RESEARCH ARTICLE

A COMPARATIVE STUDY OF EFFICACY OF INTRATHECAL BUPIVACAINE AND LEVOBUPIVACAINE FOR CAESAREAN SECTION.

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Abstract

Introduction: Spinal anaesthesia is a balance technique used for cesarean delivery. It provides rapid onset of anesthesia and complete muscle relaxation.

Objective: To assess and compare the onset of sensory and motor block, duration of sensory and motor block, neonatal outcome, cardiovascular parameters and adverse drug reactions.

Material and Methods: This was a prospective, randomized, double blind study. A total of 60 patients were enrolled and divided into 30 in each group. Group A was given 8.5 mg Isobaric Levobupivacaine with 15 μg Fentanyl and Group B was given 8.5 mg Hyperbaric Bupivacaine with 15 μg Fentanyl.

Result: The difference in the onset of sensory block and motor block and duration of sensory and motor block was statistically significant in two groups.

Conclusion: The combination of Isobaric Levobupivacaine with Fentanyl can be used as a safe and effective alternative to Hyperbaric Bupivacaine with Fentanyl for spinal anaesthesia in cesarean section as, it provides comparable sensory block characteristics, early motor recovery allowing early mobilization, stable haemodynamics and good foetal well-being.

Introduction:-

Spinal anesthesia is commonly employed for cesarean delivery. It is simple to perform, economical, produces rapid onset of anesthesia and complete muscle relaxation1.

Bupivacaine is a long acting amide local anaesthetic with duration of action of 1.5-2.0 hrs.2 However, intrathecal bupivacaine alone may be insufficient to provide complete analgesia despite the high sensory block. 13% of the patients undergoing caesarean delivery had visceral pain even after the intrathecal administration of 15 mg bupivacaine.3,4 Further more such large doses of intrathecal bupivacaine were associated with severe hypotension and delayed recovery of motor block.5

Levo-bupivacaine is the (s)-enantiomer of bupivacaine. It is a long acting local anaesthetic, provides more selective neuraxial blockade i.e. early motor recovery. Clinical profile is comparable to bupivacaine and has a superior...
pharmacokinetic profile. It is less cardiotoxic and neurotoxic than bupivacaine.\textsuperscript{6} Its baricity offers an advantage of providing a less position sensitive block.\textsuperscript{7}

Moreover, smaller doses of bupivacaine supplemented by intrathecal opioids have been recommended for spinal anaesthesia in parturients undergoing caesarean delivery.\textsuperscript{8-11} Neuraxial administration of opioids along with local anaesthetics improves the quality of intraoperative analgesia and also provide postoperative pain relief for longer duration.\textsuperscript{10-12}

Therefore, Fentanyl provides better intraoperative analgesia and a safer alternative than morphine. Spinal doses of Fentanyl 10 μg to 25 μg are commonly used for caesarean delivery anaesthesia.\textsuperscript{8,14} It has no deleterious effects and appears to be safe for the mother and the newborn.\textsuperscript{15}

In this study we observed the clinical efficacy of intrathecal Isobaric Levobupivacaine over Hyperbaric Bupivacaine, with Fentanyl for cesarean section.

**Aim and Objectives**

**Aim**
To study sensory and motor block characteristics of spinal anaesthesia in two study groups:
1. **Group A**: 0.5% Levobupivacaine 8.5 mg plus Fentanyl 15 μg intrathecally (total volume 2 ml)
2. **Group B**: 0.5% hyperbaric Bupivacaine 8.5 mg (1.7 ml) plus Fentanyl 15 μg intrathecally. (total volume 2 ml)

To study the intraoperative haemodynamic changes.

**Objectives**
To assess and compare following parameters in both the groups:
1. Onset of sensory block.
2. Maximum Cephalad spread.
3. Duration of sensory block.
4. Onset of motor block.
5. Duration of Motor blockade.
6. Haemodynamic parameters (Heart Rate and Blood Pressure-Systolic, Diastolic, Mean).
7. Neonatal outcome

**Material and Methods:**
This prospective, randomized, double blind clinical trial was conducted in the Department of Anaesthesia in MGM Medical College, Aurangabad over a period of two years from Nov 2015 to Sep 2017 after approval from ethical committee.

Sixty patients were included in the study.

**Inclusion Criteria**
1. American Society of Anaesthesiologists (ASA) Physical status I and II who were to undergo elective caesarean section under Spinal Anaesthesia
2. Patients more than 20 years of age.
3. Patients with height between 150-170 cms
4. Patients with weight between 50-80 kgs
5. Gestational age >37 weeks

**Exclusion Criteria**
1. Parturients for emergency surgery
2. Contraindication for spinal anaesthesia
3. Known allergy for LA/opioid
4. Foetal indication for LSCS
Materials:

**Injection Isobaric Levobupivacaine 0.5%**
Each ampule contains 10 ml having drug concentration of 50 mg/10 ml.

**Injection Hyperbaric Bupivacaine 0.5%**
Each ampule contains 4ml, having drug concentration of 5mg/ml.

**Injection Fentanyl**
Each ampule contains 2 ml having drug concentration of 50 μg/ml.

Methods
All patients were kept nil orally for 6 hour prior to surgery. Weight of the patient was recorded. Procedure was explained to the patient and written consent was taken for participation in study using a sealed envelope technique, 60 patients were randomly allocated to one of two groups-

**Group A**: 8.5 mg Isobaric Levobupivacaine with 15 g μg Fentanyl
**Group B**: 8.5 mg Hyperbaric Bupivacaine with 15 μg Fentanyl

After taking the patient in OT, baseline heart rate, non invasive blood pressure, oxygen saturation (SPO2), Electrocardiogram were recorded.

A wide bore IV line was established and all patients were preloaded with 10ml/kg body weight ringer lactate solution.

Spinal anaesthesia was performed in sitting postion with 25 gauge quincke spinal needle by midline approach at L3-L4 level after confirming free flow of CSF, the drug was injected in sub-arachnoid space according to the group and the patients were made supine. After spinal anaesthesia the vital parameters pulse rate, BP, respiratory rate and SPO2 were recorded at every 2 min for the first 10 minutes followed by measurements every 5 minutes till the completion of surgery.

Onset of sensory block was assessed bilaterally by pinprick method in anterior axillary line and the time from intra-thecal injection to the loss of sensation of pin prick at T10 level was taken as onset of sensory block.

The highest level of loss of sensation of pin prick was taken as the maximum height of sensory block.

Motor block was assessed by modified Bromage scale as described below:

0 = No paralysis, able to flex hip/knee joints/ankles
1= able to move knees, unable to raise extended legs
2= able to flex ankles, unable to flex knees
3= unable to move any part of the lower limb

Onset of motor block was taken as time when intra-thecal injection was given (0 min) to obtaining a motor block of grade 3.

Surgery was allowed after achieving T6 sensory level and grade 3 motor block.

Failure to achieve loss of pin prick sensation at T6 dermatome level at the end of 20 min was considered as failure of block and general anaesthesia was supplemented.

Motor block was assessed every 5 min until complete motor block was established and every 15 min after surgery till complete regression of motor block. Duration of motor block was recorded as time from time of injection to complete motor recovery (Bromage scale 0).

Intra operative Haemodynamic changes were treated as follows:-

1. Bradycardia is defined as pulse rate <50 bpm and was treated with 0.6 mg IV Atropine
2. IV boluses of mephentermine 6 mg and additional IV fluids were administered to treat hypotension (defined as systolic BP below 90 mm or decreased systolic pressure of > 25 % of baseline value)
Statistical analysis
All collected data was compiled on MS Excel sheet nad appropriate statistical tests applied.

P value of less than 0.05 is considered statistically significant.

Observation and Results:-
The study population was composed of 60 patients posted for elective caesarean section delivery. They were divided into two groups of 30 each. All the baseline parameters such as age wise distribution, weight, height and duration of surgery was not statistically significant.

Table 1:-Comparison of Time of onset of Sensory Block (TOSB) Between Two Groups

| TOSA (Min) | Group A | | Group B | |
|------------|---------|-------|---------|-------|
|            | No. of patients | Percentage | No. of patients | Percentage |
| 2-3        | 8       | 26.67% | 4         | 13.33% |
| 3-4        | 19      | 63.33% | 8         | 26.67% |
| 4-5        | 3       | 10.00% | 18        | 60.00% |
| Total      | 30      | 100%   | 30        | 100%   |

The mean time of onset of sensory block at T_{10} in Group A was 3.45 ± 0.42 minutes, in Group B was 3.92±0.45 minutes. The difference in the mean time between Group A and Group B was statistically highly significant (p= 0.000 which is <0.05).

Table 2:-Comparison of Highest Level of Sensory Block (HSLB) between Two Groups

| Level | Group A | | Group B | |
|-------|---------|-------|---------|-------|
|       | No. of patients | Percent- age | No. of patients | Percent- age |
| T_4   | 5       | 16.67% | 13       | 43.33% |
| T_6   | 25      | 83.33% | 17       | 56.67% |
| Total | 30      | 100%   | 30       | 100%   |

In Group A, maximum level of sensory block achieved was T_4 (16.67%) and minimum height achieved was T_6 (83.33%). The median value was T_6 (T_4-T_6).

In Group B, maximum level of sensory block achieved was T_4 (43.33%) and minimum height achieved was T_6 (56.67 %). The median value was T_6 (T_4-T_6).

Table 3:-Comparison of Total Duration of Sensory Block between two Groups (TDSB)

| Time for sensory regression into L_4 (min) | Group A | | Group B | |
|------------------------------------------|---------|-------|---------|-------|
|                                          | No. of patients | Percent- age | No. of patients | Percent- age |
| 110-129                                  | 21      | 70%   | 0        | 0%    |
| 130-149                                  | 9       | 30%   | 0        | 0%    |
| 150-169                                  | 0       | 0%    | 12       | 40%   |
| 170-199                                  | 0       | 0%    | 18       | 60%   |
| Total                                    | 30      | 100%  | 30       | 100%  |
In Group A, the total duration of sensory block was 117-150 minutes and the mean time was $125.43 \pm 6.88$ minutes.

In Group B, the total duration of sensory block was $171.77 \pm 7.85$ minutes.

The difference in the mean value between Group A and Group B was statistically significant (with $p=0.000$ which is $< 0.05$).

**Table 4:** Comparison of Time of onset of Motor Block (TOMB) in Two Groups

| TOMB (Min.) | Group A | Group B |
|-------------|---------|---------|
| No. of patients | Percent- age | No. of patients | Percent- age |
| 1-2 | 1 | 3.33 | 0 |
| 2-3 | 1 | 3.33 | 0 |
| 3-4 | 22 | 73.33 | 0 |
| 4-5 | 2 | 6.67 | 3 |
| 5-6 | 3 | 10.00 | 14 |
| 6-7 | 1 | 3.33 | 13 |
| Total | 30 | 100 | 30 | 100 |

In Group A, in 22 patients (73.33%) the time of onset of grade III motor block was 3-4 minutes. The mean time was $3.45 \pm 0.42$ minutes. In group B, in 14 patients (46.67%) the time of onset of grade III motor block was 5-6 minute and in 13 patients (43.33%) the time of onset of grade III motor block was 6-7 minute. The mean time is $5.55 \pm 0.33$ minutes. The difference in the mean time between Group A and Group B was statistically highly significant ($p < 0.000$).

**Table 5:** Comparison of Time of Complete Motor Recovery (TCMR) between Groups

| Time of complete motor recovery (min) | Group A | Group B |
|------------------------------------|---------|---------|
| No. of patients | Percent age | No. of patients | Percentage |
| 130-139 | 2 | 6.67 | 0 | 0.00 |
| 140-149 | 25 | 83.33 | 0 | 0.00 |
| 150-159 | 3 | 10.00 | 3 | 10.00 |
| 160-169 | 0 | 0.00 | 27 | 90.00 |
| Total | 30 | 100 | 30 | 100 |

In Group A, the mean of duration of Motor Block was $145.33 \pm 4.74$ minutes and in Group B it was $162.3 \pm 2.34$.

The difference in the mean time of total duration of motor block in Group A and Group B was statistically highly significant ($p < 0.05$).
Apgar score, SBP, DBP, RR, Oxygen saturation were not significant at various intervals in between the groups.

Figure 1. Comparison of Side Effect between two groups.

Hypotension was seen in 10%, and 36.67% of patients in Group A and B respectively.

None of the patients suffered from pruritus in Group A, but 2 patients in Group B had suffered from pruritus; it subsided without any treatment. The difference in the incidence of pruritus was not significant between the two groups.

None of the patients showed shivering and respiratory depressions. Bradycardia was found in 6.66% and 23.33 percent cases in groups A and B respectively and the difference was significant.

Discussion

Relief of pain during surgery and postoperative period is one of the mainstays of balanced anaesthesia. Spinal anaesthesia remains one of the basic techniques in modern anaesthesia despite variable popularity over many years since its introduction into clinical practice. Various drugs have been tried in subarachnoid block along with local anaesthetics with the aim of improving the quality of intra operative and post operative pain relief. 16

Caesarean delivery involves traction of peritoneum and handling of intraperitoneal organs, resulting in intraoperative visceral pain. However, intrathecal Bupivacaine alone may be insufficient to provide complete analgesia despite the high sensory block. 13% of the patients undergoing caesarean delivery had visceral pain even after the intrathecal administration of 15 mg Bupivacaine. 3,4

Further more such large doses of intrathecal Bupivacaine were associated with severe hypotension and delayed recovery of motor block. 5 Although hyperbaric Bupivacaine is the most commonly used drug for spinal anaesthesia, it too has been known to cause sudden cardiac arrest after spinal anaesthesia due to extension of the sympathetic block. 17,18 Its most serious side effect is cardiotoxicity and pregrent women are more susceptible to this effect. 19 It may cause hypotension or bradycardia after mobilisation, especially with abrupt position changes. 7

The quest for newer and safer analgesic agents has always been one of the primary needs in anaesthesiology practice. Bupivacaine, the widely used local anaesthetic in regional anaesthesia is available in a commercial preparation as a recemic mixture of its two enantiomers, Isobaric Levobupivacaine, S (-) isomer and dextro Bupivacaine. , R (+) isomer. Levorotatory isomers were shown to have a safer pharmacological profile attributed to its faster protein binding rate.

Onset of Sensory block:
In the present study the mean time of onset of sensory analgesia at T10 in Group A (i.e. 8.5 mg Isobaric Levobupivacaine and 15 µg Fentanyl group) was 3.45±0.42 minutes, in Group B (i.e. 8.5 mg Hyperbaric Bupivacaine and 15 µg Fentanyl group) was 3.92±0.45 minutes. The difference in the mean time between Group A
and Group B was highly statistically significant ($p < 0.000$). This showed that onset of sensory block is faster in group with Levobupivacaine.

**Gulen et al (2012)**

Did a study on 60 patients who were randomly divided into two groups. The combinations 10 mg Levobupivacaine (0.5%) + fentanyl (15 μcg) for Group LF (n = 30) patients, 10 mg hyperbaric bupivacaine (0.5%) + fentanyl (15 μcg) for BF (n = 30) patients were intrathecally administrated a total of 2.3 cc. The time for the onset of sensory block was 2.0±0.37 in group LF and 1.46±0.50 group BF and the difference was not significant. The result of our study are different from this study. The earlier time of onset in this study, as compared to our study, might be because they have used higher dose of the drugs.

**Bozdogan N et al (2013)**

Did a study in ninety-three patients who were randomized into 3 groups (n = 31). Patients in Group C received 0.5% Levobupivacaine (2.2 ± 0.2 mL), Group S received 2.5 μg sufentanil plus 0.5% Levobupivacaine (2.2 ± 0.2 mL), and Group F received 10 μg fentanyl plus 0.5% Levobupivacaine (2.2 ± 0.2 mL) intrathecally completed to a volume of 3 mL with the addition of saline in all groups. The time to onset of sensory block at T10 level was 3.0 min, 2.50 min and 11.00 min. in group S, group F and group C respectively ($P =0.000$). Their T10 Level was earlier in group F (2.50) as compared to our study, may be because they have used higher total volume of the drugs (2.3ml).

**Karaca F et al (2014)**

Carried out a study in which the patients were randomly allocated into two groups, so that patients in Group C received intrathecal isobaric 7.5 mg 0.5% Levobupivacaine (1.5 ml) and 20 μg fentanyl (0.4 mL), while the ones in Group B had intrathecal isobaric 7.5 mg 0.5% bupivacaine (1.5 mL) and 20 μg fentanyl (0.4 mL). The sensory block onset time in group C was 2.0 min. and in group B was also 2.0 min (p> 0.05) they have compared same two drugs with fentanyl the sensory onset time was similar in both the groups and they did not find any statistical difference between Levobupivacaine and Bupivacaine group. Whereas we found that Levobupivacaine has earlier onset of sensory block. The difference in both the studies could be attributed to difference in baricity of the local anesthetic drugs. They have used Isobaric Bupivacaine.

**Highest Level of Sensory Block:**

In the present study, majority of the patients in group A (83.33%) achieved the highest sensory level of T6. Majority of the patients in group B (56.67%) achieved the highest sensory level at T6. In group A, 16.67% of patients achieved sensory level at T4, whereas in group B 43.33 % patients achieved sensory level at T4. The difference in the two groups is significant (p=0.0242)

Our result concurs with the following study.

**Duggal R et al (2015)**

Observed in their study that the maximum sensory block height achieved in Group L was (2 out of 30 achieved T4) significantly lower than Group B ( 12 out of 30 achieved T4) ($P = 0.003$).

**Gulen et al (2012)**

Did a study on 60 patients who were randomly divided into two groups. The combinations 10 mg Levobupivacaine (0.5%) + fentanyl (15 μcg) for Group LF (n = 30) patients, 10 mg hyperbaric bupivacaine (0.5%) + fentanyl (15 μcg) for BF (n = 30) patients were intrathecally administrated a total of 2.3 cc. The maximum sensory level (T dermatome ) in group LF was achieved at T4 level (2–4) and in group BF was at 3(2–4). Our results are similar to this study. Since the dose of the drugs used was more in their study, so sensory level & median were achieved at higher level (LF was at T4 and BF was at T3). Even though in Bupivacaine group, higher sensory level was achieved than Levobupivacaine group.

**Duration of Sensory Block:**

In the present study total duration of spinal block (time for sensory regression to L1) in Group A which received 0.5% hyperbaric Levobupivacaine 8.5 mg plus Fentanyl 15 μg (2ml) intrathecally was 125.43 ± 6.88 and Group B which received 0.5% hyperbaric bupivacaine 8.5 mg plus Fentanyl 15 μg (2ml) intrathecally was 171.77 ± 7.85. The difference in the mean time between Group A, Group B was statistically highly significant ($p=0.000$). Similar results were noticed with studies carried out by Duggal R et al. and Gulen et al.

**Duggal R et al (2015)**

Did a study and the results of the study showed that the duration of sensory block (first analgesic requirement) was shorter in parturients in Group L than those in Group B (80.03 ± 8.12 vs. 103.47 ± 10.18 min), the difference being highly significant ($P < 0.001$). The time to regression by two dermatomes (min) in
group L was 54.97±4.61 and in group B was 72.93±7.34 min (p<0.001) i.e. highly significant. The researcher had used the total duration of sensory block as per these two parameters (first analgesic requirement and time to regression by two dermatomes). They also found shorter duration of sensory block in group L as compared to group B.

Gulen et al (2012)20 did a study to find that time to regression by two dermatomes and time to regress to T12 dermatome was found to be significantly long in Group BF. Time to regression by two dermatomes for the sensory block in Group LF was 71.43±12.96 whereas in group BF was 76.16±13.86 min. Regression time to T12 dermatome in Group L was 145.50±11.01 and in Group BF was 162.33±10.56 min with p<0.05 and hence difference is statistically significant. The researcher had used the total duration of sensory block as per these two parameters (first analgesic requirement and time to regression by two dermatomes). Since higher doses of drugs were used in their studies so difference in values from our study was seen.

Motor blockade characteristics:

Onset of Motor Block:
In our study the mean time of onset of grade III motor block in Group A was 3.45±0.42 and Group B was 5.55±0.33 minutes. The difference in the time of onset of motor blockade between group A and group B was statistically highly significant (p=0.000). Similar studies by other researchers have reported results as under.

Bozdogan N et al (2013)21 studied Ninety-three patients who were randomized into 3 groups (n = 31). Patients in Group C received 0.5% Levobupivacaine (2.2 ± 0.2 mL), Group S received 2.5 µg sufentanil plus 0.5% Levobupivacaine (2.2 ± 0.2 mL), and Group F received 10 µg fentanyl plus 0.5% Levobupivacaine (2.2 ± 0.2 mL) intrathecally completed to a volume of 3 mL with the addition of saline in all groups. They observed that in Group S (3.75min) and Group F (3.0), target levels of motor block was achieved more rapidly as compared to group C (10.0 min) (P = 0.000). They observed that in Group F, the onset of motor block was achieved in 3.0 min, which was comparable to our study.

Debbarma B et al (2017)24 studied 100 parturients (American Society of Anesthesiologists I-II, aged 18-40 years) who were randomized into four groups: Group I (0.5% hyperbaric bupivacaine 7.5 mg in L2-3 intrathecal space), Group II (0.5% hyperbaric Levobupivacaine 7.5 mg in L2-3 intrathecal space), Group III (0.5% hyperbaric bupivacaine 10 mg in L3-4 intrathecal space), and Group IV (0.5% hyperbaric Levobupivacaine 10 mg in L3-4 intrathecal space), respectively. They concluded that Levobupivacaine 7.5 mg can be used in lower segment cesarean section when given in L2-3 space. Onset of motor block (Bromage 3) is faster with group LF7.5 mg (180.20± 43.26 sec) as compared to group BF 7.5 mg(183.68± 58.70) but the difference is not significant (p=0.76).

Subhasi D et al (2012)25 studied eighty patients. Group BF receiving 7.5 mg (1.5 ml) hyperbaric bupivacaine and 25 mcg (0.5 ml) fentanyl, or Group LF receiving 7.5 mg (1.5 ml) hyperbaric Levobupivacaine and 25 mcg (0.5 ml) fentanyl. On set of motor block ( taken as Bromage 1) in group LF was 135.00±75.70 and in group BF was 97.89±42.82 sec. The time for onset of motor block was longer in group LF as compared to group BF (p=0.069).

In this study, the onset of Motor block was defined as Bromage 1 and in our study the onset of motor block was defined as Bromage 3.Similarly the Levobupivacaine used in Group LF was hyperbaric in baricity, while in our study it was isobaric .This maybe the reason for the difference in the results.

Duration ofMotor Block:
In the present study, the mean time for duration of motor block in Group A was 145.33±4.74 min and Group B was 162.3± 2.34 min. The difference between the time for complete motor recovery was statistically highly significant (p=0.000).

Gulen et al in (2012)20 observed that in Group BF (10 mg hyperbaric bupivacaine, 0.5 % plus fentanyl (15 µg)) regression time for motor block was 132.66±7.15 and in group LF was 99±9.13 min. The difference was statistically significant (p<0.05). This is comparable with our study. No clear cut definition for regression of motor block was mentioned in this study which maybe the reason for actual difference seen in the values of duration of motor block.

Rao A et al (2014)2 conducted a study and found that Levobupivacaine with fentanyl produces (LF group 109.50±16.37 min) less intensive motor blockade when compared to bupivacaine with fentanyl (BF group 168.00±
38.77 min ) (p<0.001). In conclusion 8.75 mg of 0.5% Levobupivacaine combined with 12.5mcg fentanyl causes early regression of motor blockade.

Byadarahalli A N, et al (2016)\textsuperscript{26} carried out a study and found that time to regression of motor block (B0) in group L was 118.83±12.26 min and in group B was 128.33 ± 10.93 and p=0.663. Hence there was no statistical difference in the time for motor recovery. The result is different from our study and this could be attributed to difference in the dose of drug and no usage of opioid combination.

Limitations of The Study
One of the limitations of our study was the limited sample size. Although certain trends could be established in this pilot study, further controlled large sample size studies are required to confirm the results. Other limitation of our study was neonatal assessment.

The clinical effects of Fentanyl on the neonate could be assessed by only APGAR score. Facilities to monitor umbilical blood gases and neurobehavioral tests were not available at our college.

Conclusion:
The combination of Isobaric Levobupivacaine (0.5%) 8.5 mg with Fentanyl 15 µg can be used as a safe and effective alternative to Hyperbaric Bupivacaine (0.5%) 8.5 mg with Fentanyl 15 µg for spinal anaesthesia in cesarean section as, it provides comparable sensory block characteristics, early motor recovery allowing early mobilization, stable haemodynamics and good foetal well being.

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