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Comparative evaluation of low-dose levobupivacaine and ropivacaine in patients undergoing inguinal herniorrhaphy under walking spinal anaesthesia as daycare surgery

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ABSTRACT

Background: Ropivacaine and levobupivacaine possess the property of sensory-motor dissociation. Hence these drugs allow a faster recovery of motor function and hence, these are potentially useful agents for walking spinal anaesthesia in daycare surgeries.

Patients and Methods: This is a prospective, double-blind, randomized study involving 120 adult ASA 1 and 2 patients who were randomly allocated into two groups. Group R (n = 60) received 7.5 mg 0.75% ropivacaine + 25 µg fentanyl + 1.5 ml sterile water. Group L (n = 60) received 5 mg 0.5% levobupivacaine + 25 µg fentanyl + 1.5 ml sterile water. Each solution was made to a total volume of 3 ml, administered intrathecally. Sensory and motor block characteristics, hemodynamic changes and postoperative recovery profile characteristics were noted. Paired/unpaired t-test and chi-square test were used wherever applicable for statistical analysis using SPSS version 15.0.

Results: Sensory block onset time and time to reach the maximal cephalic spread were comparable in both the groups, whereas time to the two-segment regression and time to first analgesic requirement were significantly shorter in group RF. Out of 60 patients in each group, 59 patients in group RF and 57 patients in group LF were MBS grade 5. Time to home discharge was also significantly shorter in group RF.

Conclusion: We concluded that both local anaesthetics could be used in the walking spinal technique; however, ropivacaine is preferred because of its favourable block characteristics and early ambulation time.

Keywords: levobupivacaine, ropivacaine, walking spinal anaesthesia, daycare surgery

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INTRODUCTION

Selective spinal anaesthesia (SSA) is a new regional anaesthesia technique in which minimal doses of intrathecal agents are used so that only the nerve root supplying the specific areas. This technique allows only the modalities that required to be anaesthetized are affected, dorsal column and motor function are mostly preserved such that patients are able to stand up and walk after the surgery. '*Walk in, walk out*' spinal with an extremely low dose of local anaesthetics and opioids for daycare procedures created the concept of walking spinal anaesthesia.[1]

Hyperbaric bupivacaine injection is the commonly used drug for spinal anaesthesia, causes a long-lasting motor block, hypotension, and bradycardia which eliminate it as the drug of choice among all the local anaesthetics for daycare surgeries. Hence the quest is on for an alternative local anaesthetics and combinations which can produce spinal anaesthesia of relatively shorter duration with better haemodynamic stability.

Ropivacaine and levobupivacaine are both pure S-enantiomers of bupivacaine. They are the two most recently introduced amide local anaesthetics which possess a lower risk of cardiotoxicity compared with racemic bupivacaine.[2] Due to their property of sensory-motor dissociation (ability to block sensory nerves to greater degree than motor nerve), these drugs allow a faster recovery of motor function and therefore are potentially useful agents for daycare anaesthesia.[3]

Fentanyl is commonly added to local anaesthetic solutions to improve anaesthesia and analgesia allowing the use of very low doses of local anaesthetics, enabling the aim of minimal motor blockade, early mobilization and ambulation, with minimal side effects. In this study, we compared equipotent doses of ropivacaine and levobupivacaine with the addition of fentanyl for the intraoperative characteristics and recovery profile of these drugs as walking spinal anaesthesia for inguinal hernia repair.

PATIENTS AND METHODS

This prospective, double-blind, randomized, controlled study was conducted after obtaining

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approval from the institutional ethical review board. After taking written informed consent, 120 patients (ASA grade 1 and 2), between 18-60 years of age, weighing 45-80 kg with a height between 150 to 180 cm, were randomly divided into two groups according to computer-generated random number list. The R group (n =60) received 1 ml of 0.75% ropivacaine + 0.5 ml of 25 microgram fentanyl + 1.5 ml sterile water. The L group (n = 60) received 1 ml of 0.5% levobupivacaine + 0.5 ml of 25 microgram fentanyl + 1.5 ml sterile water. Each of the solutions was made to a total volume of 3 ml.

All unwilling patients, known case of hypersensitivity to local anaesthetics, patients with medical complications like raised intracranial tension, anaemia, heart disease, severe hypovolemia, shock, septicaemia, hypertension, patients with coagulation disorders or on anticoagulant therapy, local infection at the proposed site of puncture for spinal anaesthesia and spinal deformities like kyphoscoliosis and lordosis, were excluded from the study.

Study drug was prepared aseptically just before intrathecal injection by another anesthesiologist. Therefore the investigator was blinded to the drug administered for intrathecal injection. Patients were placed in the lateral decubitus position. The drug solution was administered intrathecally in L3-L4 space after local infiltration of 2% lidocaine, without any barbotage. Patients were placed supine immediately after the procedure with the table maintained horizontally. Time of intrathecal injection was noted in both the groups and was labelled as '0 min' after intrathecal injection. Patients were given supplementary oxygen at 2-4 litres/min by nasal prongs.

Vital parameters were monitored at 5-minute intervals to the end of surgery. If systolic blood pressure fell below 80 mmHg or 20% below the baseline (hypotension), injection mephentermine 3 mg intravenous was given. If the heart rate fell below 50/min or 20% below the baseline (bradycardia), injection atropine sulphate 0.6 mg intravenous was given.

Sensory block was assessed every two minutes till two consecutive readings of sensory block remain the same (i.e. when the highest cephalic spread of sensory block has occurred), after which it was assessed at ten-minute intervals till the end of surgery. The onset of sensory block at T10 was noted, and the surgeon was allowed to start the surgery.

The modified Bromage scale was used to assess motor block by Breen *et al.*[4] at the same interval of time as that of sensory block. The quality of surgical analgesia was evaluated by an anesthesiologist, the surgeon and the patient him/herself and was graded as: excellent (no discomfort and no supplementary drug required), good (mild discomfort but no analgesia required), and poor (discomfort requiring rescue analgesia or general anaesthesia).

Quality of surgical field relaxation was classified as: excellent (complete relaxation), good (slight tightness but able to perform surgery), and poor (difficult to perform surgery). If adequate sensory and motor block was not attained even at twenty minutes after intrathecal injection of the drug, the patient was given general anaesthesia. Fentanyl 2 μg/kg intravenously was given as rescue analgesia.

All patients were monitored in the operative room for at least 60 minutes to keep a close watch on the hemodynamic and block characteristics, even if the surgery ended earlier. After completion of the surgery, the level of sensory block and motor block were recorded with the patient still on the operation table. This recording was labelled as the 'immediate post-operative' in the postoperative period. The patients were shifted to the Post Anaesthesia Care Unit (PACU), and they were assessed every 30 minutes for motor block until they attain complete motor recovery. Sensory block was also assessed every 30 minutes until regression of sensory block to S2 dermatome. Patients were evaluated half-hourly by Post Anaesthesia Discharge Scoring System (PADSS)[5] until a score of ≥9 was achieved, to check their readiness for discharge.

Time of request for the first analgesic was recorded. On the day after the surgery, patients were asked about any persistent symptoms like pain, nausea, vomiting, headache, backache, delayed voiding and neurologic symptoms such as tingling, numbness, and they were treated accordingly if any. They were also instructed to report if they suffered from any of the symptoms mentioned above within one week after the anaesthetic procedure. Follow up calls were made on the telephone to each patient.

In this study, the primary outcome variable was the time taken to ambulation. A sample size of 60 per group was calculated based on a difference in the time taken to ambulation between levobupivacaine and ropivacaine group, with a population variance of $(50)^2$, a two-sided alpha of 0.05, and a power of 80%.

Statistical Package for Social Sciences (SPSS) version 15.0 was used for statistical analysis. For comparing quantitative variables within each group across various follow-ups, we used paired t-test, and for comparing between the two groups, we have used the unpaired t-test. Qualitative variables between the two groups were compared using Chi-square/Fisher Exact test. A two-sided p-value of <0.05 was considered statistically significant.

RESULTS

Sensory block characteristics

As shown in Table 1, the sensory block onset at T10 was achieved in 6.33±1.37 minutes in Group L, compared to 5.92±1.48 minutes in

Table 1 Sensory block characteristics (in minutes)

Onset of sensory block	Onset at T10 level	Onset to maximal cephalic spread	2-segment regression time
Levobupivacaine (mean±SD)	6.33±1.37	14.33±2.56	94.52±10.60
Ropivacaine (mean±SD)	5.92±1.48	13.53±2.88	86.75±16.30
p-value	0.060	0.055	<0.001

SD: standard deviation

Table 2 Motoric block characteristics

	Group L	Group R	p-value
Maximum motoric block grading			
Grade 2	1 (1.72)	0 (0)	0.158
Grade 3	2 (3.45)	1 (1.67)	0.279
Grade 4	0 (0)	0 (0)	-
Grade 5	55 (94.83)	59 (98.33)	0.047
Onset to achieve maximum motoric block, minutes (mean±SD)	12.67±3.06	14.0±0.0	<0.01
Motoric block duration, minutes (mean±SD)	80.0±5.0	75.0±0.0	<0.01

SD: standard deviation

Table 4 Postoperative recovery profile characteristics (in minutes)

	Group L	Group R	p
Regression to S2	211.62±23.35	188.10±23.80	<0.001
First rescue analgesic	170.34±22.58	145.23±22.34	<0.001
Time to ambulation	230.91±26.52	210.30±23.42	<0.001
Time to urination	291.62±24.27	270.30±21.50	<0.001
Time to achieve PADSS ≥9	332.19±26.73	317.82±18.38	<0.001

Data displayed in mean±SD; SD: standard deviation; PADSS: Post Anaesthesia Discharge Scoring System

Group R (p =0.060). The mean time required for maximum cephalic spread of sensory block was 14.33±2.56 minutes in Group L, and 13.53±2.88 min in Group R and the results were comparable (p=0.055).

The time to 2 segment regression of sensory block was significantly shorter in Group R (86.75±16.30 minutes) compared to Group L (p <0.001). Hence, sensory block with ropivacaine was of quick onset and shorter duration than levobupivacaine. In Group L, two subjects failed to achieve sensory block at or above T10 dermatome and were given general anaesthesia. In comparison, all patients in Group R achieved sensory block at or above T10 dermatome (Figure 1).

Motoric block characteristics

Out of 58 subjects in Group L, 55 (94.83%) showed minimal motor blockade, i.e. MBS-5, whereas, in Group R, 59 patients (98.33%) had Grade 5 motor blockade, as shown in Table 2 (p=0.047). Only three patients in Group L and one patient in Group R showed motor block. The difference in duration of complete motor block and the total duration of motor block was statistically significant (p <0.01).

Hemodynamic parameters

We found no significant differences in both groups in terms of intraoperative and postoperative heart rate, systolic and diastolic blood pressure, and mean blood pressure (Figure 2). Intraoperatively, only two subjects developed hypotension and one subject developed bradycardia. In the recovery room, one patient in Group L developed hypotension, but none of the patients in either group developed bradycardia.

Postoperative recovery profile

We assessed the efficacy of levobupivacaine and ropivacaine in ambulatory settings by using the PADSS score. A PADSS score of ≥9 was considered satisfactory for discharge. Due to surgical constraints (lower abdominal surgery), patients in our study were encouraged to ambulate only under supervision, preferably with some assistance, once all three criteria for ambulation fulfilled, i.e. the

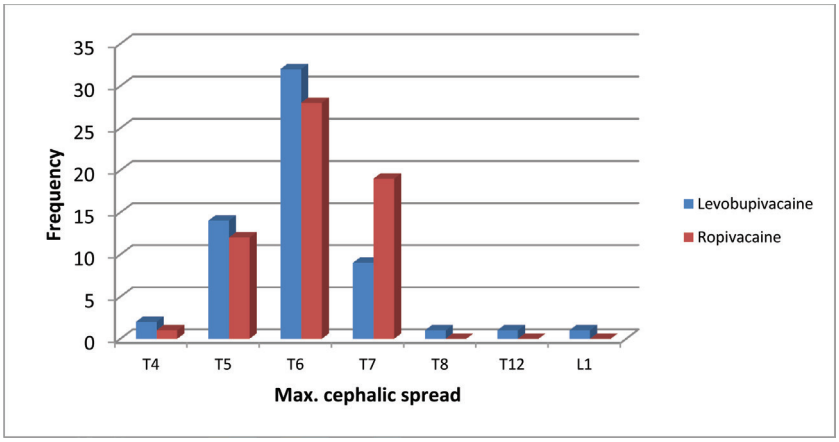

Figure 1 Distribution of maximum cephalic spread of sensory block

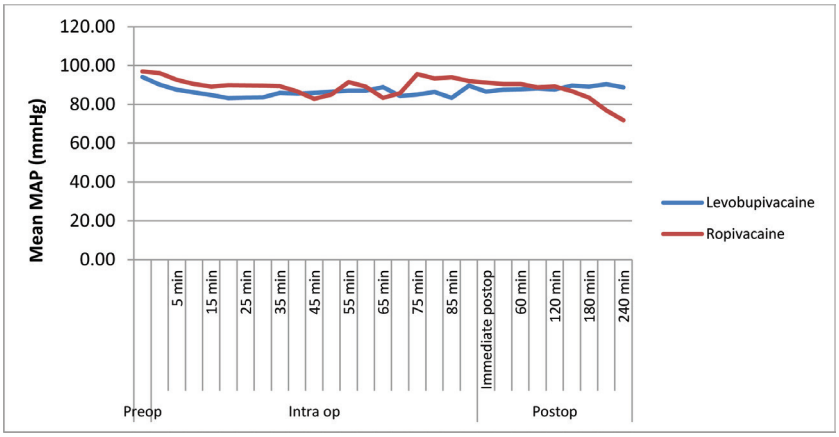

Figure 2 Intraoperative and postoperative changes in mean arterial pressure

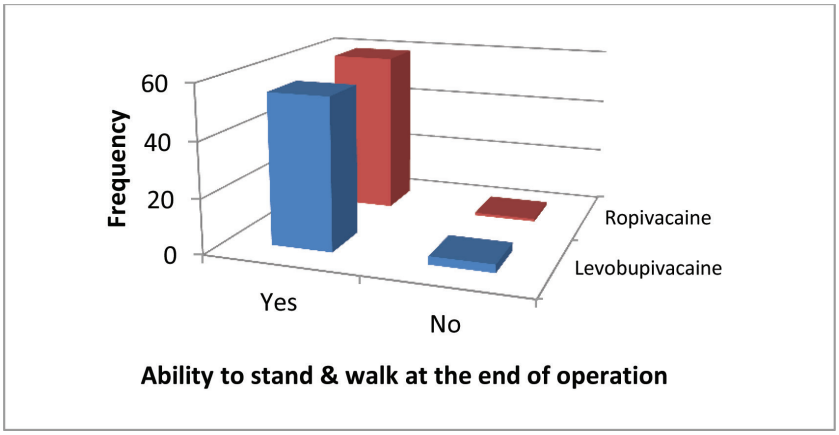

Figure 3 The ability to stand and walk at the end of surgery in both groups

sensory block regression to S2 dermatome, ability to plantar flexion and sense of proprioception returning in the great toe.[7]

As our study includes the effectiveness of walking spinal anaesthesia, we looked for the ability to stand and walk (ASW) at the end of the surgery and at 60 minutes after intrathecal administration, whatever is later. As shown in Figure 3, the ASW at the end of operation among both the groups showed no statistical significance.

As shown in Table 4, ropivacaine took less time for sensory block regression to S2 level compared to levobupivacaine (188.10±23.80 vs 211.62 ±23.35 minutes, respectively). In our study, patients were given rescue analgesia when VAS score was recorded ≥3, and the time to first rescue analgesia was noted. Patients experienced pain in the recovery room, probably due to the regression of sensory block below the line of the surgical incision. Patients in Group R experienced postoperative pain requiring rescue analgesia earlier (145.23±22.34 minutes) than patients in Group L (170.34±22.58 minutes).

Adverse events

In both groups, two patients developed hypotension, and one patient developed bradycardia. Three patients (5.00%) in the levobupivacaine group and four patients (6.67%) in the ropivacaine group complained of pruritus, which was managed with antihistamines. There was no statistically significant difference in regards to the intraoperative bradycardia and hypotension (Figure 4).

In the recovery room, one patient in levobupivacaine developed hypotension, but none of the patients in either group developed bradycardia. There was no need for sympathomimetics or anticholinergics in both the groups in the recovery room. None of the patients in either group complained of persistence of these symptoms. In our study, we found no evidence of any transient neurologic symptoms with both levobupivacaine and ropivacaine. There was no episode of postoperative nausea, vomiting pruritus, and shivering in both groups. No complaints of low back pain or dysesthesias in the lower limbs and symptoms suggested of post-dural puncture headache (PDPH) were reported in the postoperative follow-up period.

Quality of analgesia and surgical field relaxation

Quality of analgesia was categorized excellent among 45 patients (75%) in Group L and 51 patients (85%) in Group R out of 60 patients (p >0.05). It was good in 13 patients (21.67%) in Group L and nine patients (15%) in Group RF. The quality of analgesia was categorized poor in only two patients in Group L; no patient showed poor quality of analgesia in Group R (p >0.05).

Surgical field relaxation was excellent in 45 patients in Group L and 47 patients in Group R. It was good in 13 patients in each group and poor in 2 patients in Group L (converted to general anaesthesia), and no patient showed poor quality of relaxation in Group R (p >0.05).

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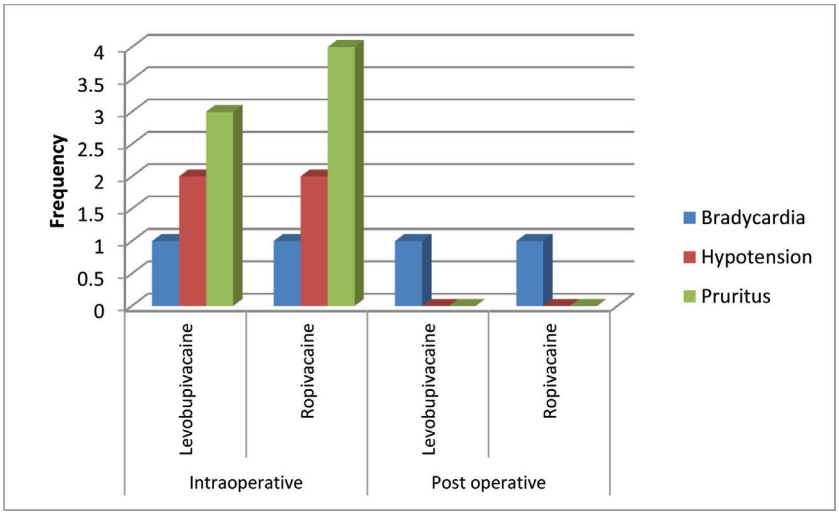

Figure 4 Incidence of intraoperative and postoperative adverse events

DISCUSSION

Ambulatory surgery is rapidly growing worldwide due to recent advances in anaesthesia and surgical practices. The benefits of ambulation of patients at the earliest and discharge on the same day are, reduced risk of hospital-acquired infection, speedier recovery, and better use of resources, shorter hospital stay, and hence better usage of high-cost operating rooms.[6]

To produce spinal anaesthesia for ambulatory inguinal hernia repair, increasing the dose of long-acting local anaesthetics will delay home readiness. Combining intrathecal opioids with local anaesthetics might be beneficial for achieving a higher sensory block and minimal motor blockade, without increasing the dose of local anaesthetics, and so early mobilisation. The use of low doses of local anaesthetics has allowed patients to achieve traditionally accepted discharge criteria.[1]

Nowadays, with shifting focus to daycare anaesthesia and ambulatory surgeries, more and more surgeries are being performed in a daycare setting. In that context, a study is needed to compare newer local anaesthetics, especially to achieve criteria's of walking spinal anaesthesia successfully. There are many studies for walking epidural analgesia, but not many studies in the context of walking spinal anaesthesia and hence, till now a topic of research. More and more researches are required in support of this with various local anaesthetics so that it can be used daily in future.

Ropivacaine was synthesised simultaneously with bupivacaine by Af Ekenstam almost 50 years ago and is first launched in 1996. It is the first pure S-enantiomer local anaesthetic to be clinically introduced. Several experimental and clinical studies confirm that ropivacaine has a lower and different toxicity profile compared to bupivacaine. The interpretation of a less intense motor block (differential motor block) and more rapid recovery of sensory and motor functions with intrathecal ropivacaine have been the subject of some controversy. Some have argued that this is a specific drug effect of ropivacaine, demonstrating an increased separation of the sensory-motor blocking effects by its lower lipid solubility[2] and therefore it blocks nerve fibres involved in pain transmission (Aδ and C fibres) to a greater degree than those controlling motor function (Aβ fibres). Others claim that the observed differences are merely due to reduced potency of ropivacaine compared with bupivacaine.[7]

Levobupivacaine is an amide, local anaesthetic, the pure S (-)-enantiomer of racemic bupivacaine. Its mechanism of action and pharmacodynamics are similar to those of bupivacaine. Its high lipid solubility makes it more potent than lower lipid-soluble agent ropivacaine and results in a longer duration of action.

As we were using these drugs for ambulatory surgery, we chose a dose which ensured the adequate duration of analgesia above T10 without prolonging duration and degree of motor blockade. In the present study, we estimated the local analgesic dose to be 5 mg for levobupivacaine and 7.5 mg for ropivacaine. We added 25 mcg of Fentanyl in both the groups. The effect of adding fentanyl to both the groups is thought to be important for achieving anaesthesia with less motor blockade using a smaller amount of local anaesthetic and providing early postoperative ambulation.[8]

Moiza *et al.*[9] reported that 8 mg levobupivacaine or 12 mg ropivacaine are acceptable alternatives to 8 mg bupivacaine when limiting spinal anaesthesia at the operative side for inguinal repair. The use of a 1.5:1 equipotency ratio between ropivacaine and levobupivacaine resulted in a shorter duration of spinal anaesthesia with ropivacaine.

Similar results have also been reported by Danelli *et al.*[10] The result of this study seem to confirm the validity of the 1:1.5 equipotency ratio between levobupivacaine and ropivacaine. For this reason, we considered both an equivalent and a supposed equipotent dose of 5 mg levobupivacaine as compared to 7.5 mg of ropivacaine.

Rate of onset and extent of the sensory block to pinprick showed no statistically significant difference between the two groups concerning the onset time to T10, the maximum extent of cephalic spread, and the time to maximum spread. These results are comparable with the results of a study done by Mantouvalou *et al.*[11] where they found no significant differences in onset and time taken for the maximum level of the sensory block between levobupivacaine and ropivacaine group($p>0.05$).

These results are also similar to the study conducted by Luck *et al.*[12]

There is a significant faster two-segment regression, and after that regression, to S2 level in the ropivacaine group as compared to the levobupivacaine group. The results are in accordance with previous studies that also reported the time taken to two-segment regression shorter in ropivacaine compared to levobupivacaine.[8,11,12]

In this study, out of 60 patients, 55 patients in the levobupivacaine group as compared to 59 patients in the ropivacaine group showed minimal motor blockade. We believe that the plausible explanation of the absence of motor block in our study may be the small volume of local anaesthetics used intrathecally.[8] Camorcia *et al.*[13] reported similar findings, where they concluded that the relative motor blocking potency ratio of ropivacaine and levobupivacaine was 0.83, showing significant trends for a greater motor block with levobupivacaine than ropivacaine.

The total duration of motor block was also significantly shorter in the ropivacaine group (75 min) in comparison to the levobupivacaine group ($p<0.01$). Luck *et al.*[12] also found that the degree and duration of motor block were significantly less in the ropivacaine group compared with the other two groups. Mantouvalou *et al.*[11] found the fact that regression of motor block from one stage of focus Bromage scale to the previous one was significantly faster in the ropivacaine group as compared to the levobupivacaine group. Similar results were found in this study. The values in our research are in line to a study by Casati *et* al.[14] that reported faster complete regression of spinal anaesthesia in patients receiving ropivacaine.

In our study, the administration time of rescue analgesia was 170.34±22.58 minutes in the LF group while it was 145.23±22.34 minutes in the RF group ($p <0.001$). Camorcia *et al.*[13] determined that the relative analgesic potency ratio for ropivacaine to levobupivacaine was 0.80 (0.70-0.92), which supported our findings. A study conducted by Taspinar *et al.*[8] also showed similar results.

The mean time for ambulation was shorter for the R group (210.30±23.42 minutes) than for the L group (230.91±26.52 minutes). Our study is in accordance with Luck *et al.*[12] who calculated time to mobilisation between L and R to be statistically significant.

Urinary retention after spinal anaesthesia may delay home discharge. A long-lasting sensory block may affect the voiding capability, which requires regression of the sensory block to at least a dermatome level of S3 to obtain normal detrusor function.[15] In our study, time to first micturition was longer (291.62±24.27 minutes) in Group L than Group R (270.30±21.50 minutes). Adjuvants such as fentanyl facilitate reductions in the dose of local anaesthetics and prolong sensory block without delaying time to void. Patients in Group R attained PADSS ≥9 (home readiness) earlier than patients in Group L, ($p<0.001$).

Cappelleri *et al.*[16] in their study found that the resolution of spinal block and time to first voiding was significantly shorter with ropivacaine than levobupivacaine ($p <0.05$). Similarly, time to home discharge was also shorter with ropivacaine ($p <0.05$), supporting the findings in our study.

Our results showed that the patients were haemodynamically stable in both the groups except a few episodes of bradycardia and hypotension. We have added opioids to the local anaesthetic solutions and applied them in over 15-20 seconds to minimize the intraoperative haemodynamic effects, and in this way, we can give a low dose of local anaesthetic with minimum hemodynamic side effects.

There was no need for sympathomimetics or anticholinergics in both the groups in the recovery room. None of these patients complained of pruritis postoperatively. In our study, we found no evidence of any transient neurologic symptoms with both levobupivacaine and ropivacaine. There were no episodes of postoperative nausea, vomiting or shivering in both the groups.

CONCLUSION

Ropivacaine produces a spinal block which has sensory block onset characteristics similar to equipotent doses of levobupivacaine, but with a less intense motor block. Both the sensory and motor blocks are also subject to a more rapid recovery with ropivacaine compared with levobupivacaine. In contrast, levobupivacaine has more analgesic potency as the administration time of rescue analgesia for levobupivacaine is more as compared to ropivacaine. Secondly, levobupivacaine provides prolonged and more intense motor blockage as compared to ropivacaine. We suggest that both anaesthetics can be used in the walking spinal technique; however, ropivacaine may be preferred because of its block characteristics and early ambulation time, for short procedures. Nowadays, with the focus shifting to daycare anaesthesia and ambulatory surgeries, further studies are required to compare these drugs in other doses with different adjuvants.

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