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Comparison of Intrathecal Bupivacaine, Ropivacaine (0.75%) and Ropivacaine (0.75%) with Clonidine (30µg) for Lower Abdominal and Lower Limb Surgeries with Regard to Quality of Anaesthesia and Safety.

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ABSTRACT

Background: A prospective randomized study was conducted to study the efficacy and safety of Bupivacaine, Ropivacaine and Ropivacaine with clonidine intrathecally for lower abdominal and lower limb surgeries. **Methods:** 120 patients undergoing lower abdominal and lower limb surgeries of 120 minutes or lesser duration were randomized into three groups, n = 40. Group A received 3 ml 0.5% Bupivacaine (15 mg)+ 0.2ml normal saline, Group B received 3 ml of 0.75% isobaric Ropivacaine (22.5 mg)+ 0.2ml normal saline and Group C received 3ml of 0.75% Ropivacaine (22.5mg)+ clonidine 30 µg. Quality of subarachnoid blockade and hemodynamic changes were compared. **Results:** Onset time and time to maximum motor blockade was rapid in all the three groups ; duration of motor blockade was significantly shorter in Ropivacaine group and comparable between Bupivacaine and Ropivacaine with clonidine group. Onset of sensory blockade and maximum sensory block level achieved were comparable between three groups. Time to, onset of maximum sensory block and regression of sensory block by 2 segments were shorter in the Bupivacaine group compared to the other 2 groups. Better hemodynamic profiles were noted in Ropivacaine groups compared to Bupivacaine group. There were no statistically significant differences between the Quality of sedation and the side effects between the groups. **Conclusion:** Hemodynamic profile was better with Ropivacaine and onset, quality, duration of analgesia, etc. were comparable with Bupivacaine when clonidine 30µg was added as adjuvant.

Keywords: Bupivacaine, Clonidine, Intrathecal, Ropivacaine.

INTRODUCTION

The increased popularity of ambulatory surgeries has resulted in more frequent use of sub arachnoid blocks with local anaesthetics. Bupivacaine has been the agent of choice for spinal anaesthesia traditionally, though its undesirable side effects like bradycardia, hypotension, cardiotoxicity and central nervous system toxicity has been a matter of concern.[1,2] Bupivacaine has been associated with cardiotoxicity when used in high concentration or when accidentally administered intravascularly.

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Ropivacaine, a long-acting regional anaesthetic is a pure S(-) enantiomer, unlike Bupivacaine, which is a racemate, developed for the purpose of reducing potential toxicity and improving relative sensory and motor block profiles.[3] Ropivacaine is less lipophilic than bupivacaine and that, together with its stereo-selective properties[4], contributes to a significantly higher threshold for cardiotoxicity and CNS toxicity than bupivacaine in animals[4,5] and healthy volunteers.[6]

Motor block is similar to bupivacaine, but with a later onset and a shorter duration.[7] Clonidine is a partial agonist of the α-2-adrenoreceptor, which acts as an analgesic and sedative. During spinal anesthesia, clonidine is administered as an adjuvant to local anaesthetic to decrease the time to onset of block, increase its depth and duration, lower the dose of local anaesthetic, reduce systemic absorption and therefore prevent side effects.

MATERIALS AND METHODS

After obtaining approval from hospital ethics committee and written informed consent, 120 patients of American Society of Anesthesiologists Grade I and II, aged between 20 and 60 years scheduled for elective lower abdominal and lower

limb surgeries of 120 mts or lesser duration under spinal anesthesia were included in the study.

Study was conducted in the Department of Anaesthesiology, KMCT Medical college, Calicut between June 2012-2015. Exclusion criteria included bleeding disorders, infection at puncture site, morbid obesity, emergency surgeries, other contra-indications for spinal anesthesia, allergies to amide local anaesthetics, patients with baseline heart rate < 55beats/mt, and history of uncontrolled hypertension and diabetes. All patients were pre-medicated with Tab. Lorazepam 1mg, Tab. Rantac 150mg and Tab. Domstal 10mg 1-2 hrs before surgery.

Patients were randomly assigned into three groups (n=40) using sealed envelope method to receive 3 ml of 0.5% Bupivacaine(H) (15 mg) +0.2ml Normal saline for Group A, 3 ml of 0.75% isobaric Ropivacaine (22 mg)+ 0.2ml Normal saline for Group B and 3 ml of 0.75% isobaric Ropivacaine (22 mg)+ 30µg Clonidine for Group C.

Before commencement of spinal anesthesia, patients were instructed on the methods of sensory or motor assessments. Intravenous line secured, Ringer's lactate solution (10 ml/kg) was infused for 15 min before the initiation of the procedure. Non-invasive monitors connected and baseline values of heart rate, blood pressure and oxygen saturation were noted before the procedure. Spinal anesthesia was performed in left lateral position with 25 G Quincke babcock's spinal needle with a midline approach at the L3-4 interspace and drug administered. Level of sensory block was checked with cold spirit cotton swab in the axillary line by a blinded anaesthetist/ anesthesia technician. Motor block was assessed by Modified Bromage scale [Table 1]. Degree of sedation was assessed with Ramsay Sedation Score [Table 2].

Table 1: Modified Bromage Scale

Score	Criteria
0	No motor block
1	Inability to raise extended leg; able to move knees and feet
2	Inability to raise extended leg and move knee; able to move feet
3	Complete block of motor limb

Table 2: Ramsay Sedation Scale

Score	Response
1	Anxious or restless or both
2	Cooperative, orientated and tranquil
3	Responding to commands
4	Brisk response to stimulus
5	Sluggish response to stimulus
6	No response to stimulus

Level of Sensory – Motor block and sedation was evaluated at 3, 6, 10, 15, 20, 30, 45, 60, 75, 90 & 120 mts. Onset time of sensory or motor blockade was defined as the interval between intrathecal administration and time for maximum level of sensory block or a Bromage score of 3 respectively. Duration of sensory or motor blockade was defined as interval from intrathecal administration to the point of complete resolution of the sensory block or to the point in which Bromage score was back to zero respectively. Thus, the maximum level of sensory block, onset time, duration of sensory and motor blockade as well as the interval from intrathecal administration to the point of a two-segment regression of sensory blockade was recorded. Maximum deviation of systolic/diastolic blood pressure and heart rate from the baseline were recorded. Hypotension (>20% decrease from baseline value) was treated with I.V Mephentermine 6mg and crystalloids. Bradycardia treated with 0.6mg Atropine I.V. Side-effects including Nausea, vomiting, post-operative headache, urinary retention and shivering were noted and treated. Surgery was started when a sensory block at or above T6 dermatome was established.

Statistical Analysis

All Statistical analyses were carried out with ANOVA (Analysis of Variance), except Quality of sedation and Side effects, which were analysed by Chi-square statistics. P-value <0.05 was considered as significant. There was no significant difference between the two groups with respect to age, height, weight, sex and duration of surgery [Table 3].

Maximum deviation of Heart rate, Systolic BP and Diastolic BP [Table 4] from the baseline was statistically significant and in the following order; Bupivacaine group > Ropivacaine-Clonidine group > Ropivacaine group. Change in respiratory rate per minute from baseline was not significant between the groups [Table 4].

Table 3: Demographic Data

Variable	Group I (n=40)	Group II (n=40)	Group III (n=40)	P-Value
Age(yrs)	47.28 ± 6.6	48.5 ± 7.4	48.64 ± 7.14	0.639
Weight(kg)	66 ± 10.22	67.78 ± 7.6	64.6 ± 10.83	0.339
Height(cm)	171.32 ± 5.96	171.85 ± 4.81	170.75 ± 4.53	0.633
Operative time (mts)	65 ± 27.7	68 ± 28.4	66 ± 26.8	0.885

RESULTS

Onset of sensory block was similar in the 3 groups. Most of the patients in Group I (85%), Group II (92.5%) and Group III (95%) had a maximum sensory level of T6 [Graph I]. Time to maximum sensory block (in mts) was more rapid in the Bupivacaine group followed by Ropivacaine-

Clonidine group and Ropivacaine group (P-value <0.05). The mean time for regression of sensory block by 2 segment was more for the Ropivacaine-Clonidine group followed by Ropivacaine and then Bupivacaine group, indicating comparatively longer sensory block time with Ropivacaine-clonidine group. Mean onset time for motor block was comparable between the 3 groups. Mean onset time to maximum motor block was faster and duration of motor block was comparatively more in the Bupivacaine and Ropivacaine-Clonidine group than the Ropivacaine group (P-value <0.05) [Table 5].

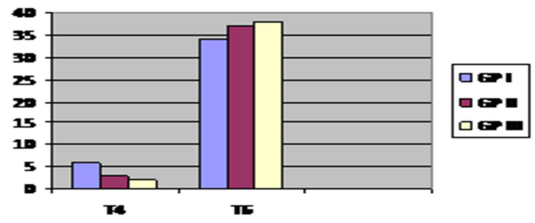
Table 4: Comparison of Vital Parameters

Parameter	Gp I (n=40) Mean ± SD	Group II (n=40) Mean ± SD	Group III (n=40) Mean ± SD	ANOVA				
				SS	df	Ms	F	P-Value
Max. deviation of HR(beats/mt) from baseline. (0-120mts of surgery)	18 ±6.21	8.8±3.4	16 ±7.01	B:1873.067 W:3871.304	2 117	936.533 33.08	28.304	0.000
Max. deviation of Systolic BP (mm Hg)from baseline. (0-120mts of surgery)	22±8.31	8±6.21	14±7.13	B:3946.667 W:6179.827	2 117	1973.333 52.819	37.360	0.000
Max. deviation of Diastolic BP (mm Hg)from baseline. (0-120mts of surgery)	8±3.14	4±2.41	6±3.02	B:320 W:966.736	2 117	160 8.263	19.364	0.000
Change in Resp. Rate/mt from baseline	3.3±1.02	3.01±1.1	3.11±1.01	B:1.736 W:127.55	2 117	0.868 1.090	0.796	0.453

Table 5: Sensory and Motor block characteristics (Mean ± SD)

Parameter	Group I (n=40) Mean ± SD	Group II (n=40) Mean ± SD	Group III (n=40) Mean ± SD	ANOVA				
				SS	df	Ms	F	P-Value
Onset of sensory block (mts)	1.06 ±0.38	1.61±0.72	1.27 ±0.42	B:6.163 W:32.729	2 117	13.081 0.280	11.015	0.000
Time to maximum sensory block(mts)	6.6±2.42	16.02±3.1	12.11±1.81	B:1791.795 W:730.95 8	2 117	895.897 6.248	143.401	0.000
Regression of sensory block by 2 segments (mts)	102.6±18.22	116.8±13.8	139.2±18.7	B:27239.467 W:34011.83	2 117	13619.733 290.699	46.852	0.000
Onset of Motor block (mts)	1.08±0.25	2.03±0.35	1.33±0.41	B:19400 W:13.771	2 117	9.7 0.118	82.413	0.000
Time to onset of maximum motor block (mts)	4.22±1.20	8.33±1.81	5.61±1.33	B:349.635 W:252.915	2 117	174.817 2.162	80.892	0.000
Duration of motor block (mts)	181.2±22.3	142.5±9.6	177±19.7	B:36074.400 W:38124.06	2 117	18037.2 325.847	55.355	0.000
Time to 1st rescue analgesic	218±32.61	182.2±23.2	211±21.38	B:28801.067 W:80291.50	2 117	14400.533 686.252	20.984	0.000

(ss: sum of squares, df: degrees of freedom, Ms: Mean squares, F:Ratio of between groups mean square over within groups mean square)



Graph 1: Maximum Sensory Block

Time to first rescue analgesic was also more in the Bupivacaine and Ropivacaine-Clonidine group [Table 5]. Quality of sedation was comparable between the groups with majority of the subjects having a Ramsay sedation score of 2. 10% of the subjects in the Ropivacaine-Clonidine group had a sedation score of 3 [Table 6]. Side effects were more in the Bupivacaine group, but statistically insignificant [Table 7].

Table 6: Quality of Sedation in the groups

Ramsay sedation score	Group I (n=40)	Group I (n=40)	Group I (n=40)	P-Value
2	40	39	36	0.066335
3	0	1	4	

(Chi-square statistic is 5.4261)

Table 7: Side effects in the study groups

Side effects	Group I (n=40)	Group I I (n=40)	Group III (n=40)	P-Value
Nausea & Vomiting	2	0	1	0.837932
Bradycardia	5	1	3	
Hypotension	6	0	3	

(Chi-square statistic is 1.4359)

DISCUSSION

Subarachnoid block with its relatively good safety profile and high success rate is still the most preferred anesthesia technique, especially for day care surgeries, among the practicing anaesthesiologists. Traditionally used Bupivacaine with its undesirable side effects and cardiotoxicity is still the preferred local anaesthetic. Lesser lipophilic, shorter acting Ropivacaine with a better safety profile, if the duration of anaesthesia it can provide can be prolonged by addition of a suitable adjuvant, can be a good alternative to Bupivacaine. We conducted this study to compare the block characteristics, duration of anaesthesia etc between Bupivacaine, Ropivacaine and Ropivacaine with an adjuvant (clonidine) added. In our study, the deviation of heart rate, systolic and diastolic BP from baseline values were comparatively more in the Bupivacaine group. Griffin et al.[8]demonstrated the similar hypotensive effects of intrathecally administered Ropivacaine and Bupivacaine. Danelli et al.[9] noticed no difference in clinical hypotension in 60 women undergoing elective caesarean delivery under spinal anesthesia with either Ropivacaine or Bupivacaine. Sonal N. Bhat et.al[10] in their study noted that the fall in systolic and the diastolic blood pressure from the 5 min interval was more in the Ropivacaine group, which was almost comparable with Bupivacaine group by the end of the surgery. De Kock et al.[11], McNamee et al.[12] & Malinovsky et al.[13] in their studies reported statistically significant intra-operative hypotension with higher concentrations of intrathecally administered Ropivacaine, which was different from our study findings. In our study, onset time of sensory block was similar in the 3 groups and most of the patients in all the three groups had a maximum sensory level of T6. Time to maximum sensory block was comparatively more rapid in the Bupivacaine group followed by Ropivacaine-Clonidine group and Ropivacaine group. The mean time for regression of sensory block by 2 segment was more for the Ropivacaine-Clonidine group followed by Ropivacaine and then Bupivacaine group, indicating comparatively longer sensory block time with Ropivacaine-clonidine group. Malinovsky et al.[13], McNamee et al.[12] and Sonal N. Bhat et. al[10] in their study comparing intrathecal isobaric ropivacaine versus bupivacaine, found that cephalad spread of sensory blocks was higher with Bupivacaine than with Ropivacaine. Volume of diluted anaesthetic solutions may alter the cephalad extent of anesthesia. However, there are large inter individual variations in the total volume of cerebrospinal fluid [14] and dilution does not significantly affect the spread of intrathecal anesthesia[15]. The major determinant for the spread of intrathecal anesthesia is the dose of local anaesthetic injected[16]. Kallio et al.[17] proved in their study that, time of onset and duration of sensory block was comparable between both the drugs. In our study, the two segment regression time was comparatively more in Ropivacaine-clonidine and Ropivacaine group, which was comparable with the findings of Sonal N. Bhat et. al [10]. Çınar et al.[18] and Klimscha et al.[19] Gonul Sagiroglu et al[20] and De Kock et al.[11] compared sensory and motor blocks by intrathecally administering ropivacaine with various doses of clonidine and there were no differences between the groups in terms of time to onset of maximum sensory and motor blocks. However, compared to the clonidine free group, two segment reduction time were longer in clonidine groups, which supported our findings.

In our study, mean onset time of motor block was comparable between the 3 groups and these observations are in accordance with the similar studies conducted by McNamee et al.[12], Kallio et al[17] and Sonal N Bhat et al.[10] We observed that the mean onset time to maximum motor block was faster and duration of motor block was comparatively more in the Bupivacaine and Ropivacaine-Clonidine group than the Ropivacaine group. Sonal N bhat et al.[10] noted longer mean duration of motor and sensory blockade in the Ropivacaine group. Quality of sedation in our study was also comparable between the groups with majority of the subjects having a Ramsay sedation score of 2. Carabine et al.[21] also found sedation rates to be similar in their study in which bupivacaine alone or in combination with clonidine was used in spinal anesthesia. 10% of the subjects in our study in the Ropivacaine-Clonidine (30µg) group had a sedation score of 3. In the study performed by De Kock et al.[11] including 120 patients, various doses of clonidine were added to 8 mg ropivacaine. Sedation developed in two patients in the 75 µg clonidine group. Gonul Sagiroglu et al[20] observed sedation in five out of 25 cases in the Ropivacaine plus 30 µg Clonidine group.

We observed more side effects in the Bupivacaine group, but statistically insignificant. 13 out of the 40 subjects had either nausea & vomiting, bradycardia or hypotension, compared to 7 in Ropivacaine-Clonidine group and 1 in Ropivacaine group.

CONCLUSION

Our study revealed that Ropivacaine, with reduced potential for CNS and Cardiotoxicity, appears to be a safe alternative to Bupivacaine when administered intrathecally and further an adjuvant like Clonidine when added, can provide similar or better onset, quality, duration of analgesia, sensory and motor blockade as that of Bupivacaine.

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