IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 18, Issue 6 Ser. 18 (June. 2019), PP 28-45
www.iosrjournals.org

A Comparison of Spinal Anaesthesia with Levo-Bupivacaine and Hyperbaric Bupivacaine combined with Fentanyl in Elective Caesarean Section

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Abstract:
Aim: *The Aim of the study is to evaluate following factors when Levobupivacaine 0.5% 9mg + 10mcg Fentanyl and hyperbaric Bupivacaine 0.5% 9mg + 10mcg Fentanyl given intrathecally in elective caesarean section.*
Study design: *Randomized control trial.*
Place and duration of study: *Anesthesia Department, Siddhartha Medical College / Government General Hospital, Vijayawada from January 2017 to June 2018.*
Methodology:*120 parturient with American Society of Anesthesiologists I-II undergoing elective caesarean section were enrolled for study with their informed consent. They were randomly divided equally to either Group BF receiving 1.8ml of 0.5% HyperbaricBupivacaine(9mg)+ 0.2ml Fentanyl(10mcg), or Group LF receiving 1.8ml of 0.5% IsobaricLevobupivacaine(9mg)+ 0.2ml Fentanyl(10mcg). Sensory and motor block characteristics of the groups were assessed with pinprick, cold swab, and Bromage scale; observed hemodynamic changes and side-effects were recorded. Effects on the neonate were observed by Modified Bromage Scale and umbilical cord blood gas analysis.*
Results: *Hemodynamic parameters like mean arterial pressure of Group BF were found to be lower. Group BF exhibited maximum motor block level whereas in Group LF, max sensorial block level and postoperative visual analog scale scores were higher. Umbilical blood gas pCO_2 was slightly higher, and pO_2 was marginally lower in Group BF. Onset of motor block time, time to max motor block, time to T10 sensorial block, reversal of two dermatome, the first analgesic need were similar in both groups.*
Conclusion:*plain Levobupivacaine 0.5% which is pure s – enantiomer of Bupivacaine is a good alternative for caesarean section in spinal anesthesia as it have less CVS and CNS toxicity when compared with Bupivacaine Hydrochloride. Early recovery of motor blockade leading to early mobilization of the mother and analgesia almost similar to racemic hyperbaric Bupivacaine . Addition of low dose Fentanyl 10mcg with Levobupivacaine has dose sparing effect of opiods on local anesthetics, better postoperative analgesia and early recovery from motor block. Action of isobaric Levobupivacaine is independent of gravity in spinal anesthesia.*
Key Words: *Cesarean sections, fentanyl, hyperbaric bupivacaine, isobaric levobupivacaine.*

Date of Submission: 16-06-2019 Date of acceptance: 02-07-2019

I. Introduction

The incidence of women going for caesarean section dramatically increased in last 20years. The number of Caeserian section deliveries in India has been more than doubled in the past decade, going up from 8.5 percent of total births in 2005-06 to 17.2 percent in 2015-16. During the same period, institutional deliveries also doubled from 38.7% to 78.9%, data released by National Family Health Survey-4 in 2017. The challenges presented by a pregnant women requiring anaesthesia or analgesia, or both, make the role of obstetric anaesthesiologist both challenging and rewarding. Those providing the anaesthetic services to labour and delivery suite must be familiar with the unique physiology of parturient and effects of numerous drugs and techniques on parturient and fetus. The safety of obstetric anaesthesia has increased primarily as a result of awareness of local anaesthetic toxicity and increased use of regional anaesthesia and analgesia.

Spinal anesthesia is a most commonly used technique for caesarean section. Hyperbaric Bupivacaine in 8% glucose is often used. Plain or glucose-free, Bupivacaine has been frequently referred to as "isobaric" in the literature. Recently, several studies have confirmed that plain Bupivacaine is indeed hypobaric in comparison with human CSF.[2-4] Clinically, this manifests as an unpredictable median sensory block height differs with a inter-individual spread and is occasionally associated with block failure when the spinal block has

not spread high enough for surgery.[5,6] For this reason, hyperbaric Bupivacaine is favoured in obstetric anaesthesia. Although hyperbaric local anaesthetic solutions have a remarkable record of safety, their use is aiso associated with some risk. [7-9] To prevent unilateral or saddle blocks. Patients should move from the lateral or sitting position rapidly to supine position.Because of the extension of the sympathetic block cardiac arrest may occur with hyperbaric solutions..[10,11] The use of isobaric solutions may prove less sensitive to position issues and Hyperbaric solutions may cause hypotension or bradycardia after mobilization; isobaric solutions are favoured with respect to their less sensitivity to postural changes.[12]

Levobupivacaine is a S(-)enantiomer of racemic Bupivacaine which is less toxic to the cardiovascular system and central nervous system[13,14] and has shorter duration of motor block. The Levobupivacaine has been shown to be genuienly isobaric with respect to CSF of pregnant women.[4,15] Its use in this setting may, therefore, has uniquel advantages because this property may translate to a more likely spread.

Fentanyl, an opioid administered intrathecally improves the quality of sensory blockade intraoperatively without increasing sympathetic or motor blockade. It also enhances the quality and duration of postoperative analgesia to a significant extent. Fentanyl has no significant adverse outcome on the foetus.

In present study we compare the intraoperative and immediate postoperative clinical effects of intrathecal 0.5% plain Levobupivacaine (9mg) + Fentanyl (10micrograms) and 0.5% hyperbaric Bupivacaine (9mg) + Fentanyl(10micrograms).

II. Aims And Objectives

The Aim of the study is to evaluate following factors when Levobupivacaine 0.5% 9mg + 10mcg Fentanyl and hyperbaric Bupivacaine 0.5% 9mg + 10mcg Fentanyl given intrathecally in elective caesarean section.

1. Onset and duration of sensory block
2. Onset and duration of motor block
3. Intraoperative hemodynamic changes
4. Postoperative analgesia
5. Adverse effects.

III. Materials And Methods

This clinical study is prospective randomized comparative and conducted on 120 adults of ASA physical status I & II in the age group of 20 to 30 years, posted for elective LSCS under spinal anaesthesia after Institutional Ethical committe approval and written informed consent by patients at Government General Hospital, Vijayawada during the academic year from January 2017 to June 2018.

Patients were randomly divided on an alternative basis into two groups of 60 each.

Group LF (Levobupivacaine – Fentanyl) : Received 1.8ml of 0.5% IsobaricLevobupivacaine(9mg)+ 0.2ml Fentanyl(10mcg)

Group BF (Bupivacaine – Fentanyl) : Received 1.8ml of 0.5% HyperbaricBupivacaine(9mg)+ 0.2ml Fentanyl(10mcg)

3.1Inclusion criteria

- Age: 20-30years.
- A patient who fits into American society of anaesthesiologists(ASA) physical status criteria I and II posted for elective caesarean section under subarachnoid block.
- Patients who are willing and able to give informed written consent.
- Concomitant medications: The patient can take relevant medication for concomitant diseases like diabetes, hypertension etc.

3.2 Exclusion criteria

- Patient refusal.
- Age> 30 years or <20 years.
- ASA Grade III or IV.
- Patient with pre-existing neurological and spine deformities
- Patients allergic to Local Anaesthetics and Opioids.
- Patient on anticoagulants/known coagulation disorder.
- Short stature.
- Localinfection at the site of proposed puncture for spinal anaesthesia

3.3 Method of Study

Pre anaesthetic check up was carried out on the previous day of surgerywith a detailed history, general physical examination, systemic examination, airway assessment and spine examination were done. Routine

investigations like complete haemogram, fasting blood sugar, renal function tests, ECG and others (if required) were done. Patient's weight and height was also recorded. All patients were kept nil orally for 8-10 hours.
All patient were given orally the previous night of the elective surgery.

1. T. Ranitidine 150mg
2. T. Alprazolam 0.5mg

Preoperatively: Nil per oral status was confirmed.
The procedure of subarachnoid block was explained, and the patient was informed to communicate to the anaesthesiologist about perception of pain or discomfort during surgery.

3.4 Materials Used :

1**. Spinal anaesthesia kit :**

- 25G spinal needle (Quincke)
- 2cc disposable syringes – 3 nos.
- 0.5% hyperbaric Bupivacaine ampoule
- 0.5% Levobupivacaine ampoule
- 2ml Fentanyl (50µg/ml) ampoule
- Naloxone hydrochloride ampoule.

2. **Safety measures for mother:**

All safety measures were taken for cardiovascular and pulmonary resuscitation. The following equipment and drugs were checked and kept ready.

- Boyle's apparatus
- Laryngoscope with blades,
- Endotracheal tubes – 6.5, 7, 7.5 and 8 mm ID sizes
- Suction apparatus
- Emergency drugs : Inj. Mephentermine / Inj. Adrenaline / Inj. Atropine / Inj. Hydrocortisone / Inj. Dopamine / Inj. Deriphylline / Inj. Thiopentone sodium / Inj. Succinylcholine / Inj. Sodium bicarbonate.

3. **Neonate resuscitation trolley:**

- Infant laryngoscopes with blades
- Endotracheal tubes – 2.5 & 3 mm ID sizes
- Ambu bag.
- Micro drip set, 24G IV cannula,
- Baby tray with mucous sucker, nasogastric tube, disposable 10cc, 5cc, and 2cc syringes,
- Emergency drugs: 25% dextrose ampoule / Inj. Sodium bicarbonate / Inj. Adrenaline / Inj. Atropine / Inj. Vit. K / Inj Naloxone.

3.4 Procedure

Following arrival into the operation theatre:

- Patient was shifted onto the OT table, and intravenous access established on the forearm with 18 Gauge IV cannula and Lactated Ringer's solution 10ml/kg was infused intravenously before the block.
- Multipara monitors (ECG, non-invasive blood pressure, pulse oximeter) were attached, and baseline parameters was recorded.
- Patient in sitting or left lateral position , under aseptic precautions subaracnoid block was performed by midline approach using 23 G Quinke Babcock spinal needle at L3-L4 OR L4-L5 intervertebral space and the patient received one of the two study drugs.

[**Group LF:** 1.8 ml 0.5% isobaric Levo bupivacaine(9 mg) +0.2ml fentanyl(10mcg)]
[**Group BF:** 1.8 ml 0.5% hyperbaric bupivacaine(15mg) +0.2ml fentanyl(10mcg)]

- Heart rate, blood pressure were measured at 0,2,4,6,8,10,30,60,45,90,120 minutes.
- Hypotension was defined as 20% decrease in blood pressure from baseline values and was treated with intermittent IV boluses of ephedrine 6mg.
- Bradycardia was defined as heart rate less than 50 bpm and treated with IV atropine 0.6mg.
- Patients were continuously monitored using non invasive blood pressure, pulse oximeter, ECG.
- After administration of spinal anaesthesia, oxygen(4l/min) by facemask was given. Fluid therapy was initiated with lactated Ringer's solution (10ml/kg/hour).

Assessment of sensory blockade :

1. Onset of analgesia(sensory block): Is defined as the time interval between administration of local anaesthetic into the subarachnoid space to the loss of pin-prick sensation at the site of surgical incision.
2. Highest level of sensory block was noted.

Duration of analgesia(sensory block) : Is the time from onset of analgesia to timeof request for rescue analgesics.

Degree of sensory block:

Assessment of degree or intensity of sensory block was done using Visual Analogue Scale Score on a 10cm scale:

0-4 mm	No Pain
5-44mm	Mild Pain
45-74mm	Moderate Pain
75-100mm	Severe Pain

Assessment of motor blockade:

Assessed by **Modified Bromage scale**

1. Onset of motor block: The time interval between injection of drug into subarachnoid space, to the patient's inability to lift the straight extended leg(grade 3).
2. Duration of motor block: Duration of motor block was recorded from onset the time to time when the patient was able to lift the extended leg (grade 0).

Modified Bromage Score	**Degree of Block / Score**
A) No motor block, free movements of legs & feet with ability to raise extended leg	**None – Grade 0**
B) Inability to raise extended leg and knee flexion is decreased but extension of feet and ankle is present	**Partial – Grade 1 33%**
C) Inability to raise leg, no flexion of knees, flexion of ankle and feet present	**Partial- Grade 2 66%**
D) Inability to raise leg, flex knee or ankle Completely or move toe	**Complete – Grade 3**

Complications such as bradycardia, hypotension, nausea & vomiting, pruritis, shivering, if any are noted intra operatively.

3.5 Statistical Method:

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean+_ SD (Min-Max), and results on categorical measurements are presented in Number (%) with Student 't' test and Chi Sqare test.

IV. Observation And Results

The 120 patients admitted in our hospital selected for study are divided into two equal and comparable groups. Those patients who were subjected were considered as Group BF, and Group LF.

Table 1Comparison of Age Distribution

Variable	Group BF		Group LF		P- Value
	Mean	SD	Mean	SD	
Age	23.23	2.92	23.83	3.04	0.273

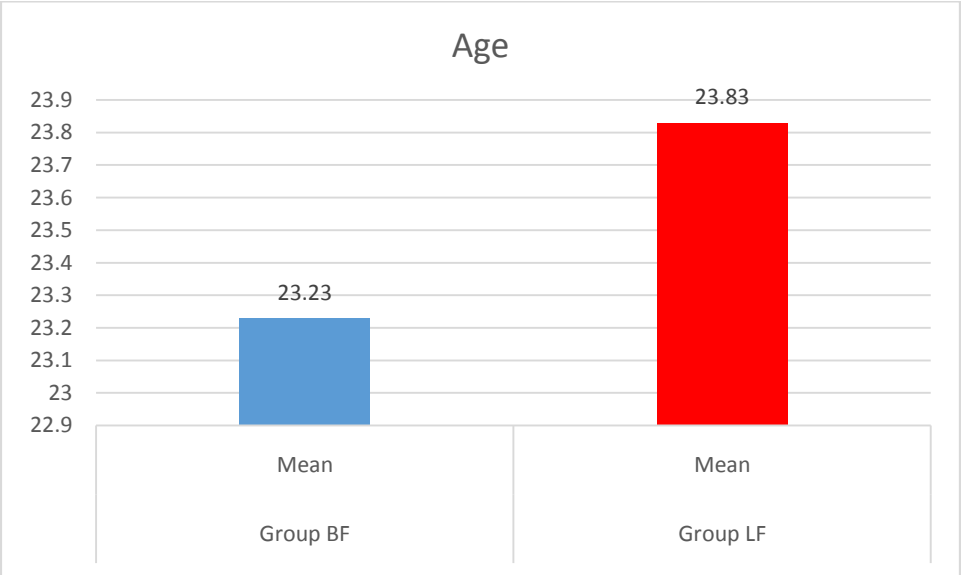


Table 2 : Weight

Variable	Group BF		Group LF		P- Value
	Mean	SD	Mean	SD	
Weight	64.47	6.75	65.83	6.52	0.262

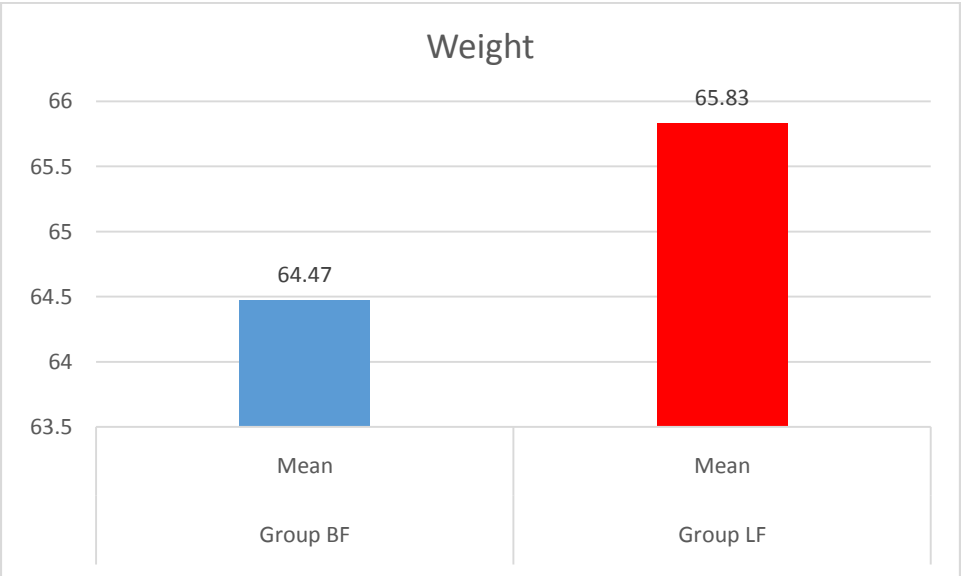


Table3 : PULSE RATE (Mean + SD) and t – test for samples

PR	Group-BF		Group-LF		P-value
	Mean	SD	Mean	SD	
at PRE OPE	85.50	11.15	82.93	10.19	.191
at 2 min	83.80	11.17	82.48	10.35	.504
at 4 min	78.80	15.41	78.13	13.59	.802
at 6 min	78.90	14.32	78.22	12.39	.780
at 8 min	80.80	13.52	78.10	12.30	.255
at 10 min	82.00	12.45	78.50	11.50	.112
at 15 min	82.30	11.16	79.12	10.56	.111
at 30 min	82.75	10.51	79.53	10.09	.090
at 45 min	82.23	10.15	79.73	10.32	.184
at 60 min	82.23	9.19	79.57	10.20	.135
at 120 min	82.00	8.75	80.30	10.51	.338

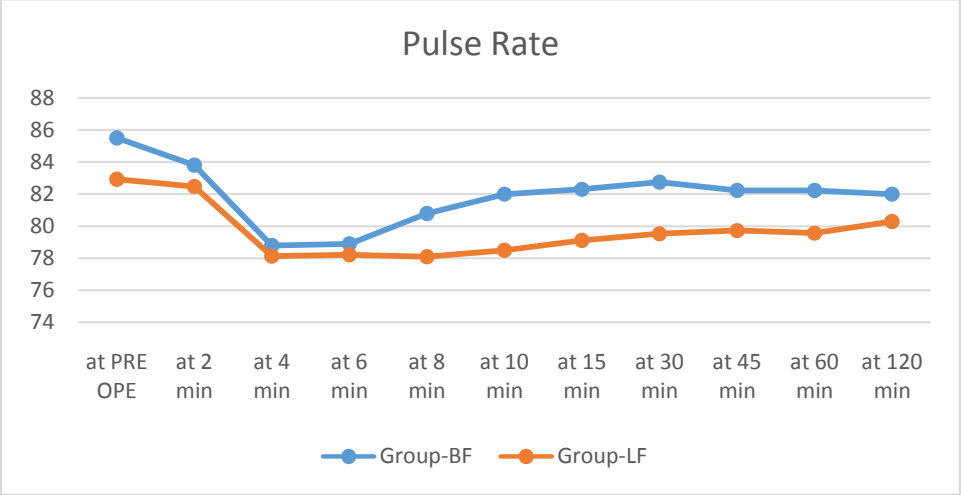


Table 4: SBP

SBP	Group-BF		Group-LF		P-value
	Mean	SD	Mean	SD	
at PRE OPE	113.20	10.50	111.70	11.20	.451
at 2 min	109.97	10.38	111.27	11.19	.511
at 4 min	103.33	15.27	104.25	15.65	.746
at 6 min	101.67	14.64	102.13	11.76	.848
at 8 min	102.67	12.63	100.77	11.10	.383
at 10 min	105.27	10.45	102.82	10.27	.198
at 15 min	107.07	10.04	105.23	9.50	.306
at 30 min	107.70	10.02	106.30	9.71	.438
At 45 min	109.30	9.66	108.07	9.44	.481
at 60 min	110.43	8.77	109.33	8.82	.495
at 120 min	111.20	8.21	110.23	9.04	.541

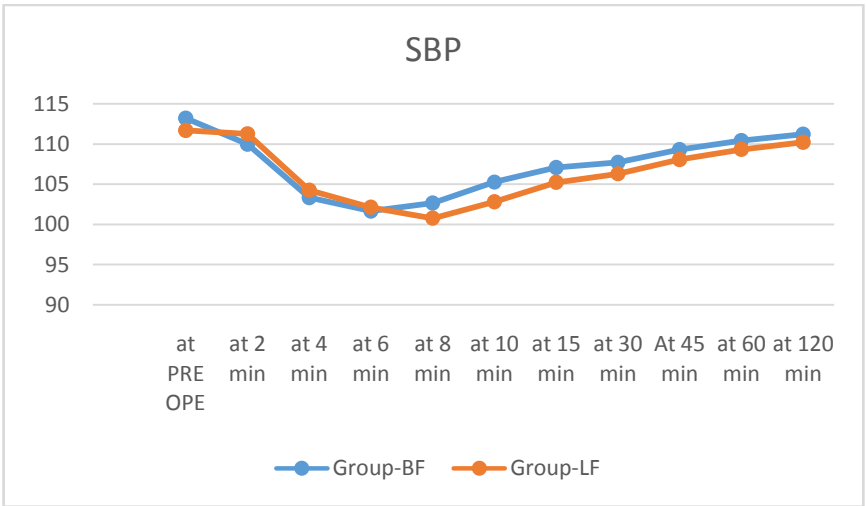


Table 5 : DBP

DBP	Group-BF		Group-LF		P-value
	Mean	SD	Mean	SD	
at PRE OPE	74.72	10.48	71.60	10.01	.098
at 2 min	71.90	11.91	71.20	10.04	.728
at 4 min	66.97	13.98	66.80	12.12	.945
at 6 min	67.73	11.97	65.87	10.26	.361
at 8 min	69.03	10.29	65.38	9.06	**.041**
at 10 min	70.00	9.38	67.17	9.50	.103
at 15 min	70.67	9.25	68.60	8.50	.205
at 30 min	71.13	8.92	69.97	8.34	.461

at 45 min	71.77	8.71	70.70	8.04	.487
at 60 min	72.03	7.76	70.93	8.06	.448
at 120 min	72.43	7.35	71.23	7.74	.386

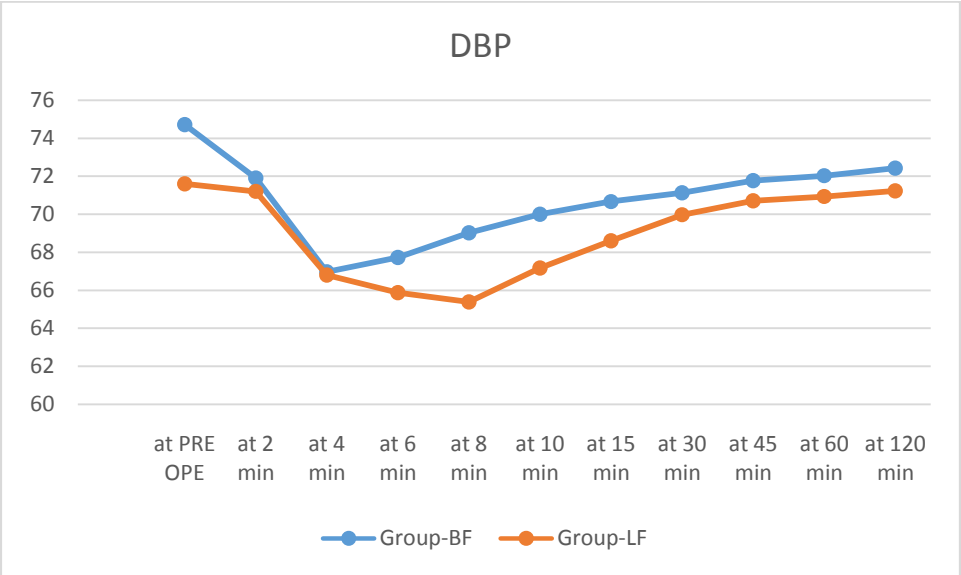


Table6 : Respiratory Rate

RR	Group-BF		Group-LF		P-value
	Mean	SD	Mean	SD	
at PRE OPE	18.53	1.08	17.73	1.09	**<0.001**
at 2 min	18.63	1.13	17.90	1.05	**<0.001**
at 4 min	18.68	1.62	18.12	1.54	.052
at 6 min	18.62	1.89	17.98	1.59	**.049**
at 8 min	18.62	2.06	17.78	1.62	**.015**
at 10 min	18.57	1.51	17.73	1.30	**.002**
at 15 min	18.42	1.28	17.67	1.17	**.001**
at 30 min	18.20	1.05	17.57	1.00	**.001**
at 45 min	18.18	0.93	17.47	1.11	**<0.001**
at 60 min	18.13	1.02	17.57	1.00	**.003**
at 120 min	18.33	0.99	17.85	1.01	**.009**

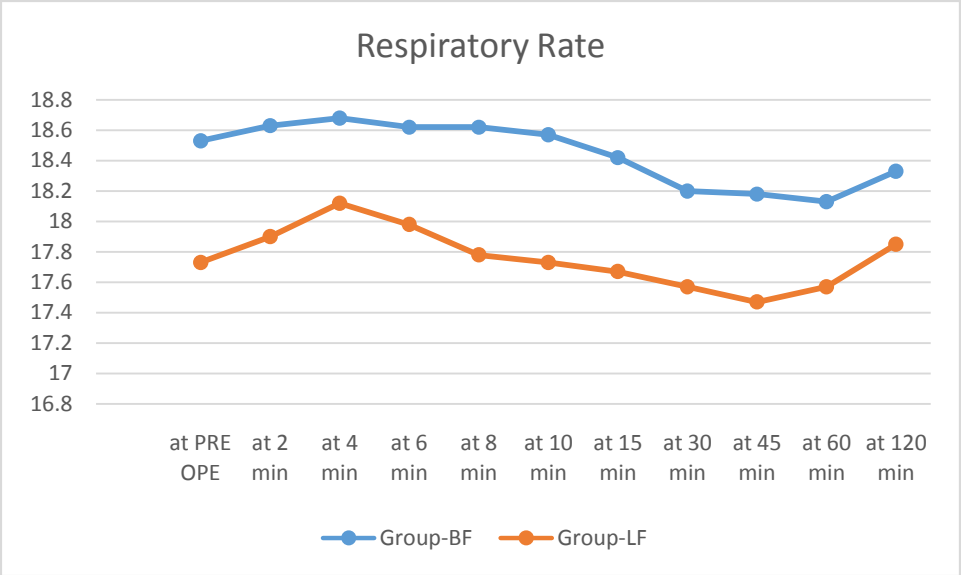


Table- 7 : SPO2

SPO2	Group-BF		Group-LF		P-value
	Mean	SD	Mean	SD	
at PRE OPE	99.18	0.97	99.32	1.08	0.478
at 2 min	98.65	1.89	99.22	1.11	**0.047**
at 4 min	98.5	2.43	99.1	1.91	0.135
at 6 min	98.6	2.37	99.27	1.07	0.05
at 8 min	98.65	2.43	99.4	0.89	**0.027**
at 10 min	98.92	2.04	99.68	0.65	**0.006**
at 15 min	99.37	1.46	99.72	0.67	0.094
at 30 min	99.32	1.27	99.83	0.56	**0.005**
at 45 min	99.67	0.79	99.83	0.49	0.17
at 60 min	99.65	0.78	99.88	0.42	**0.043**
at 120 min	99.65	0.71	99.9	0.44	**0.022**

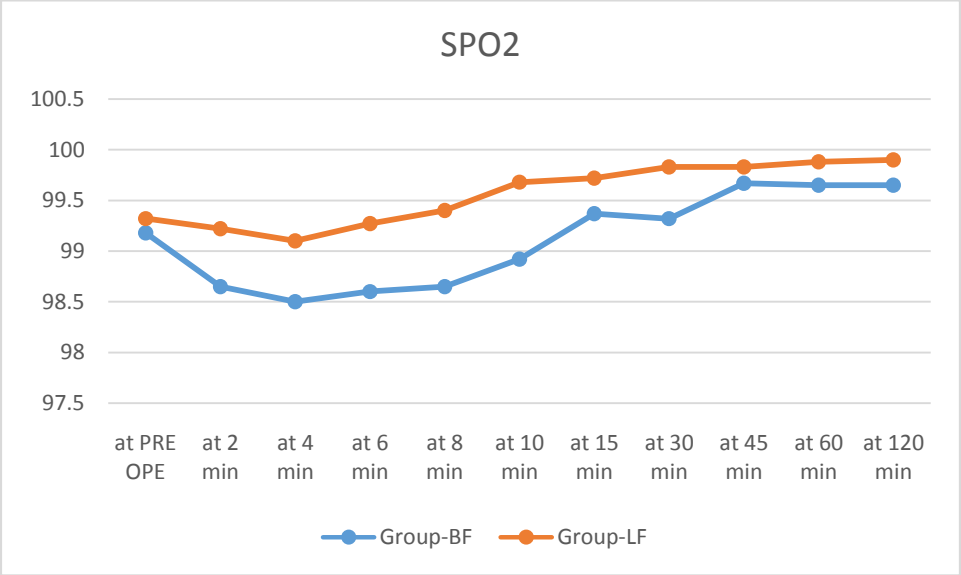


Table-8 : Characteristics of Sensory Blockade (Mean ± S.D) and t-test

Variable	Group BF		Group LF		P- Value
	Mean	SD	Mean	SD	
Onset of Sensory Block(Min)	1.46	0.18	2.29	0.30	<0.001

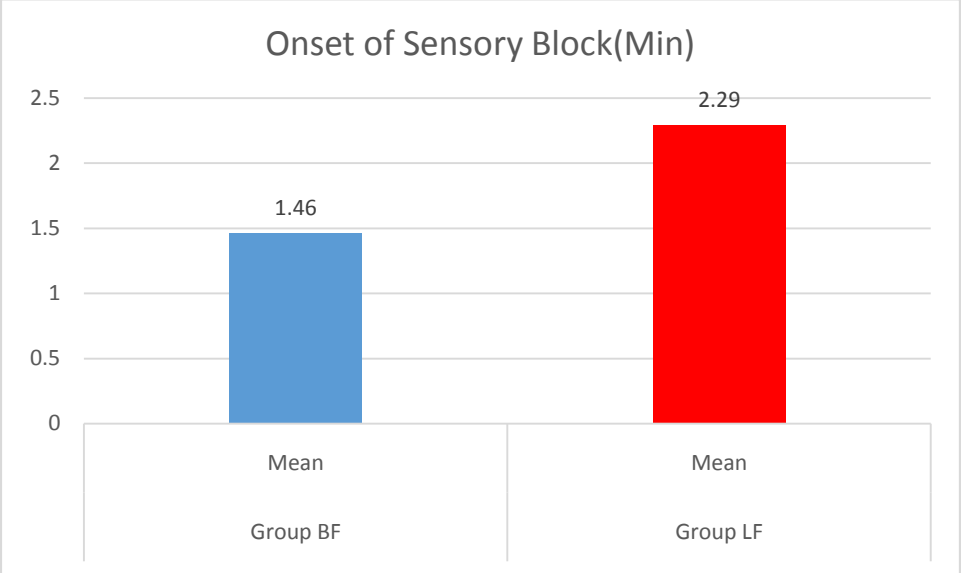


Table-9 : VAS Score

Variable	Group BF		Group LF		P- Value
	Mean	SD	Mean	SD	
Intensity of Analgesia(VAS Score)	1.15	0.36	1.13	0.34	0.796

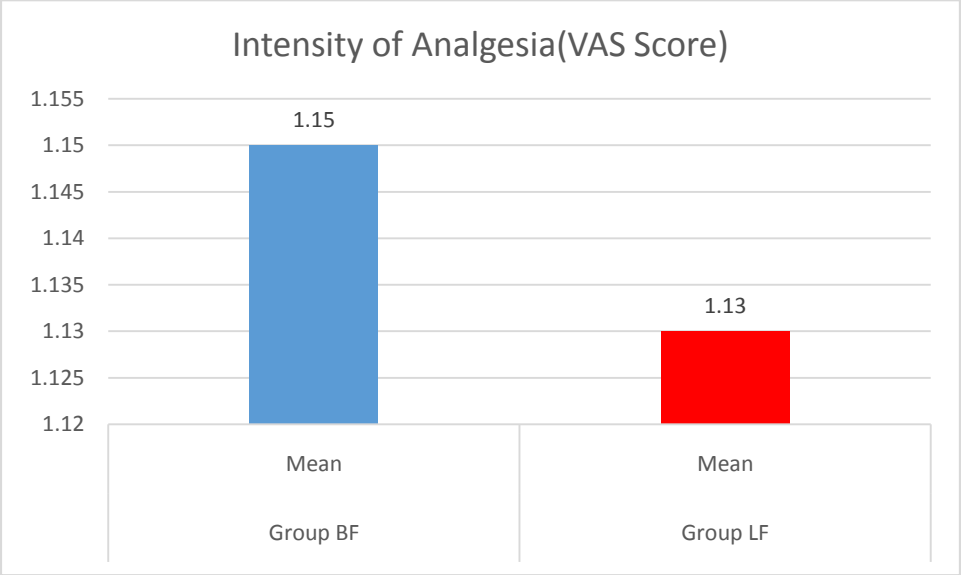


Table 10- Comparion between two groups

Variable	Group-BF		Group-LF		P-value
	Mean	SD	Mean	SD	
TIME OF 2 SEGMENT REGRESSION(MIN)	89.30	4.40	83.83	5.91	**<0.001**
TIME OF SEGMENT REGRESSION(MIN) to T12 SEGMENT	139.57	9.57	112.28	7.84	**<0.001**
1ST ANALGESIC DOSE TIME (MIN)	157.92	9.80	135.07	10.87	**<0.001**

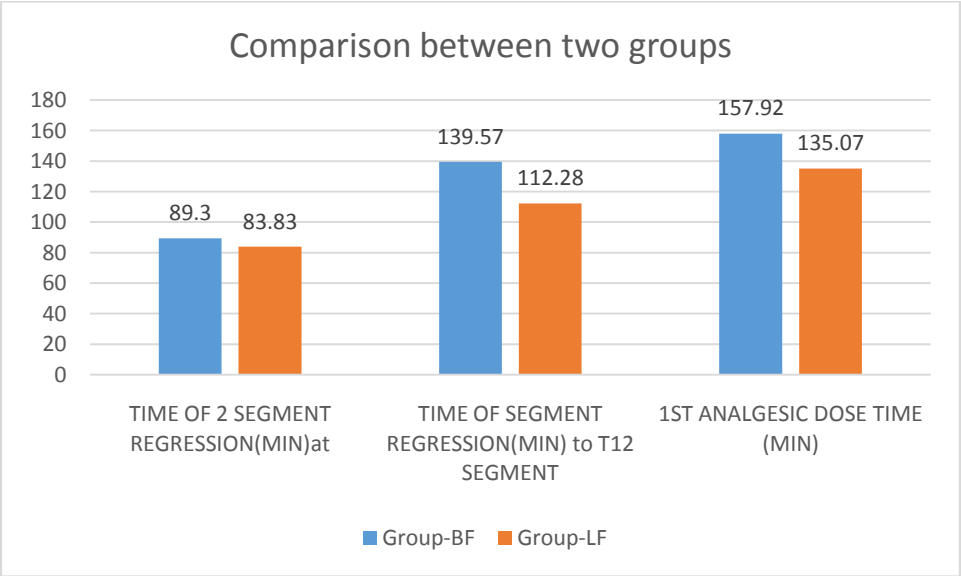


Table-11 : Characteristics of Motor Block (Mean ± S.D)

Variable	Group BF		Group LF		P- Value
	Mean	SD	Mean	SD	
Onset of Motor Block(Min)	5.58	0.48	6.07	0.53	<0.001

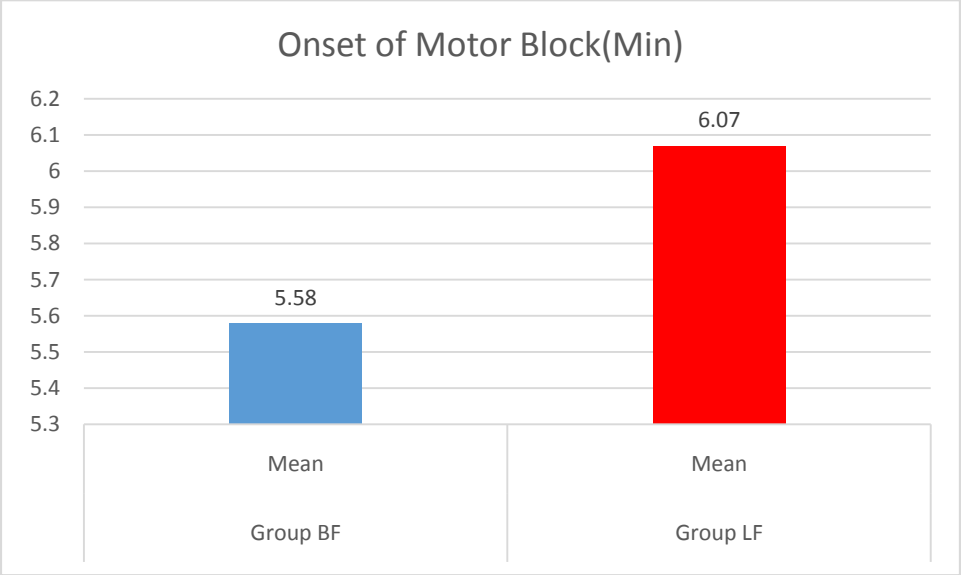


Table-12 : Grade Of Motor Blockade (Modified Bromage Score)

Variable	Group BF		Group LF		P- Value
	Mean	SD	Mean	SD	
Grade of Motor Blockade (Modified Bromage Score)	2.82	0.39	2.87	0.34	0.457

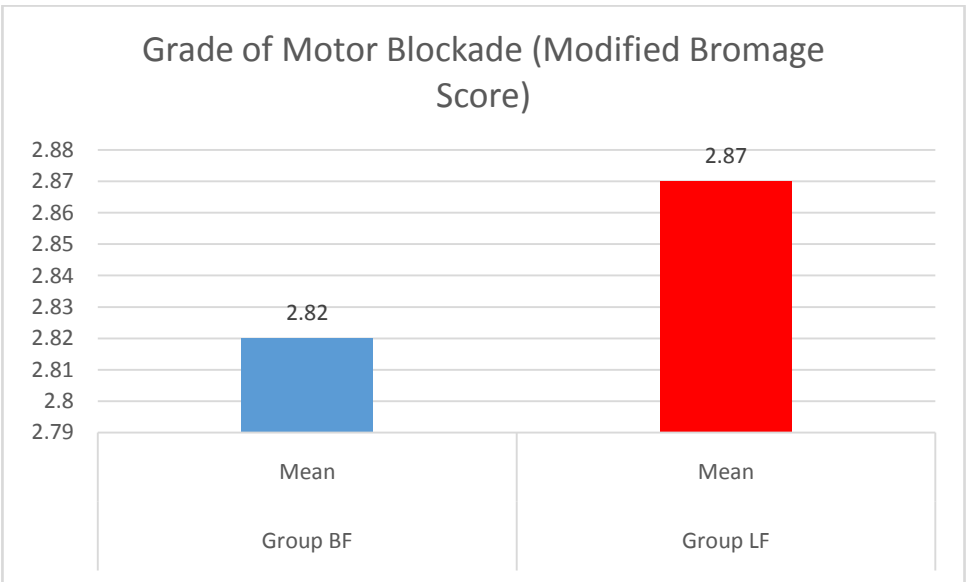


Table-13 : Duration of Motor Blockade in (MIN)

Variable	Group BF		Group LF		P- Value
	Mean	SD	Mean	SD	
Duration of Motor Blockade in (Min)	142.85	5.99	97.30	5.49	<0.001

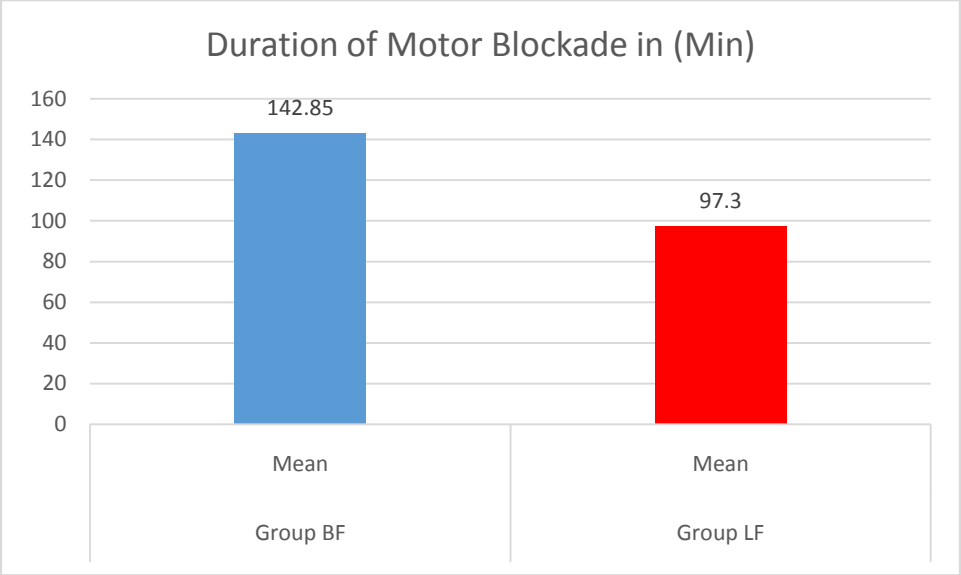


Table-14 : Incidence of Side Effects - Intraoperative

Adverse Effects	Group-BF		Group-LF	
	Count	%	Count	%
Bradycardia	1	1.7%	0	0.0%
Headache	2	3.3%	1	1.7%
Headache,Nausea	1	1.7%	0	0.0%
Hypotension	2	3.3%	4	6.7%
Hypotension,Bradycardia	10	16.7%	2	3.3%
Hypotension,Bradycardia,Resp.Deprression	2	3.3%	0	0.0%
Nausea	11	18.3%	2	3.3%
Vomiting	1	1.7%	1	1.7%
Nil	30	50.0%	50	83.3%
Total	60	100.0%	60	100.0%
P=0.006				

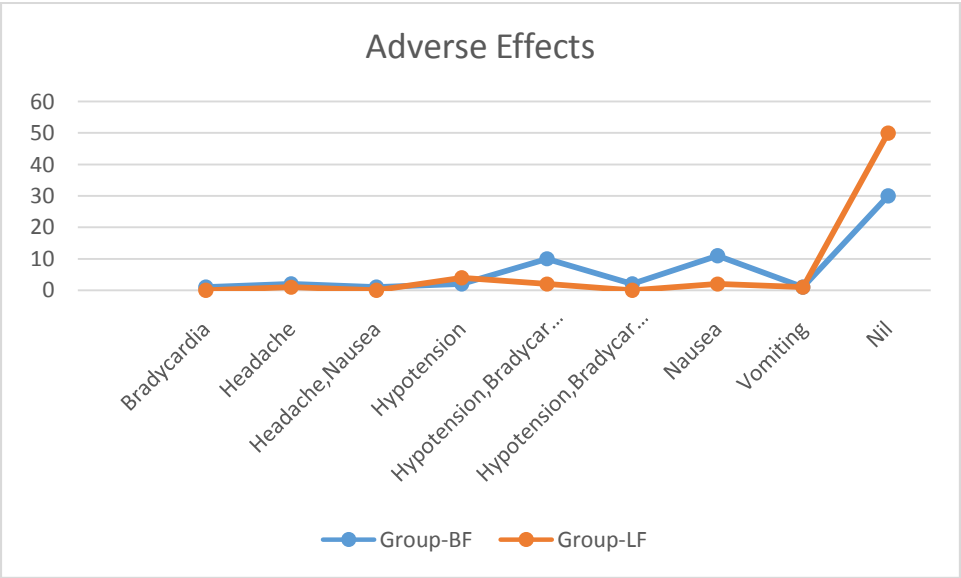
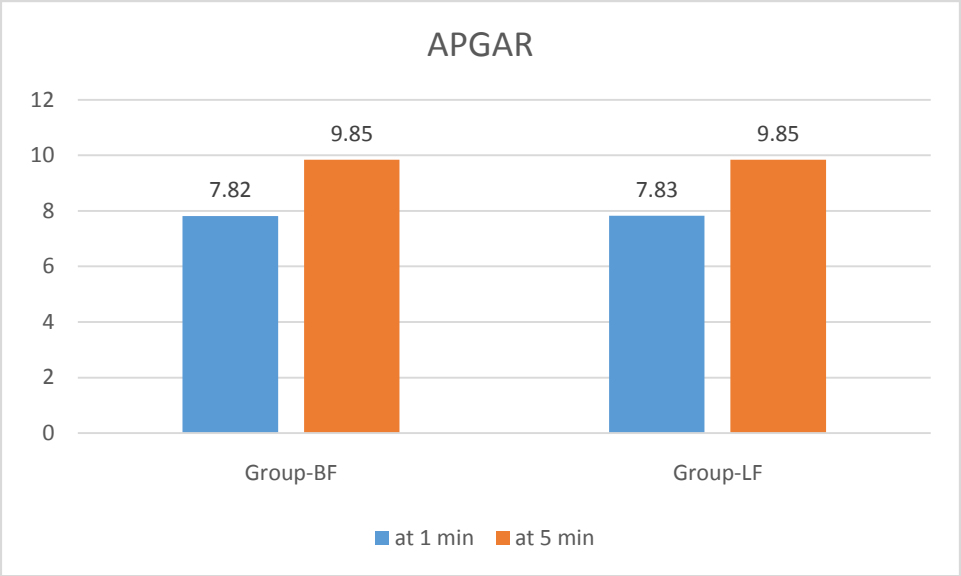


Table-15 : Neonatal Parameters

APGAR	Group-BF		Group-LF		P-value
	Mean	SD	Mean	SD	
at 1 min	7.82	0.50	7.83	0.53	.860
at 5 min	9.85	0.40	9.85	0.36	1.000



V. Discussion

Recent trends in obstetric anaesthesia show increased popularity of regional anaesthesia among obstetric anaesthetists. General anaesthesia in caesarean section is associated with increased morbidity and mortality rate when compared to regional anaesthesia. Regional anaesthesia has its own demerits which are primarily related to excessively high spinal blocks and toxicity of local anaesthetics. Reduction in doses and improvement in technique to avoid high level blocks and increased awareness of toxicity of local anaesthetics have contributed to reduction in complications related to regional anaesthesia.

Levobupivacaine is pure S - enantiomer of racemic Bupivacaine is less toxic to CVS and CNS, and it causes less duration of motor block leading to early mobilization of the patient which were proved in following studies **Gulen Guler et al.,Prabha P et al., Dilek Subasi et al., Dimarzio G et al., and NK Girgin et al.**

Levobupivacaine has been shown to be truly isobaric to CSF of pregnant women, and its use in the setting may, therefore, offer special advantages because this property may translate to a more predicatble spread[4,15]. The spread of isobaric Levobupivacaine in spinal anaesthesia is not dependent on gravity this is proved by a study by **Fabio Gori et al 2010** who conducted a study on two groups in sitting and in supine position with same amount of drug and concluded that isobaric Levobupivacaine in women at term produces a subarachnoid block, the dermatome level of which does not depend on gravitational forces. In our study, all the patients in both groups were placed in left lateral decubitus position for spinal anethesia, and the sub arachnoid block was given in L3 – L4 intervertebral space Fentanyl, a lipophilic opiod in small doses added to local anaesthetics during sub arachnoid block produces a more rapid onset, surgical block of better quality (than local anaesthetics alone) and leads to more rapid recovery of motor function which then allows a quicker discharge post surgery[32-37]. Intrathecally, it exerts its effects by combining with opiod receptors in the dorsal horn of spinal cord and may have a supraspinal spread and action. **Choi et al. 2000**[38] reported that the combination of 8mg Bupivacaine and 10mcg Fentanyl is as effecient as 12mg of hyerbaric Bupivacaine.

In the present study, 60 full term parturients of ASA Grade 1 and 2 posted for elective caesarean section under spinal anaesthesia were divided in to two groups:

GROUP LF (n = 60)– received 1.8ml (9mg) Levobupivacaine 0.5% + Fentanyl10mcg (0.2ml).
GROUP BF (n = 60)– received 1.8ml (9mg) hyperbaric Bupivacaine 0.5% +Fentanyl 10mcg (0.2ml).

Parturients with twin pregnancy, pre eclampsia, eclampsia, diabetes complicating pregnancy, heart disease complicating pregnancy, height less than 150cms and ASA 3, 4 were not taken into our study.

We chose to give 9mg of isobaric Levobupivacaine 0.5% because which according to previous studies was sufficient for good operative analgesia as proved in studies by **Prabha P et al. 2014** , 8.75mg of isobaric Levobupivacaine 0.5% was used along with 15mcg Fentanyl, and there was 100% patient and surgeon

satisfaction with good perioperative analgesia and with less intraoperative complications , similarly in the study by **Gunusen I et al 2011** comparision of different doses of Levobupivacaine in spinal anaesthesia in caesarean section was done and they concluded that the incidence of hypotension was higher in Levobupivacaine 10mg group even though this group presented more effective anaesthesia and greater patient surgeon satisfaction compared with the Levobupivacaine 5mg and 7.5mg groups. As a result, they concluded that levobupivacine 7.5mg + 15mcg Fentanyl is suitable for combined spinal epidural anesthesia in elective caesarean section. A study by **Bremerich DH et al. 2007** who concluded that 10mg Levobupivacaine is recommended for parturients undergoing caesarean section with spinal anaesthesia . We choose 9mg as we were not planning CSE technique and choose low dose Fentanyl as it prolongs the analgesia time.

The parameters measured in the two groups included haemodynamic measurements (pulse rate , systolic blood pressure , diastolic blood pressure) , respiratory parameters (respiratory rate , oxygen saturation) , charecteristics of sensory block , charecteristics of motor block , intraoperative and post-operative complications like nausea , vomiting ,Headache . In the neonate, Apgar score was measured to assess any effects of drugs on the neonate.

5.1 **DEMOGRAPHIC DATA**

The demographic data compared between two goups were age and weight

All the patients were between 20 – 29 yrs of age and the mean age was 23.83 yrs in LF group and 23.23 yrs in BF group which was comparable with the study by **Prabha P et al. in 2014,** where the mean age was 24.05 yrs in Bupivacaine groupand 25.85yrs in Levobupivacaine group.

The mean weight was 65.83 kgs in LF group and 64.47 kgs in BF group this was comparable with the study by **Prabha P et al. in 2014 , where** the mean weight was 62.95kgs in Bupivacaine group and 58.90 in Levobupivacaine group .

The difference in the mean values of the demographic parameters was not significant ($p > 0.05$).

5.2 : HAEMODYNAMIC PARAMETERS:

In the present study, there was no statistical significance between both groups in the preoperative mean pulse rate values. Intraoperatively there was significant difference in pulse rate 2 min , 4 min and 6 min respectively with group BF having less mean heart rate than group LF at those time intervals .

Incidence of bradycardia was 2 case (3.3%) in LF group where as it was 13 cases (21.7%) in group BF , there was statistically significant difference in both groups (p < 0.05) . Bradycardia was treated with single dose of injection atropine 0.5mg intravenously.

Incidence of bradycardia was comparable with study by **Gulen Guler et al. in2012** (n=30),.where incidence of bradycardia was 6.67% (2 cases) in LF groupand 30% (9 cases) in BF group

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5.3 : Brady Cardia :

	LFGroup (n=60)	BF Group(n=60)
PRESENT STUDY	2(3.3%)	13(21.7%)
Gulen Guler et al. 2012	2(6.67%)	9(30%)

A study by Dilek Subasi et al. in 2012 the incidence of bradycardia was different, and it was 35% in LF group and 16% in BF group , it may be due to the use of hyperbaric levobupivacaine in their study and their crieteria for bradycardia .

In a study by Prabha P et al. in 2014 the incidence of bradycardia was negligible in both groups.

The present study shows that there is less incidence of bradycardia in Levobupivacaine group compared to Bupivacaine group. It may be due to the difference in baricity of levobupivacaine which is isobaric and leads to less sympathetic blockade compared to hyperabaric bupivacaine .

The fall in systolic blood pressure was more in BF group with significant fall at 2min , 4 min , 8min and 10minutes and the incidence of hypotension was observed 6 patients (10%) in LF group and 14 patients (23.3%) in BF group and the hypotension was treated with iv crystalloid boluses and mephentermine 3-6mg per dose iv . There was significant difference in diastolic blood pressures in two groups ($p<0.05$).

5.4 : Hypotension

	LF GROUP	BF GROUP
PRESENT STUDY	6(10%)	14 (23.3%)
Gulen Guler et al	5 (6.67%)	11 (36.67%)

Hypotension is the most common complication in the spinal anaesthesia [38]. It is known that besides its effects on the mother, it causes acidosis by altering uteroplacental perfusion.Administering hydration using crystalloid or colloid before spinal anaesthesia has proven insufficient [39,40,41]. Titti et al. reported that rate of occurunce of hypotension was 62% in elective caesarean section operations in which they administered spinal anaesthesia with 2.5ml 0.5% Bupivacaine . Gulen Guler et al. reported the incidence of hypotension in their study as 36.6% in Bupivacaine 0.5% 2ml + 15mcg Fentanyl group (BF) and 16.6% in (LF) 10mg Levobupivacaine + 15mcg Fentanyl group and they believed that this reduced incidence was due to decreased dose of local anaesthetic and added Fentanyl .

A study by Dimarzio G et al. 2011[20] there was higher incidence of hypotension in group B (Bupivacaine) . Diastolic blood pressure suffered a great reduction 3 minutes after injection of local anaesthetic , in 7 patients of group B there was marked hypotension with placenta hypoperfusion and fetal acidosis without significant impact on 1 minute and 5 minute APGAR score .

In present study, the incidence of hypotension was 5 patients (16.67%) in LF group, and (40%) 12cases in BF group which was treated with doses of mephentermine 3-6mg and total dose used was in LF 30mg and in BF group was 72mg . The less incidence of hypotension in LF group can be attributed to the isobaricity of plain levobupivacaine which causes less sympathetic block level and is less sensitive to postural changes when compared to hyperbaric Bupivacaine group (BF) preventing cephalad spread of drug while positioning the patient leading to higher blockade .

5.5 CHARACTERISTICS OF SENSORY BLOCKADE:

The onset of sensory block was similar in the two groups with mean onset time in LF 2.29 min and BF group 1.46 min and there was statistical difference ($p < 0.001$) In study by Gulen Guler et al. 2012 this was not similar where there was no significant difference between onset of sensory block time and time to reach T10 dermatome levels in both groups .

In study by Prabha P et al. 2014, the mean time from induction of drug to skin incision was longer in group L (Levobupivacaine + Fentanyl) than group B (Bupivacaine + Fentanyl) group. In a study by Glaser et al. they concluded that the intergroup difference between Levobupivacaine and Bupivacaine were insignificant both with regard to onset time and duration of sensory blockade.

The time for two segment regression of sensory dermatome was 83.33 minutes in group LF and 89.30 minutes in group BF which was statistically significant which means the 2 segment regression time is longer in BF group which is comparable to result of study by Gulen Guler et al. 2012 in their study the two segment regression time was 71 minutes in group LF and 76.16 minutes in group BF with statistically significant difference ($p < 0.05$) . In study by Dilek Subasi et al 2012 there was no significant difference between two segment regression time in both groups ($p > 0.05$) with mean 2 segment regression time being 89.95minutes in LF group and 82.74 minutes in BF group this may be due to use of hyperbaric Levobupivacaine and hyperbaric Bupivacaine as compared to isobaric Levobupivacaine in our study .

In this study, the mean T12 regression time for sensory block was 112.28 minutes in group LF and 139.57 minutes in group BF which is statistically significant ($p< 0.001$). The regression time was longer in Bupivacaine group which is comparable to study by **Gulen Guler et al2012** where the mean T12regression time was 145.50minutes in group LF and 162.33 minutes in group BF which is statistically significant ($p < 0.05$) . In study by **Prabha P et al. 2014,** the time for regression of sensory block to below L1 was 211 minutes in group L (Levobupivacaine) and 183 minutes in group B (Bupivacaine) which is statistically significant ($p < 0.05$) indicating prolonged surgical analgesia in group L . In the study by **Dilek Subasi et al.** there was no difference in onset of sensory block and regression time of sensory dermatomes in both groups.

In this study, the mean time for first analgesic dose was 135.07 minutes in group LF and 157.92 minutes in group BF which was statistically significant ($p< 0.05$) indicating the early need for analgesia in Levobupivacaine group compared to Bupivacaine group . In study by **Gulen Guler et al. 2012,** the mean first analgesic time was 145.4 minutes in LF group and 161.3 minutes in BF group with significant statistical significance ($p< 0.05$) which is similar to this study. In study by **DilekSUBASI et al. 2012** the first analgesic need was 162.55 minutes in LF group and173.05 minutes in BF group but without significant difference ($p > 0.05$). In the study by **Prabha P et al. 2014,** the request time of analgesia was 220 minutes in Bupivacaine group and 229.25 minutes in Levobupivacaine group with p value > 0.05 indicating no significant difference in both groups in analgesia time.

5.6 : MOTOR BLOCK CHARACTERISTICS :

In present study, the onset of motor block was longer in group LF is 6.07 minutes than group BF is 5.58 minutes which was statistically significant ($p < 0.05$) and same results were seen in **Gulen Guler et al. 2012** study. Onset of motor block was slower in LF group (4.1minutes) when compared to BF group (2.36

minutes). In the study by **Prabha P et al. 2014** time for onset of motor block was 3 minutes in LF group and 1.5 minutesin BF group with significant statsical difference of $p < 0.05$.

A study by **Dilek Subhasi et al. 2012** the time for motor block onset was 2.25 minutes in LF group and 1.45 minutes in BF group without significant statistical difference ($p > 0.05$) and in a study by **NK Girgin et al.** there was no significant difference between two groups in onset of motor block time . This may be due to the difference in the baricity of Levobupivacaine which in **Dilek Subhasi** study was hyperbaric.

Degree of motor block in this study was grade 2.8 (mean) as per modified Bromage scale by the end of 10 minutes in both groups in all patients; this was similar to study by **Guler et al. Gulen 2012** where complete motor block was obtained within 20 minutes in every patient in both groups (Bromage 3). In contrast , study by **Prabha P et al. 2014** maximum motor block was Bromage 3 in group BF whereas only 12 of 20 (60%) in group had Bromage 3 motor block and 8 (40%) had Bromage 2 which was statistically significant between both groups ($p<0.05$).

Bromage score of Prabha P et al. 2014 study:

	BROMAGE SCORE		TOTAL	P value
	3	2		
Group B (%)	20 (100%)	0 (0%)	20	0.003*
GROUP L (%)	12(60%)	8 (40%)	20	0.003

In the study by **Dilek Subasi et al. 2012,** there was significant difference between maximum motor blocks between groups ($p < 0.05$).

5.7 REGRESSION OF MOTOR BLOCKADE TIME:

In present study, the mean regression of motor block time was 97.30 minutes in group LF and 142.85 minutes in group BF which was statistically significant with $p<0.001$and similar results were seen with following studies :

In a randomized, double blind study by **Gulen Guler et al. 2012,** the regression time for motor block was 99 minutes in LF (isobaric Levobupivacaine + Fentanyl) group and 132.66 minutes in BF (hyperbaric Bupivacaine + Fentanyl) group showing that there is rapid recovery from motor block with Levobupivacaine group. In a study by **Prabha P et al. 2014** similar results were found where regression of motor block time was 109 minutes in LF group and 168 minutes in BF group with statistically significant difference ($p< 0.05$). In a study by **NK Girgin et al.** for outpatient herniorrhaphy , similar results were seen with recovery of motor blocktime was 201 minutes in Levobupivacaine group and 287 minutes in Bupivacaine group. A study by **Dilek SUBASI 2012** et al. also there was significant difference between both groups ($p< 0.05$) with Levobupivacaine group showing early recovery from motor block.

The effects of baricity on block charecteristics have been contradictory in literature , while some studies that report the difference in baricity does not affect the block characteristics[42], on the other hand there are also studies reporting that motor block develops and receeds fast when hypobaric solutions are used [43] .

5.8 INTRAOPERATIVE COMPLICATIONS:

Intraoperative complications encountered in present study were hypotension which was defined as fall in systolic or diastolic blood pressure to more than 25% from baseline totally in our study. There were 6 patients (10%) in LF group and 14 patients (23.3%) in BF group which was statistically significant ($p< 0.05$) and similar results were seen in study by Gulen Guler et al. where in a group of 30 (n) 5 patients in group LF (16.67%) and 11 patients in group BF (36%) experienced hypotension which was treated with 6mg of mephentermine iv and iv fluid bolus crystalloids. **Titti et al.** reported that rate of occurence of hypotension was 62% in elective caesarean operations in which they administered 2.5ml of 0.5% Bupivacaine. We believe that difference in our results were due to the fact that We decreased the dose of local anaesthetic (9mg) and added Fentanyl (10mcg).

In a study conducted by **Bremerich DH et al. 2007** for a dose finding investigation, they concluded that 10mg of Levobupivacaine is recommended for parturients undergoing elective caesarean section under spinal anaesthesia. Wetook 9mg and added 10mcg Fentanyl which reduces the local anaesthetic dose required, hastens the onset of block, provides good analgesia and promotes early motor recovery. **Gunusen et al. 2011** have compared different doses of Levobupivacaine-Fentanyl combination in caesarean section and reported that 10mg Levobupivacaine with 10mcg Fentanyl combination provides 100% effective anesthesia, but incidence of hypotension was high. The higher incidence of hypotension rates reported by **Gunsen et al.** may be related to the difference in the definition of hypotension between studies; while they considered 20% reduction SBP from baseline values as hypotension, we accepted the 25% decline as hypotension.

In the study by **Prabha P et al. 2014,** the incidence of bradycardia was negligible, the fall in mean arterial pressure noted in group B (Bupivacaine + Fentanyl) is statistically significant with about 30% fall in SBP noted in about 10 patients . In a study by **Dimarzio G et al. 2011** comparision of spinal anesthesia in

caesarean section between isobaric Levobupivacaine and hyperbaric Bupivacaine and there was a higher incidence of hypotension in group B .

In our study the next common seen complication was bradycardia. It was seen in 1 patient (3.37%) in LF group and 7 patients (23.34%) in BF group which was statistically significant . Baradycardia was defined as pulse rate below 50 per minute and was treated with bolus dose of injection atropine 0.6mg. Similar results were seen in study of **Gulen Guler et al. 2012** where the incidence of bradycardia was 2 patients (6.67%) in LF group and 9 patients (30 %) in BF group

Glasser et al. in line with our study reported that Levobupivacaine , comparedwith Bupivacaine , causes less bradycardia and that reduces arterial pressure less .

Coppejans H C, Vercauteren 2004 in their study compared effects ofspinal Levobupivacaine with Bupivacaine for caesarean section and found lower incidence of hypotension with the S-enantiomer Levobupivacaine.

Gulen Guler et al. 2012 study the incidence of nausea was 3 patients in LFgroup and 10 patients in BF group which was statistically significant ($p < 0.05$). There was no incidence of vomiting , shivering , headache or backache in both groups .

Nausea and vomiting can occur due to few factors. The most important reason is that cerebral blood flow decreases in consequence of hypotension . Other reasons are related to the level where block reaches. It may also occur as a result of an increase in the block level or because of the fact that structures related to peritoneal stretch during operation due to an inadequate block level.We can explain the reduced incidence of nausea occurred in Levobupivacaine group with the fact that the doses we administered,developed adequate blocks and caused less hypotension.

5.9 RESPIRATORY PARAMETERS:

There was no significant difference between the both groups ($p > 0.05$) in respiratory rate and oxygen saturation; there was no incidence of any respiratory depression in both groups due to intrathecal Fentanyl. Hence intrathecal Levobupivacaine with low dose Fentanyl is a good option for caesarean section as it is less cardiotoxic, and recovery of motor block is fast with good perioperative analgesia .

5.10 NEONATAL PARAMETERS:

All the babies in the two groups had APGAR scores from 7-10 at 1 minute and 5minutes after birth. There was no statistically significant difference in APGAR scores between two groups, and none of them required aggressive resuscitation. The same results were seen in study by **Prabha P et al. 2014** where all the neonates had an APGAR score of 10 at 5 minutes to conclude that both local anaesthetic and opiod has no adverse effects on neonate.

A Study by **Belzarena HD1992** concluded that combination of Bupivacaine and a low dose of Fentanyl (25 µg) provided excellent surgical anaesthesia with no change in APGAR scores and long lasting postoperative analgesia and very few negative side effects.

In the prersent study, there were no postoperative complications like hypotension, headache, PDPH , backache in both groups .

In our present study the overall difference between two groups were, there was no statistical significant difference between time of onset of sensory block , onset of motor block , maximum sensory dermatome level reached(T4) , degree of motor block (Bromage 3), respiratory parameters and neonatal APGAR scores between isobaric Levobupivacaine group (LF) and hyperbaric Bupivacaine group (BF), which was similar to study by Gulen Guler et al 2012 , **Prabha Pet al 2014** .the 2segment regression time and T12 dermatome regression time of sensory block was earlier in LF group similar to Gulen Guler et al. 2012 study and the time for first analgesic time was also earlier in LF group .

Time for maximum motor block was earlier in BF group, and it lasted longer than LF group with statistically significant difference this shows the early regression of motor block in Levobupivacaine spinal anesthesia which is consistent with many previous studies like **Gulen Guler et al. 2012 , Prabha P et al. 2014 , BremerichDH etal 2007 , NK Girgin et al2008 and DilekSUBASI etal 2012** all concluded thatthe duration of motor block in Levobupivacaine is significantly shorter than racemic Bupivacaine and is advantageous for early mobilisation of the patient .

In hemodynamic parameters, the incidence of hypotension and bradycardia was more in Levobupivacaine group with a statistically significant difference ($p<0.05$) indicating the less CVS toxicity of Levobupivacaine which is attributed to its high protein binding capacity (>97%) less amount of free drug is available for causing adverse reactions in other tissues. This is also comparable to previous study by

Gulen Guler et al. 2012 , Prabha P et al. 2014 , Bremerich DH etal 2007 , NKGirgin et al2008 and DilekSUBASI etal 2012 who concluded that Levobupivacainewas less cardiac and neurotoxic than racemic Bupivacaine. In a study by **HazelBardsley et al. 1998,** they studied for cardiovascular effects of

Levobupivacaine andracemic Bupivacaine following intravenous administartion and concluded that Levobupivacaine produces significantly less effects on cardiovascular function than racemic Bupivacaine.

VI. Conclusion

From present study findings and correlating it to the previous studies and literature plain Levobupivacaine 0.5% which is pure s – enantiomer of Bupivacaine is a good alternative for caesarean section in spinal anesthesia as it have less CVS and CNS toxicity when compared with Bupivacaine Hydrochloride. Early recovery of motor blockade leading to early mobilization of the mother and analgesia almost similar to racemic hyperbaric Bupivacaine . Addition of low dose Fentanyl 10mcg with Levobupivacaine has dose sparing effect of opiods on local anesthetics, better postoperative analgesia and early recovery from motor block. Action of isobaric Levobupivacaine is independent of gravity in spinal anesthesia.

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Dr.M.Neeraja. "A Comparison of Spinal Anaesthesia with Levo-Bupivacaine and Hyperbaric Bupivacaine combined with Fentanyl in Elective Caesarean Section.". IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 18, no. 6, 2019, pp 28-45.