylaxis was given using injection ondansetron 0.08 mg/kg and injection ranitidine 1 mg/kg.

The patient was made to sit for administration of spinal anesthesia. Under all strict aseptic precautions, after disinfecting the skin and infiltrating with 2% lignocaine, lumbar puncture was performed at L2-L3 interspace with 25 gauge (Quincke needle). After obtaining clear flow of cerebrospinal fluid, Group 1, the patient was given 0.5% of isobaric levobupivacaine 15 mg (3 ml) with 0.2 ml normal saline intrathecally, while Group 2 patient was given 1% isobaric chloroprocaine 30 mg (3 ml) with 30 mg clonidine (0.2 ml). Total volume of 3.2 ml in each group was given intrathecally within 10 s.

After completion of the spinal injection, the patient was immediately made to lie supine. The patient was evaluated for sensory and motor block, for every 2 min for the first 20 min, then every 3 min for next 30 min, then every 5 min for 40 min, and then every 10 min for 60 min and finally every 15 min until the sensory block has regressed to S1 dermatome. The patient was administered Injection midazolam 1 mg i.v. after spinal anesthesia. During the surgery, patient's pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and arterial oxygen saturation were recorded every 3 min for 30 min and then every 5 min until completion of the surgery.

The sensory level of the block was assessed in a caudal to cephalad direction with loss to pin prick sensation, and the C5-C6 dermatome was used as an unblocked reference point. The motor block was assessed using the modified bromage scale.

**Table 1: Demographic**

| Variables | Group 1 | Group 2 | *P*-value |
|---|---|---|---|
| | Mean±SD | Mean±SD | |
| Age (in years) | 39.63±13.14 | 38.27±13.85 | 0.697# |
| Gender | | | |
| Male | 27 (90%) | 26 (86.7%) | 0.687# |
| Female | 3 (10%) | 4 (13.3%) | |
| Weight (in kg) | 62.09±8.79 | 63.50±6.08 | 0.472# |

#Statistically not significant

**Table 2: Block quality**

| Sensory block | Group 1 | Group 2 | *P*-value |
|---|---|---|---|
| | Mean±SD | Mean±SD | |
| Onset | 6.89±1.97 | 3.90±1.12 | <0.001* |
| Time to peak | 14.26±3.19 | 7.70±1.56 | <0.001* |
| Duration | 312.71±51.94 | 101.00±14.99 | <0.001* |
| Two-segment regression | 119.31±34.87 | 76.63±15.69 | <0.001* |
| Motor block | | | |
| Onset | 10.91±3.47 | 4.40±1.28 | <0.001* |
| Duration | 249.57±38.34 | 91.80±14.47 | <0.001* |

*Statistically significant

**Table 3: Side effects**

| Side effects | Group 1 | Group 2 | *P*-value |
|---|---|---|---|
| TNS | 0 | 0 | |
| Hypotension | 4 | 3 | |
| Bradycardia | 2 | 2 | |
| PONV | 1 | 3 | 0.980# |
| Respiratory depression | 0 | 0 | |
| Pruritus | 0 | 0 | |
| Shivering | 3 | 4 | |

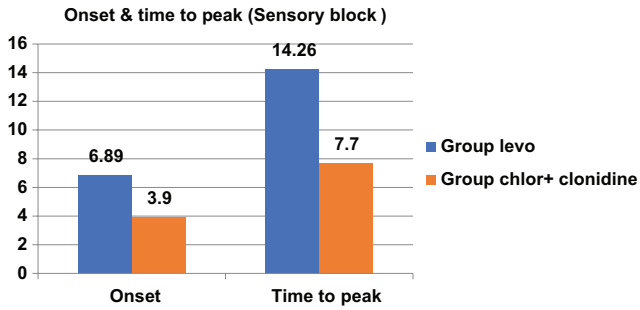
#Statistically not significant, PONV: Postoperative nausea and vomiting

Readiness for the surgery was defined as loss of pin prick sensation ≥T10 with modified bromage ≥2.

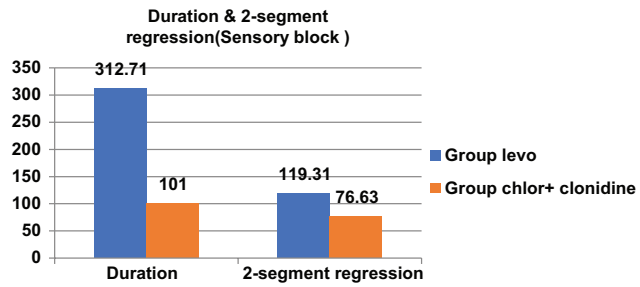
During surgery, evaluation of the motor block was suspended until the end of the procedure. If the patient complained of pain, injection diclofenac 75 mg i.v. was administered. If additional sedation is needed, midazolam 1 mg i.v. was administered. The total dose of any given medication was recorded. If the patient still felt pain, general anesthesia was provided and the case excluded from the study. Any complications, side effects and adverse effects up to 24 h postoperatively were noted.

## RESULTS

A total of 60 patients were assessed. The age, weight, and gender were comparable in both the groups [Table 1]. The onset of both sensory and motor blocks was faster in Group 2 [Table 2]. The time to peak sensory block was also earlier in Group 2 but it attained a lower dermatomal blockade as compared to Group 1 [Table 2]. The duration of both sensory and motor blockade was longer in Group 1 [Table 2]. The two-segment regression time was also shorter in Group2 [Table 2]. The differences were statistically significant in all the parameters ($P < 0.001$) [Table 2]. In Group 1, four patients had hypotension, and two had bradycardia while in Group 2, three patients had hypotension and two patients had bradycardia [Table 3]. Shivering was complained by three patients in Group 1 as compared from four in Group 2 [Table 3]. One patient complained of nausea in Group 1 while three patients had nausea in Group 2 [Table 3]. There was a greater fall in MAP after 6 min of spinal anesthesia in Group 1 as compared to Group 2, but the difference was not found to be statistically significant.




Group 1: Group levo, Group 2: Group chlor + clonidine

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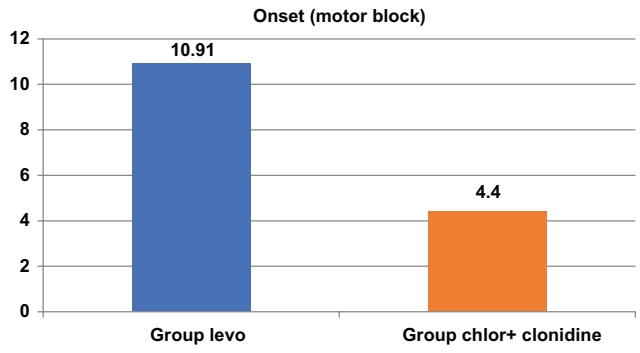


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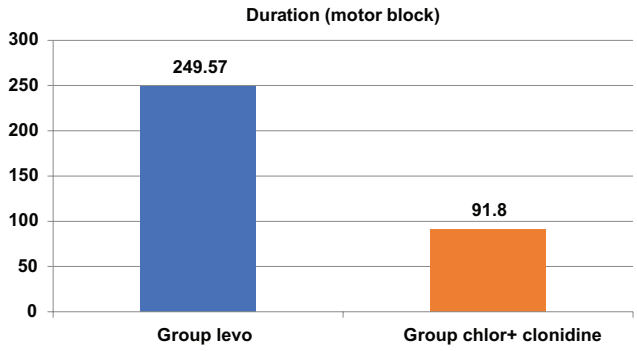


Group 1: Group levo, Group 2: Group chlor + clonidine

## DISCUSSION

A faster recovery for the patients not only benefits the patients but also reduces the burden from the already overburdened health-care services in our country. In the present world, day care surgeries have become the new trend as everybody wishes to resume to their normal activity as soon as feasible. As none of the local anesthetic agents can be used in all the surgeries, the time demands different a more suitably acting drug which covers all aspects of the surgery and does not over drive the requirement.

In our study, the dose of chloroprocaine was selected to be 30 mg as there were a limited number of studies conducted at this dosage. Most of the studies had been conducted on 40 mg and 50 mg. Given the limited number of studies, there was limited clarity on the feasibility of the usefulness of the selected drug dosage. Casati *et al*.[2] concluded that the chloroprocaine 30 mg had insufficient duration of spinal blockade and suggested adding adjuvants. Kopacz *et al*.[7] concluded that the 10 mg is a no effect dose, 20 mg and 30 mg produced adequate sensory anesthesia but limited motor blockade with occasional sacral sparing. Therefore, we selected the lowest dose of 30 mg 1% chloroprocaine 3 ml for patients planed for lower limb surgery, in view that this dose could be sufficient for surgical anesthesia. The mean heart rate rose following administration of spinal anesthesia in both the groups which was more in Group 1 but not statistically significant. After 21 min of anesthesia, the heart rate started to decline, but the decline was not statistically significant when compared to Group 2. This may be due to higher spinal level blockade in Group 1 than Group 2.

The mean onset time of sensory blockade, in our study, was significantly early in Group 2 (3.90 ± 1.12 min) as compared with Group 1 (6.89 ± 1.97 min) and the difference was statistically significant. The study conducted by other authors[8,9] on 0.5% levobupivacaine 15 mg had similar results. While few authors[10-12] using other doses of Levobupivacaine had a different mean onset sensory block due to the dose variations.

The mean time of peak height for sensory block was significantly early in Group 2 compared with Group 1 [Table 2] and the difference was statistically significant ($P < 0.001$) [Table 2]. The study by Gonter *et al*.[12] and Smith *et al*.[13] on chloroprocaine had

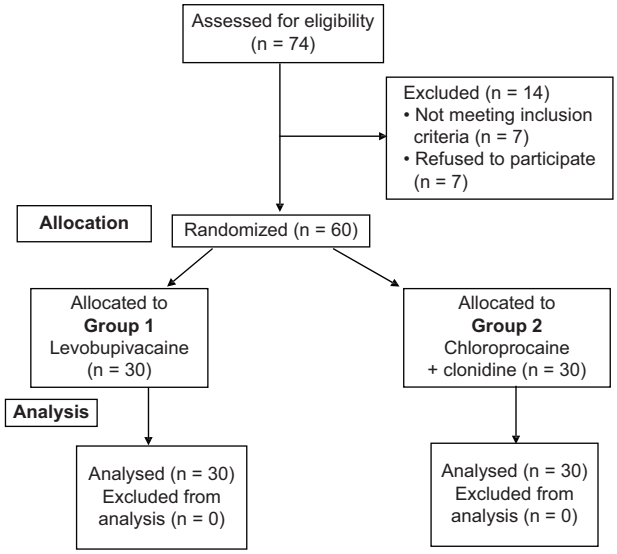


**Figure 1: Consort diagram**

a similar mean time of peak height for sensory block. The study on 40 mg chloroprocaine by other authors[14-18] had a different mean duration of two-segment regression of sensory block readily attributed to the higher dose used in the study. The study by Burke *et al*.[19] and Kataraia *et al*.[8] on 0.5% levobupivacaine 15 mg had a similar result, while Mantouvalou *et al*.[10] and Sahin *et al*.[9] had a different mean duration of two-segment regression, while Mantouvalou *et al*.[10] used L3-4 interspace for spinal anesthesia, Sahin *et al*.[9] had the patient in prone position for the entire duration of the surgery.

The time to onset of motor blockade was significantly less in Group 2 compared with Group 1 and the difference was statistically significant ($P < 0.001$) [Table 2]. To the best of our knowledge, there was no study on 1% chloroprocaine 30 mg, which showed the onset of motor block. The study on 0.5% levobupivacaine 15 mg by various authors[8,10,19,20] had similar result regarding onset of motor block.

The time of duration of motor block was significantly less in Group 2 compared with Group 1 and the difference was statistically significant ($P < 0.001$) [Table 2]. The study on chloroprocaine 30 mg by Gonter *et al*.[12] found that with chloroprocaine, the mean duration of motor block was 54 min and the gastrocnemius regained 90% of the power by 70 min when tested with isometric force dynamometer. Davis *et al*.[21] had mean duration of motor block of 65 min with 3% 30 mg chloroprocaine. The gastrocnemius regained 90% of the power by 69 min when tested with isometric force dynamometer. The study with 0.5% levobupivacaine 15 mg by various author[9,10,19,20] had similar result in view of duration of motor block. Similarly, in our study, we found an early recovery from motor block with chloroprocaine with clonidine as compared to levobupivacaine.

Hypotension was seen in both the groups and was treated with injection mephentermine 6 mg iv and 200–250 ml boluses of iv fluids. It was found to be statistically insignificant when compared between both groups.

## CONCLUSION

In this study, we found chloroprocaine with clonidine has early onset of both sensory and motor as well as shorter duration of two-segment regression, sensory and motor effects when used intrathecally as compared to levobupivacaine. Thus, we conclude that the use of chloroprocaine with clonidine is more suitable for short duration lower limb surgeries less than 2 h to ensure early ambulation on comparing with levobupivacaine. Levobupivacaine can be preferred for longer duration surgeries.

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