ORIGINAL RESEARCH PAPER

Volume - 12 | Issue - 04 | April - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

COMPARATIVE STUDY OF CLONIDINE AND FENTANYL AS ADJUVANTS TO INTRATHECAL ROPIVACAINE TO ASSESS THE DURATION OF ANALGESIA IN LOWER LIMB SURGERIES.

Anaesthesiology

Dr. Punithavathy*	Assistant Professor, Department of Anaesthesia, KMCH Institute of Health Sciences & Research *Corresponding Author
Dr. K. Deepa	Resident, Department of Anaesthesia, Kovai Medical Center & Hospital, Coimbatore
Dr. A. T. Sathiya Vinotha	Associate Professor, Department of Pharmacology, KMCH Institute of Health Sciences Research,Coimbatore
Dr K. Chandramohan	Consultant, Department of Anaesthesia, Kovai Medical Center & Hospital, Coimbatore
Dr. S. Jeevithan	Professor, Department of Community medicine, KMCH Institute of Health Sciences Research, Coimbatore

ABSTRACT

Objective: Ropivacaine has the benefit of providing appropriate intraoperative anaesthesia and effective postoperative analgesia when used for lower limb procedures under spinal anaesthesia, but some patients still experience pain after the medication has taken its full course of action. Adjuvants added to local anaesthetics have the advantage of extending the sensory-motor block's duration and lowering the overall dose necessary.4 This study compared Clonidine and Fentanyl as adjuvants to intrathecal ropivacaine in enhancing the quality of anaesthesia by postponing the requirement for analgesics. **Methods:** 100 Patients who were undergoing lower limb surgeries were selected for the study and divided into two groups of 50 each. Patients were randomly allocated to one of the two groups using envelope method for blinding the investigator. GROUP A patients received 2.5ml 0.75% Ropivacaine(18.75mg) + Clonidine(60µg) 0.2ml, GROUP B patients received 2.5ml 0.75% ropivacaine(18.75mg) +Fentanyl (20mcg) 0.2ml. The following parameters were noted: Time of injection of subarachnoid block, Time of onset of sensory block at T10 level, Time of onset of motor block, Duration of motor block, Degree of sedation. **Results and discussion:** No difference in the onset of sensory and motor blockade between the two groups. There was statistically significant prolongation in the duration of motor blockade in clonidine group 195.6 minutes when compared with fentanyl group 157.8 minutes ($p < 0.001$). Analgesic duration was significantly higher in clonidine group 321.70 ± 48.93 min when compared with fentanyl group 273.60 min ($p = < 0.001$).The difference in haemodynamic parameters – heart rate, systolic & diastolic blood pressure, mean arterial pressure (except for systolic blood pressure at 150 minutes) were statistically insignificant between both the groups. Sedation was slightly higher in the fentanyl group when compared to clonidine group but was statistically insignificant. None of the patients required supplemental oxygen, analgesia, or anxiolysis intraoperatively. No significant difference in the incidence of complications like bradycardia, hypotension, respiratory depression etc between the two groups. **Conclusion:** In our study subarachnoid block with 0.75% isobaric ropivacaine (2.5ml) for lower limb surgeries with addition of clonidine 60mcg as anaesthetic adjuvant has advantage over fentanyl 20 mcg, as it increases the duration of spinal anaesthesia and increases postoperative analgesic duration. No significant complications were recorded in both study groups.

KEYWORDS

Ropivacaine, Lower limb surgeries, Clonidine, Fentanyl, Adjuvants

INTRODUCTION

Subarachnoid block is a safe and efficient type of neuroaxial anaesthetic technique practised routinely for lower limb surgeries, due to its more dependable block with a lower failure incidence (1). Various elements, such as the overall dose, the solution's baricity, the injection site, and the patient's position following the block determines the block's length and quality. There is a continuous research to find the ideal, safe drug that has minimal or no adverse effects and provide great surgical anaesthesia (2).Commonly used local anaesthetic Bupivacaine is cardio toxic in large doses(3). Ropivacaine, a long-acting amide and a pure S enantiomer of propivacaine is found to have a similar sensory blockade and a lower degree motor blockade. Ropivacaine has the benefit of good intraoperative anaesthesia and effective postoperative analgesia when used for lower limb procedures under spinal anaesthesia, but some patients still experience the pain after the drug has taken its full course of action. Adjuvants are added to local anaesthetics to address these short comings (4). When opioids like fentanyl are added to ropivacaine, the effects are cumulative and the sensory block is denser which enhances anaesthesia quality. Pruritus, vomiting, and respiratory depression are side effects of intrathecal opioids (5) leading to search for a better non opioid adjuvant. Clonidine, a partial alpha 2 agonist, has sedative and analgesic properties. Intrathecal clonidine has the advantages of a denser block and a longer post - operative analgesic duration. Bradycardia, hypotension, and sedation are among the side effects (6).The purpose of this study is to evaluate the effects of ropivacaine combined with the adjuvants clonidine and fentanyl.

The aim of this study is to compare the efficacy, analgesic effect, postoperative analgesia of clonidine and fentanyl along with ropivacaine given via intrathecal route for patients undergoing lower limb surgeries. The parameters studied are duration of analgesia, duration of motor blockade, time of onset of sensory block at T10, hemodynamic parameters, sedation score and time of first rescue analgesia using VAS score. We also recorded the Side effects if anything was reported by the patient. Gaurav Kuthiala et al (7) in 2011 reviewed the pharmacological use of ropivacaine. Less lipophilic than bupivacaine, ropivacaine. In contrast to A fibres, which carry the motor function, it penetrates the big myelinated motor fibres less and hence acts only on the A and C nerves, which transmit pain. Luck et al (8) used equal doses of hyperbaric bupivacaine, ropivacaine and levobupivacaine (15 mg) intrathecally for elective surgery, and found that ropivacaine had a shorter duration of subarachnoid block than levobupivacaine and bupivacaine, and researchers came to the conclusion that ropivacaine is useful for orthopaedic procedures and other situations requiring early mobilisation.

Equipotent doses of different local anaesthetics have been tried in various surgeries to suit the surgical needs (9,10). Dose finding and comparative studies on different dosages of adjuvants with local anaesthetics have been done in this regard(9,10). Chaudhary A et al(11) noticed shorter period of total motor block in spinal anaesthesia using ropivacaine1.8 ml(0.75%) with 10 mcg fentanyl, when compared with the pure ropivacaine 2 ml, in group of 60 patients undergoing TURP surgery. Dose finding and comparative studies on different dosages of adjuvants with local anaesthetics have been done in this regard (12,13). N Boztug et al(14) for outpatient arthroscopic knee surgery, compared the use of intrathecal ropivacaine to ropivacaine + fentanyl. The administration of an intrathecal solution (3 ml) containing either 10 mg of isobaric ropivacaine or 8 mg of isobaric ropivacaine with 25 micrograms of fentanyl was randomly assigned to 50 patients in equal groups. The ropivacaine with fentanyl group experienced less anaesthesia time. In comparison to ropivacaine + fentanyl, the cephalad distribution of sensory blocking was greater

with ropivacaine. They came to the conclusion that using 10 mg of ropivacaine alone results in a longer duration of anaesthesia than adding 25 microg of fentanyl to 8 mg of ropivacaine. Thus, arthroscopic knee surgery can use lower dosages of ropivacaine combined with a fentanyl addition without risk .Abhishek et al (15) in 2022 performed a random study using ropivacaine in intravenous adjuvants for lower limb operations. 70 adult patients between the ages of 20 and 60 who had signed up for elective lower limb surgery were split into two groups. 3 mL of 0.5% isobaric ropivacaine and 1.0 mcg/kg of clonidine were administered intravenously to Group C. 3 mL of 0.5% isobaric ropivacaine and 0.5 mcg/kg of dexmedetomidine were administered intravenously to Group D. They came to the conclusion that it is simple to treat the temporary hypotension and substantial bradycardia caused by dexmedetomidine and clonidine. When compared to clonidine, dexmedetomidine has the advantage of sensory block, motor block, drowsiness, and postoperative analgesia lasting longer with a lower frequency of serious side effects.

MATERIALS AND METHODS

This study was conducted after institutional human ethical committee approval in the tertiary-care hospital Kovai Medical Center and Hospital, Coimbatore, India from December 2020 to December 2021. It is a 1050 bedded multispecialty NABH accredited hospital. Patient on anticoagulants, antiarrhythmics, beta blockers, antipsychotic drugs, tricyclic antidepressants, alpha adrenergic agonist, Patients with contraindications or history of hypersensitivity to the study drugs, Patients with contraindications for spinal anaesthesia were excluded from the study. Informed written consent was obtained from the patients before the initiation of the study.100 Patients who were undergoing lower limb surgeries were selected for the study and divided into two groups of 50 each. Patients were randomly allocated to one of the two groups using envelope method for blinding the investigator. **GROUP A -**2.5ml 0.75% Ropivacaine (18.75mg) + Clonidine (60µg) 0.2ml ,**GROUP B -**2.5ml 0.75% ropivacaine (18.75mg) +Fentanyl 20mcg0.2ml. After routine preoperative preparations like recording of basal line vital parameters, and standard monitoring, patients were given sub arachnoid block in right lateral position with a 26 G Quincke's needle at the L3/4 interspace in the midline. The following parameters were noted: Time of injection of subarachnoid block. Time of onset of sensory block at T10 level. Time of onset of motor block, duration of motor block, degree of sedation, duration of surgical procedure. Hemodynamic parameters.Systolic and Diastolic blood pressure, Mean Arterial Blood pressure, pulse rate and oxygen saturation were recorded at 0,3,6,9 and 15th minute and thereafter every 30 minutes till 180 minutes. Any discomfort like nausea, vomiting, shivering, pruritus and adverse events such as hypotension, bradycardia respiratory depression were noted. On completion of surgery, patient was shifted to the post anaesthesia care unit for observation. Patients were transferred to postoperative ward after complete resolution of motor blockade and stabilisation of blood pressure. Vital signs and oxygen saturation were monitored until recovery of patients from anaesthesia.

Statistical analysis:

Data analysis was done with the help of computer by using SPSS software and Sigma Stat 3.5 version (2012). Using this software, percentage, mean, standard deviation and 'p' value were calculated through one way ANOVA, and Chi square test and a P value of < 0.05 was taken as significant

RESULTS

The time to reach T10 sensory level between the two groups is statistically not significant. The onset of motor block between the two groups is statistically not significant. There was statistically significant prolongation in the duration of motor blockade in clonidine group 195.60 min when compared with fentanyl group 157.8 min ($p = < 0.001$).There was statistically significant prolongation in the duration of analgesia in clonidine group 321.70 min when compared with fentanyl group 273.60 min ($p < 0.001$) (Table 1)

All haemodynamic parameters – heart rate, systolic & diastolic blood pressure, mean arterial pressure except for systolic blood pressure at 150 minutes was statistically insignificant between both groups.(Table 2) Sedation was slightly higher in the fentanyl group when compared to clonidine group but was statistically insignificant. None of the patients required supplemental oxygen, analgesia, or anxiolytics intraoperatively. No significant difference in the incidence of complications like bradycardia, hypotension, respiratory depression etc between the two groups.

Table 1: Clinical parameters observed in both groups.

Clinical parameter	Group A(Fentanyl)	Group B (Clonidine)
Onset of sensory block	4.98 ± 1.78	4.96 ± 1.84
Onset of motor block	9.36 ± 2.06	9.00 ± 2.09
Duration of motor block	157.8 ± 24.84	195.60 ±22.05***
Duration of analgesia	273.60 ± 36.53	321.70 ± 48.93***

Data is expressed as mean ± SD. p value is expressed as * $p<0.05$,** $p< 0.01$,*** $p< 0.001$

Table 2: Haemodynamic parameters observed in both groups

Min	Heart rate		SBP		DBP		MAP	
	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B
0min	78.36± 7.21	77.40 ±5.84	117.64 ±7.98	120.06 ±9.22	74.06± 7.86	75.62 ±8.91	87.78 ±8.68	89.16± 9.79
3 min	79.48± 8.88	77.82 ±8.29	113.56 ±7.33	113.70 ±9.31	71.60± 7.24	71.44 ±8.79	84.16 ±7.36	83.42± 9.91
6 min	77.80± 6.73	78.00 ±8.24	111.64 ±9.04	111.44 ±9.07	69.88± 8.06	69.22 ±8.01	82.94 ±8.10	81.32± 8.77
9 min	76.24± 7.94	77.46 ±9.35	110.46 ±9.42	111.84 ±10.7	68.70± 8.87	67.24 ±8.59	81.26 ±8.36	80.00± 9.79
12 min	74.48± 6.92	74.84 ±6.99	109.52 ±9.53	110.14 ±9.26	68.54± 7.35	67.64 ±8.81	81.24 ±7.44	80.46± 9.56
15 min	75.34± 7.79	75.96 ±8.28	110.48 ±8.46	111.38 ±7.88	68.70± 6.64	69.46 ±7.92	81.86 ±6.35	82.02± 9.11
30 min	76.02± 6.61	76.12 ±7.54	110.76 ±9.37	112.60 ±7.92	68.12± 7.84	69.26 ±8.74	81.56 ±7.95	82.42± 8.73
45 min	76.68± 6.26	76.82 ±6.93	112.92 ±7.32	113.50 ±7.75	70.30± 6.75	70.92 ±7.97	84.12 ±5.93	83.44± 9.03
60 min	77.60± 7.21	77.46 ±7.29	113.60 ±9.37	114.34 ±7.12	71.14± 7.14	70.12 ±7.86	84.70 ±6.74	82.96± 7.81
90 min	77.54± 7.20	77.46 ±7.12	113.70 ±8.37	114.94 ±7.94	71.96± 5.93	72.00 ±7.81	85.42 ±5.71	85.34± 7.41
120 min	76.88± 6.64	77.30 ±6.87	115.38 ±7.80	116.10 ±6.23	71.84± 6.46	72.58 ±8.37	85.42 ±6.62	85.70± 7.74
150 min	76.92± 6.10	76.98 ±6.54	114.30 ±7.77	117.42 ±5.77	72.34± 5.45	73.38 ±8.31	86.16 ±4.87	87.28± 7.54
180 min	77.10± 5.79	77.02 ±5.71	115.90 ±6.00	116.84 ±5.85	72.42± 6.53	72.58 ±8.63	86.06 ±6.00	86.30± 7.39

Data is expressed as mean ± SD. p value is expressed as * $p<0.05$, ** $p< 0.01$, *** $p< 0.001$

DISCUSSION

In lower limb procedures, subarachnoid block with 0.75% ropivacaine had a better safety profile than lignocaine and bupivacaine(16).As an alternative to bupivacaine, we suggested researching the effectiveness of ropivacaine when used in spinal anaesthesia for lower limb procedures, using the same equi-milligram dose (18.5 mg) as Sharan et al(17).. In patients undergoing total hip arthroplasty, McNamee et al(18) investigated the effectiveness of two intrathecal ropivacaine concentrations, 2.5 mL of 0.75% (18.75 mg) and 1% (25 mg), without adjuvants. The group that received 25 mg of ropivacaine had a longer period of anaesthesia. In our study, adjuvants were added to reduce the dose of ropivacaine. The quality of spinal anaesthesia can be improved by adding analgesic adjuvants to low dose local anaesthetics, (5, 6, and 7). Intrathecal opioids in doses below therapeutic levels has shown to improve and lengthen the duration of sensory block, without improving the duration of motor blockade and also without extending the postoperative recovery from motor blockade, when added to bupivacaine and ropivacaine (19). In a similar study, the effects of low dose intrathecal ropivacaine with and without fentanyl during arthroscopic knee surgery were examined by Boztug et al. They came to the conclusion that using merely 10 mg of ropivacaine alone resulted in a sensory and motor blockage lasting longer than when 25 mcg of fentanyl was added to 8 mg of ropivacaine. According to the existing research, clonidine has been used in spinal anaesthesia at various doses ranging from 30 to 150 mcg, creating a range of postoperative analgesic requirements (20, 21). De Kock et al. (22) examined the relationship between intrathecal clonidine (15, 45, or 75 mcg) and subarachnoid ropivacaine (8 mg) in four groups for ambulatory surgery. High intrathecal clonidine dosages can prolong the postoperative motor blockade and have negative hemodynamic effects including bradycardia and hypotension. Recent studies have demonstrated that low dose intrathecal clonidine at a dose of 1-2 mcg/kg is sufficient to extend the effects of ropivacaine spinal

anaesthesia 5. To obtain appropriate analgesia and hemodynamic stability in our study, we employed an intrathecal clonidine dosage of 60 mcg(23).We used the period in minutes from the drug's intrathecal injection to the moment the patient requested analgesia or the VAS was greater than two to compare the efficacy. We evaluated haemodynamic effects as well as side effects such as nausea, vomiting, pruritus, and shivering in order to compare safety. In order to determine the duration of analgesia following lower limb procedures, we evaluated fentanyl and clonidine as adjuvants to intrathecal ropivacaine in our study. In order to prevent bias brought on by the influence of confounding variables, the general demographic features of the participants in both groups, such as age, height, and weight, were matched before statistical analysis of the resulting results. According to statistical analysis of the two groups, the mean age of the fentanyl group's participants was 45.28 years, whereas the mean age of the clonidine group's subjects was 41.48 years. With a p-value of 0.12 (p-value > 0.05), this is statistically insignificant according to analysis. The mean weight in the fentanyl group was 71.66 kg and that in the clonidine group was 71.18 kg, which was statistically not significant with a p-value of 0.78 (p-value > 0.05) and the mean height in the fentanyl group was 162.7cm and that in the clonidine group was 162.9cm. Therefore, both groups could be compared. The onset of sensory blockage at T 10 was found in our investigation. The interval between the injection of anaesthetic solution and the disappearance of pain at the T10 dermatome was used to determine the beginning of sensory block. Concerning the time at which sensory block began, no appreciable variation was discovered. They also showed no discernible differences in how quickly motor blockage set in. In situations of lower limb procedures, the length of motor blockage after spinal anaesthesia should be appropriate. Less time could result in spinal anaesthesia wearing off before it even lasts the entire surgery. Unnecessarily extending the motor blockade's length can result in a patient's delayed release from the post-anesthesia care unit and poor patient satisfaction. In this investigation, the duration of motor blockage was statistically significantly prolonged in the clonidine group (195.6 ±222.05 minutes) compared to the fentanyl group (157.8 ±24.84 minutes) (p< 0.001). According to studies by Sharan et al.6 (clonidine 30 mcg) and Chhabra et al.21, the duration of motor blockage was significantly prolonged in the clonidine group compared to the fentanyl group. In a research by Kock et al., 15 ropivacaine 8 mg combined with 75 mcg of clonidine resulted in noticeably prolonged sensory and motor anaesthesia (195 ± 40 min and 164 ± 34 min, respectively; p< 0.05).In our study, the clonidine group had a substantially longer analgesia duration (321.70 ± 48.93 min) compared to the fentanyl group (273.60 ± 36.53 min) (p 0.001). Our findings agreed with a number of other studies (24).In contrast to earlier investigations, the analgesia in this trial lasted longer. The variable clonidine, fentanyl, or ropivacaine doses utilised in those studies may be the reason for this. Baseline haemodynamic parameters like heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure was comparable between both groups. The mean heart rates between both the groups even at these time points were within the physiological range. So this can be considered clinically not significant. Overall, there is no statistically significant difference in the intraoperative heart rate between the two groups. Bradycardia, a feared side effect of clonidine, (HR<50/min) did occur in 2 patients but was statistically insignificant. The findings in our study was similar to Sharan et al[6], Chhabra et al[21]**.** In our study, at only 150 minutes after the block, a statistically significant difference in mean SBP (114.30 mm Hg) in clonidine group compared to (117.42 mm Hg) in fentanyl group was seen. Other than this, there was no statistically significant difference in SBP between the two groups. When analysed in terms of the number of episodes of hypotension (as defined by a fall in systolic blood pressure >20% from baseline), it was not statistically significant between the two groups. In this study, the diastolic blood pressure difference between the two groups was not statistically significant. In our study, MAP difference between the two groups was not statistically significant. There was a statistically significant difference (P < 0.05) in SPO2 of both the groups at 15 minute (97.96) and at 120 minute (97.92). To assess the degree of sedation, Ramsay's sedation score was used. There was a statistically significant difference (P < 0.05) in Sedation score at 6 minutes,15 minutes, 90 minutes. But none of the patients in both groups had excessive sedation. Shivering occurred in 1 patient in the fentanyl group and 2 patients in the clonidine group. But the difference was not statistically significant. Nausea occurred in 2 patients in the fentanyl group and 1 patient in the clonidine group, which was statistically not significant. Pruritis occurred in 4 patients of fentanyl group and was statistically insignificant.

CONCLUSION

In our study subarachnoid block with 0.75% ropivacaine (2.5ml) for lower limb surgeries with addition of clonidine 60mcg as anaesthetic adjuvant has advantage over fentanyl 20 mcg, as it increases the duration of spinal anaesthesia and increases postoperative analgesic duration. No significant complications were recorded in both study groups. The main limitations of this study are the duration of sensory blockade, the time of mobilise the patient and the return of bowel and bladder functions were not measured.

REFERENCES:

1. Kamel I, Ahmed F, Sethi A. Regional anaesthesia for Orthopaedic procedures: What orthopaedic surgeons need to know? World journal of Orthopedics.2022;13(1):11-35.
2. Bhat N, Himaldev, Upadya M. Comparison of efficacy and safety of ropivacaine with bupivacaine for intrathecal anaesthesia for lower abdominal and lower limb surgeries. Anaesthesia Essays and Researches.2013;7(3):381-385.
3. Malinovsky JM, Charles F, Kick O, Lepage JY, Malinge M, Cozian A, Bouchot O, and Pinaud M. Intrathecal Anesthesia: Ropivacaine Versus Bupivacaine. Anaesthesia Analgesia.2000; 91:1457-60.
4. Seetharam R, Bhat G. Effects of isobaric ropivacaine with or without fentanyl in subarachnoid blockade:A prospective double-blind, randomised study. Anaesthesia Essays and Researches.2015; 9(2): 173-177.
5. Bathari R, Bhalotra R, Anand R, Kumar V. A randomised trial to compare the effect of addition of clonidine or fentanyl to hyperbaric ropivacaine for spinal anaesthesia for knee arthroscopy. Southern African Journal of Anaesthesia and Analgesia. 2016; 22(1):20-24.
6. Sharan R, Verma R, Dhawan A, Kumar J.Comparison Of clonidine and fentanyl as adjuvant to ropivacaine in spinal anesthesia in lower abdominal surgeries. Anesth Essays Res. 2016; 10(3): 526–53
7. Kuthiala G, Chaudhary G. Ropivacaine: A review of its pharmacology and clinical use. Indian Journal of Anaesthesia 2011; 55:104-10.
8. Luck JF, Fettes PD, Wildsmith JA. Spinal anaesthesia for elective surgery: A comparison of hyperbaric solutions of racemic bupivacaine, levobupivacaine, and ropivacaine. British Journal of Anaesthesia 2008; 101:705 10.
9. Koltka K, Uludag E, Senturk M, Yavru A, Karadeniz M, Sengul T. Comparison of equipotent doses of ropivacaine fentanyl and bupivacaine fentanyl in spinal anaesthesia for lower abdominal surgery. Anaesthesia Intensive Care 2009; 37:923-8.
10. Gupta K, Sharma D, Gupta K, Krishnan A, Pandey MN. Intrathecal fentanyl as an adjuvant to 0.75% isobaric ropivacaine for infraumbilical surgery under subarachnoid block: A prospective study. Saudi journal of Anaesthesia. 2014; 8(1):64-8.
11. Chaudhary A, Bogra J, Singh P, Saxena S, Chandra G, Verma R. Efficacy of spinal ropivacaine versus ropivacaine with fentanyl in transurethral resection operations. Saudi Journal of Anaesthesia. 2014;8(1):88-91.
12. Hughes D, Hill D, Fee JP. Intrathecal ropivacaine or bupivacaine with fentanyl for labour. British Journal of Anaesthesia. 2001 Nov; 87(5):733-7.
13. Wahedi W, Nolte H, Klein P. Ropivacaine for spinal anaesthesia. A dose finding study. Anaesthetist. 1996; 45(8):737-44
14. Chhabra A, Dawoodi S, Jagtap S. Comparison of clonidine versus fentanyl as an adjuvant to intrathecal ropivacaine for major lower limb surgeries: A randomised double-blind prospective study. Indian Journal of Pain. 2013;27(3):170-4.
15. Abhishek MS, Nagraj TR. Randomized Controlled Study Using Ropivacaine with Intravenous Adjuvants in Spinal Anaesthesia in Lower Limb Surgeries. Anaesthesia Essays and Researches.2020;14(2):208-212.
16. Thakur R, Aske R, Keshari U. Comparative Evaluation of Intrathecal Administration of Isobaric Levobupivacaine (0.5%) and Isobaric Ropivacaine (0.75%) in Patients Undergoing Lower Limb Surgeries. International Journal of Contemporary Medical Research.2018;5(2).
17. Parveen S, Jan M, Hussain A, Saleem B, Habib M. Efficacy and Appropriate Dosage of isobaric Ropivacaine for Spinal Anaesthesia in patients Undergoing Elective Lower Limb Orthopaedic Surgeries. Journal of Dental and Medical Sciences.2016;1(1):8-12.
18. McNamee DA, Parks L, McClelland A, Scott S, Milligan K, Ahlen K. Intrathecal ropivacaine for total hip arthroplasty: double-blind comparative study with isobaric 7.5 mg ml −1 and 10 mg ml −1 solutions. British Journal of Anaesthesia. 2001;87(5):743–7.
19. Varun S, Srivastava M, Maurya I, Garg R, Dhama V, Manik V. A clinical prospective, randomized study to compare intrathecal isobaric bupivacaine – fentanyl and isobaric ropivacaine – fentanyl for lower abdominal and lower limb surgeries. Anaesthesia, Pain and Intensive care. 2012; 16(3): 237-242.
20. Filos KS, Goudas LC, Patroni O, Polyzou V. Intrathecal clonidine as a sole analgesic for pain relief after caesarean section. Anesthesiology 1992;77(2):267-74.
21. Benhamou D, Thorin D, Brichant JF, Dailland P, Milon D, Schneider M. Intrathecal clonidine and fentanyl with hyperbaric bupivacaine improves analgesia during caesarean section. Anaesthesia Analgesia. 1998;87(3):609-13. 6.
22. Kock MD, Gautier P, Fanard L, Hody JL, Lavand'Homme P. Intrathecal Ropivacaine and Clonidine for Ambulatory Knee Arthroscopy. Anesthesiology. 2001; 94(4):574–8.
23. Swain A, Nag D S, Sahu S, Samaddar D P. Adjuvants to local anaesthetics: Current understanding and future trends. World Journal Clinical Cases. 2017; 5(8): 307-323.
24. Shukla U, Prabhakar T, Malhotra K. Postoperative analgesia in children when using clonidine or fentanyl with ropivacaine given caudally. J Anaesthesiol Clin Pharmacol.2011;27(2): 205-210. 38. 37.