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Original Research Article

Comparative Study of Intrathecal Bupivacaine and Levobupivacaine with Fentanyl for Cesarean Section: A Prospective, Randomised Controlled, Double Blinded Study

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Conflict of interest: Nil

Abstract:

Objectives: To compare the effects of intrathecal hyperbaric bupivacaine (1.8ml) with fentanyl (10µg) and isobaric levobupivacaine (1.8ml) with fentanyl (10µg) in cesarean section in terms of the onset, peak, duration, regression and duration of analgesia of sensory and motor blockage.

Material and Methods: After written informed consent, study included 60 patients of ASA I, II, aged >20 years, posted for cesarean section under spinal anaesthesia. Patients were divided into two groups of 30 patients each. During induction group B patients were received 0.5% hyperbaric bupivacaine (1.8ml) with fentanyl (10µg) and group L were received 0.5% isobaric levobupivacaine (1.8ml) with fentanyl (10µg). Patients were assessed for onset, peak, duration, regression and duration of analgesia of sensory and motor blockage in both the groups. Hemodynamic parameters (heart rate, systolic blood Pressure, diastolic blood pressure, mean arterial pressure, SpO2), adverse effects and Neonatal outcome were recorded.

Results: The time for onset, time to peak and time to duration of sensory blockade were significantly lesser in group B. The time to onset, times to peak of motor blockage were significantly lesser in group B in compared to group L. The duration of motor blockade was significant prolonged in group B. The duration of analgesia was significantly prolonged in group L. Incidence of side effects such as hypotension were more in group B.

Conclusion: It is concluded that Levobupivacaine had prolonged sensory blockade, prolonged analgesia, and earlier regression of motor blockade, stable hemodynamic and decreased incidence of adverse effect. So levobupivacaine less cardiotoxic and had no adverse effects on neonates.

Keywords: Cesarean Section, Intrathecal Bupivacaine, Fentanyl, Levobupivacaine.

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Introduction

Sub-arachnoid block or Spinal anaesthesia is the most common central block used in a surgical setting, which is being the most versatile and commonly used regional block worldwide today was first administered by J. Leonard Corning's in New York in 1885. The first planned spinal anaesthesia for surgery in man was administered by August Bier on 16 August 1898, in Kiel, where he injected 3ml of 0.5% cocaine into intrathecal space. [1]

More than a century has passed and even now, it is one of the most popular techniques for both elective and emergency surgical procedures such as caesarean sections, lower abdominal procedures, orthopedic and urological surgeries. The spinal technique is easy to perform and has a very high success rate. Spinal anaesthesia has been shown to blunt the stress response to surgery, decrease intraoperative blood loss, and lower the incidence of postoperative thromboembolic events. It can be used to extend analgesia into post-operative period, where its use has been shown to provide better analgesia than can be achieved with parenteral opioids. [2-5]

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Postoperative pain is a major cause of fear and anxiety in hospitalized patients. It is the duty of

anesthesiologist to provide the essential four A's of rapid outpatient recovery – Alertness, Analgesia, Alimentation, and Ambulation. Various adjuvants like opioids (morphine, fentanyl and sufentanyl) and other drugs [such as dexmedetomidine, clonidine, magnesium sulfate, neostigmine, ketamine and midazolam] are tested as adjuvants to local anesthetics. Spinal anaesthesia is widely used, providing a fast onset and effective sensory and motor blockade.

Bupivacaine is available as a racemic mixture of its enantiomers, levobupivacaine and dextrobupivacaine.6 In recent years, its pure S-enantiomers, levobupivacaine, ropivacaine, have been introduced into clinical practice because of their lower toxic effects for cardiovascular and central nervous system and hemodynamic effects.

The aim of study was to compare and evaluate the effects of intrathecal administration of 0.5% hyperbaric bupivacaine (1.8ml) and 10 µg of fentanyl with 0.5% isobaric levobupivacaine (1.8ml) and 10 µg of fentanyl in cesarean section with respect to compare and assess sensory and motor block, hemodynamic parameters, first request for analgesic and neonatal outcome.

Material and Methods

After getting approval from Institutional Review Board (IRB No.1002/2020) and informed written consent from patients, this prospective, randomized, double blind study was carried out in the Department of Anaesthesiology, Govt. Medical College and Sir. T. Hospital, Bhavnagar, Gujarat. Trial was registered under Clinical Trial Registry India (CTRI registration No. REF/2020/10/037815).

60 patients of ASA grade I and II, scheduled to undergo cesarean section under spinal anaesthesia were included in this study as per below mentioned inclusion and exclusion criteria.

Inclusion criteria

1. American Society of Anesthesiologists (ASA) physical status I & II who will undergo cesarean section under spinal anesthesia.
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 more than 37 weeks.

Exclusion criteria

1. Patients who had contraindication to spinal anesthesia.
2. Clinically significant coagulopathy.
3. Allergy to local anesthetic.
4. Infection at injection site.
5. Patients with spine deformities.
6. Patients with moderate aneamia (Hb<10gm %).

Preoperative Evaluation:

A detailed pre-anaesthetic examination was done comprising of history, clinical examination (general physical examination, systemic examination and airway examination), routine baseline investigations (complete hemogram, random blood sugar, renal profile, serum electrolyte and Electrocardiogram (ECG)) were done.

In pre-anaesthesia preparation room:

Monitoring was established according to minimum monitoring standards. Monitoring includes recording of baseline vital parameters – heart rate (HR), noninvasive blood pressure (NIBP), peripheral arterial oxygen saturation (SpO2).

Each patient was informed in detail regarding nature, course and purpose of the study. Patients were explained 0–10-point visual analogue scale (VAS) on a sheet paper where, (0) labeled as NO PAIN and (10) as WORST POSSIBLE PAIN.

Patients were randomly allocated to one of the two groups of 30 patients each by distributing computer generated random number sequence in sealed envelopes. Thirty envelopes of each group were made with group mentioned inside and were mixed up. Patient was asked to pick one envelope in pre-anaesthetic room.

One member (not assigned for recording outcome measures) from the team except from principal Investigator (PI), asked to open the envelope and filled up the drug as per group assigned to patient. PI was responsible for performing the procedure and recording primary and secondary outcome measures of the study.

- Group B received 0.5% hyperbaric bupivacaine 1.8 ml with fentanyl 10 µg.
- Group L received 0.5% isobaric levobupivacaine 1.8 ml with fentanyl 10 µg.

In every patient included in the study, peripheral IV(Intravenous) line was secured with 18G IV line and premedicated with Inj. Ondansetron 4 mg IV, Inj. Metoclopramide 10 mg IV and Inj. Ranitidine 50 mg IV slowly and then patient were shifted to operating room.

In the operation theatre:

Preloading was done with Inj. Ringer Lactate 10ml/kg. All equipment and drugs necessary for resuscitation and general anaesthesia were kept ready. Under strict aseptic and antiseptic precaution subarachnoid block was performed in left lateral position, using midline approach with 25G spinal needle in L3 – L4 intervertebral space.

Mixture of drugs according to group assign was injected after obtaining free and clear flow of CSF. Principle investigator, who performed the

subarachnoid block, was unaware about the contents of drug solution injected in subarachnoid space.

Immediately after the block, patient was turned supine. The time of injection was noted as time "0". Assessment of sensory and motor characteristics of SAB was done as per the grading shown in the Tablet every 30 seconds interval till peak of the blockade achieved.

All participants were given supplemental oxygen by transparent face mask at a flow rate of 6L/min. The sensory block was assessed by skin sensation to pin prick, using the sterile 23G hypodermic needle. The motor block was assessed according to Modified Bromage Scale.

Time of onset of sensory block at L1, T10 and maximum level attained were noted. Pulse rate, respiratory rate, non-invasive blood pressure and oxygen saturation were recorded at 1,5,10,15,20,25,30,40,50,60 minutes till the completion of surgery and then at 1-hour interval till 4 hours post operatively.

After 4 hours, monitoring of patient at 4 hours interval till 24 hours. Any supplementation required for inadequate block or side effects like haemodynamic disturbances, nausea, vomiting, Shivering was recorded

After the completion of surgery:

Patients were shifted to Post Anaesthesia Care Unit (PACU) where sensory and motor blockade were assessed at 30 minutes interval till regression of sensory and motor blockade. Thereafter participants were monitored at 4 hourly intervals for next 24 hours for complications and adverse events if any.

Time of analgesia request was noted in post-operative period. At the time of analgesia request, the patients were asked to rate their intensity of pain as per „Visual Analog Scale" (VAS).

Neonatal outcome was evaluated by APGAR score

Interpretation:

- 7≥: Normal4-6: Low
- ≤3: Critically Low

Results

Table 1: Demographic Parameters

Parameters	Groups	n (Sample size)	Mean	SD (Standard Deviation)	p value
Age	Group B	30	25.57	3.50	0.94
	Group L	30	25.63	3.65	
Weight	Group B	30	63.90	10.03	0.53
	Group L	30	62.40	8.26	
Height	Group B	30	156.70	3.54	0.06
	Group L	30	158.67	4.46	
Duration of Surgery	Group B	30	50.93	4.96	0.27
	Group L	30	52.57	6.37	

Table 1 showed that patients "Demographic parameters in terms of age, weight and height were comparable in both the groups (p value >0.05). Duration of surgery was comparable in both the groups (p value >0.05).

Table 2: Time to onset of Sensory block

Groups	n (Sample size)	Mean	SD (Standard Deviation)	p value
Group B	30	1.31	0.15	<0.0001
Group L	30	3.71	0.45	

Table 2 showed that time to onset of sensory blockade were significant lesser in group B in compared to Group L (p value <0.0001)

Table 3: Time to onset of motor block

Groups	n (Sample size)	Mean	SD (Standard Deviation)	p value
Group B	30	2.44	0.35	<0.0001
Group L	30	5.20	0.58	

Table 3 showed that time to onset of motor blockade were significant lesser in group B in compared to Group L (p value <0.0001)

Table 4: Time to regression of sensory block

Groups	n (Sample size)	Mean	SD (Standard Deviation)	p value
Group B	30	181.57	4.93	<0.0001
Group L	30	210	6.43	

Table 4 showed that time to regression of sensory blockade (Duration of sensory block)were significant less in group B in compared to Group L (p value <0.0001).

Table 5: Time to regression of motor block

Groups	n (Sample size)	Mean	SD (Standard Deviation)	p value
Group B	30	181.43	7.35	<0.0001
Group L	30	130.83	6.83	

Table 5 showed that time to regression of motor blockade (Duration of motor block) was significant high in group B in compared to Group L (p value <0.0001).

Table 6: First request of analgesia

Groups	n (Sample size)	Mean	SD (Standard Deviation)	p value
Group B	30	199.16	8.71	<0.0001
Group L	30	214.5	6.06	

Table 6 showed that time for first request of analgesia were significant longer in group L in compared to Group B (p value <0.0001). Vital Parameters like Heart Rate, Systolic Blood Pressure, Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial Pressure and SPO2 were comparable in Both Groups. (p value >0.05)

Table 7: Side effects

Side Effects	Group B		Group L		P value
	F	%	f	%	
Hypotension	14	46.67	3	10	0.0042
Bradycardia	3	10	1	3.34	0.6048
Vomiting	3	10	2	6.67	0.6404
Shivering	1	3.34	2	6.67	0.5536

Table 7 showed that incidence of hypotension was significant less in group L in compared to group B(p value 0.0042). Other side effects like Bradycardia, Vomiting and Shivering were comparable in both the group.

Table 8: Neonatal outcome

	Group B	Group L	p value
0 min	8.1±0.30	8.14±0.34	0.69
5 min	8.97±0.18	9.0±0.0	00

Table 8 showed that neonatal outcome was comparable in both the group.

Discussion

Spinal anaesthesia is the most preferred technique in lower segment cesarean section, because of easy and rapid induction, effective sensory and motor blockade and has no significant effect on the fetus. Addition of opioids prolonged the duration of analgesia and anaesthesia without any adverse outcome in fetus.

For cesarean section, adequate sensory and motor blockade and better hemodynamic stability with minimum adverse effect is necessary. Hypotension and bradycardia are the most common complications of sub arachnoid block and are even more serious in caesarean section because of aorta-caval compression by the graviduterus. [7-9]

In our study we evaluated the efficacy of sensory blockade, efficacy of motor blockade, duration of analgesia, hemodynamic parameters, side effects and neonatal outcome of intrathecal administration of 0.5% hyperbaric bupivacaine 1.8ml and 10 µg of fentanyl in compared to 0.5% isobaric levobupivacaine 1.8ml and 10 µg of fentanyl.

In our study we noted that patients Demographic parameters in terms of age, weight and height were comparable in both the groups (p value >0.05). Duration of surgery was comparable in both the groups (p value >0.05).

Times for onset of sensory blockade were significantly lesser in group B in compared to Group L. The results of our study were in consonance with the study by Ayesha Goyalet al, 2015 [7], observed that, the mean time for onset of sensory blockade was slower in group LF. The time to attain maximum sensory (T6) level were significantly lesser in group B in compared to Group L. Prabha. P et al 2014 [10] conducted randomized double blinded study into two groups. Group B received 8.75 mg of 0.5% hyperbaric bupivacaine with 12.5 mcg of fentanyl. Group L received 8.75mg of 0.5% isobaric levobupivacaine with 12.5 mcg of fentanyl. She noticed that the time to achieve maximum sensory blockade and time for regression of sensory blockade were longer in group L.

Duration of sensory blockade was significantly longer in group L in compared to group B. Ayesha Goyal et al, 2015 [7], found that total duration of

sensory block for group BF was 112.46 ± 19.32 min and for group LF was 128.34 ± 14.63 min and it was statistically significant which is in accordance with our study.

Time to onset of motor blockade were significantly lesser in group B in compared to Group L. Sakshi Thakore et al 2018 [11], evaluated the efficacy of low dose levobupivacaine versus bupivacaine with fentanyl for subarachnoid block in patient undergoing MTP. She found that time for onset of motor blockade in group B was 2.3 ± 1.0 and in group L was 3.3 ± 1.3. So, the time for onset of motor blockade in group B was shorter in group B. Gulen Guler et al 2012 [12], conducted study in 60 pregnant women scheduled for elective cesarean section to investigate the clinical efficacy of Levobupivacaine compared with hyperbaric bupivacaine for spinal anaesthesia for caesarean section. Patients were randomly divided into two groups. The combination of 10mg Levobupivacaine (0.5%) and fentanyl (15 mcg) for group LF (n=30) patients and 10 mg 0.5 % hyperbaric bupivacaine and fentanyl (15 mcg) for BF (n=30) patients were intrathecally administered to a total volume of 2.3 ml. He observed that time for onset of motor blockade and time for maximum motor blockade was shorter in group BF.

In our study we noted that the time to achieve maximum motor block for group B was 6.24 ± 0.70 min and for group L was 7.88 ±0.47 min with p value of<0.0001 which was statistically significant. Thus, the time to attain maximum motor block were significantly shorter in group B in compared to Group L.

Duration of motor blockade was significant prolonged in group B in compared to Group L. The results of our study were in consonance with the study by Bremerich DH et al., He studied variable doses of Levobupivacaine (7.5 mg/10 mg/12.5 mg) without any additives. They recommended 10 mg of Levobupivacaine for patients who underwent elective caesarean section with spinal anaesthesia. They observed that Levobupivacaine showed significantly shorter and less dense motor blockade when compared to Bupivacaine in subarachnoid block in elective caesarean section.

Mean duration of analgesia (1st request of analgesia)were 199.16 ± 8.71 min in group B and 214.5 ± 6.06 min in group L withp value of<0.0001 which was statistically significant. The results of our study were in consonance with the study by Turkmen et al 2012 [8]. He concluded that the duration of analgesia was longer in group L compared to group B and concluded that levobupivacaine is a good alternative to bupivacaine. The results of our study were in also consonance with the study by Idowu et al. [13] He observed that the addition of 25 mcg of fentanyl to 2.5ml of 0.5 % hyperbaric bupivacaine increased the duration of analgesia.

Vital Parameters like Heart Rate, Systolic Blood Pressure, Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial Pressure and SPO2 were comparable in Both Groups. The results of our study were in consonance with the study by Erdil et al., noted in spinal anaesthesia, that low dose Levobupivacaine plus fentanyl had better hemodynamic stability when compared with low dose Bupivacaine plus fentanyl. The results of our study were in consonance with the study by Prabha P et al [10] observed that the fall in Mean Arterial Pressure noted in group B was statistically significant, and also noted about 30 % fall in systolic BP in 10 patients.

In our study we recorded that incidence of side effects such as hypotension; bradycardia and vomiting were more in group B. The results of our study were in consonance with the study by Prabha P et al 2014 [10]. Levobupivacaine with fentanyl produced better hemodynamics stability and lesser incidence of adverse effects like bradycardia, hypotension than bupivacaine with fentanyl group. They concluded that levobupivacaine was a good alternative to bupivacaine in LSCS.

In our study we noted that the mean APGAR score at 0 min and 5 min were about 9 in both the groups and it showed that study drug had no adverse effect in neonate. The results of our study were in consonance with the study by Lirk et al., he found in his study that intrathecal bupivacaine, ropivacaine, levobupivacaine and fentanyl used for LSCS had no adverse effect as evaluated by APGAR and the pH of arteries in umbilical cord.

Conclusion

We concluded that 1.8 ml of 0.5 % Isobaric Levobupivacaine with 10 µg fentanyl when given intrathecally in caesarean section had prolonged sensory blockade, earlier regression of motor blockade, stable hemodynamic and decreased incidence of adverse effect such as hypotension than 1.8 ml of 0.5 % Hyperbaric Bupivacaine with 10µg fentanyl. So levobupivacaine is less cardiotoxic. Early motor recovery beneficial for early mobilisation and less chances of deep venous thrombosis. APGAR score at 0 min and 5 min was about 9 in both the groups and it showed that study drugs had no adverse effect in neonates.

So, we concluded that 0.5 % Isobaric Levobupivacaine with fentanylis a better alternative to 0.5 % Hyperbaric Bupivacaine with fentanyl in caesarean section.

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