Original Article

Comparison of block characteristics of intrathecal isobaric levobupivacaine versus isobaric ropivacaine for infra-umbilical surgeries in school-age children: A prospective randomised double-blind study

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ABSTRACT

Background and Aims: Levobupivacaine and ropivacaine are effective local anaesthetic drugs used in regional anaesthesia with low cardio-neurotoxicity profile than bupivacaine, but comparative studies are limited in children. So, we compared these two drugs intrathecally to study their efficacy and safety in school-age children. **Methods**: This study was carried out in 60 American Society of Anesthesiologists class I, II and III patients aged 6–12 years, of either sex undergoing infra-umbilical surgeries. After institutional ethical committee approval and written informed consent, the patients were randomly divided into two groups. Group A received isobaric levobupivacaine (0.5%, 0.3-0.4 mg/kg), whereas group B received isobaric ropivacaine (0.5%, 0.5 mg/kg) intrathecally. Fentanyl (0.2 μg/kg) was used as an adjuvant in both the groups. Onset, peak and duration of sensory and motor blockade, duration of post-operative analgesia, time for micturition, perioperative haemodynamic parameters and complications were compared. **Results**: Onset and peak of sensory and motor block were earlier in group A. Significantly longer duration of sensory and motor block was achieved in group A (251 ± 41 min, 201 ± 40 min) compared to group B (211 ± 21 min, 102 ± 16 min) ($P < 0.001$). The time to first rescue analgesic was also significantly prolonged in group A (270 ± 39 min) compared to group B (233 ± 18 min) ($P < 0.001$). Time to micturition was much early in group B (157 ± 27 min) compared to group A (225 ± 31 min) ($P < 0.001$). **Conclusion**: Intrathecal isobaric levobupivacaine and ropivacaine with fentanyl produces effective surgical anaesthesia and postoperative analgesia without any adverse effects. Early regression of sensorimotor blockade makes ropivacaine better in comparison to levobupivacaine for short infra-umbilical surgeries in children.

Key words: Fentanyl, intrathecal, levobupivacaine, ropivacaine, school-age children

INTRODUCTION

Regional anaesthesia plays a vital role in modern paediatric anaesthesia practice. Spinal Anaesthesia (SA) is regaining popularity in recent times due to advanced paediatric equipment and skill enhancement. It is an easy and safe technique in patients with difficult airway and provides excellent analgesia with good muscle relaxation.[1] SA has good control on cardiovascular and stress responses, provides good postoperative pain relief, shortens the hospital stay and is thus cost-effective.[2]

An important concern with SA in children is the risk of local anaesthetic (LA) toxicity because of thinner and less myelinated nerve fibres, immature hepatic metabolism and low plasma proteins.[3] Introduction of safer LA drugs like levobupivacaine and ropivacaine and understanding their pharmacokinetics, dynamics

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and toxicities is the key to success for modern regional anaesthesia techniques.[4] Levobupivacaine and ropivacaine are S (-) enantiomers of bupivacaine with a safe neuro-cardiotoxic profile.

Short duration of surgical anaesthesia is one of the major drawbacks of paediatric SA. To overcome this, adjuvants are added with LA drugs.[5-7] Fentanyl is a popular opioid adjuvant as it shortens the onset time and prolongs the duration of sensory block.[8]

Although data are available on the individual use of levobupivacaine and ropivacaine, comparative studies between these two drugs in children are still lacking. The aim of our study was to compare the efficacy (onset, peak level, and duration of sensory and motor block), duration of postoperative analgesia and safety of the isobaric form of these two drugs.

METHODS

This prospective randomised double-blind parallel group comparative study was conducted from 10-02-2020 to 10-02-2021 after institutional ethical committee approval and Clinical Trials Registry-India (CTRI) registration. Written informed consent of either the patient's mother or father and assent from children above 8 years was taken. Sixty patients of either sex aged 6–12 years of American Society of Anesthesiologists (ASA) class I, II or III posted for infra-umbilical surgery (appendicectomy, herniotomy, orchidopexy etc.) were included. Parent refusal, allergy to study drugs, those with coagulation defects, local site infection, raised intracranial pressure and severe hypovolaemia were excluded. The primary outcome of the study was to compare the onset, peak level and duration of sensory and motor block, whereas the secondary outcome was to observe the duration of postoperative analgesia, analgesic consumption in the first 8 hours, perioperative haemodynamic changes, side effects and complications.

Patients were randomised 1:1 using computer-generated series into two groups of 30 each. Allocation concealment was done using sealed opaque envelope technique and study drug was prepared by an anaesthesiologist not involved in the study. Group A received intrathecal isobaric levobupivacaine 0.5% (<15 kg: 0.4 mg/kg, >15 kg: 0.3 mg/kg) with fentanyl (0.2 μg/kg) and group B received intrathecal isobaric ropivacaine 0.5% (0.5 mg/kg) with fentanyl (0.2 μg/kg) [Figure 1].

Thorough pre-anesthesia check-up was done a day prior to surgery that is, detailed history, general physical examination, systemic examination, airway assessment and lumbar spine examination. Patients were kept nil by mouth 6 hours for light meal, 4 hours for human milk, 2 hours for clear fluids before surgery. The anaesthesia plan was explained to the parents.

One hour prior to surgery, Eutectic mixture of LA (EMLA) and occlusive dressing were applied at sites of lumbar puncture and venipuncture. Oral midazolam 0.5 mg/kg (Inj. midazolam mixed with honey) was given to all the patients 30 minutes prior to surgery in preoperative room.

Anaesthesia workstation, equipment for subarachnoid block (SAB) and equipment for resuscitation were kept ready. Patient was shifted to operation room (OR) and counseled regarding the procedure. Multipara monitor was attached. Baseline heart rate (HR), blood pressure (BP) and oxygen saturation (SpO2) were recorded and monitored throughout the procedure. Intravenous line was secured with 22G/24G intravenous (IV) cannula and injection ringer lactate was administered according to Holliday-Segar formula. Proper counseling, use of pre-anesthetic oral midazolam and EMLA were sufficient in cooperative patients to perform SAB. Uncooperative patients were sedated with sevoflurane via mask and Jackson Rees/ Bain's circuit before SAB to make them calm and this was turned off immediately after spinal block.[9]

The patient was put in lateral decubitus position. With all aseptic precautions, lumbar puncture was done in the midline at L4-L5 intervertebral space with 27G Quincke cutting spinal needle (length: 60 mm/90 mm, needle hub dead space: 0.02 ml). After confirmation by free aspiration of cerebrospinal fluid, the predetermined volume of the study drug was injected intrathecally and the patient was turned supine. Caution was taken not to elevate the lower extremities to avoid high/ total SA. Lumbar puncture was done by the same anaesthesiologist in all the patients.

Sensory and motor block were assessed every 2 minutes till complete blockade. Sensory block was assessed with bilateral nontraumatic pin prick with a 23-gauge blunt needle and the facial expression or child's movement was observed. Onset of sensory block [when patient feels dull sensation to prick/pinch at T10 level], time for complete sensory block [complete loss of sensation to prick/pinch (temperature, touch

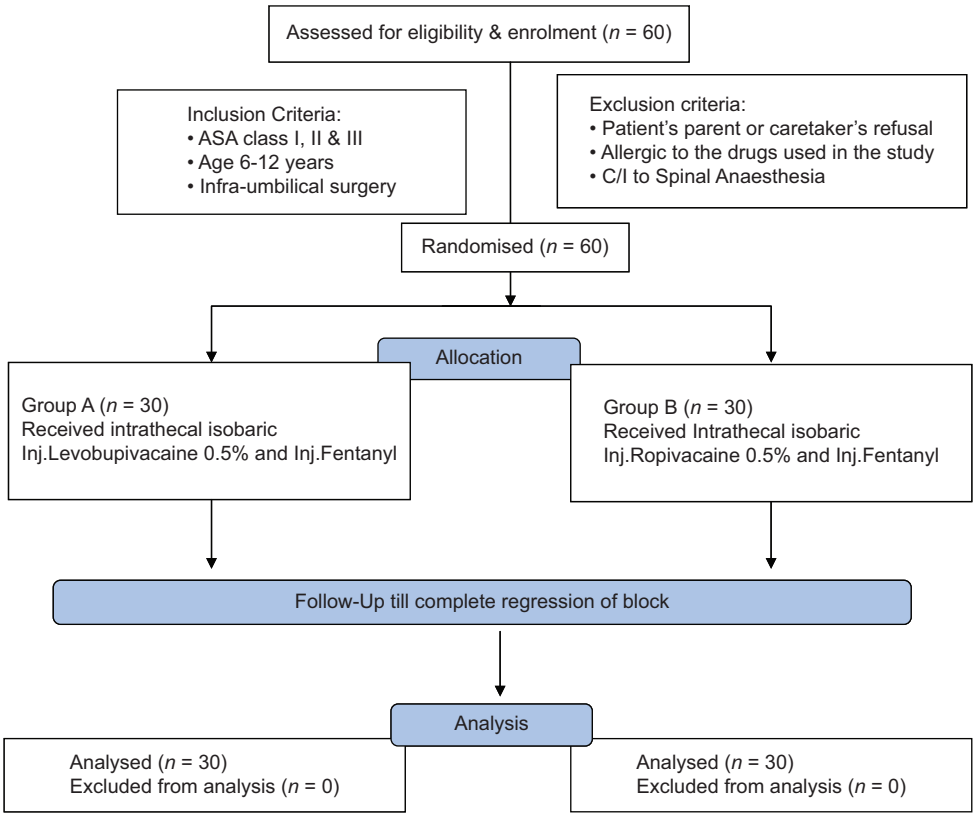

Figure 1: CONSORT chart of patients recruited and analysed. ASA: American Society of Anesthesiologists; C/I: Contraindication

and pain)], peak level [highest dermatome showing sensory blockade] and total duration of sensory block [time interval between spinal drug injection and complete regression of sensory block up to lateral side of foot (S1)] were noted. Sensory block assessment was done with subjective pain scale in children who could express verbally (score 0: Sharp pain, score 1: Touch sensation only, score 2: Not even touch sensation) and observational pain scale in children who could not express verbally (based on rise of blood pressure, heart rate and crying) [Table 1]. Motor block was assessed by modified Bromage score (1: complete block, 2: almost complete block, 3: partial block, 4: detectable weakness of hip flexion, 5: no detectable weakness of hip flexion, 6: able to perform partial knee bend).

The surgeon was allowed to start surgery once the sensory block level of T10 and modified Bromage score of 2 was achieved. It was considered as a failed SAB if the peak sensory block level was below T10 and modified Bromage score <4 after 10 minutes of SAB. These patients were given general anaesthesia (GA) and excluded from the study.

Postoperative HR, BP and SpO2 were noted at 30 minutes, 1 hour, 2 hours, 4 hours, 6 hours and so on. Sensory and motor block were also assessed every 30 minutes after surgery. The study was discontinued after 8 hours or till complete recovery of motor and sensory function, whichever was earlier.

Table 1: Observational pain scale (for sensory block assessment)

	Criteria	Score
Rise in Heart Rate	>10%-<20% of preoperative level	0
	20% to 30% of preoperative level >30% of preoperative level	1 2
Rise in Blood Pressure	>10%-<20% of preoperative level	0
	20% to 30% of preoperative level >30% of preoperative level	1 2
Crying	Not crying	0
	Crying but responds to tender loving care	1
	Crying and does not respond to tender loving	2

If the child complained of pain or observational pain score ≥3, intravenous paracetamol infusion (15 mg/kg) was given as rescue analgesic according to institutional protocol and this duration from spinal injection to first rescue analgesic consumption was noted as duration of analgesia. All patients were observed for side effects like nausea, vomiting, shivering and complications like hypotension, bradycardia, haematoma, local anaesthetic systemic toxicity and urinary retention.

The sample size was calculated based on a study by Soni *et al*.[10] comparing mean time to complete motor block in the two groups. Pooled standard deviation (SD) (σ) =0.79, Difference of Means (δ) = 0.9, Type I error (α) =5%, Z_{α} =1.96 and Type II error (β) =5%, $Z_{1-\beta}$ =1.65 were calculated. Substituting in formula, assuming 95% power and 95% confidence interval, the minimum required sample size was 21 in each group. We took 30 patients in each group to account for dropouts.

$$\text{Sample size N} = \frac{2(z_{\alpha} + z_{1-\beta})^2 \sigma^2}{\delta^2}$$

Data was recorded in Microsoft Excel software. Group comparisons were made using t-test/Mann–Whitney U test for normally/non-normally distributed continuous data, respectively. Chi-square test was used for categorical variables. Statistical Package for Social Sciences (SPSS) version 23 was used for analysis. $P < 0.05$ was taken as the cut-off for statistical significance.

RESULTS

In our study, the demographic characteristics age, sex and weight were comparable. Significant differences were not seen between the two groups in terms of ASA class, type, and duration of surgery [Table 2].

The onset of block, time for complete sensory and motor block were early in group A [Table 3] and the differences were significant ($P < 0.001$). Level of peak sensory block was T6.6 (T6-T8) and T6.7 (T6-T8) in group A and group B, respectively, which was comparable.

All the patients in group A attained modified Bromage score 1 at peak motor block, whereas in group B 90% patients attained score 1 and 10% patients attained score 2 and there was no significant difference between the two groups.

Duration of sensory and motor blockade and duration of analgesia were higher in group A compared to group B [Table 3] and the differences were statistically significant ($P < 0.001$).

In the first 8 hours, 90% of patients in group A and 83.3% in group B received single rescue analgesic dose (Inj. Paracetamol 15 mg/kg IV) and remaining 10% of patients in group A and 16.7% in group B required two rescue analgesic doses [Figure 2].

Table 2: Comparison of demographic characteristics between the two groups

	Group A	Group B	*P*
Mean Age (year)[a] (mean±SD)	9.70±1.91	9.57±1.94	0.787
Sex (Male/Female)[b] (number)	23/7	25/5	0.519
Weight (kg)[c] (mean±SD)	28.07±7.08	27.97±7.93	0.959
Duration of surgery (min)[a] (mean±SD)	38.33±5.83	38.47±5.41	0.812

Values expressed as mean (SD) or number as analysed by Wilcoxon Mann-Whitney U test[a], Chi-square test[b], *t*-test. [c]*P*<0.05 is significant. SD: Standard deviation

Time to micturition was earlier in group B (157.70 ± 27) compared to group A (225 ± 31) and the difference was significant ($P < 0.001$) [Table 3].

Baseline haemodynamic parameters were comparable between the two groups. MAP and HR in both groups showed change at different time-points [Figure 3]. Though the change over time within each group was significant, none of the patients developed severe hypotension and bradycardia.

None of the patients needed additional sedation, GA, or airway management. Postoperatively, two patients in group A and one patient in group B suffered from vomiting, which was treated with IV ondansetron (0.08 mg/kg) and two patients in each group developed shivering, which was managed with warm blankets.

DISCUSSION

Isobaric levobupivacaine and ropivacaine provide adequate surgical anaesthesia and postoperative analgesia without haemodynamic perturbations. It can be achieved with small doses of safer LA, alleviating the side-effects of polypharmacy. The flexibility of a child's spine, easy palpation of intervertebral space with wide interpedicular diameter at lumbar level makes paediatric spinal anaesthesia an effortlessly safe technique.

Levobupivacaine, due to its faster protein binding, has minimal unwanted effects and toxicity. Ropivacaine shows sensorimotor block differentiation at low dose and has lesser toxicity because of its poor lipid solubility. So, these two LAs are considered as safe alternatives to bupivacaine.

Few studies have showed that adding opioid as adjuvant provides dose-sparing effect of levobupivacaine and ropivacaine with improved quality of block and less haemodynamic variations during the intraoperative period.[11]

Table 3: Comparison of block characteristics between the two groups

	Group A	Group B	*P*
Onset of sensory block (min)[c] (mean±SD)	2.10±0.26	2.63±0.33	<0.001
Peak level of sensory block[b] (block level)	T6.6 (T6-T8)	T6.7 (T6-T8)	0.682
Complete sensory block (min)[c] (mean±SD)	5.26±0.50	6.59±0.45	<0.001
2-segment regression time (min)[c] (mean±SD)	85.53±5.93	80.17±12.77	0.043
Duration of sensory block (min)[a] (mean±SD)	251.07±41.87	211.67±21.24	<0.001
Onset of motor block (min)[c] (mean±SD)	2.24±0.24	3.45±0.33	<0.001
Complete motor block (min)[c] (mean±SD)	10.92±1.01	12.48±0.75	0.237
Modified bromage scale at peak motor block[d] (percentage)	30 (100%) 0 (0%)	27 (90%) 3 (10%)	0.237
Duration of motor block (min)[c] (mean±SD)	201.50±40.82	102.70±16.81	<0.001
Duration of analgesia (min)[c] (mean±SD)	270.43±39.84	233.83±18.02	<0.001
Rescue analgesic doses in first 8 hours[d] (percentage)	One dose: 90% Two doses: 10%	One dose: 86.7% Two doses: 13.3%	0.706
Time of micturition (min)[c] (mean±SD)	225.50±31.68	157.70±27.39	<0.001

Values expressed as mean (SD), level or percentage as analysed by Wilcoxon-Mann-Whitney U test[a], Chi-square test[b], *t*-test[c], Fisher's Exact test[d]. *P*<0.05 is significant. SD: Standard deviation

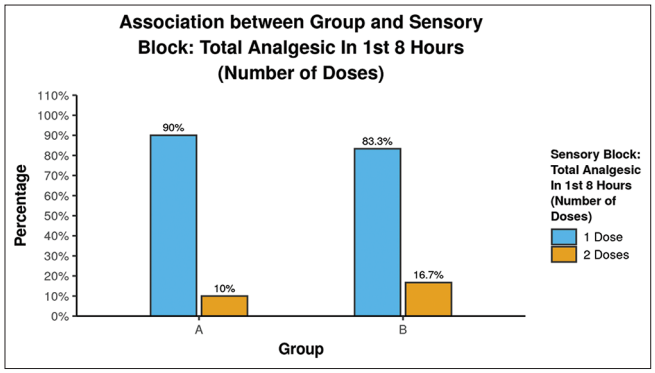

Figure 2: Bar graph depicts the total number of analgesic doses consumed in first 8 hours in both the groups (in terms of percentage of patients)

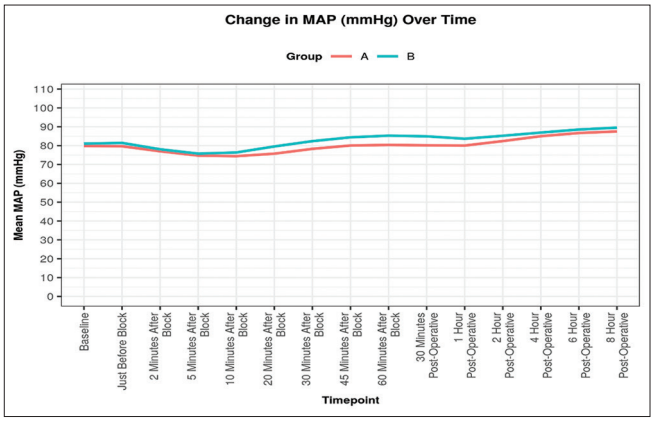

Figure 3: Line diagram depicting change in mean MAP (Mean Arterial Pressure) over time

Onset of sensory block was earlier in our study with levobupivacaine group (2.10 ± 0.26 min) and ropivacaine group (2.63 ± 0.33) as compared to the study[12] done on levobupivacaine alone (4.9 ± 0.8 min) and levobupivacaine with clonidine (3 ± 0.7 min) in paediatric SA (5-15 years). However, this could be due to distinct site of action of fentanyl and clonidine at spinal level and inter-observer variation in sensory block assessment.

Peak level of sensory block with levobupivacaine and ropivacaine in our study was T6.6 (T6-T8) and T6.7 (T6-T8), respectively. On the contrary, the study[1] done in children aged 1–14 years with levobupivacaine (0.2-0.5 mg/kg), sensory peak level was T4.4 (T2-L1) and in another study[13] on isobaric ropivacaine 0.5% (0.5 mg/kg) for children aged 1–17 years, sensory peak level was T5.5 (T2-T12). This difference in peak level of sensory block might be due to the wide age group and variation in pain quantification.

Two-segment regression of sensory block was 85.53 ± 5.93 min and 80.17 ± 12.77 min in levobupivacaine and ropivacaine group, respectively in our study. Dissimilar results were seen with the studies done on levobupivacaine[1] (80.66 ± 27 min) and ropivacaine[13] (92 ± 27 min). This could be due to difference in perception of pain.

The 2-segment regression with hyperbaric bupivacaine was merely 43 ± 10 minutes in infants and children.[14] This prompted us to add fentanyl as an adjuvant with LA to overcome short duration of block.

Mean duration of sensory and motor block in levobupivacaine group was 251 ± 41 minutes and 201 ± 40 minutes, respectively, in our study. However, in another study,[12] sensory and motor block with levobupivacaine alone was 173 ± 17 minutes and 136 ± 12 minutes and with levobupivacaine and clonidine was 297 ± 24 minutes and

232 ± 43 minutes, respectively in 60 patients aged 5–15 years undergoing SAB. These studies showed that addition of adjuvant to LA has improved the sensorimotor block duration.

No ample literature is available for comparison of mean duration of sensory and motor blockade of ropivacaine. Although a study done on isobaric ropivacaine 0.5% in which the mean time of regression of sensory block to T10 was 96 minutes (range: 34-210 minutes) as observed by the authors,[13] results have not been drawn on duration of complete sensory and motor block. Mean duration of sensory block in ropivacaine group was 211.67 minutes (range: 178-242 minutes) in our study.

Also, in our study, there was no significant difference between the two groups for the requirement of total number of analgesic doses in first 8 hours. 27 patients (90.0%) in Group A and 25 patients (83.3%) in group B required single dose of rescue analgesic in first 8 hours and rest of the patients required two doses of rescue analgesic.

Duration of analgesia was longer in levobupivacaine group as compared to ropivacaine group (270.43 ± 39.84 minutes vs. 233 ± 18 minutes). Till now, none of the studies have compared the block characteristics for these two local anaesthetics in paediatric SAB.

Early return of desire to micturate was observed in ropivacaine group (157.70 ± 27 minutes vs. levobupivacaine group 225.5 ± 31 minutes). Previous studies[15,16] showed that postoperative urinary retention (POUR) is common after SA than GA. In our study, none of the patients suffered from POUR. This might be because of the shorter duration of blockade in children due to high regional blood flow and use of isobaric form of LA whose block regression is earlier than hyperbaric form.

Limitations of our study were difficult pain quantification in children; height was not taken into consideration and discharge statistics were not collected. These limitations might have influenced our results.

CONCLUSIONS

Intrathecal isobaric levobupivacaine and ropivacaine with fentanyl produces effective surgical anaesthesia and postoperative analgesia without any adverse effects. Early regression of blockade makes ropivacaine better in comparison to levobupivacaine for short infra-umbilical surgeries in children.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published, and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Kokki H, Ylönen P, Heikkinen M, Reinikainen M. Levobupivacaine for pediatric spinal anesthesia. Anesth Analg 2004; 98:64-7.
2. Rawal N. Analgesia for day-case surgery. Br J Anaesth 2001; 87:73-87.
3. Finster M. Toxicity of local anesthetics in the fetus and the newborn. Bull N Y Acad Med Vol. 1976; 52:222-5.
4. Goyal R, Jirtjil K, Baj B, Singh S, Kumar S. Paediatric spinal anesthesia. Indian J Anaesth 2008; 52:264-72.
5. Ture P, Ramaswamy AH, Shaikh SI, Alur JB, Ture AV. Comparative evaluation of anaesthetic efficacy and haemodynamic effects of a combination of isobaric bupivacaine with buprenorphine vs. isobaric levobupivacaine with buprenorphine for spinal anaesthesia – A double blinded randomised clinical trial. Indian J Anaesth 2019; 63:49-54.
6. Bakshi U, Chatterjee S, Sengupta S, Gupta D. Adjuvant drugs in central neuraxial analgesia A review. Internet J Anesthesiol 2009;26. Available from: https://ispub.com/IJA/26/1/6383. [Last accessed on 2021 Sep 22].
7. Sharma I, Rana S, Choudhary B, Dhiman T, Sharma S, Kumar M. Comparative analgesic efficacy of intravenous vs intrathecal dexmedetomidine as an adjuvant to hyperbaric bupivacaine in subarachnoid block for below knee orthopaedic surgery. Indian J Anaesth 2020; 64:463-9.
8. Singariya G, Choudhary K, Kamal M, Bihani P, Pahuja H, Saini P. Comparison of analgesic efficacy of intrathecal 1% 2-chloroprocaine with or without fentanyl in elective caesarean section: A prospective, double-blind, randomised study. Indian J Anaesth 2021; 65:102-7.
9. Baghele A, Dave N, Dias R, Shah H. Effect of preoperative education on anxiety in children undergoing day-care surgery. Indian J Anaesth 2019; 63:565-70.
10. Soni P, Sharma LM, Tungria H, Singh Y. A comparative evaluation of equipotent doses of isobaric Levobupivacaine and Ropivacaine with neuraxial adjuvant Fentanyl for lower abdominal and lower extremity surgery. Indian J Clin Anaesth 2019; 6:59-65.

11. Duman A, Apiliogullari S, Duman I. Effects of intrathecal fentanyl on quality of spinal anesthesia in children undergoing inguinal hernia repair. Paediatr Anaesth 2010; 20:530-6.
12. Cham SC, Ramtani U, Kamble S, Cham C. Spinal anaesthesia in children: Comparative study of isobaric Levobupivacaine 0.5% with or without Clonidine. Indian J Clin Anaesth 2015; 2:141-6.
13. Kokki H, Ylönen P, Laisalmi M, Heikkinen M, Reinikainen M. Isobaric ropivacaine 5 mg/ml for spinal anesthesia in children. Anesth Analg 2005; 100:66-70.
14. Verma D, Naithani U, Gokula C, Harsha. Spinal anesthesia in infants and children: A one-year prospective audit. Anesth Essays Res 2014; 8:324-9.
15. Aziz Niazi AA, Aziz Taha MA. Postoperative urinary retention after general and spinal anesthesia in orthopedic surgical patients. Egypt J Anaesth 2015; 31:65-9.
16. Haleem S, Ozair A, Singh A, Hasan M, Athar M. Postoperative urinary retention: A controlled trial of fixed-dose spinal anaesthesia using bupivacaine versus ropivacaine. J Anaesthesiol Clin Pharmacol 2020; 36:94-9.