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Comparision of Anaesthetic Effects of L-Bupivacaine V/S Isobaric Ropivacaine with Fentanyl as An Adjuvant In Lower Limb Surgeries Under Spinal Anaesthesia: A Randomized Double Blind Interventional Study

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Abstract

Background: This study is designed to compare the efficacy of intrathecal ropivacaine with fentanyl v/s L-bupivacaine with fentanyl for onset and duration of sensory and motor block, duration of analgesia, sedation and to evaluate the side effects, if any.

Methods: The study was conducted in orthopedics Operation theatre, Department of Anaesthesiology, S.M.S. Medical College and Attached group of hospitals, Jaipur with due permission from institution ethics committee and review board and written informed consent from patients were obtained.

Results: Duration of sensory and motor blockade was statistically significant between the groups and was longer in group with levobupivacaine with fentanyl. The difference in the time to first dose rescue analgesic in the two groups is statistically significant. Levobupivacaine with fentanyl gives prolonged post operative analgesia. Hypotension was seen in both the groups which was not statistically significant (P>0.05). The difference in incidence of bradycardia in the two groups were not significant (P>0.05). The incidence of postoperative complications were not statistically significant.

Conclusion: This study shows that the intrathecal 3.5 ml of 0.75% ropivacaine with fentanyl 25 micrograms provides adequate anaesthesia for lower limb surgeries.

Keywords: Ropivacaine, Fentanyl, Levobupivacaine

Introduction

Pain as defined by the International Association for the Study of Pain (IASP) is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage"[1]

Effective management of postoperative pain relieves suffering and leads to earlier mobilization, fewer pulmonary and cardiac complications, a reduced risk of deep vein thrombosis, faster recovery with less

likelihood of the development of neuropathic pain, reduced cost of care and increased patient satisfaction[2].

Post-operative pain management remains a challenge despite recent advances in our understanding of the physiology of acute pain, the development of new opioid and non-opioid analgesics, novel methods of drug delivery (systemic, regional and local) and more widespread use of pain-reducing minimally invasive surgical techniques[3].

Ropivacaine has an improved safety profile over bupivacaine with less toxic effect on central nervous system and cardiovascular system and hence gaining popularity. Presently, hyperbaric preparations of ropivacaine are commercially not available because of difficulty in maintaining the pharmacological stability of hyperbaric solutions for clinical use.[4].

Due to its long duration of action racemic bupivacaine is the commenest local anaesthetic used. However profound myocardial depression and even cardiac arrest can occur after accidental intravascular injection. Levo bupivacaine is the s(-) enantiomer of racemic bupivacaine.

The cardiotoxicity is less then that of racemic bupivacaine due to its lesser affinity for cardiac sodium channels.[5]

This study is designed to compare the efficacy of intrathecal ropivacaine with fentanyl v/s L-bupivacaine with fentanyl for onset and duration of sensory and motor block, duration of analgesia, sedation and to evaluate the side effects, if any.

Material & Methods

Study area: The study was conducted in orthopedics Operation theatre, Department of Anaesthesiology, S.M.S. Medical College and Attached group of hospitals, Jaipur with due permission from institution ethics committee and review board (reference no. 52/MC/EC/2019 dated 08/01/2019) and written informed consent from patients were obtained.

Study design: Hospital based randomized double blind interventional study.

Study period: From october 2018 to August 2019.

Sample size: The required sample size was 30 in each group at 95% confidence interval and 80% power to verify the expected minimum difference of 37.5(±26.1) in mean duration of motor block in both groups. This sample size was adequate to cover all other study variable too.

Sample technique: 60 patients satisfying inclusion criteria were selected using simple random technique by sealed enveloped method.

Blinding: This trial was so planned that neither the investigator nor the patients were aware of the groups and the drugs used.

Randomization: It is a statistical procedure by which the participants were allocated into 2 different groups. In this study randomization was done by sealed enveloped method. One of the colleagues allotted the patients to group A and group B. Study drug was prepared and administered by the colleague to the patient observations were done by me.

Study universe: -Cases undergoing lower limb surgeries under spinal anaesthesia.

Study groups: The study was conducted in the following 2 groups of patients. Each group consist of 30 patients (n=30/group)

Group A: 30 Patients received injection ropivacaine, 3 ml (0.75%) with injection fentanyl, 0.5 ml (25 µg) intrathecally.

Group B: 30 Patients received injection levo-bupivacaine, 3 ml (0.5%) with injection fentanyl, 0.5 ml (25 µg) intrathecally.

Inclusion criteria : Adult patients aged between 18 and 65 years of both gender undergoing lower limb surgeries under spinal anaesthesia. Patients belonging to American Society of Anaesthesiologist (ASA):- Grade I: Without co-morbid condition. Grade II: Controlled co-morbid conditions

Exclusion criteria: Patients not willing to participate in the study. H/O hypersensitive reactions to local anaesthetics. Medical complications such as anaemia, heart disease, severe hypovolemia, shock, septicemia, and hypertension. Patients on anticoagulant therapy and H/O coagulation disorders. Local infection at the proposed site of puncture for spinal anaesthesia. Patients with neurological and psychiatric disorders. If the optimal effect of anaesthesia was not achieved by spinal anaesthesia, the patient was excluded from the study.

Pre anaesthetic checkup was done a day before the surgery that includes : Complete medical and surgical history of patient including any known drug allergy. General and systemic examination. Vital parameters like Blood Pressure, pulse, temperature & respiratory rate. Weight of the patient was also noted.

Procedure : After taking informed written consent and confirming overnight fasting, patient was taken on the operation table, monitors attached and baseline vitals like Blood pressure, pulse rate, SpO_2, respiratory rate was recorded. An 18 gauge intravenous (IV) cannula was inserted, lactated Ringer's solution was administered as a bolus of 10 ml/kg before subarachnoid block to all patients. Vitals was noted just before lumbar puncture. Spinal anaesthesia was performed at L3-L4 interspace with the patient in left lateral position by using a 25 Gauge Quincke needle under strict aseptic conditions. Free flow of cerebrospinal fluid was verified before injection of the anaesthetic solution 3.5 ml volume, which was administered over 30 seconds. The direction of the needle aperture was caudal during the injection. All patients was immediately placed in a supine position. Monitoring was done using continous electrocardiography, heart rate, non-invasive blood pressure and continous pulse oximetry and patients were given 4.0 L/min of oxygen by venti-mask. Vitals was checked every 5 minutes for first 30 minutes then every 10 minutes till surgery and then every 60 minutes for 12 hours postoperatively.

Results

Table 1: Age Distribution (Mean ± SD)

	Group A	Group B	P value
Age (Yrs)	34.93±11.11	32.67±9.59	0.401 (NS)
Sex (M:F)	25:5	28:2	0.421
Weight (Kg)	66.27± 9.12	65.17 ± 6.24	0.587
ASA	29:1	30:0	1.00

Table 2: Duration of Sensory and Motor Block [Mean ± SD] (95% confidence interval)

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Sensory	128.67	9.00	157.67	12.78	P<0.001 (S)
Motor	152.00	11.26	181.67	14.16	P<0.001 (S)

Table 3: Duration of analgesia [Mean ± SD] (95% confidence interval)

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Duration of Analgesia (min)	349.33	16.60	417.33	29.35	P<0.001 (S)

Table 4: Mean time to two segment regression [Mean ± SD] (95% confidence interval)

	Group A		Group B		P value
	Mean	SD	Mean	SD	
2 segment sensory regression time (min)	102.33	6.91	101.33	6.91	0.577 (NS)

Table 5: Mean Onset time of Sensory Block and motor block (Mean ± SD) (95% confidence interval)

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Sensory	9.79	1.16	9.25	1.09	0.070 (NS)
Motor	14.44	1.61	14.27	1.55	0.666 (NS)

Table 6: Comparison of Post operative VAS Score among study groups (Mean ± SD)

	Group A		Group B		P value
	Mean	SD	Mean	SD	
1 hr	0.00	0.00	0.00	0.00	-
2 hr	0.00	0.00	0.00	0.00	-
3 hr	0.00	0.00	0.00	0.00	-
4 hr	0.13	0.35	0.00	0.00	P<0.001 (S)
5 hr	1.13	0.35	0.27	0.45	P<0.001 (S)
6 hr	3.00	0.00	1.10	0.31	P<0.001 (S)
7 hr	0	0	3.00	0.00	P<0.001 (S)
8 hr	0	0	0	0	
9 hr	0	0	0	0	
10 hr	0	0	0	0	
11 hr	0	0	0	0	
12 hr	0	0	0	0	

Table:7Comparison of Post operative Sedation Score among study groups

	Group A		Group B		P value
	Mean	SD	Mean	SD	
1 hr	1.00	0.00	1.00	0.00	-
2 hr	1.03	0.18	1.07	0.25	0.561 (NS)
3 hr	1.07	0.25	1.00	0.00	0.155 (NS)
4 hr	1.03	0.18	1.00	0.00	0.321 (NS)
5 hr	1.00	0.00	1.03	0.18	0.321 (NS)
6 hr	1.03	0.18	1.00	0.00	0.321 (NS)
7 hr	1.00	0.00	1.00	0.00	-
8 hr	1.00	0.00	1.00	0.00	-
9 hr	1.00	0.00	1.00	0.00	-
10 hr	1.00	0.00	1.00	0.00	-
11 hr	1.00	0.00	1.00	0.00	-
12 hr	1.00	0.00	1.00	0.00	-

Table: 8 Frequency of complications among study groups

	Group A		Group B	
	No.	%	No.	%
Hypotension	5	16.67	5	16.67
Bradycardia	0	0.00	3	10.00
Nausea	3	10.00	5	16.67
Vomiting	2	6.67	5	16.67
None	20	66.67	12	40.00
Total	30	100.00	30	100.00

Chi-square = 6.786 with 4 degrees of freedom; P = 0.148 (NS)

Discussion

Spinal anaesthesia is the most convenient anaesthetic technique that offers many advantages over general anaesthesia, including reduced stress response and improved post operative pain relief. Spinal anaesthesia is the technique of choice and is the gold standard for lower abdominal and lower limb surgeries.[4]

Ropivacaine is safer as compared to bupivacaine. It has less toxic effects on central nervous system and cardiovascular system thereby gaining popularity. Presently, hyperbaric preparations of ropivacaine are commercially not available because of difficulty in

maintaining the pharmacological stability of hyperbaric solutions for clinical use.[5]

Intrathecal opioids are synergistic with local anaesthetics and intensify the sensory block without increasing the sympathetic block

Due to its long duration of action, racemic bupivacaine is the commonest local anaesthetic used. However, profound myocardial depression and even cardiac arrest can occur after accidental intravascular injection. Levobupivacaine is the s (-) enantiomer of racemic bupivacaine. The cardiotoxicity is less than that of racemic bupivacaine due to its lesser affinity for cardiac sodium channels.[5]

The mean duration of sensory block in Group A was 128.67 ± 9.00 min and in Group B was 157.67 ± 12.78 min. The p- value was < 0.001 between the groups which was statistically significant. The mean duration of motor block in Group A was 152.00 ± 11.26min and in Group B was 181.67 ± 14.16 min. The p- value was < 0.001 between the groups which was also statistically significant. Duration of sensory and motor blockade was shorter in group A. **Layek A et al[6],** in their study concluded that the duration of motor block was longer (median 245 min) in levobupivacaine group compared to (median 150 min) in ropivacaine group which was significant with p value <0.001.**Hoda w et al[7],** also observed that Intrathecal isobaric levobupivacaine-fentanyl combination produces a significantly longer duration of sensory block and motor block (201.74 ± 18.51 minutes) than isobaric ropivacaine-fentanyl combination (152.88± 20.41 minutes) which was significant with p value <0.001. **Koltka K et al[8]**, compared equipotent doses of ropivacaine-fentanyl and bupivacaine-fentanyl in spinal anesthesia for lower abdominal surgery. They found that duration and intensity of motor block was shorter with ropivacaine as compared with bupivacaine. Thus, Our results coincides with above mentioned studies in term of mean duration of sensory and motor blockade.

Ropivacaine is a long acting S‑enantiomer, amide local anaesthetic, with low lipid solubility, which blocks nerve fibres involved in pain transmission Aδ and C fibers to a greater degree than those controlling motor functions Aβ fibers.[4]

Ropivacaine has a shorter duration of sensory and motor block, hence it may be preferred in day care surgery.[6]

Saran a et al[9] also observed that the Duration of sensory blockade was not significantly different [in group ropivacaine with fentanyl 191.38 ± 3.562 and in group levo-bupivacaine with fentanyl 191.24 ± 3.414 min (p = 0.841)]. These results does not coincides with our study. It could be because of the lesser dose of levobupivacaine 0.5%, 10 mg + fentanyl 20 microgram and ropivacaine 0.75%,15 mg+ fentanyl 20 microgram.

The mean duration of 1st dose of rescue analgesia was 349.33±16.60minutes in Group A and 417.33±29.35 minutes in group B. Which was longer in group B compared to group A. The differences among the groups were found to be statistically highly significant. **Jagtap S et al [4],** found that time for rescue analgesia was prolonged in group bupivacaine with fentanyl(Group BF) (263.33 ± 63 min) when compared to group ropivacaine with fentanyl(Group RF) (234.44 ± 58.76 min), *P* = 0.021 which coincides with our study. **McNamee et al[10],** found that the time to first rescue analgesic was significantly shorter in the ropivacaine group (median 3.4 hours) than in the bupivacaine group (median 4.9 h) with P<0.001 which also coincides with our study. Similar finding was reported by **Mantouvalou *et al*[11]**

Levobupivacaine exerts its pharmacological action through reversible blockade of neuronal sodium channels. Myelinated nerves are blocked through exposure at the nodes of Ranvier more readily than unmyelinated nerves; and small nerves are blocked more easily than larger ones. In general, the progression of anesthesia is related to the diameter, myelination and conduction velocity of the affected nerve fibers. Specifically, the drug binds to the intracellular portion of sodium channels and blocks sodium influx into nerve cells, which prevents depolarization. It blocks nerve conduction in sensory and motor nerves mainly by interacting with voltage sensitive sodium channels on the cell membrane. It also interferes with impulse transmission and conduction in other tissues.[16]

While Ropivacaine reversibly interferes with the entry of sodium in the nerve cell membranes, leading to decreased permeability to sodium. It blocks generation and conductance of nerve impulses. Blockade of Aα and Aβ is slow and hence produces lesser motor blockade than bupivacaine.[12,13]

The mean time to two segment regression in Group A was 102.33 ± 6.91 (min) and in Group B was 101.33 ± 6.91(min).The p- value was > 0.05 between the groups which was statistically not significant. **Gautier et al[14]**, in their study noted the time for two segment regression was similar between the two groups and was 89±33 mins in the bupivacaine group and was 98±30 mins in the ropivacaine group when administered intrathecally. These results coincides with our study **Srilakshmi k et al[15]** found that time from injection to two dermatomal regression was 112.7±21.3 minutes in Group R (Ropivacaine 0.75% ,2.5 ml with fentanyl 0.5 ml , 25 microgram) and 129.9±15.7 minutes in Group B (Levobupivacaine 0.5% , 2.5 ml with fentanyl 0.5 ml ,25 microgram), when compared it was found to be highly significant statistically with a p value of < 0.001.which does not coincides with our study.

The mean onset of sensory block was 9.79±1.16minutes in group A, while 9.25±1.09 minutes in group B and the difference was statistically not significant(p>0.05). The mean onset of motor block for Group A was 14.44 ± 1.61(min) and for Group B was 14.27± 1.55 (min) and the difference was statistically not significant (p>0.05). **Vampugalla PS et al[16]**, observed that The mean time for onset of peak sensory block in ropivacaine with fentanyl(Group R) was 8.28±2.2 mins and in levobupivacaine with fentanyl(Group L) was 7.98±2.2 mins, with p=0.49, which was statistically not significant. the mean time for onset of motor block (Bromage 3) was 13.9±2.9 mins for Group R and 12.9±3.9 mins for Group L with p=0.16, which was clinically and statistically not significant. Thus, our results correlates with the above-mentioned study in terms of onset time of sensory block and motor block.Our study also coincides with **Malinowski et al[17]** who compared intrathecal isobaric ropivacaine, 15 mg and isobaric bupivacaine, 10 mg for transurethral resection of bladder or prostrate. It was found that the onset of sensory blockade was similar and was 13±8 mins for ropivacaine group compared to 11±7 mins in the bupivacaine group. This was statistically not significant.**Kallio et al[18] and McNamee et al[10]** also reported the same observations.

The mean VAS score in group A was 0.13 ± 0.35 at 4 hours , 1.13 ± 0.35 at 5 hours and 3.00±0.00 at 6 hours.In group B the mean VAS score was 0.00 ± 0.00 at 4 hours, 0.27 ± 0.45 at 5 hours,1.10±0.31 at 6 hours and 3.00±0.00 at 7 hours .The differences among the groups were found to be statistically highly significant (p<0.001).

In group A, 5 patients experienced hypotension. In group B also 5 patients experienced hypotension and was treated by giving fluid and injection mephentermine 6 mg intravenously.there was not of any statistical significance. hypotension in both group at any point of time which coincides with findings of **Layek A et al** [6].

In our study, no patients had developed bradycardia in group A while 3 patients developed bradycardia in group B. Bradycardia was treatet by giving injection Atropine 0.6 mg intravenously.It was statistically not significant . In group A, 3 patient's developed Nausea amd 2 patients developed vomitting .In group B, 5 patients developed Nausea and 5 patient's developed vomitting . This was also statistically not significant.

In our study, the two groups neither intraoperatively nor post operatively differ significantly with respect to heart rate at any interval. The changes in Mean pulse rate, mean systolic blood pressure, mean diastolic blood pressure and mean arterial blood pressure was statistically not significant. Our results coincides with **Koltka et al**[8] observed that The groups did not differ in haemodynamic parameters in the operating room . Intraoperative hypotension requiring treatment with ephedrine occurred in eight of the patients in the bupivacaine group (32%) and five of the patients in the ropivacaine group (20%) . The patients requiring treatment with atropine for bradycardia did not differ.

In our study no cases of allergy or respiratory depression were reported.

Many studies are being conducted with Levo-bupivacaine and Ropivacaine with adjuvant as fentanyl for prolonging the post-operative analgesia. The aim of these studies is to determine which combination is providing long duration of analgesia and shorter duration of motor blockade to provide early ambulation and physiotherapy with least side effects.

Conclusion

This study shows that the intrathecal 3.5 ml of 0.75% ropivacaine with fentanyl 25 micrograms provides adequate anaesthesia for lower limb surgeries. Ropivacaine provides a lesser duration of sensory and motor blockade then levo-bupivacaine.so it can be used for lower limb surgeries or requiring short duration and early ambulation. Furthermore, fentanyl as an adjuvant to both ropivacaine and levo-bupivacaine enhances the duration of the sensory block.

Hence, ropivacaine with fentanyl in spinal anesthesia for lower lower limb surgeries is a better alternative compared to levo-bupivacaine with fentanyl favouring day care ambulatory surgeries.

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