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Efficacy and Appropriate Dosage of Isobaric Ropivacaine for Spinal Anesthesia in Patients Undergoing Elective Lower Limb Orthopaedic Surgeries.

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Abstract:
Background: *The dose response of ropivacaine has not been extensively determined yet. This study was conducted to estimate minimum effective local anaesthetic dose and to assess the duration of sensory and motor block, and side effects if any, of intrathecal administration of ropivacaine for lower limb surgeries.*
Materials and Methods: *120 patients aged between 20 years and 60 years of either sex belonging to ASA Class I and Class II posted for elective lower limb orthopaedic surgeries were randomly selected for the study. The study population was randomly divided by a set of random numbers into 3 groups (Group I= 10mg of isobaric Ropivacaine, Group II= 15mg of isobaric Ropivacaine, Group III= 20mg of isobaric Ropivacaine Statistical comparisons were performed using analysis of variance with post hoc analysis*
Results: *All three groups were comparable regarding the age and gender of the patients and the variation in age and gender distribution between groups was statistically insignificant. Onset of sensory block was statistically significant in three groups. Overall 58 patients (48.3%) successfully completed their surgery. According to our definition the spinal anaesthesia was effective in 10 (25%), 20 (50%), 36 (90%) in 10mg, 15mg and 20mg groups respectively. Based on this result we determined ED 50 (50% CI) to be 15mg (13-16) and ED 95 (95% CI) to be 20mg (18.5-22.5).*
Conclusion: *We conclude that ropivacaine is a suitable agent for spinal anaesthesia in lower limb orthopaedic surgeries and adequacy of spinal anaesthesia is related to the dose and degree of motor block.*
Abstract Word Count : 251

I. Introduction

Spinal anaesthesia is one of the commonest methods of anaesthesia for orthopaedic lower limb procedures. Till recently Bupivacaine 0.5% heavy was the only drug used for spinal anaesthesia after the discontinuation of lidocaine's intrathecal use. In 2009 ropivacaine another aminoamide local anaesthetic having all the advantages but less the cardio and CNS toxicity of bupivacaine has been introduced in India. Ropvacaine is unique amongst this group in that it is prepared for clinical use as the pure s-enantiomer rather than a racemic mixture[1,2,3]. The advantage of ropivacaine is that it produces less motor block when used in lower doses and can be very useful for ambulatory surgeries and also better safety profile in terms of cardiac and CNS toxicity. There are many reports who have described the intrathecal use of ropivacaine[4-12]. As ropivacaine has been recently introduced in India and not many studies have been done in India regarding use of ropivacaine for spinal anaesthesia. Hence a study was conducted to know minimum effective local anesthetic dose and to assess the duration of sensory and motor block and side effects if any of intrathecal administration of ropivacaine for lower limb surgeries.

II. Methods

120 patients aged between 20 years and 60 years of either sex were taken up for the study. These were posted for elective lower limb orthopaedic surgeries in the year 2014 in a tertiary orthopaedic care centre and were randomly selected for the study after obtaining approval from the Institutional Ethical Committee along with written and informed consent from patients participating in the study. The study population included ASA class I and II (American society of Anesthesiologists class I and II). The study population was randomly divided by a set of random numbers into 3 groups (Group I= 10mg of isobaric Ropivacaine, Group II= 15mg of isobaric Ropivacaine, Group III= 20mg of isobaric Ropivacaine). The numbers were kept equal in each group by a method of permuted randomization with 40 patients in each group (n=40). Patient who refuse to subarachnoid block or with known allergy to amide local anesthetic were excluded from the study. Patients with lower extremity peripheral neuropathy or with severe cardiac and respiratory diseases were also excluded from this study. All Patients were premedicated on the night before surgery and preloaded before anesthesia with intravenous ringer lactate. Before commencement of anaesthesia patients were instructed regarding methods of sensory and motor assessment and baseline. Monitoring was done using multiparameter monitor having pulse oximetry, ECG NIBP and SPO_2. Patients were placed in sitting position. Under all aseptic precautions the space was identified at $L_4 - L_5$ or $L_3 - L_4$ interspace. A 25 G Quincke spinal needle was passed through through midline approach and study drug was injected after confirmation of needle tip in the subarachnoid space by free flow of CSF. The study solution was prepared randomly in syringe with dose of 10mg, 15mg and 20mg. The investigator assessing the effects of drug was blinded for the study. Onset of sensory and motor blockade and maximum level of the same was noted. Time for two segment sensory regression and total duration of sensory blockade and motor blockade were also observed. Monitoring during surgery and peri-operative period was done by means of multiparameter monitors which displays heart rate, systolic blood pressure (SBP) diastolic blood pressure (DBP), mean arterial pressure (MAP), ECG and SPO_2. till complete sensory and motor recovery.

Sensory blockade was tested using pinprick method with a blunt 27G needle at 2mins interval after the spinal injection and subsequently at 5 mins interval during first 30 mins, then at 15 min intervals between 30 and 120 mins, and thereafter at 30 min intervals until complete recovery. Quality of motor blockade was assessed by modified Bromage scale. Total duration of surgery, total duration of analgesia and side effects were also noted.

Patients were evaluated for 24 hours regarding total duration of analgesia, postoperative analgesic requirements, vital parameters (heart rate, blood pressure, respiratory rate, and oxygen saturation), adverse affects and other sequelae. Postoperatively, the pain was recorded by using visual analogue scale (VAS) between 0 and 10 (0 = no pain, 10 = most severe pain); initially every hourly for 4 hours, then every 4 hourly for the next 24 hours. Injection Diclofenac (75mg) was given intramuscularly as rescue analgesia when visual analogue scale was $\geq$4.

Statistical analysis

Results were presented as mean and SD or median and range where appropriate. Statistical comparisons were performed using analysis of variance with post hoc analysis. Inter-group comparisons were performed using one-way analysis of variance. We used linear regression and chi-square test to determine dose response relation of motor block. Analysis was performed using SPSS version 14.0. If p value was significant, then multiple comparison tests were applied to see the significance between each pair of groups using one-way analysis of variance.

Effective dose was defined as a dose that provides adequate sensory dermatomal anaesthesia to pinprick to T8 or above. Data for successful response in each group were used to construct a working probit-log (dose) plot.

III. Results

In 10mg group age ranged from 20-55 years with a mean of 39.40$\pm$4.882. In 15mg group age ranged from 25-60 years with a mean of 43.05$\pm$6.939. In 20mg group age ranged from 2-58 years with a mean of 44.40$\pm$8.519. The statistic analysis between the groups was statistically not significant (p = 0.131). All three groups were comparable regarding the gender of the patients and the variation in gender distribution between groups was statistically insignificant (p = 0.817). Majority of patients in study population belonged to ASA Class I in all the groups. The variation in ASA class distribution of patients among different group was statistically insignificant (p = 0.243). The height (cm) in 10mg group ranged between 154 to 173cm with a mean height of 168.95$\pm$7.052cm. In 15mg group height (cm) ranged between 157-175cm with a mean height of 166.15$\pm$7.415. In 20mg group height (cm) ranged between 156-174cm with a mean height of 165.65$\pm$8.293. When values were compared statistically the difference was found insignificant (p = 0.342).

Duration of surgery ranged between 35 to 75 minutes with a mean duration of 44.55$\pm$11.26 minutes in 10mg group. 45 to 75 minutes with a mean duration of 59.55$\pm$11.843 minutes in 15mg group and 48 to 80

minutes with a mean duration of 65.55±10.490 minutes in 20mg group. The statistical difference between the groups was insignificant with a p value of 0.273. The time from injection to highest level of sensory block among the groups was statistically significant ($p \leq 0.0001$).[Table 1]

In 10mg group, onset of sensory block ranged from 5.9-8.7 minute with a mean of 7.1±0.648. In 15mg group onset of sensory block ranged from 5.7-9.0 minute with a mean of 7.3±1.061 and in 20mg group, onset of sensory block ranged from 6.0-10.2 minute with a mean of 7.5±1.161. The difference was statistically insignificant among the groups with a p value of 0.348. The time from injection to highest level of sensory block in 10mg group ranged from 9-14 minutes with a mean of 12.7100±1.21304 min. In 15mg group it ranged from 8-12 minutes with a mean of 11.3050±2.08818 minutes and in 20mg group it ranged from 7-11 minutes with a mean of 9.1400±0.63528. The statistical difference among the groups was significant ($p \leq 0.0001$). Multiple comparison test among the study groups was significant (Table 2).

Time for two segment regression from highest level of sensory block ranged between 85 to 110 minutes with a mean of 92.75±1.997 in 10mg group, 92 to 120 minutes with a mean of 104.50±3.000 in 15mg group and 100 to 130 minutes with a mean of 108.50±0.946 in 20mg group. The statistical difference among the group was significant with a p value of < 0.000. Multiple comparison test among the study groups was significant (Table 3).

The time of onset of motor block to Bromage 4 ranged from 9.9 to 14.3 minutes with a mean of 12.06±1.08 minutes in 10mg group. 8.2 to 14.1 minutes with a mean of 11.40±1.38 minutes in 15mg group. 8.52 to 14.2 minutes with a mean of 11.24±1.54 minutes in 20mg group. The statistical difference among the group was not significant with p value of 0.08.

The time of regression of motor blockage to Bromage 0 ranged from 90-125 minutes with a mean of 115.30±4.725 minutes in 10mg group. 110-140 minutes with a mean of 133.45±1.849 minutes in 15mg group and 122-158 minutes with a mean of 138.25±1.118 minutes in 20mg group. The statistical difference between the groups was significant ($p < 0.0001$).

Overall as per our definition, spinal anaesthesia was effective in 10 (25%), 20 (50%), 36 (90%) in 10mg, 15mg and 20mg groups respectively. Based on this result we determined ED 50 (50% CI) to be 15mg (13-16) and ED 95 (95% CI) to be 20mg (18.5-22.5).

The incidence of hypotension, bradycardia, nausea and vomiting were similar among the groups. No patient had residual neurologic changes or back pain when examined 24 hours after operation.

IV. Discussion

In this study we have shown a dose dependent relation between the duration of sensory analgesia and the extent and duration of motor block and the success rate of spinal anaesthesia for lower limb surgeries. The rate of onset of analgesia and motor blockade and number of segment blockade were not influenced by the dosage. The primary aim of this study was to determine an effective dose of spinal ropivacaine for orthopedic surgeries of lower limb because one potential benefit of use of the spinal ropivacaine would be for ambulatory surgery of short duration in order to decrease hospital burden and thereby providing cost effective management. Different doses have been used in previous studies for spinal anesthesia for lower limb surgeries ranging from 15mg to 33.75mg [4,9,13,14,15] but the most suitable effective dose for elective lower limb surgeries of more than 50 minutes duration has not been studied well.

Using probit analysis, we determined the ED 50 (95% CI) to be 15mg (13-16.8mg) and ED95 (95% CI) to be 20mg (18.5-22.5mg). The estimation of dose requirement for intrathecal ropivacaine from this study is incomparable with earlier study by Lee YY et al [12] who defined ED 50 and ED 95 as 7.6 and 11.4 mg respectively but their shortcomings were small sample size and CI were wide. They considered time period up to 50 minutes as successful criteria and did not monitor progression and regression of sensory and motor block.

Sell et al [16] defined ED_{50} of ropivacaine for patients having hip replacement surgery as 12.8mg (95% CI: 12.2-13.4mg) and used the technique of continuous spinal anaesthesia with spinal catheter and updown sequential analysis. Loss of sensation to pinprick and tetanic electrical stimulation at T_{12} dermatome, complete motor block at 20 min after intrathecal injection were used as criteria for success by them. They used spinal catheter that would produce a different spread of local anaesthetic compared with injection through needle. These differences in successful criteria and technique of intrathecal injection of study solution render direct comparison of our results impossible.

Hemodynamic complications like bradycardia and hypotension were dose independent as reported in other studies[17,18,19]. We had high failure rates with low doses when the surgery used to get prolonged that limited the benefits of our study in those groups. We further recommend that facilities for other modalities of anesthesia should also be kept available while using ropivacaine in low doses.

V. Conclusion

In conclusion we found that ropivacaine is a suitable agent for spinal anaesthesia in lower limb orthopedic surgeries. When used for this purpose, we calculated ED_{50} of spinal ropivacaine to be 15mg and ED_{95} to be 20mg. Adequacy of spinal anaesthesia was related to dose and to the degree of motor block but poorly correlated with upper level of sensory change assessed by pinprick.

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Tables

Table 1: Highest level of sensory block

Study Group	**Highest level of sensory block**				**Total**
	T4	**T5**	**T6**	**T8**	
10mg	0	0	6	14	20
	0.0%	0.0%	30.0%	70.0%	100.0%
15mg	2	4	11	3	20
	10.0%	20.0%	55.0%	15.0%	100.0%
20mg	3	9	8	0	20
	15.0%	45.0%	40.0%	0.0%	100.0%
Total	**5**	**13**	**25**	**17**	**60**
	83%	**21.6%**	**41.6%**	**28%**	**100.0%**

Table 2: Multiple Comparison test among the study groups

Study Group (A)	**Study Group (B)**	**Mean Difference (A&B)**	**P value**
10mg	15mg	1.40500*	.003
	20mg	3.57000*	.000
15mg	10mg	-1.40500*	.003
	20mg	2.16500*	.000
20mg	10mg	-3.57000*	.000
	15mg	-2.16500*	.000

Table 3: Two segment regression from highest level of sensory block (min)

	N	**Mean**	**Std. Deviation**	**P value**
10mg	20	92.75	1.997	< 0.000
15mg	20	104.50	3.000	
20mg	20	108.50	.946	
Total	60	101.92	7.065	