Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/17011
DOI URL: http://dx.doi.org/10.21474/IJAR01/17011

RESEARCH ARTICLE

COMPARISON OF 0.5% LEVOBUPIVACAINE- FENTANYLAND 0.5% ROPIVACAINE-FENTANYL IN INFRAUMBILICAL SURGERIES

Dr. Megha S.[1] and Dr. Raghunandana P.[2]

1. Junior Consultant, Rainbow Children's Hospital, Hebbal, Bangalore.
2. Assistant Professor SIMSRC, Bangalore.

Manuscript Info

Manuscript History
Received: 23 March 2023
Final Accepted: 27 April 2023
Published: May 2023

Key words:-
Infraumbilical, Spinal Anaesthesia, Regional Analgesia

Abstract

Spinal anaesthesia is a commonly performed procedure when the surgical site is located on the lower abdomen, perineum or lower extremities. The advantages are an awake and spontaneously breathing patient, minimal drug costs, reduction of poly-pharmacy and rapid patient turnover. Regional anesthesia techniques have seen numerous modifications over the last two decades with the advent of many new and safer local anesthetics. Presently, hyperbaric bupivacaine is the most commonly used drug for administration of spinal anaesthesia. Levobupivacaine and ropivacaine have recently become available in India for clinical use. Very few studies have been done comparing these two drugs in India. Hence, present study was undertaken to compare 0.5% Levobupivacaine (isobaric)-fentanyl(25µg) and 0.5% Ropivacaine (isobaric)-fentanyl(25µg)with regards to onset and duration of blockade infra umbilical surgeries in spinal anaesthesia. Methods and materials- this is a hospital based randomized double blinded comparative clinical study. Adult patients scheduled for elective infra umbilical surgeries under spinal anaesthesia. Eighty patients were randomized to two groups: group LF and RF (n=40 for each group). All patients received drug volume of 3.5ml containing 3 ml isobaric levobupivacaine (15 mg) + 0.5 ml (25 mcg) fentanyl in group LF, and 3ml isobaric ropivacaine (15mg) + 0.5 ml (25 smcg) fentanyl in group RF. The time for completion of intrathecal administration of study drugs injection is considered as TIME 0. The following parameters were observed – time of onset and duration of sensory block, motor block.

Results: In the present study, mean onset of sensory block was faster in Group LF (5.25±0.74 min) than in Group RF (6.53 ± 0.51 min) and was statistically significant (p value < 0.001). In the present study, mean onset of motor block was faster in Group LF (7.25±0.98 min) than in Group LF (11.2 ± 0.61 min) and was statistically significant (p value <0.001).

Conclusion: LF group provided better sensory and motor blockade with higher dermatome coverage than RF group.

Corresponding Author:- Dr. Megha S.
Address:- Junior Consultant, Rainbow Children's Hospital, Hebbal, Bangalore.

Introduction:-

Spinal anaesthesia is a commonly performed procedure when the surgical site is located on the lower abdomen, perineum or lower extremities. The advantages are an awake and spontaneously breathing patient, minimal drug costs, reduction of poly-pharmacy and rapid patient turnover. It is a simple, effective and safe technique. Hence it has become the method of choice for such surgeries.

Spinal anaesthesia is performed by injection of a local anaesthetic with or without adjuvant in the sub-arachnoid space producing intense sensory, motor and sympathetic blockade. Anesthesiologists, all across the world, have been trying to make spinal anaesthesia as safe as possible by providing adequate intra and post-operative analgesia and at the same time promoting early ambulation post– surgery.

Regional anesthesia techniques have seen numerous modifications over the last two decades with the advent of many new and safer local anesthetics. Presently, hyperbaric bupivacaine is the most commonly used drug for administration of spinal anaesthesia. It's levorotatory or S (−) stereoisomer known as levobupivacaine, which is less cardiotoxic than bupivacaine has been available in India since 2014 emerged as a safer alternative for regional anaesthesia than its racemic parent. Clinically levobupivacaine is well tolerated in a variety of regional anaesthesia techniques either bolus administration or continuous infusion. In clinical anesthesia, levobupivacaine produces comparable surgical sensory and motor block with bupivacaine in spinal anaesthesia.[1] At present in India only isobaric 0.5% levobupivacaine is available for intrathecal use, and since it is isobaric it may be ideal drug to be used in infra-umbilical surgeries as the level of block will be much lower when compared to hyperbaric drug, when SAB is administered and patient turned into supine position.[2]

Ropivacaine was introduced into clinical practice in 1996 and in India by 2009. It was the first commercially available local anaesthetic in its category as a pure S-enantiomer. Ropivacaine resembles bupivacaine structurally. It's a long acting amide local anesthetic cause's differential sensory nerve block, with a dose-dependent motor blockade and a safer cardiac profile. It has demonstrated an improved safety profile over bupivacaine, with a reduced central nervous system and cardiotoxicity, together with a wide clinical utility at different doses and for a wide range of indications.[3]Although these concerns are not clinically relevant to spinal anaesthesia because of the smaller doses required, there has, nevertheless, been an increased interest in these agents for intrathecal use.[4]Ropivacaine also available in india as 0.5%, 0.75%, and 1% isobaric preservative free drug for intrathecal use. It is less potent when compared levobupivacaine but studies have found out higher concentration of 0.5% and above, both the drugs behave equipottently.

The aim of using adjuvants with local anaesthetics is to improve analgesic intensity, to increase duration of action, to achieve faster onset and to achieve acceptable, effective prolonged post - operative analgesia with lower drug doses and thus reduced risks of side-effects. Efforts to find an ideal adjuvant in regional anaesthesia have been going on since a long time. Thus opioids like fentanyl[5] have been used intrathecally as adjuvants to the local anaesthetics for improvement in quality and extending the duration of spinal blockade.

Levobupivacaine and ropivacaine have recently become available in India for clinical use. Very few studies have been done comparing these two drugs in India. Hence, present study was undertaken to compare 0.5% Levobupivacaine (isobaric)-fentanyl(25µg) and 0.5% Ropivacaine (isobaric)-fentanyl(25µg)with regards to onset and duration of blockade infra umbilical surgeries in spinal anaesthesia.

Material and Methods:-

This study was conducted as a one year hospital based randomized double blinded comparative clinical study.Adult patients scheduled for elective infra umbilical surgeries under spinal anaesthesia at APOLLO BGS HOSPITALS, Mysore between December 2017 to November 2018. The study population consisted of 80 patients randomly allocated into two groups by a computer generated chart.

1. Group LF – 3ml 0.5% isobaric Levobupivacaine-fentanyl(25µg) Group – (40)
2. Group RF - 3ml 0.5% isobaric Ropivacaine-fentanyl(25µg) Group – (40)

Patients undergoing elective infra umbilical surgeries lasting for 60 to 120 min, 18 to 65 years group and ASA class I and class II patients were included in the study.

Patients with Contraindications to sub-arachnoid block, Pre-existing neurological deficits in the lower extremities, and co-existing cardiovascular, respiratory, neurological, psychological, hepatic, or renal disease, allergy to the drug being studied, Pregnant patient and Obese patients were excluded from the study

The Descriptives procedure displays univariate summary statistics for several variables in a single table and calculates standardized values (z scores). Variables can be ordered by the size of their means (in ascending or descending order), alphabetically, or by the order in which the researcher specifies.

The Crosstabs procedure forms two-way and multiway tables and provides a variety of tests and measures of association for two-way tables. The structure of the table and whether categories are ordered determine what test or measure to use. Cramer's V test was employed in the present study.

The Independent-Samples T Test procedure compares means for two groups of cases. Ideally, for this test, the subjects should be randomly assigned to two groups, so that any difference in response is due to the treatment (or lack of treatment) and not to other factors.

Demographic data of the patients like name, age, sex and history obtained through an interview. The physical and medical examination was conducted. These findings were recorded on a predesigned and pretested proforma.

Patients were preloaded with 10ml/kg of Ringer Lactate within half an hour of administering spinal anaesthesia. Lumbar puncture with a 27(G) Quincke's spinal needle was performed with the patient in sitting position after thorough skin preparation. Intrathecalinjection of study drugseither ropivacaine with fentanyl or levobupivacaine with fentanyl were given according to groups they belong to after noting the clear free flow of CSF with the operating table kept flat. These study drugs were prepared by another anaesthesiologist who was also involved with randomization of patient and was not involved further with observations of the patients, thus the patient and the observer were blinded for study drugs. Patients are turned to supine immediately and are given supplemental oxygen with face mask at 5L/minute.

Sensory block was checked using alcohol swab for cold sensation. Since both cold sensation and fine pain sensation are carried by A fibres, we did not use needle prick to avoid discomfort for the patient.

Eighty patients were randomized to two groups: group LF and RF (n=40 for each group). All patients received drug volume of 3.5ml containing 3 ml isobaric levobupivacaine (15 mg) + 0.5 ml (25 mcg) fentanyl in group LF, and 3ml isobaric ropivacaine(15mg) + 0.5 ml (25 smcg) fentanyl in group RF.

The time for completion of intrathecal administration of study drugs injection is considered as TIME 0. The following parameters were observed – time of onset and duration of sensory block, motor block.

Onset of Sensory block:
Was taken from time 0 to the time taken to reach the level of T10, and assessed using alcohol swab in mid-axillary line

Maximum level of sensory block achieved was also checked

Onset of Motor block:
The time taken to reach modified Bromage score 3 fromtime 0
Bromage0: Free movement of legs and with ability to raise extended leg.
Bromage1:Inability to raise extended leg and knee flexion is decreased, but full flexion of ankle and feet is present.
Bromage2:Inability to raise leg or flex knees, flexion of ankle and feet present.
Bromage3:Inability to raise leg, flex knee or ankle or move toes.

Duration of blockade
Sensory block:
Duration of sensory block is from time 0 till the recovery of sensory block at the level of L1

Motor block:
Total duration of motor block is taken as the time for return to modified Bromage score 0.

Sensory and motor block were assessed at time intervals: 0, 5, 10, 15, 30, 45, 60, 90, 120 minutes after injection. The assessments were continued at 15 minutes interval thereafter until the motor block regressed completely (i.e. modified Bromage score=0). All durations were calculated considering the time of injection as time zero. Any complications associated with these drugs if seen were noted.

Blood pressure and Heart rate were recorded at 2, 4, 6, 8, 10, 15, 20, 25, 30 minutes and thereafter, every 15 minutes till the end of surgery.

Hypotension was defined as decrease in systolic B.P by 20% from baseline values or a systolic B.P less than 90 mm of Hg and was treated with incremental intravenous boluses of ephedrine 5 to 10 mg and a bolus administration of 250 ml of Ringer Lactate solution over 10 minutes.

Bradycardia was defined as decrease in heart rate less than 50 beats per minute and was treated with intravenous Atropine 0.6 mg.

Results:-

In this study 75% were males and 25% were females in group LF and 72.5% were males and 27.5 % were females in group RF, suggesting both the groups had comparable demographic characteristics (p=0.799).

In Group LF, 85.0 % patients were ASA Grade I and 15.0 % were ASA Grade II. In Group RF, 87.5 % patients were ASA Grade I and 12.5% were ASA Grade II, suggesting that ASA Grades in both groups were comparable (p=0.745).

In the present study no statistically significant difference was observed between group LF and group RF with regards to mean age (41.72± 11.68 and 38.22 ± 13.87 years respectively; p = 0.226), mean weight (64.15 ± 7.58 and 61.52 ± 7.83 kg respectively; p = 0.132) and mean height (164.12 ± 6.14 and 163.50 ± 5.58 cm respectively; p = 0.556).

Table 1:- Onset and duration of sensory block.

Group	**Onset (minutes)**		**Duration(minutes)**	
	Mean	**Standard deviation**	**Mean**	**Standard deviation**
Group LF	5.250	0.74	169.5	7.15
Group RF	6.525	0.51	144.25	5.94
p value	< 0.001		< 0.001	

In the present study, mean onset of sensory block was faster in Group LF (5.25±0.74 min) than in Group RF (6.53 ± 0.51 min) and was statistically significant (p value < 0.001) The mean duration of sensory block was longer in Group LF (169.5±7.15 min) than in Group RF (144.25 ± 5.94 min) and was statistically significant (p value < 0.001).

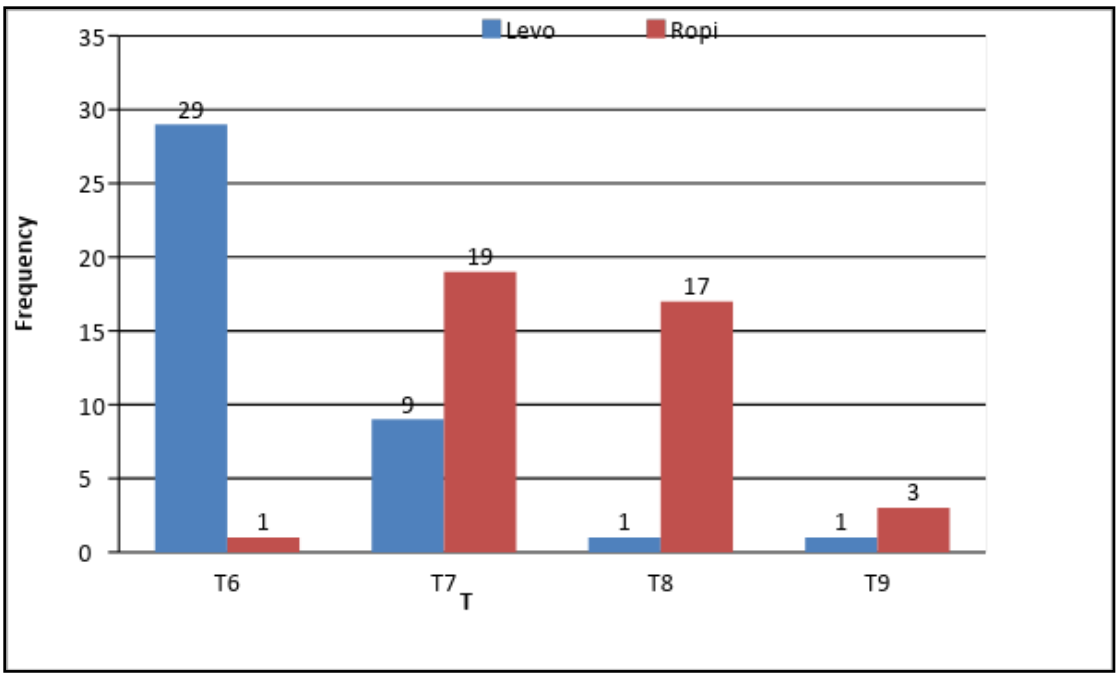

Figure 1:- Highest sensory dermatome block level.

In the present study higher number of patients were noted with T_6 sensory dermatome level block in group LF (72.5%) compared to group RF (2.5%) and was statistically significant (p value < 0.001).

Table 2:- Onset and duration of motor block.

Group	Onset (minutes)		Duration(minutes)	
	Mean	Standard deviation	Mean	Standard deviation
Group LF	7.25	0.98	219.5	6.39
Group RF	11.20	0.61	171.25	7.23
p value	< 0.001		< 0.001	

In the present study, mean onset of motor block was faster in Group LF (7.25±0.98 min) than in Group LF (11.2 ± 0.61 min) and was statistically significant (p value <0.001) The mean duration of motor block was longer in Group LF (219.5±6.39 min) than in Group RF (171.25 ± 7.23 min) and was statistically significant (p value < 0.001).

In this study the mean heart rate in group LF at beginning was noted as 81.43±8.18 bpm which decreased to 70.75 ± 8.38 bpm at 60 minutes interval and reached 71.28±7.45 bpm at 120 minutes. In group RF,themeanheart rate at beginning was 81.85 ± 8.78 bpm which reduced to 71.67 ± 6.88 bpm at 60 minutes interval and reached 75.4 ± 6.55 at 120 minutes. However at all the intervals the mean heart rate in group LF and RF was comparable (p > 0.05).

In this study, the mean systolic blood pressure in group LF, at two minutes interval was 128.60 ± 8.15 mm Hg which decreased to 116.25 ± 8.38 mm Hg at 10 minutes interval and reached 113.40 ± 8.73 mm Hg at 120 minutes. Similarly, in group RF, the systolic blood pressure at two minutes interval was 126.35 ± 8.95 mmHg which decreased to 111.95 ± 9.03 mm Hg at 10 minutes interval and reached 121.40± 5.52 mm Hg at 120 minutes. However the mean systolic blood pressure at all the intervals in group LF and RF were comparable (p > 0.05) except at 10 minutes duration when it was significant (p value = 0.03).

In the present study, preoperatively the mean diastolic blood pressure in group LF and RF was almost similar and hence statistically not significant (82.63 ± 7.15 and 82.63 ± 8.78 mm Hg respectively; p = 1). There was a decrease in mean diastolic blood pressure at 30 minutes interval that is, 67.75± 5.90 mm Hg in group LF and 68.57 ± 5.91 mm Hg in group RF but this difference was statistically not significant (p = 0.53). Further at 120 minutes also the mean diastolic blood pressure in group LF and RF were comparable (74.61±4.27 and 79.20 ± 6.38 mm Hg respectively; p=0.06).

In the present study, preoperatively the mean MAP in group LF and RFwas almost similar and hence statistically not significant (98.40 ± 6.71 and 97.42 ± 8.42 mm Hg respectively; p value = 0.57). There was a decrease in mean MAP at 30 minutes interval, 81.17 ± 6.43 mm Hg in group LF and 81.67 ± 5.83 mm Hg in group RF but this difference was statistically not significant (p = 0.69). Further at 120 minutes also the mean MAP in group LF and RF were comparable (85.22 ± 4.08 and 93.23 ± 5.84 mm Hg respectively; p = 0.15).

Table 3:- Complications/ Side – Effects observed.

	Group LF (n=40)	**Percentage**	**Group RF (n=40)**	**Percentage**
Hypotension	6	15	4	10
Nausea and Vomiting	2	5	1	2.5
Bradycardia				

In 15% of cases in group LF and 10% of cases in group RF, hypotension was observed. Other incidences observed were nausea and vomiting in the two groups.

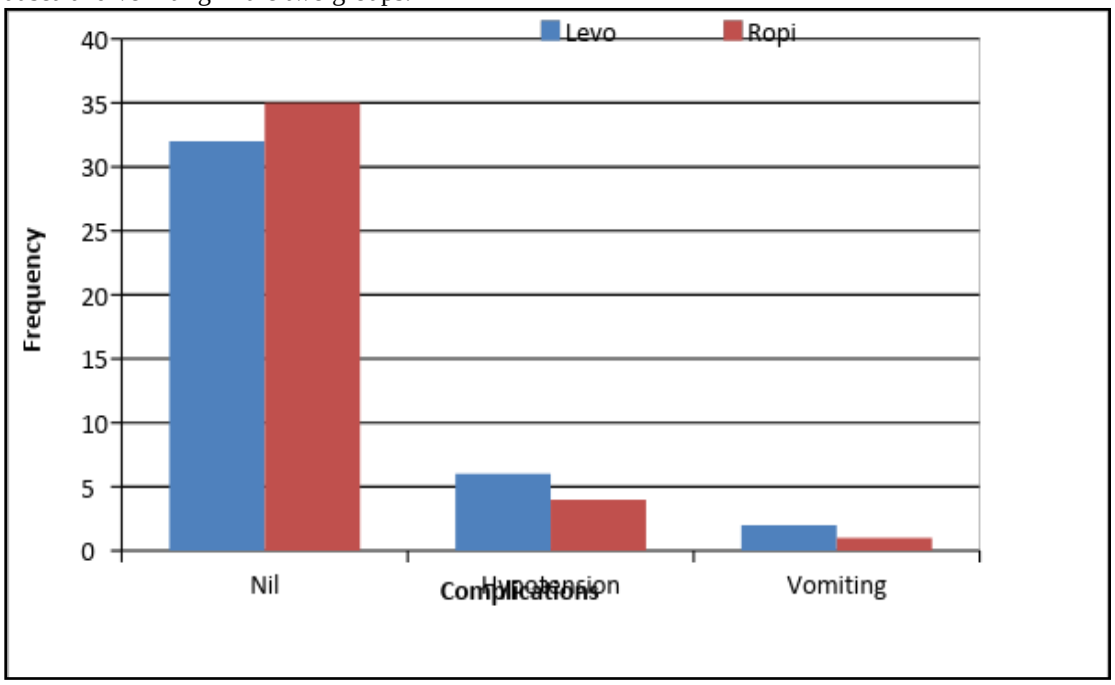

Figure 31:- Complications / Side Effects observed.

Discussion:-

In our study we selected levobupivacaine and ropivacaine as study drugs because, Clinical studies in various patient populations**Ying et al,Kannai et al** and **Sinnot et al, Allery et al**, **Gautier et al** showed that bupivacaine is the most potent local anesthetic equivalent to levobupivacaine followed by ropivacaine([6,7-10])It was believed that levobupivacaineand bupivacaine produce comparable surgical sensory blockLevobupivacaine has not entirely replaced bupivacaine in clinical anaesthesia practice. The equipotency of the twodrugs has been recently questioned. And Ropivacaine is less potent because of its lower lipid solubility but that it has an advantage of stronger differentiation between sensory and motor block, a feature that is particularly useful when early mobilization is important to enhance recovery.When Ropivacaine is used in a concentration of 0.5% the efficacy is comparable with 0.5% Bupivacaine, even though the equipotent doses of Ropivacaine to Bupivacaine is 1.5:1

Our study was done using isobaric solutions. In current clinical practice hyperbaric bupivacaine is most commonly used for intrathecal administration.Since in India levobupivacaine, ropivacaine available only in isobaric forms, we conducted study comparing isobaric solution. It would be useful to do further study comparing hyperbaric levobupivacaine, hyperbaric ropivacaine and hyperbaric bupivacaine for intrathecal usage

In our study demographic parameters like age, sex, weight, height and ASA status were comparable between the two groups.

Study shows that the intrathecal administration of either 15 mg ropivacaine or 15 mg levobupivacainewas well tolerated and an adequate block for lower abdominal surgery was achieved in all patients in each group.

In our study, **onset of sensory block** was defined as the time taken to achieve than in Group RF (6.53 ±0.51 min) and was statistically significant (p value <0.001).In the study conducted by**Das et al**[11] observed onset of sensory block values for Group L was 4.2± 1.99mins and ingroup R was 7.73±3.04 min, which is similar to our study. values obtained for Group L in our study also correlate well with thatof **Mehta et al**[12] (5.46±1.72 min), and onset time observed by **Fattoriniet al**[13] (12±6 min) in group L was slightly longer; the difference may be due to the use of lower dose (8 mg) of Levobupivacaine in their study

In our study, **duration of sensory block** was defined as two dermatome regression of anaesthesia from the highest level. It was longer in Group LF (169.5±7.15 minutes) than in Group RF (144.25 ± 5.94 minutes) and was statistically significant (p value <0.001). Majority of patients had T_6 sensorydermatome block level in Group LF while T_7 sensory dermatome block level was observed in Group RF.

Das et al[11] and **Mehta et al**[12] found that the duration of sensory blockade for levobupivacaine was 145±28 mins and 189.4±42.9 min respectively and that for Ropivacaine was 122.47 + 25.4 mins and 144.32 + 32.1 mins respectively. The minimal difference in results in the studies may be because of different parameters used for calculating duration. Das et al considered 2 segment regression from the maximum sensory block height as the duration of sensory blockade, whereas Mehta et alconsidered time from the onset of sensory block to the time when the patient required first dose of analgesia.

Breebaart et al, in their study, concluded that the total duration of sensory block with 10 mg of levobupivacaine and 15 mg of ropivacaine was 173 ± 47 minutes and 167 ± 49 minutes,[14] which was quite similar to our study.

A study done by **Mantouvalou et al**, comparing characteristics of spinal anaesthesia in patients undergoing lower abdominal surgery between 15 mg of levobupivacaine with 15 mg of bupivacaine and 15 mg ropivacaine, showed the duration of sensory block was 230 minutes, 240 minutes and 200 minutes respectively suggesting levobupivacaine was longer acting than ropivacaine.[15]In this study total duration of sensory block was measured and not just two segment regression, hence a slight difference can be noted in the duration between that and our study.

In our study, **onset of motor block** was defined as the time to reach Modified Bromage Grade 3. The mean onset of motor block was faster in Group LF (7.25±0.98 min) than in Group RF (11.2 ± 0.61 min) and was statistically significant (p value <0.001).

Itcorrelates with study by **Das et al**,[11] who found that onset of motor block inLevobupivacaine group was 7.37±3.26 mins and 11.07+3.04 mins in Ropivacaine group which is similar to our study.

Total **duration of motor block** was defined as the time for return to Modified Bromage Grade 0in our study. It was longer in Group LF (219.5 ± 6.39 min) than in Group RF (171.25 ± 7.23 min) and was statistically significant (p value < 0.001).

Rajni Thakur1 et al (2018) compared60 patients of ASA I and II of age 20 to 50 years of either sex patients Undergoing Lower Limb Surgeries, for Group I with 3 ml 0.5% isobaric Levo Bupivacaine (15 mg) and groupII (3ml 0.75% isobaric Ropivacaine (22.5mg). The mean duration of motor blockade in Group I was 224.20 ± 19.17 mins compared to 178.20 ± 31.14 mins in Group II which was statistically significant, its similar to our study.[16]

Varun et al conducted a study on 100 patients undergoing lower abdomen and lower limb surgeries under spinal anaesthesia. The patients were randomly divided intotwo groups receiving either 3 ml 0.5% isobaric bupivacaine + 20 mcg fentanyl or 3 ml 0.5% isobaric ropivacaine + 20 mcg fentanyl. Time for Motor recovery to Modified Bromage scale 0 was 180.20±41.66 minutesin the former group and 173.00±17.76 minutes in the latter group, the results being similar to our study.[17]

In our study, the baseline hemodynamic parameters i.e., mean heart rate, mean systolic blood pressure, mean diastolic blood pressure and mean arterial pressure were comparable in Group LF and Group RF at all the intervals since beginning (p value> 0.05). Hypotension was observed in 15% of the patients in Group LF while 10% of the patients in Group RF had hypotension. It was corrected with 5 mg of ephedrine and 250 ml of fluid bolus. Similar hemodynamicswere observed in the study by Jagtap et al.[18]Hypotension requiring treatment was observed in 3.3%patients in Group Ropivacaine-Fentanyl as compared to 10% patients in Group Bupivacaine Fentanyl.

The other side effects observed were nausea and vomiting and pruritus in the two groups. Group LF had an incidence of 5% of nausea and vomiting while Group RF had an incidence of 2.5% of nausea and vomiting. Similar results were observed in the study by Jagtap et al where the incidence of nausea and vomiting was 3.3% in Ropivacaine - fentanyl group[18]. It was treated with Inj. ondansetron 4 mg i/v in our study.

To evaluate the pharmacodynamic effects of different intrathecal drugs, a clinical model should be developed to determine the relative potencies of local anesthetics with adjuvants. This involves the estimation of the median effective dose (ED_{50}) to determine the spinal potency ratios for sensory and motor block. Ropivacaine, levobupivacaine, and bupivacaine belong to the pipecolylxylidine homologous series of local anesthetics that have an ability to cause differential sensory and motor neural blockade. Previous studies have compared ED_{50} values of levobupivacaine/ropivacaine and ropivacaine/bupivacaine when given intrathecally for surgical anesthesia. However most of these studies have been done without the use of fentanyl as adjuvant. Hence more studies need to be done with fentanyl to add to the already existing knowledge.

Conclusion:-

Our study showed that intrathecal0.5% isobaric levobupivacaine + fentanyl ismore potent than intrathecal 0.5% isobaric ropivacaine + fentanyl with respect to the duration of sensory and motor block with with good haemodynamic stability in lower abdominal surgeries.Intrathecal0.5% isobaric ropivacaine+fentanyl provides satisfactory anaesthesia with shorter duration of motor block compared to intrathecal0.5% isobaric levobupivacaine + fentanyl which is a desirable feature for early ambulationbetter drug for day care surgeries.Levobupivacaine has faster and prolonged sensory and motor blockade compared to Ropivacaine,which is better for surgeries of prolonged duration.Both the drugs can be used as alternative to bupivacaine intrathecally with no risk of major side effects/complications, when used intrathecally.

Bibliography:-

1. Weinberg L, Hu R, Chen SP. Levobupivacaine for Regional Anaesthesia and Pain Management. Clinical Medicine Reviews in Therapeutics. 2011;3:371-97.
2. Greene NM. Uptake and elimination of local anaesthetics during spinal anaesthesia. AnaesthAnalg. 1985;64:715-30.
3. Kuthiala G, Chaudhary G. Ropivacaine: A review of its pharmacology and clinical use. Indian J Anaesth. 2011;55:104-10.
4. Luck FJ, Fettes PDW, Wildsmith JAW. Spinal anaesthesia for elective surgery: a comparison of hyperbaric solutions of racemic bupivacaine, levobupivacaine, and ropivacaine. Br J Anaesthesia. 2008;101(5):705-10.
5. Bouvet L, Da-Col X, Chassard D, Dalery F, Ruynat L, Allaouchiche B, et al. ED_{50} and ED_{95} of intrathecal levobupivacaine with opioids for Caesarean delivery. Br J Anaesthesia. 2011;106(2):215-20.
6. Lee YY, NganKee WD, Fong SY, Liu JTC, Gin T. The median effective dose of bupivacaine, levobupivacaine, and ropivacaine after intrathecal injection in lower limb surgery. AnesthAnalg. 2009;09:1331.
7. Kanai Y, Katsuki H, Takasaki M. comparison of the anesthetic patency and intracellular concentration of s (-) and r (+) bupivacaine and ropivacaine in crayfish giant axon in vitro. AnesthAnalg. 2000;90:415-20.
8. Sinnott CJ, Strichartz GR. Levobupivacaine versus ropivacaine for sciatic nerve block in the rat. RegAnesth Pain Med. 2003;28(4):294-303.
9. Alley EA, Kopacz DJ, McDonald SB, Liu SS. Hyperbaric spinal levobupivacaine: a comparison to racemic bupivacaine in volunteers. AnesthAnalg. 2002;94(1):188-93.
10. Gautier PE, De Kock M, Van Steenberge A, Poth N, Lahaye-Goffart B, Fanard L et al. Intrathecal ropivacaine for ambulatory surgery. Anesthesiol. 1999;91(5):1239-45.

11. Mehta A, Gupta V, Wakhloo R, Gupta N, Gupta A, Bakshi R, et al. Comparative evaluation of intrathecal administration of newer local anaesthetic agents Ropivacaine and Levobupivacaine with Bupivacaine in patients undergoing lower limb surgery. The Internet Journal of Anesthesiology. 2007;17(1).
12. Das A, Hazra R, Halder B, Ghosh S, Chakraborty S, Basu R, et al. Comparison of the effects of Intrathecal Bupivacaine, levobupivacaine and Ropivacaine in lower abdominal surgery: a double-blind, randomized controlled trial using isobaric preparations. International Journal of Information Research and Review. 2015;2(04):636-41.
13. Fattorini F, Ricci Z, Rocco A, Romano R, Pascarella A, Pinto G. Levobupivacaine versus racemic bupivacaine for spinal anaesthesia in orthopaedic major surgery. Minerva Aaestesiol. 2006;72:637-44.
14. Breebaart MB, Vercauteren MP, Hoffmann VL, et al Urinary bladder scanning after day-case arthroscopy under spinal anaesthesia: comparison between lidocaine, ropivacaine, and levobupivacaine. Br J Anaesth. 2003;90:309-13
15. Mantonvalon M, Ralli S, Amontoglon H, Zirs GT, Papadopoulos G. Spinal Anaesthesia: comparison of plain ropivacaine, levo bupivacaine for lower abdominal surgery. Acta Anaesthesia Belgium. 2008;59:65-71.
16. Thakur R, Aske R, Keshari U. Comparative evaluation of intrathecal administration of isobaric levobupivacaine (0.5%) and isobaric ropivacaine (0.75%) in patients undergoing lower limb surgeries. International Journal of Contemporary Medical Research. 2018;5(2):B6-B8.
17. Varun S, Srivastava M, Maurya I, Garg R, Dhama V, Manik YK. A clinical prospective, randomized study to compare intrathecal isobaric bupivacaine-fentanyl and isobaric ropivacaine - fentanyl for lower abdomen and lower limb surgeries. Anaesthesia Pain and Intensive Care. 2012;16(3):237-42.
18. Jagtap S, Chhabra A, Dawoodi S, Jain A. Comparison of intrathecal ropivacaine-fentanyl and bupivacaine-fentanyl for major lower limb orthopaedic surgery: A randomised double-blind study. Indian J Anaesth. 2014;58:442-6.