Original Article ISSN (O):2395-2822; ISSN (P):2395-2814

Comparative Study of Levobupivacaine with Fentanyl Versus Ropivacaine with Fentanyl for Labor Analgesia.

Razia Husain[1], Tauqir Anwar[2], Shumaila Aftab Khan[3], Saira Jamshed[4], Zainab S Khan[5], Munira Murtaza Khomusi[6]

[1]Consultant Anesthesiologist, Saify Hospital. Ex Professor, Hamdard College of Medicine and Dentistry, Hamdard University Hospital, Karachi, Pakistan.

[2]Consultant Gynaecologist Saify Hospital, Ex Associate Professor, Hamdard College of Medicine and Dentistry, Hamdard University Hospital, Karachi, Pakistan.

[3]Specialist Gynecologist, Al Qasmi Womens Hospital ,Sharjah U A E. Ex Assistant Professor, Hamdard College of Medicine and Dentistry, Hamdard University Hospital, Karachi, Pakistan.

[4]Assistant Professor, Hamdard College of Medicine and Dentistey, Hamdard University Hospital, Karachi, Pakistan

[5]Resident, Gangaram Hospital FJ MU, Lahore, Pakistan.

[6]Resident, JPMC Hospital, Karachi, Pakistan.

Received: April 2019
Accepted: May 2019

ABSTRACT

Background: Effective pain relief is one of the important components of management of normal labor. Adequate pain relief is associated with reduction in maternal sympathetic activity and considerably decreased maternal anxiety level. Epidural analgesia is being increasingly used for this purpose. Many local anesthetic drugs are being used for providing epidural analgesia. We conducted this study to compare Ropivacaine and Levobupivacaine in terms of onset and duration of analgesia, motor involvement, hemodynamic effects and neonatal outcome. **Methods:** This was a prospective comparative study in which 100 patients presenting in spontaneous labour were included in this study on the basis of a predefined inclusion and exclusion criteria. Patients were divided into 2 groups on the basis of drug used. Group A patients received Ropivacaine along with fentanyl whereas group B patients received Levobupivacaine along with fentanyl. VAS score, Sensory and motor block and vital parameters were recorded before giving epidural and 5,15, 30 and 60 minutes and thereafter every hourly till delivery took place. Sensory block was assessed by pin prick sensation whereas motor block was assessed by modified bromage scale. Statistical analysis was done using SSPS 21 software and p value less than 0.05 was taken as statistically significant. **Results:** Parameters such as height, weight, body mass index, ASA grades, gravidity and duration of labor were found to be comparable in both the groups with no statistically significant difference in between 2 groups (P>0.05). Mode of delivery and conversion to LSCS was also similar in both the groups. Mean time for onset of analgesia was comparable in both the groups. The mean VAS scores in group A were found to be less as compared to group B during initial 1 hour after the bolus dose and the difference was found to be statistically significant (P<0.0001). After 1 hour the VAS scores were found to be comparable in both the groups with no statistically significant difference in the mean VAS scores of patients in both the groups (P>0.05). The need for top-up analgesia was found to be statistically significantly higher in group B as compared to group A (P=0.0277). The motor sparing was better in group A as compared to group B and the difference was found to be statistically significant (P=0.0026). Hemodynamics and neonatal outcome were found to be comparable in both the groups (P>0.05). **Conclusion:** Ropivacaine is a better local anesthetic drug as compared to Bupivacaine for labor analgesia. Its use is associated with better analgesic effect, superior motor sparing and less need for top up analgesic doses.

Keywords: Labor Analgesia, Ropivacaine, Bupivacaine, VAS Score, Neonatal Outcome.

INTRODUCTION

Visceral as well as somatic pain is an essential part of normal vaginal delivery. Normal labor consists of uterine contractions and cervical dilatation which result in visceral pain. Somatic pain is usually due to pressure on pelvic floor and vagina by descending part, usually head, of the fetus.[1] Obstetric analgesia consists of providing anaesthesia below T8 to T10 of spinal level so as to abolish pain sensation in this region. Epidural analgesia is being increasingly used for painless labor and has the advantage of superior pain relief, giving painless episiotomies and same epidural analgesia can be extended to providing anaesthesia for cesarean section if needed.[2] It also has the distinct advantage of controlling blood pressure in patients with pregnancy induced hypertension and blunting of hemodynamic

Name & Address of Corresponding Author
Dr Razia Husain
103, Almas Square, SD-5, Block-G,
North Nazimabad
Karachi,
Pakistan. 74700

responses in patients in whom cardiac status is compromised such as in cases of maternal valvular heart disease.[3] Though commonly used in developed countries its use is restricted to some tertiary care hospitals in developing countries including Pakistan because of unavailability of skilled manpower and also non affordability of the cost incurred.. But with increasing availability of skilled anesthesiologists the practice of labor analgesia is slowly but steadily gaining popularity.[4]
The indications for labor analgesia include maternal obesity, pregnancy induced hypertension, maternal cardiovascular, neurological or respiratory diseases. In fact, American Society of Anesthesiologists recommends that any maternal request for labor analgesia is a sufficient ground for giving labor analgesia.[5] It should be avoided if serious maternal hemorrhage is anticipated. It is also contraindicated in patients having hypotension, thrombocytopenia, coagulopathies, sepsis, raised intracranial tension and infections at the site of epidural placement.[6]
Different local anesthetic drugs have been in use either alone or in combination with opioids for providing labor analgesia depending upon the experience of anesthetist and patient profile. Various agents which have been used for this purpose include Bupivacaine, Ropivacaine and Levobupivacaine.[7] Opioids such as fentanyl, morphine and meperidine can be used in combination with local anesthetic agents for epidural analgesia. Addition of opioids has a sparing effect on local anesthetic drug thereby reducing the requirement of local anesthetic agent and thereby reducing its toxicity.[8]

Levobupivacaine is an amino-amide local anesthetic which belongs to the family of n-alkyl substitute pipecoloxylidide. It acts by reversible blocking of neuronal sodium channels. It has been extensively used for subarachnoid block, epidural analgesia and anaesthesia and peripheral nerve blocks.[9] The common adverse effects associated with levobupivacaine include hypotension, nausea, vomiting and headache. Its cardiovascular adverse effect particularly hypotension and ECG changes has been a cause of concern for many anesthetists. On the other hand, Ropivacaine is a long-acting amide anesthetic agent that also acts by inhibition of neuronal sodium channels but is less likely to produce profound motor blockade because of its inability to penetrate large motor fibers because of which its use result in higher degree of motor sensory differentiation as compared to levobupivacaine.[10]

We conducted this prospective comparative study to assess the quality of labor analgesia, hemodynamic stability and motor involvement with levobupivacaine and ropivacaine in patients during normal vaginal delivery.

MATERIALS AND METHODS

This was a prospective comparative study in which 100 patients presenting in spontaneous labor were included in this study on the basis of a predefined inclusion and exclusion criteria. Institutional ethical committee approved the study and informed written consent was obtained from all the patients.
Demographic data such as age, weight, height and BMI were noted in all the cases. Obstetric data such as gravidity and parity of the patients along with gestational age was noted down. All the basic investigations such as complete blood count including platelet count, INR and serological markers such as HBsAg, HIV and ELISA was noted. The patient was positioned in the sitting position and epidural space was identified. The epidural space was identified at L3/L4 or L4/L5 with an 18-guage Tuohy's needle using loss of resistance technique with air. An epidural catheter (20-guage) was inserted for about 5to 7 cms in epidural space. The patient received local anesthetic drug depending upon the group they belonged to.
Group A: 50 patients were included in this group and they received initial test dose of 2ml 0.5% Ropivacaine followed by 8ml Ropivacaine along with 50 microgram fentanyl as bolus when the cervical dilatation was found to be between 3-5 cms and after that 0.2% with 1 microgram per ml fentanyl at 6to 8 ml per hr.
Group B: Remaining 50 patients in this group received levobupivacaine 0.5 % with fentanyl 50 microgram 10 ml and after that 0.2% levobupivacaine with 1 microgram per ml fentanyl at 6to 8 ml per hr.
The patients were assessed by VAS scores and VAS score less than or equal to 3 was considered as adequate analgesia. Duration of analgesia was noted in both the groups. VAS score, Sensory and motor block and vital parameters were recorded before giving epidural and at 5,10,15, 20,25,30, 45 and 60 minutes and thereafter every 15 minutes till delivery of the baby. Sensory block was assessed by pin prick sensation whereas motor block was assessed by modified bromage scale.

Table 1: Modified Bromage Scale

Modified Bromage Scale	
0	No motor Paralysis
1	Inability to raise extended leg
2	Inability to flex knee
3	Inability to flex ankle

Parameters like onset of analgesia (from injection of local anesthetic to a point where VAS is equal to or less than 3), duration of analgesia (request for first analgesic dose). Motor block assessment was done by Breen modified bromage scale (BMBS). BMBS was also assessed before giving epidural and 5,15, 30 and 60 minutes and thereafter every hourly till delivery occurs. A continuous monitoring of fetal

heart rate was done using cardiotocography. Neonates were assessed by APGAR score at 1 minute. The statistical analysis was done using SSPS 21 software and p value less than 0.05 was taken as statistically significant.

Inclusion Criteria:

1. ASA I and II status.
2. Singleton pregnancy.
3. Patients in spontaneous active Labour.
4. Those requested for labor analgesia.
5. Gave informed consent to be part of study.

Exclusion Criteria:

1. Those who refused consent.
2. Patients in whom epidural analgesia was contraindicated.
3. Allergy to anesthetic drugs.
4. Multiple or preterm pregnancies.

RESULTS

This was a prospective comparative study in which 100 patients belonging to ASA I and II and requesting for labor analgesia were included on the basis of a predefined inclusion and exclusion criteria. The patients were divided into 2 groups of 50 patients each on the basis of drug used for epidural analgesia. First demographic details of the patients in both the groups were studied. The most common age group in Group A (50%) as well as group B (44%) was between 18-25 years. The mean age was found to be comparable in both the groups (P=0.146) with no statistically significant difference.

Table 2: Age Groups of the studied cases

	Group A		Group B	
	No Of Patients	Percentage	No Of Patients	Percentage
18-25 years	25	50.00%	22	44.00%
26-30 years	13	26.00%	11	22.00%
31-35 years	9	18.00%	10	20.00%
> 35 years	3	6.00%	7	14.00%
Total	50	100.00%	50	100.00%
Mean Age	26.12 +/- 4.84		27.32 +/- 5.39	
P= 0.244 (Not Significant)				

Table 3: Distribution Of Patient Characteristics Among The Two Groups.

Patient Characteristics	Group A	Group B	P Value
Height (cms)	154.12 ± 16.22	150.32 ± 14.76	0.2234
Weight (Kg)	58.22 ± 9.34	61.48 ± 7.52	0.0571
BMI kg/m2	24.12 ± 2.32	24.48 ± 2.02	0.4100
ASA (I:II)	42:8	38:12	0.4539
Primi:Multigravida	30:20	28:22	0.8396
Duration of Labour (min)	388.6 +/- 142.20	402.2 +/- 130.44	0.6237

Similarly, parameters such as height, weight, body mass index, ASA grades, gravidity and duration of labor were found to be comparable in both the groups with no statistically significant difference in between 2 groups (P>0.05).

The analysis of the patients on the basis of mode of delivery showed that amongst group A patients 25 (50%) patients normal vaginal delivery occurred whereas instrumental delivery was done in 13 (26%) patients. Conversion to LSCS had to be done in 12 (24%) patients. In group B normal and instrumental delivery occurred in 22 (44%) and 15 (30%) patients. Conversion to LSCS was required in 13 (26%) patients. The mode of delivery as well as need for conversion to LSCS was found to be comparable in both the groups with no statistically significant difference.

Table 4: Mode of Delivery and need for conversion to LSCS.

	Group A		Group B		P Value
	No Of Patients	Percentage	No Of Patients	Percentage	
Normal Vaginal Delivery	25	50.00%	22	44.00%	0.6889
Instrumental Delivery	13	26.00%	15	30.00%	0.8240
Conversion to LSCS	12	24%	13	26.00%	1.000

The mean time for onset of analgesia in group A and group B was found to be 7.24 +/- 2.12 minutes and 7.38 +/- 3.24 minutes respectively. The statistical analysis of the mean duration for onset of analgesia showed that Ropivacaine group had a relatively fast onset of analgesia but the difference was found to be statistically insignificant (P>0.05).

Table 5: Onset Of Analgesia in Studied cases.

Onset Of Analgesia	Mean Time	Std Deviation
Group A	7.24	2.12
Group B	7.38	3.24
P>0.05 , 95% CI -0.9466 to 1.2266		

The analysis of the patients on the basis of adequate analgesia showed that Mean VAS score during first stage of labor was found to be 0.46 ± 0.38 and 1.98± 0.92 in group A and group B respectively. Similarly, during 2nd stage of labor mean VAS scores in group A and group B were found to be 0.73 ± 0.42 and 2.12 ± 1.09 respectively. The mean VAS scores in group A were found to be less as compared to group B during initial 1 hour after the bolus dose and the difference was found to be statistically significant (P<0.0001). After 1 hour the VAS scores were found to be comparable in both the groups with no statistically significant difference in the mean VAS scores of patients in both the groups (P>0.05).

Table 6: Comparison of mean VAS scores Up to 6 hours postoperatively.

VAS score	Group A	Group B	P Value
Before Giving Bolus	9.22 ± 0.58	9.34 ± 0.62	P= 0.320 (Not Significant)
5 minutes	7.38 ± 0.72	8.12± 0.92	P < 0.0001 (Significant)
10 minutes	0.73 ± 0.42	1.12 ± 1.09	P =0.020 (Significant)
30 minutes	0.80 +/- 0.62	1.10 +/- 0.80	P=0.0387 (Significant)
60 minutes	0.74+/- 0.58	0.98 +/- 0.60	P=0.04 (Significant)
90 minutes	2.12 +/- 0.98	2.38 +/- 0.80	P=0.149 (Not Significant)
2 hours	2.48 +/- 0.80	2.62 +/- 0.78	P=0.3778 (Not Significant)
3 hours	2.50 +/- 0.92	2.52 +/- 0.90	P=0.9127 (Not Significant)
4 hours	2.22 +/- 0.80	2.12 +/- 0.78	P=0.5283 (Not Significant)
5 hours	2.31 +/- 0.78	2.40 +/- 0.80	P=0.5703 (Not Significant)
6 hours	2.80 +/- 0.90	2.94 +/- 0.82	P=0.4181 (Not Significant)

2 patients in group A and 10 patients in group B required top-up analgesia during 1st or 2nd stage of labor. 4 patients in group B required multiple doses of top-up analgesia. The need for top-up analgesia was found to be statistically significantly higher in group B as compared to group A (P=0.0277).

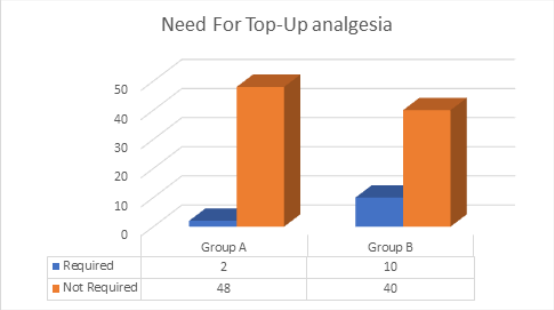

Figure 1: Need For Top-Up Analgesia in Studied cases.

The analysis of the patients for motor involvement on the basis of Bromage scale showed that out of 50 patients in Group A all patients had a Bromage scale of 1 whereas in group B out of 50 patients 41 patients had a bromage scale of 1 and remaining 9 patients were found to have Bromage scale of 2. The motor sparing was better in group A as compared to group B and the difference was found to be statistically significant (P=0.0026).

Table 7: Bromage Scale In Studied Cases.

Bromage Scale	Group A	Group B
0	0	0
1	50	41
2	0	9
P= 0.0026		

The Mean mean arterial pressure (MAP) in Group A was 76.24 +/- 6.12 whereas in group B MAP was found to be 74.66 +/- 6.82. The analysis of mean arterial pressures (MAP) of patients up to 12 hours showed that Mean arterial pressures were comparable in both the groups with no statistically significant difference (P=0.2257).

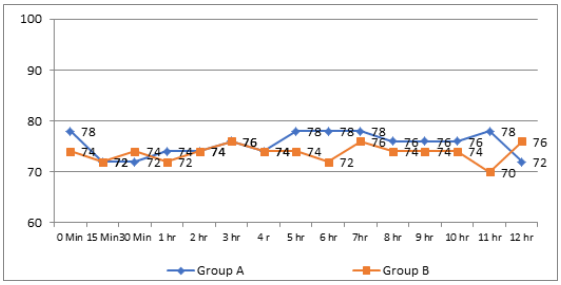

Figure 2: Mean Arterial Pressures in studied cases.

The analysis of heart rates showed that the mean heart rate in Group A was 79.77 +/- 5.98 whereas in group B mean heart rate was found to be 79.29 +/- 4.22. The analysis of mean heart rate of patients up to 12 hours showed that there was no statistically significant difference in mean heart rate of patients in both the groups (P=0.64).

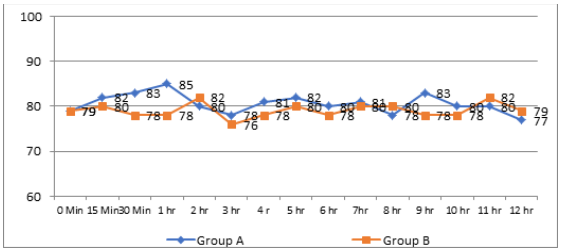

Figure 3: Mean Heart Rates in studied cases.

Table 8: Apgar score at 1 MIN

Gravida	Group A		Group B	
	No. of cases	%	No. of cases	%
< 6	2	4 %	3	6 %
=/> 6	48	96 %	47	94 %
Total	50	100%	50	100%
P value > 0.05(Not Significant)				

APGAR scores of all the neonates were recorded. APGAR score less than 6 was taken as suggestive of birth asphyxia. 2 (4%) and 3 (6%) neonates were found to have an APGAR score less than 6 at 1 minutes in Group A and Group B respectively. The APGAR score at 1 minute of the neonates was found to be comparable with no statistically significant difference (P>0.05).

DISCUSSION

Newer local anesthetics such as levobupivacaine and Ropivacaine have a better safety profile and its use has been reported to be associated with less systemic toxicity and less motor involvement as compared to Bupivacaine. In present study we compared use of Levobupivacaine and Ropivacaine for labor analgesia in terms of onset and duration of analgesia,

motor differentiation, Post-Operative VAS score and hemodynamic stability of the patients. In our study the patient profile in both the group was similar and patients were found to be comparable in terms of mean age, weight, Body mass index and ASA grades. Moreover, we also found that in both the groups conversion to LSCS was comparable and the usual indication for conversion to LSCS was fetal distress suggested by fetal bradycardia.

We took VAS score less than 3 as adequate analgesia and found that the mean time for onset of analgesia in group A and group B was found to be 7.24 +/- 2.12 minutes and 7.38 +/- 3.24 minutes respectively The statistical analysis of the mean duration for onset of analgesia showed that Ropivacaine group had a relatively fast onset of analgesia but the difference was found to be statistically insignificant (P>0.05). Gunduz S et al conducted a study of one hundred women who requested epidural analgesia in active labor were randomly allocated into two groups; one group received 20 mL of ropivacaine 0.125% with fentanyl 50 µg and the other received 20 mL of bupivacaine 0.125% with fentanyl 50 µg. The authors found that there were no differences between the two study groups in the measured obstetric and neonatal outcomes. The onset time, duration of analgesia, and sensory levels were similar between the groups. The authors concluded that Both ropivacaine and bupivacaine provide equivalent labor analgesia with high maternal satisfaction and tolerable adverse effects in the clinically used dose range.[11] Similarly, Bawdane et al reported Ropivacaine and Bupivacaine were similar with respect to hemodynamic stability, onset of analgesia, quality of analgesia, sensory blockade, neonatal outcome, requirement of drugs, duration of labor, and incidence of side effects.[12]

One of the important aspects of using Ropivacaine for labor analgesia is that it has been uniformly reported to be having a better sensory motor differentiation profile. The analysis of the patients for motor involvement on the basis of Bromage scale showed that out of 50 patients in Group A all patients had a Bromage scale of 1 whereas in group B out of 50 patients 41 patients had a bromage scale of 1 and remaining 9 patients were found to have Bromage scale of 2. The motor sparing was better in group A as compared to group B and the difference was found to be statistically significant (P=0.0026). One of the important implications this have in labor analgesia is that a drug which profoundly affects motor system is likely to hamper normal delivery thereby increasing conversion to LSCS rate though in our study LSCS conversion rates were found to be comparable in both the groups. Writer WD undertook a meta-analysis analyses effect of epidural analgesia with ropivacaine for pain in labor on neonatal outcome and mode of delivery compared with bupivacaine. The authors found that Spontaneous vaginal deliveries occurred more frequently overall with ropivacaine than with bupivacaine (58% vs 49%; P < 0.05) and instrumental deliveries (forceps and vacuum extraction) less frequently (27% vs 40%; P < 0.01), while the frequency of Caesarean section was similar between groups.[13] Many studies have reported a clear advantage of Ropivacaine over Levobupivacaine as far as motor involvement was concerned.

We found that there was no statistically significant difference in hemodynamics of both the groups. Similar comparable hemodynamics have also been reported by the authors such as Padalwar S et al,[14] and Pinder AJ.[15] Finally, in Our study Neonatal outcome as assessed by APGAR score was found to be comparable in both the groups.

CONCLUSION

Ropivacaine is a better local anesthetic drug as compared to Bupivacaine for labor analgesia. Ropivacaine is associated with better analgesia, superior motor sparing and less need for additional analgesic doses. Maternal hemodynamics and neonatal outcome as assessed by APGAR score at 1 minute was found to be comparable and in this regard Bupivacaine as well as Ropivacaine appears to be reasonably similar.

REFERENCES

1. Labor S, Maguire S. The Pain of Labour. Rev Pain. 2008;2(2):15–19.
2. Silva M, Halpern SH. Epidural analgesia for labor: Current techniques. Local Reg Anesth. ;3:143–153.
3. Luthra A, Bajaj R, Jafra A, Jangra K, Arya VK. Anesthesia in pregnancy with heart disease. Saudi J Anaesth. 2017;11(4):454–471.
4. Dobson M. Opinion: Labour Analgesia in the Developing World; Why Not. Rev Pain. 2011;5(3):2–3.
5. ACOG Committee Opinion #295: pain relief during labor. Obstet Gynecol. 2004 Jul;104(1):213.
6. Pandya ST. Labour analgesia: Recent advances. Indian J Anaesth. 2010;54(5):400–408.
7. Swain A, Nag DS, Sahu S, Samaddar DP. Adjuvants to local anesthetics: Current understanding and future trends. World J Clin Cases. 2017;5(8):307–323.
8. Li Y, Hu C, Fan Y, Wang H, Xu H. Epidural analgesia with amide local anesthetics, bupivacaine, and ropivacaine in combination with fentanyl for labor pain relief: a meta-analysis. Med Sci Monit. 2015;21:921–928. Published 2015 Mar 29.
9. Bajwa SJ, Kaur J. Clinical profile of levobupivacaine in regional anesthesia: A systematic review. J Anaesthesiol Clin Pharmacol. 2013;29(4):530–539.
10. Kuthiala G, Chaudhary G. Ropivacaine: A review of its pharmacology and clinical use. Indian J Anaesth. 2011;55(2):104–110.
11. Gündüz Ş, Eriş Yalçın S, Karakoç G, Akkurt MÖ, Yalçın Y, Yavuz A. Comparison of bupivacaine and ropivacaine in combination with fentanyl used for walking epidural anesthesia in labor. Turk J Obstet Gynecol. 2017;14(3):170–175.

12. Bawdane KD, Magar JS, Tendolkar BA. Double blind comparison of combination of 0.1% ropivacaine and fentanyl to combination of 0.1% bupivacaine and fentanyl for extradural analgesia in labour. J Anaesthesiol Clin Pharmacol 2016;32:38-43
13. Writer WD, Stienstra R, Eddleston JM, Gatt SP, Griffin R, Gutsche BB, Joyce TH, Hedlund C, Heeroma K, Selander D. Neonatal outcome and mode of delivery after epidural analgesia for labour with ropivacaine and bupivacaine: a prospective meta-analysis. Br J Anaesth. 1998 Nov;81(5):713-7.
14. Paddalwar S, Nagrale M, Chandak A, Shrivastava D, Papalkar J. A randomized, double-blind, controlled study comparing Bupivacaine 0.125% and Ropivacaine 0.125%, both with Fentanyl 2 µg/ml, for labor epidural analgesia. Indian J Pain 2013;27:147-53
15. Pinder AJ, Dresner M. Intrathecal ropivacaine or bupivacaine with fentanyl for labour. Br J Anaesth. 2002 Apr;88(4):611; author reply 611-2.

How to cite this article: Husain R, Anwar T, Khan SA, Jamshed S, Khan ZS, Khomusi MM. Comparative Study of Levobupivacaine with Fentanyl Versus Ropivacaine with Fentanyl for Labor Analgesia. Ann. Int. Med. Den. Res. 2019; 5(3):AN19-AN24.

Source of Support: Nil, **Conflict of Interest:** None