COMPARATIVE EVALUATION OF HAEMODYNAMIC CHANGES AND COMPLICATIONS ASSOCIATED WITH TWO DIFFERENT DOSES OF ROPIVACAINE HYDROCHLORIDE (0.75% AND 0.5%) IN SPINAL ANAESTHESIA IN LOWER LIMB ORTHOPAEDIC SURGERIES

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ABSTRACT

BACKGROUND

The introduction of safe drugs enhanced the popularity of spinal anaesthesia. Lofgren and Lundqvist introduced the most commonly used drug, Lignocaine. One of the disadvantages of Lignocaine was the association with transient neurological symptoms, which presents as low backache and lower extremity dysesthesia. Bupivacaine was introduced by Ekenstam in 1957. It is a well-established long-acting local anaesthetic used for spinal anaesthesia. It has been used frequently in spinal anaesthesia with a very little incidence of transient neurological symptoms. But it is associated with cardiovascular and central nervous system toxicity when used in high concentration or when accidentally administered intravascularly. Ropivacaine was introduced into clinical practice in 1996. It was initially used in epidural anaesthesia in lower extremity surgery, where it was compared with bupivacaine where they concluded that ropivacaine produced similar sensory and motor blockade with less cardiotoxicity. In a study, different concentrations of intrathecal ropivacaine 0.5% and 0.75% were compared for vascular surgery, which concluded that 15 mg of plain ropivacaine 0.75% is effective and safe and gives complete spinal anaesthesia in high risk patients without side effects and cardiovascular modifications.

The aim of this study was to compare and evaluate the haemodynamic changes and side effects associated with equal volumes of two different doses of ropivacaine hydrochloride (0.75% and 0.5%) used in spinal anaesthesia in lower limb orthopaedic surgeries.

MATERIALS AND METHODS

It is a prospective, randomised, double blind study conducted in a tertiary care hospital in which 80 patients of age group 20 - 65 years of either sex which were scheduled to undergo lower limb orthopaedic surgeries under spinal anaesthesia with two different doses of Ropivacaine Hydrochloride were included. The patients were randomly divided into 2 groups of 40 each. Group A received 22.5 mg (3 mL) of 0.75% isobaric Ropivacaine Hydrochloride. Group B patients received 15 mg (3 mL) of 0.5% isobaric Ropivacaine Hydrochloride.

RESULTS

The haemodynamic profile of both the groups was comparable, both intra- as well as post-operatively. In terms of safety, both doses of intrathecal ropivacaine provided high degree of cardiovascular stability with a low incidence of bradycardia and hypotension. On comparing side effects and complications, both the doses of intrathecal ropivacaine had low incidence of adverse effects.

CONCLUSION

Both ropivacaine 0.75% and 0.5% produced minimal side effects and complications as well as provided high degree of cardiovascular stability, hence recommended for anaesthetic use in prolonged lower limb orthopaedic surgeries.

KEYWORDS

Ropivacaine, Spinal Anaesthesia, Bradycardia, Hypotension, Toxicity.

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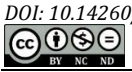

BACKGROUND

Central neuraxial blockade remains an important part of anaesthesiologists' armamentarium. Various drugs have been tried in the past for subarachnoid block, not only to provide excellent surgical anaesthesia but also to be free from inadvertent side effects. Local anaesthetics are the drugs producing reversible conduction blockade of impulses along central and peripheral nerve pathways after regional anaesthesia.[1] The introduction of safe drugs enhanced the popularity of spinal anaesthesia. Lofgren and Lundqvist

introduced the most commonly used drug Lignocaine in 1943, but it was used clinically by Gordh at Karolinska Hospital, Stockholm in 1948.[2] One of the disadvantages of Lignocaine was the association with transient neurological symptoms, which presents as low backache and lower extremity dysesthesia with radiation to hip, thigh and lower limbs beginning within 24 hours of spinal anaesthesia and lasting as long as 5 - 7 days.[3] Bupivacaine was introduced by Ekenstam in 1957[4] and was used clinically for the first time by Telivuo in 1963.[5] It is a well-established long-acting local anaesthetic used for spinal anaesthesia. It has been used frequently in spinal anaesthesia with a very little incidence of transient neurological symptoms. But it is associated with cardiovascular toxicity and central nervous system toxicity when used in high concentration or when accidentally administered intravascularly.[6] Ropivacaine is an amino-amide local anaesthetic drug, which was first synthesised in 1957[7] and was introduced into clinical practice in 1996[8] and has consistently demonstrated an improved safety profile over bupivacaine with a reduced central nervous system and cardiotoxic potential.[9] It has low lipid solubility which blocks nerve fibres involved in pain transmission (A delta and C fibres) to a greater degree than those controlling motor functions (A beta fibres).[10] Ropivacaine was initially used in epidural anaesthesia in lower extremity surgery, where it was compared with bupivacaine where they concluded that ropivacaine produced similar sensory and motor blockade with less cardiotoxicity.[11] In a study, different concentrations of intrathecal ropivacaine 0.5% and 0.75% were compared for vascular surgery (Saphenectomies, peripheral aneurysms). It was concluded that 15 mg of plain ropivacaine 0.75% is effective and safe and gives complete spinal anaesthesia in high risk patients without side effects and cardiovascular modifications.[12]

As there are limited studies on effects of ropivacaine in spinal anaesthesia, so we conducted a dose comparison study of ropivacaine with an aim to know the clinical haemodynamic changes and side effects associated with two different doses (0.5% and 0.75%) of ropivacaine in patients undergoing lower limb orthopaedic surgeries under spinal anaesthesia.

MATERIALS AND METHODS

It is a prospective, randomised, double blind study in which 80 patients of American Society of Anaesthesiologists (ASA) physical status I and II of age group 20 - 65 years of either sex were admitted in a tertiary care superspeciality hospital over a span of 2.5 years from August 2011 to February 2014.

Inclusion Criteria

Patients who were scheduled to undergo lower limb orthopaedic surgeries under spinal anaesthesia were included after the approval of ethical and scientific committee of the institution along with the informed written consent from the patients.

Exclusion Criteria

The type of patients excluded from the study were unwillingness of the patient, any life-threatening disease, neurological disorders, coagulation disorders, morbid obesity, any signs of sepsis, deformity or previous surgery of spine, any anticipated difficulty in regional anaesthesia, any history of allergy to study drug and infection at injection site.

Sample Size

From the previous study by Veena et al, the mean time for two-dermatome regression has been reported in the range of 112 to 131 minutes with a populated standard deviation (Sigma) of 29 minutes.[13] This parameter was selected, as it could be the earliest indicator of fading effect of anaesthesia. For 95% confidence interval and 80% power of the study- 37 patients would be needed in each group using following formula –

$$N = \frac{2[(a+b)^2\sigma^2]}{(\mu 1-\mu 2)^2},$$

where a and b are a = conventional multiplier for alpha = 0.05,

b = conventional multiplier for power = 0.80, μ1 − μ2 = the difference between the means from the previous study (131 - 112 minutes), σ^2 is populated standard deviation (29 minutes).

To allow for dropouts, sample size was fixed at 40 patients in each group.

Study Protocol

Pre-anaesthetic assessment was carried out in every case one day before surgery. All the patients were given Tab. Alprazolam 0.25 mg a night before surgery in the orthopaedic ward. Inj. Midazolam 0.04 mg/kg body weight was given by intravenous route just before procedure in all the groups in the operating room.

A total of 86 patients met the inclusion criteria and were included in the study. Patients were randomly divided into two groups in a double-blind manner. In the operating room, patients were randomised by sealed envelope method (wherein, externally computer-generated numbers were used) to the groups. The randomisation code allotted to the patients was kept separately and investigators were blinded to it until the study was completed. Different concentrations (0.75% and 0.5%) isobaric ropivacaine hydrochloride were covered with opaque sacks by the pharmacist in the 1:1 ratio. Only the pharmacist was aware of the code given to the type of solution in the vials. This ensured the double blinding.

Out of 86 patients who met the inclusion and exclusion criteria, 6 patients' procedure was converted to general anaesthesia due to orthopaedic problems. These 6 patients were not considered for analysis. Standard proforma was made for all the patients included in the study. Group A (40 patients) received 22.5 mg (3 mL) of 0.75% isobaric ropivacaine hydrochloride. Group B (40 patients) received 15 mg (3 mL) of 0.5% isobaric ropivacaine hydrochloride.

Multi-parameter monitor was applied and baseline heart rate, non-invasive blood pressure, respiratory rate, oxygen saturation and ECG were recorded on the concerned proformas. Intravenous line was secured with 18-G intracath and the patients were preloaded with 10 mL/kg body weight of ringer lactate over 15 - 20 mins. The patients were placed in the lateral decubitus position with the affected limb in the dependent position. Spinal anaesthesia was administered with 26-G Quincke's spinal needle using the standard midline

approach at L2 - L3 interspace. Then 3 mL of the study drug was injected into the subarachnoid space. After administration of study drug, the patient was immediately turned to the supine horizontal position.

Sensory block was assessed by loss of sensation to pin prick in the midclavicular line starting from caudad and moving cephalad using 27-G short bevel needle. The sensory parameters noted were: onset of sensory blockade at T10, maximum level of sensory block, time to regression to T10, L5 and S1 and total duration of sensory blockade (time to regression to S1). Motor blockade was checked according to modified Bromage scale.[14,15] Motor blockade was also assessed immediately after the assessment of sensory block until the return of normal motor function.

Oxygen was routinely administered via oxygen mask at oxygen flow rate of 5 L/min. Bradycardia (Defined as heart rate less than 60 bpm) was treated with 0.6 mg diluted intravenous Atropine. Hypotension (Defined as systolic blood pressure less than 100 mmHg or 30% less than the base value) was treated with IV mephentermine (diluted- 30 mg in incremental doses) with additional ringer lactate solution. The operation was started when full surgical anaesthesia developed. In case of failed neuraxial blockade, where patients required general anaesthesia were excluded from the study. Continuous multipara monitoring (Respiratory rate, pulse rate, non-invasive blood pressure, oxygen saturation, ECG) was done and readings were recorded.

The primary outcome of the study was to assess the haemodynamic changes and the secondary outcome were the complications produced. Patients were monitored for side-effects and complications during intraoperative period and next 24 hours after the operation and measures to combat them were kept ready beforehand. Side effects include hypotension, bradycardia, headache, nausea and vomiting, backache, total spinal, pruritus, local anaesthetic toxicity, urinary retention, neurological changes or any other complication.

Statistical analyses were performed using the SPSS (Statistical Package for the Social Science System version SPSS 17.0 Chicago, SPSS Inc.) version 17.0 program for Windows. We conducted a Shapiro-Wilk test to verify the distribution of the data. All data were summarised as the mean ± SD.

RESULTS

Demographic Parameters	Group A	Group A	Group B	Group B	
	Mean +/- SD	Min - Max	Mean +/- SD	Min - Max	P value
Age (years)	40.60 ± 7.85	33-48	38.85 ± 7.75	31-47	0.319
Weight (kgs)	64.67 ± 4.28	52 – 70	63.43 ± 4.83	50 - 70	0.225
Sex (Female/male)	13/27	NA	16/24	NA	0.642
ASA Grade (I/II)	28/12	NA	31/9	NA	0.446

Table 1. Demographic Parameter comparison between the Two Groups

The mean pulse rate in the pre-operative period at the time of spinal anaesthesia (0 min), then at an interval of 5 minutes for first 60 minutes of spinal anaesthesia and then at an interval of 15 minutes till 180 minutes was comparable in both the groups and was found to be statistically insignificant ($p > 0.05$).

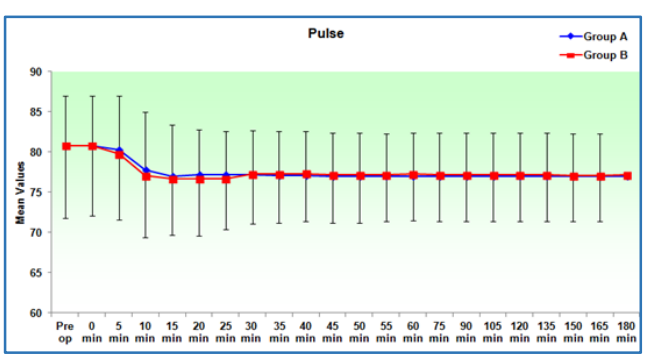

Figure 1. Mean Pulse Rate (minutes) from Pre-Operative Period till 180 Minutes

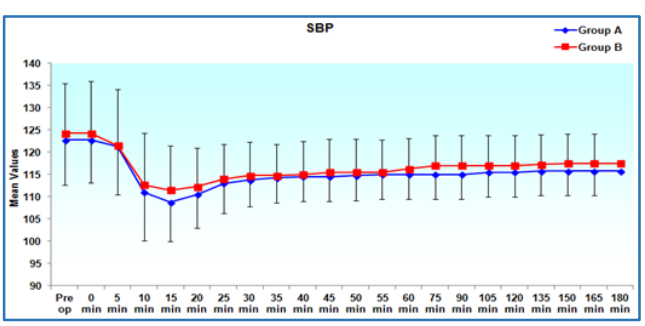

Figure 2. Mean Systolic Blood Pressure from Pre-Operative Period till 180 Minutes

The mean systolic blood pressure in the pre-operative period, at the time of spinal anaesthesia (0 minutes), then at an interval of 5 minutes for first 60 minutes, and then at an interval of 15 minutes till 180 minutes, was found to be statistically insignificant in both the groups.

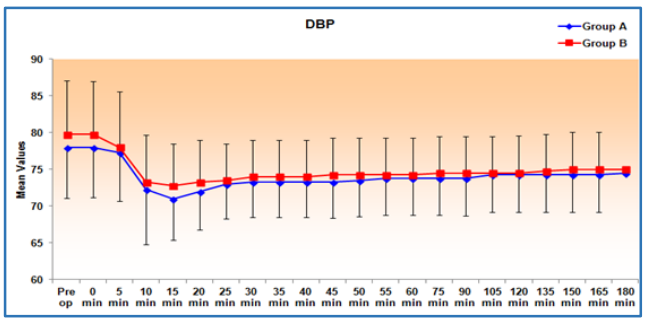

Figure 3. Mean Diastolic Pressure from Pre-Operative Period till 180 Minutes

The mean respiratory rate in the pre-operative period, then at the time of spinal anaesthesia (0 min), then at an interval of 5 minutes for first 60 minutes of spinal anaesthesia and then 15 minutes from 60 minutes till 180 minutes was comparable in both the groups and was found to be statistically insignificant (p > 0.05).

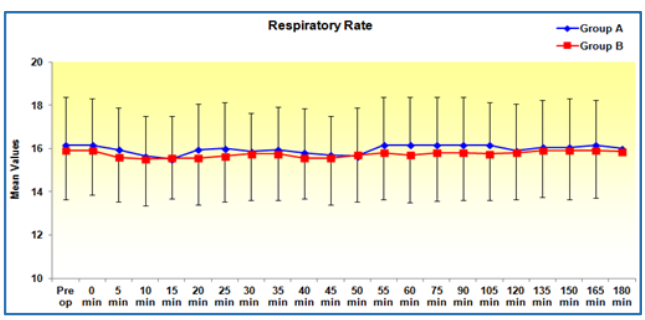

Figure 4. Mean Respiratory Rate (per minute) from Pre-Operative Period till 180 Minutes

The mean oxygen saturation in pre-operative period, at the time of spinal anaesthesia (0 min), then at an interval of 5 minutes for first 60 minutes and then at an interval of 15 minutes till 180 minutes was comparable in the two groups and it was found to be statistically insignificant (p > 0.05).

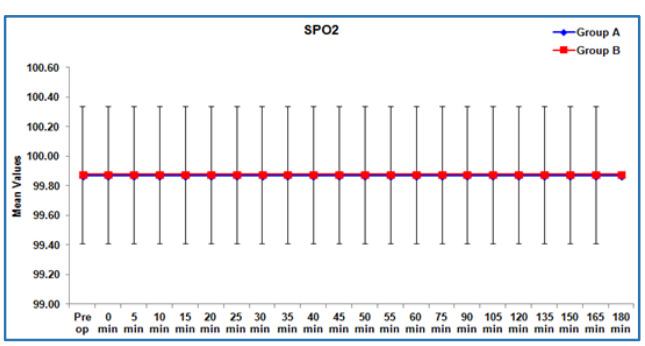

Figure 5. Mean Oxygen Saturation- SpO2 (%) from Pre-Operative Period till 180 Minutes

	Group A (n=40)		Group B (n=40)		P Value
	Frequency	Group A	Frequency	Group B	
Hypotension	7	17.5%	6	15%	1.000
Bradycardia	5	12.5%	3	7.5%	0.712
Headache	2	5%	3	7.5%	1.000
Nausea/ Vomiting	8	20.0%	6	15.0%	0.556

Table 2. Side Effects and Complications during Intra-operative and Post-operative Period

17.5% of patients in Group A and 15% of patients in Group B had hypotension intraoperatively. But the difference between the two groups was found to be statistically insignificant (p > 0.05); 12.5% of patients in Group A and 7.5% patients in Group B had bradycardia intraoperatively and the difference between the two groups was found to be statistically insignificant (p > 0.05); 5% of the patients in Group A and 7.5% patients in Group B had headache post-operatively. The difference between the two groups was found to be statistically insignificant (p > 0.05); 20% patients in Group A and 15% patients in Group B had episodes of nausea and vomiting. The difference between the two groups was found to be statistically insignificant (p > 0.05). There was no case of total spinal, retention of urine, local anaesthetic toxicity or pruritus in either of the group.

DISCUSSION

Ropivacaine is a long-acting local anaesthetic agent that is structurally related to bupivacaine. The present study was designed to compare the haemodynamic changes and complications associated with two different concentrations of ropivacaine, i.e. 0.5% and 0.75% in spinal anaesthesia in patients undergoing lower limb orthopaedic surgery. Both the groups were comparable with regard to age, sex, weight, ASA physical status and duration of surgery [Table 1].

The difference in mean pulse rate measured at various intervals intraoperatively and postoperatively was found to be statistically insignificant between the two groups. Only 5 patients receiving ropivacaine 0.75% and 3 patients receiving 0.5% ropivacaine had bradycardia during first 60 minutes, which was treated with intravenous injection atropine 0.6 mg (Diluted). The difference in the mean systolic and diastolic blood pressure measured at various intervals intraoperatively and postoperatively was found to be statistically insignificant between the two groups. Only 7 patients receiving ropivacaine 0.75% and 6 patients receiving ropivacaine 0.5% developed hypotension (Systolic blood pressure below 100 mmHg or below 30% of baseline) during first 60 minutes, which was treated with Inj. mephentermine (Diluted) and intravenous fluid-lactated ringer. In terms of safety, both doses of intrathecal ropivacaine provided high degree of cardiovascular stability with a low incidence of bradycardia and hypotension. The results correspond with other studies,[16,17,18] in which it was found that there was high degree of cardiovascular safety and there was no difference in various groups receiving different doses of ropivacaine.

The difference in the mean respiratory rate measured at various intervals intraoperatively and postoperatively was found to be statistically insignificant between the two groups. The mean SpO2 measured at various intervals intraoperatively and postoperatively was comparable between both the groups with the difference being statistically insignificant. Steinbrook et al in his study observed that spinal anaesthesia was not associated with statistically significant changes in tidal volume, respiratory rate, minute ventilation, mean inspiratory flow rate or response to the single-breath CO2 test.[19]

The side effects and complications between the two groups, both intraoperatively and postoperatively were comparable statistically. In terms of safety, both doses of intrathecal ropivacaine provided a high degree of

cardiovascular stability with a low incidence of bradycardia and hypotension. Only 5 patients in Group A (ropivacaine 0.75%) and 3 patients in Group B (ropivacaine 0.5%) had bradycardia intraoperatively. Only 7 patients in Group A and 6 patients in Group B developed hypotension. It was statistically insignificant, which was well in accordance with the various studies found in literature.[16,17,18] In our study, only 5 patients out of 80 patients had post dural puncture headache, which was managed with intravenous fluids and a non-steroidal anti-inflammatory drug. It was in accordance with the study done by Wahedi et al, in which 12 out of 40 patients had post dural puncture headache and was statistically insignificant.[18] In another study by Kallio et al, in which hyperbaric and plain ropivacaine 15 mg were compared in spinal anaesthesia in lower limb orthopaedic study, only 5 patients out of 56 patients had post dural puncture headache.[20] There is no study indicating that the incidence of post dural puncture headache is drug related.[9] In our study, only 8 patients in Group A and 6 groups in Group B had nausea and vomiting intraoperatively and postoperatively. Nausea and vomiting intraoperatively might have occurred due to concurrent hypotension, whereas post-operatively nausea and vomiting possibly could be due to Inj. Tramadol. Our study was in accordance with various studies,[16,17] who also found insignificant changes with respect to nausea and vomiting. There was no case of local anaesthetic toxicity, pruritus or total spinal in both the groups. There was no case of neurological deficit in both the groups. There was no case of backache or urinary retention in both the groups during first 24 hours after surgery.

CONCLUSION

Regional anaesthesia remains the choice of anaesthesia for lower limb orthopaedic surgeries. The haemodynamic profile of both the groups was comparable both intra- as well as post-operatively. In terms of safety, both doses of intrathecal ropivacaine provided high degree of cardiovascular stability with a low incidence of bradycardia and hypotension. On comparing side effects and complications, both the groups were statistically comparable. Ropivacaine with its efficacy, reduced potential for CNS toxicity and cardiotoxicity is an important option for regional anaesthesia.

Both ropivacaine 0.75% and 0.5% produced minimal side effects and complications as well as provided high degree of cardiovascular stability, hence recommended for anaesthetic use in prolonged lower limb orthopaedic surgeries.

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