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COMPARATIVE EVALUATION OF CLONIDINE AND FENTANYL AS ADJUVANTS TO INTRATHECAL ISOBARIC ROPIVACAINE FOR LOWER LIMB SURGERIES - A RANDOMISED, DOUBLE BLIND PROSPECTIVE STUDY.

Anesthesiology

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ABSTRACT

Background: Ropivacaine is a safer local anaesthetic than bupivacaine and lignocaine. To improve its quality of anaesthesia and analgesia, the use of adjuvants is recommended.

Aim: To compare the efficacy of clonidine and fentanyl as adjuvants to intrathecal isobaric ropivacaine for lower limb surgeries.

Design: Randomized double-blind prospective study.

Methods: Seventy patients were randomly divided in two groups. Ropivacaine-Clonidine group (RC) received 60 mcg of clonidine with 15 mg of 0.5% isobaric ropivacaine, whereas ropivacaine-fentanyl group (RF) received 25 mcg of fentanyl with 15 mg of 0.5% isobaric ropivacaine intrathecally. Maximum sensory block level, time to achieve maximum sensory block, time for sensory block to regress to L1 dermatome, time to achieve maximum degree of motor block and its regression to Bromage I, sedation score, hemodynamic parameters, and side-effects were noted.

Results: The mean onset of maximum sensory block in RC group was was slower than in the RF group ($p < .05$) .The highest dermatomal level achieved in both groups was T 6. The mean time of sensory regression to L-1 was higher in in RC group (p-value <0.0001). The mean time to achieve Bromage grade IV motor block in RC group was higher ($p > 0.05$). The motor block was of shorter duration and was subject to rapid recovery in RF group. The mean duration of sensory loss for RC group was higher (p=0.0001). Three patient (8.6%) in the clonidine group had hypotension as compared to one patient (2.8%) in the fentanyl group . Nausea/vomiting and shivering was experienced by one patient each in the fentanyl group. Pruritus was present in three patients (8.6%) in the fentanyl group.

Conclusion: Ropivacaine in combination with clonidine or fentanyl provided adequate subarachnoid block for major surgeries, wherein clonidine has advantage over fentanyl as it increased the duration of subarachnoid block and prolonged the postoperative analgesia.

KEYWORDS:

Clonidine, fentanyl, ropivacaine, intrathecal

Introduction

Isobaric ropivacaine, an amino-amide local anaesthetic has now been proven as a safer drug compared to bupivacaine and lignocaine due to the cardiotoxicity of the former and neurotoxicity of latter. [1,2] Recovery from sensory and motor block due to ropivacaine is rapid,thus making it useful for day- care surgeries. Different studies have evaluated the effects of intrathecal ropivacaine in parturients and patients undergoing minor surgeries [3,4].Very few studies have evaluated its use for major surgeries.[5]

In order to improve the benefits of intrathecal ropivacaine with respect to the quality of anaesthesia and analgesia, various adjuvants have been used which include opioids, α- agonists(dexmedetomidine, clonidine), magnesium, etc. The faster onset of both sensory and motor blockade, prolonged duration of analgesia, dose sparing action of local anaesthetics and stable cardiovascular parameters make these agents very effective adjuvants in regional anaesthesia.[6] However, worrisome adverse effects such as pruritis,urinary retention, nausea/ vomiting and delayed respiratory depression with opoids has prompted further research to use non-opoids. Clonidine, a partial α-2 agonist administered intrathecally improves the quality of block and post-operative analgesia.[7,8] We conducted this study to evaluate and compare clonidine and fentanyl as adjuvants to intrathecal isobaric ropivacaine for lower limb surgeries.

Methods

This prospective randomised double blind study entitled "Compar ative evaluation of clonidine and fentanyl as adjuvants to intrathecal isobaric ropivacaine for lower limb surgeries." was undertaken in the department of anaesthesiology in a tertiary care hospital over a period of 18 months. After institutional ethical committe approval, 60 patients of ASA grade I & II of either sex, aged 20 – 60 years undergoing elective lower limb surgeries were randomly allocated to two groups of 30 patients each. Group RC comprising 30 patients received 3 ml (15mg) of isobaric 0.5% ropivacaine with 60 µgs of Clonidine(0.5ml) making total volume of 3.5 ml. Group RF comprising 30 patients received 3 ml (15mg) of 0.5% isobaric ropivacaine with 25µgs of fentanyl (0.5ml) making total volume of 3.5 ml. Pre-anaesthetic evaluation was carried out 24 hour prior to surgery. An informed consent was taken from all the patients included in the study.Inclusion criteria were ASA Grade 1 and Grade II, procedure lasting up to 2 hours, patients free from cardio-respiratory and autonomic dysfunction. Exclusion criteria were ASA Grade III and Grade IV patients, contraindication to regional anaesthesia (patient refusal, coagulopathy, pre-existing neurological defect), known allergy to any of the study drugs, patients on antihypertensive and antidepressant drugs, patients with morbid obesity, sepsis or local site infection, anatomical deformities of spine, space occupying lesion of brain, hypovolemia. Visual analogue score (VAS) for pain was explained to the patient pre-operatively on a 10 point scale where '0'indicates no pain and '10' indicates worst imaginable pain.

On arrival to the operation theatre, patient's heart rate, blood pressure (BP), oxygen saturation (SpO2), and electrocardiogram (ECG) monitors were attached. Intravenous access was established and patients preloaded with 500 mL of Ringer Lactate solution. After ensuring sterile conditions, spinal anesthesia was performed by accessing the subarachnoid space with 27 G Quincke spinal needle via the L4-5 intervertebral space in the sitting position. After ensuring free flow of cerebrospinal fluid, patients received one of the two study drugs. The drug combinations were prepared by the first anaesthesiologist not involved in the study. However, observations were made by the second anaesthesiologist who was blinded to the drug administered. Throughout the study pulse, BP, respiratory rate, ECG, and SpO2 were monitored. A decrease of more than 25% from the baseline in the systolic blood pressure (SBP) was considered hypotension and inj. ephedrine 6 mg intravenous (IV) was administered as bolus dose. A decrease in the heart rate below 50 beats/min was considered bradycardia and inj. atropine 0.5 mg,(IV) was administered. The level of sensory block and the grade of motor

block was evaluated at 2, 4, 6, 8,10 and 15 min and thereafter at 15 min interval till the end of surgery. The sensory block level was evaluated with the ice cubes test and the motor block level was determined according to the Bromage Scale as follows : Grade1: Free movement of legs and feet, Grade II: Just able to flex knees with free movement of feet, Grade III: Unable to flex knees but with free movement of feet, Grade IV: Unable to move legs or feet. During the tracking of the sensory block in patients, a maximum sensory block level, time to achieve maximum sensory block and the time for sensory block to regress to L1 dermatome was monitored. While tracking the motor block, time to achieve maximum degree of motor block and its regression to Bromage I was noted. The level of sedation was assessed using sedation score described by Chermik and Gilling as follows : Grade 0: Wide awake, Grade 1: Calm and comfortable, responding to verbal commands, Grade 2: Sleeping but arousable, Grade 3: Deep sleep, not arousable.

VAS score was monitored in post-operative period hourly after completion of surgery till 6th hour, subsequently 2 hourly till 12th hour then 3 hourly till completion of 24 hours. In the postoperative period, the time to first analgesic demand was noted and inj.diclofenac 75 mg was administered in patients with VAS>3. Patients were observed for any discomfort, nausea, vomiting, shivering, pruritus, bradycardia, and any other side-effects. All patients were observed in the post anesthesia care unit (PACU) and later in the ward. Severe pruritus and nausea/vomiting was treated with inj. chlorpheniramine maleate 10 mg and inj. Ondensetron 4 mg, respectively. In addition,haem odynamic changes (pulse rate, systolic blood pressure, diastolic blood pressure), respiratory rate and oxygen saturation were observed in all the patients throughout the study.

Stastical analysis :

SPSS (version 16.0, SPSS Inc. Chicago, IL., USA) was used for statistical calculation. Data was expressed either as mean and standard deviation or number and percentage. Continuous variables age, BMI, duration of surgery, duration of sensory and motor blockade were compared using ANOVA test. P value of <0.05 was considered significant and <0.001 was considered highly significant. Paired and unpaired t-test and analysis of variance was used for statistical calculations. Categorical data was analyzed using chi-square test.

Observations and Results

There was stastistically no significant difference between the two groups with respect to the haemodynamic parameters like heart rate, systolic blood pressure, diastolic blood pressure and SpO2. The two groups were also comparable in relation to age,height, weight, gender, duration of surgery and ASA status p-value > .05. (table 1, figure 1)

The mean onset of maximum sensory block in ropivacaine-clonidine group was 7.80 ± 0.4 min. and that in ropivacaine fentanyl group was 6.50 ±0.6 min. (p > .05) . The highest dermatomal level achieved in both groups was T 6. 18 cases in RC group and 19 cases in RF group attained T-6 level.(p-value >0.05). The mean time of sensory regression to L-1 in RC group was 298 ±17.6 min. and that in the RF group was 214.50 ±16.7 min (p-value <0.0001). The mean time to achieve grade IV motor block in RC group was 7.18 ± 0.5 min . and that in the RF group was 5.86±5.51 min., p-value >0.05. The mean duration for recovery to grade I motor block in RC group was 245.89 ± 21.73 min. and that in the RF group was 203.50±12.87min, p-value <0.001, indicating that the motor block was of shorter duration and was subject to rapid recovery in RF group as compared to RC group. The mean duration of sensory loss (total analgesia time) for RC group and RF group was 339.67 ± 25.89 min & 256±25.81 min., respectively (p=0.0001) .Thus, we observed that sensory block lasted longer with ropivacaine clonidine group as compared with ropivacaine fentanyl group.(Table 2)

Three patient (8.6%) in the clonidine group had hypotension (drop >25% SBP) as compared with one patient (2.8%) in the fentanyl group and responded to inj. ephedrine, 6 mg along with IV fluids. In the clonidine group, three patients had bradycardia requiring inj. atropine 0.6 mg. Nausea/vomiting and shivering was experienced by one patient each in the fentanyl group. Pruritus was present in three patients (8.6%) in the fentanyl group [Table 3]. They responded to inj. ondensetron, 4 mg, and inj. chlorpheniramine 10 mg, respectively. In the fentanyl group, 15 patients (43%) had a sedation score of 1-2 as compared with 28 patients (80%) in the clonidine group who were calm and sleeping comfortably [Table 4]. None of the patients in either group had respiratory depression.

Discussion

Spinal anaesthesia is widely used for lower limb and perineal surgeries. It is safe, economical, easy to perform and effective technique which provides rapid and reliable anaesthesia with muscle relaxation, increased pain relief and comfort to patients with severe pain involving lower abdomen and lower limb with use of less medicine.[9]

In the present study, intrathecal ropivacaine (15 mg) with adjuvants, fentanyl (25 mcg), and clonidine (60 mcg) provided satisfactory anaesthesia for lower limb surgeries. Patients who received clonidine as adjuvant with ropivacaine in the spinal block experienced a prolonged sensory anaesthesia, dense and a longer duration of motor block and a significantly prolonged postoperative analgesia as compared with the ropivacaine-fentanyl group. Ropivacaine has been proved to be a well-tolerated regional anaesthetic. For intrathecal use, its efficacy as compared with bupivacaine is in the ratio of 3:2, that is, 15 mg ropivacaine provided similar motor and hemodynamic effects but less potent anaesthesia than 10 mg bupivacaine.[10] The quest for providing long duration anesthesia of optimum quality while maintaining the advantage of ropivacaine led to the use of analgesic adjuvants with intrathecal ropivacaine. A study by Boztug et al.,[11] evaluated the effects of low dose intrathecal ropivacaine with and without fentanyl for arthroscopic knee surgery. They concluded that although 25 mcg of fentanyl added to 8 mg ropivacaine provided shorter sensory and motor blockade than 10 mg ropivacaine alone. Small doses of ropivacaine and fentanyl can be safely used for arthroscopic knee surgery, thus reiterating the safety of intrathecal ropivacaine with adjuvant for ambulatory surgeries. Yegin et al.,[12] evaluated the effect of intrathecal fentanyl 25 mcg added to 18 mg of ropivacaine for trans-urethral resection of prostrate and found significant improvement in the duration and quality of anesthesia without causing substantial increase in frequency of major side effects. This is in concordance with our study. Intrathecal clonidine provides effective relief of pain. Many studies have shown that clonidine when combined with a local anesthetic may improve the quality of subarachnoid block and prolong the postoperative analgesia.[13,14] In our study, we have compared 60 mcg clonidine and 25 mcg fentanyl with 0.5% isobaric ropivacaine (15 mg) intrathecally. Sensory and motor blockade were significantly prolonged with clonidine group as compared with fentanyl group. The time for demand for first rescue analgesia was also prolonged with clonidine group. Similar results have been observed in other studies. De Kock et al.,[15] evaluated the association of small dose of intrathecal ropivacaine (8 mg) with different doses of intrathecal clonidine (15, 45, 75 mcg) in four groups, for ambulatory surgery, and found similar results. Sagiroglu et al.,[16] also obtained similar results.

McNamee et al.,[5] studied the efficacy of two concentrations of intrathecal ropivacaine, 2.5 mL of 0.75% (18.75 mg) and 1% (25 mg), without adjuvants, in patients undergoing total hip arthroplasy. The duration of sensory and motor blockade was prolonged in the group that received 25 mg of ropivacaine. Intraoperative hypotension requiring treatment with inj. ephedrine occurred in 24% of patients in both the groups. This could be because of higher concentration of ropivacaine used. In the present study, we reduced the dose of local anesthetic and supplemented with analgesic adjuvants. The incidence of hypotension and bradycardia observed was 8.6% with the clonidine group and 2.8% in the fentanyl group. De Kock et al., and Sagiroglu et al., reported a statistically significant reduction in mean BP in which higher doses of clonidine was added to ropivacaine.[15,16] Anita R Chhabra, et al compared clonidine versus fentanyl as an adjuvant to intrathecal ropivacaine for major lower limb surgeries.[17] The highest sensory level achieved was T6 in both groups. The time required to reach the peak sensory dermatome was faster in the fentanyl group (6.86 ± 3.73 min) as compared with the clonidine group (8.61 ±7.18 min) P < 0.05. They found a significant difference in the time of onset of sensory block obtained between the two group.our study results were comparable with this study.

Intraoperative pruritus is a disturbing side effect of fentanyl. Incidence of pruritis was very less in our study (8.6% in the fentanyl group) as compared to studies done by Pramod Patra, Kapoor MC, et al [18] who reported incidence of 46%,and M.S. Khanna, Ikwinder KJP Singh et al. [19] A total of 80% of our patients in the clonidine group were well-sedated which is a desirable feature since it reduces the perioperative requirement of sedation and keeps the patient calm and sleeping comfortably. Our aim of providing good-quality anesthesia and prolonged postoperative analgesia for lower limb surgeries was

satisfactorily met by using adjuvants, fentanyl (25 mcg), and clonidine (60 mcg) with 15 mg ropivacaine intrathecally. Clonidine prolonged the subarachnoid block and the postoperative analgesia compared with fentanyl. The hemodynamic parameters need to be closely monitored when adjuvants are used and more caution exercised with clonidine usage. Further research is desirable to calibrate the various dosage combinations of ropivacaine and clonidine for optimum response.

Tables and figures:

Parameter	RC group	RF group	p- value
Age	34.03 ± 8.76	33.63 ± 9.10	.551
Height	161.43 ± 6.60	158.70 ± 4.38	.099
Weight	62.97 ± 7.48	60.93 ± 7.17	.375
Male : Female ratio	24 : 6	19 : 11	.141
Duration of surgery	88.3 ± 9.13	87.0 ± 9.31	.770

Table 1 : Demographic profile

Parameter	RC group	RF group	p- value
Highest sensory level achieved(dermatome)	T 6	T 6	>.05
Time to reach peak sensory level (min)	6.5 ± 0.6	7.8 ± 0.4	< .05
Sensory regression to L 1 (min)	214.50 ± 16.7	298 ± 17.6	< .001
Time to reach Bromage 4 motor block (min)	5.86 ± 5.51	7.8 ± 0.5	> .05
Time to Bromage 1 motor regression (min)	203.50 ± 12.87	245.89 ± 21.73	< .01
Total analgesia time (min)	256 ± 5.81	339.67 ± 5.87	< .001

Table 2 :Spinal block characteristics

Parameter	RC group	RF group	p- value
Hypotension	3	2	0.533
Bradycardia	2	1	0.240
Nausea/vomiting	0	1	0.312
Respiratory depression	0	0	1.000
Shivering	0	1	0.312
Pruritis	2	3	0.096

Table 3 :Side effect profile

Sedation score	RC group	RF Group
0	1	20
1	10	14
2	1	18
3	0	0

Table 4: Comparison of sedation score in between the two groups

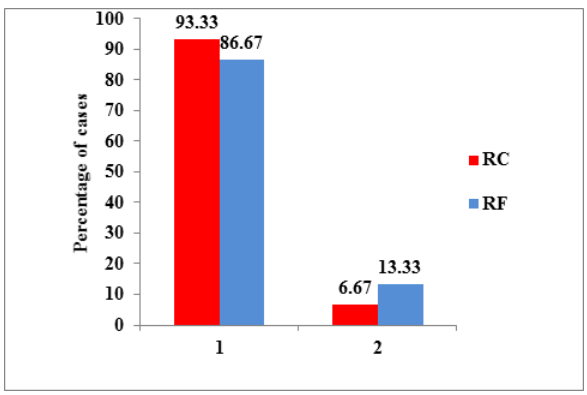

Figure 1: ASA status of patients between the two groups

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