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0.5 % Isobaric Levobupivacaine, 0.5 % Isobaric Levobupivacaine With Fentanyl And 0.5 % Hyperbaric Bupivacaine -Comparative Study In Infraumbilical Surgeries.

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***Aim**: To compare the characteristics of spinal blockade following intrathecal administration of isobaric 0.5% levobupivacaine (12.5mg) to 0.5% isobaric levobupivacaine (10 mg) with 25µg fentanyl and 0.5% hyperbaric bupivacaine (12.5mg) in patients undergoing elective sub umbilical surgery.*
***Methodology**: This is a prospective double blinded comparative study involving 120 patients assigned into 3 groups, Group A- Isobaric 0.5%levobupivacaine (12.5mg) to Group B - 0.5% hyperbaric bupivacaine (12.5mg) and Group C - 0.5% isobaric levobupivacaine (10 mg) with 25µg fentanyl. All patients received a standard volume of 2.5 ml for subarachnoid blockade and the following sensory and motor parameters were analyzed - time to achieve T10 level blockade, maximum level of sensory blockade, time taken to achieve maximum level of sensory blockade, 2 segment regression time from the maximum level of block, time taken for regression of sensory blockade to T12, time taken to achieve grade 1 Bromage score was taken as onset of motor blockade, time taken to achieve grade 3 Bromage score and time taken for regression of motor blockade to grade 0. Hemodynamic changes and side effects were also monitored.*
***Results**: The onset of sensory, motor and maximum level of blockade were prolonged with 0.5 % isobaric levobupivacaine alone. Rapid onset of sensory, motor and maximum level of blockade with delayed recovery of motor power was noted with hyperbaric bupivacaine. Addition of fentanyl 25 mcgs to 10 mgs of isobaric levobupivacaine produced blockade equivalent to 12.5 mg of hyperbaric bupivacaine in terms of onset of sensory block, maximum level of blockade, sensory regression to T12, but with quick recovery of motor power.*
***Conclusion:** In our study, intrathecal administration of 0.5% levobupivacaine 12.5 mgs resulted in prolonged onset time of sensory and motor blockade with increased sensory regression time compared to hyperbaric bupivacaine and levobupivacaine with fentanyl. Addition of fentanyl 25 mcgs to 10 mgs of isobaric levobupivacaine produced blockade equivalent to 12.5 mg of hyperbaric bupivacaine in terms of onset of sensory block, maximum level of blockade, sensory regression to T12, but with quick recovery of motor power.*
***Keywords:** Isobariclevobupivacaine,Isobaric levobupivacaine and Hyperbaric levobupivacaine ,infraumbilcal surgeries*

I. Introduction

'Cocainisation of the spinal cord' was first described by August Bier in the year 1899[1]. The technique of subarachnoid blockade has been refined since and various drugs have been used to provide analgesia and anesthesia for surgeries involving the lower limb and sub umbilical abdominal procedures. The ease and rapidity of achieving blockade with good success rate has resulted in spinal anesthesia as one of the most popular as well as effective technique of choice for all sub umbilical surgeries.

Lignocaine was used previously for spinal blockade, because of its rapid onset, dense blockade, and shorter duration of action. But the occurrence of transient neurological symptoms associated with intrathecal administration of lignocaine resulted its usage in modern anesthesia practice obsolete[2]. The use of local anesthetics with reliable onset of neural blockade and high margin of safety with regard to central nervous system and cardiovascular system is the prime focus for choosing the local anesthetics for regional anesthesia. The introduction of ropivacaine and levobupivacaine with better margin of safety for local anesthetic systemic toxicity is preferred for continuous infusions and for large volume regional blocks[3–5]. Various studies have evaluated the effectiveness of these newer drugs for spinal anesthesia using hyperbaric and isobaric solutions with reliable rate of success.[6–8]

The control of the spread of the drug in the cerebrospinal fluid that produces predictable levels of sensorimotor blockade without any major complication is the prime challenge in spinal anesthesia[9]. The spread of drugs in the CSF is governed by multiple factors such as drug related issues, patient related variables and the technique factors that ultimately influences the time of onset, height and the duration of neural blockade[9]. The baricity, defined as the density of local anesthetic solution relative to cerebrospinal fluid density and, is one of the major determinants of the extent of subarachnoid blockade.

Hyperbaric solutions tend to produce predictable sensory blockade and a higher level of blockade than plain solutions[9]. Isobaric solution of drugs often has variability with regard to onset, spread and duration of sensory and motor blockade in spinal anaesthesia[9]. But the use of truly isobaric solutions is less sensitive to changes in position and do not produce higher levels of sympathetic blockade that result in severe hypotension or bradycardia[10].

Levobupivacaine – a type of amide local anesthetic i.e., S-enantiomer of racemic bupivacaine has clinical profile resembling that of bupivacaine. The relative potencies of these drugs when given intrathecally for labor analgesia and LSCS have been studied separately[5,11], because of the differences in pharmacokinetic and dynamic response in pregnant patients, the results of these studies may not be applicable to other surgical population. The use of opioids along with levobupivacaine to augment the characteristics of spinal blockade has been investigated with varying doses of levobupivacaine which were compared either to hyperbaric or isobaric[12]. But there is limited research comparing isobaric levobupivacaine with or without fentanyl to hyperbaric bupivacaine as a single study. So in our study, we evaluated the characteristics of sub arachnoid blockade using plain isobaric 0.5% levobupivacaine, hyperbaric 0.5%bupivacine and isobaric 0.5% levobupivacaine with fentanyl 25mcgs in non-obstetric patients scheduled for sub umbilical surgeries.

II. Methodology

With the Institute Ethics Committee's approval (CSP- MED/14/APR/14/97 dated 14-04-2014) and informed consent from all patients, this prospective randomized double blinded study was done on 120 patients who underwent elective sub umbilical surgery under subarachnoid blockade. The sample size was 120 with 40 in each group that had a power of 80 with an alpha error of 5%. Patients of age 18-65 with ASA Physical status I-II and Body Mass Index < 29 kg/m^2, undergoing elective sub umbilical surgeries were included in the study. Patients of ASA III &IV, patients with spinal deformities and neurological diseases, surgeries involving non supine positions including lithotomy positions and pregnant patients were excluded from the study.

The patients were randomly allocated in to 3 groups by picking lots from a sealed bag containing 120 slips,
Group A received 2.5ml of 0.5% Isobaric levobupivacaine (12.5mg),
Group B received 2.5ml of 0.5% Hyperbaric bupivacaine (12.5mg) and
Group C received2.0ml of 0.5% Isobaric levobupivacaine (10mg) with 0.5 ml (25 mcg) of fentanyl. The drug solution was prepared by the anesthesia resident who was not a part of the study. The other anesthesiologist (the primary investigator) who was blinded to the loaded drug performed the block and monitored the physiological data and the details of the blockade.

After shifting the patient to operating room, routine monitors were connected which included electrocardiogram, pulse oximetry, noninvasive blood pressure and the baseline parameters were documented. An intravenous line was secured with 18G cannula and Ringer lactate was connected and given at 10 ml/kg over 30 minutes. Oxygen 6 Lit per minute was given through Hudson mask. Under aseptic precautions, the spinal block was given for all patients in L3-L4 space in the sitting position using 27G Pencan spinal needle. The drug was deposited in the space after ensuring free flow of cerebrospinal fluid from the needle. The patients were placed in supine position immediately. The time of intrathecal injection was considered as zero and the following parameters were observed.

Sensory block

The sensory block was assessed using temperature discrimination using cold ice packs in all patients. parameters analyzed were

- Time to achieve T10 level blockade
- The maximum level of sensory blockade
- Time taken to achieve maximum level of sensory blockade
- The 2 segment regression time from the maximum level of block
- Time taken for regression of sensory blockade to T12

Motor block

The motor block was assessed using Modified Bromage Score.

- ❖ 0 = no motor block
- ❖ 1 = inability to raise extended legs
- ❖ 2 = inability to flex knees and
- ❖ 3 = inability to flex ankle joint

- The time taken to. achieve grade 1 Bromage score was noted as onset of motor blockade
- The time taken to achieve grade 3 Bromage score
- The time taken for regression of motor blockade to grade 0

The assessment was started at 3 minutes after the intrathecal injection and was continued every 3 minutes for 15 minutes. Time taken for maximum level of sensory blockade was noted. Further periodic assessments were done for every 5 minutes for 45 minutes and then every 15 minutes till recovery of motor blockade to Bromage score Zero.

Heart rate, pulse oximetry and respiratory rate were monitored continuously and blood pressure was recorded every 5 minutes in the intra operative period. The monitored physiological data were documented every 15 minutes throughout the surgery and continued in the post anesthesia recovery room till sensory regression to T12 and Bromage score 0 were attained.

III. Results

120 subjects were enrolled in the study. None of the subjects were excluded or given general anesthesia for inadequate level of blockade. The data collected were analyzed using SPSS 15.0 software version, and the results were expressed as mean, standard deviation and percentage. A p-value of less than 0.05 was considered significant.

3 groups were comparable with respect to their **age, weight and height**. There was no statistical significance among the three groups. (Table 1). **The mean duration of surgery** between all the three groups were compared using ANOVA test. The mean duration of surgery was 74.13 ± 11.97 minutes in Group A, 72.25 ± 11.81 minutes in Group B and 73.25 ± 11.57 minutes in Group C with a p value of 0.77 which was not significant.The type of surgeries in the three groups were compared using the Pearson Chi square test and were found to be similar with a p value of 0.292. (Table 2).**The type of surgeries** in the three groups were compared using the Pearson Chi square test and were found to be similar with a p value of 0.292(Table 3).

The mean time to attain T10 level of sensory blockade was 6 ±1.17 minutes in Group A, 3.38 ±1.69 minutes in Group B and 4.13±2.51 minutes in Group C. The onset of blockade to T10 level was achieved at 6 minutes in Group A, which was comparatively longer when compared to Group B and Group C. The time taken to attain T10 level of sensory blockade between groups were analyzed using the Tukey HSD test. There was a statistically significant difference in the onset time of sensory blockade to T10 when Group A was compared to Group B and C with a p value of 0. 000. The onset time of sensory blockade was longest in Group A. There was no difference in the onset time of sensory blockade to T10 level between Group B and Group C (p value 0.178). (Table 4).

The highest level of blockade achieved in the study was at T4 level. But 75% (30) of patients in Group A and 37.5% (15) of patients in Group C attained T4 as maximum level. A maximum level of T6 was observed in 75 % (30) of patients in Group B and 60% (24) in Group C. (Table 5& figure 2).

The mean time taken to achieve the highest level of sensory blockade was 21.08 ± 4.95 minutes in Group A, 15.75 ± 3.31 minutes in Group B and 17.60 ± 3.88 minutes in Group C. The onset time for maximum level of sensory blockade was prolonged in Group A (21.08 ± 4.95 minutes) compared to Group B and Group C which was statistically significant with a p value of 0.00.There was statistically significant difference in the time required to achieve highest level of sensory blockade when group A was compared to group B and Group C with a p value of 0.000 and 0.001 respectively. Multiple comparison between Group B and Group C showed no difference in the time required to achieve highest level of sensory blockade (p value 0.113). (Table 6 & Figure 3).

The mean time for onset of Bromage score 1 was 6.07±0.47 minutes in Group A, 3.87 ±0.13 minutes in Group Band 4.97 ±1.45 minutes in Group C.The three groups were compared using ANOVA and it was observed that the time to achieve Bromage score 1 was prolonged significantly in Group A when compared to Group B and C (p value 0.000).On multiple comparison between the groups there was a difference in the onset time of motor blockade to Bromage score 1 between all the groups which was statistically significant. (Table 7 & Figure 4).

The mean time to attain Bromage Score 3 was 18.43 ± 3.11 minutes in Group A, 13.25 ± 2.66 minutes in Group B and 10.28 ± 3.98 minutes in Group C. Subjects in Group A took a longer duration to attain maximum level of motor blockade(Bromage score 3) when compared to Group B and Group C with a p value of 0.000. On multiple comparison between the three groups using Tukey HSD test, the time to attain Bromage level 3 was significant between all groups with a p value of 0.00 (Table 8 & Figure 5).

The mean time for two segment regression in group A was 129.38 ± 26.75 minutes, 109.70 ± 23.87 minutes in Group B and 77.43 ± 17.92 minutes in Group C with a p value of 0.00. The three groups were compared using ANOVA and it was observed that the time for two-segment regression was significantly prolonged in Group A compared to Group B and Group Subjects in Group C had the shortest two segment regression time. The two segment regression was longer in Group A when compared to Group B and C.On multiple comparison done between the three groups using Tukey HSD test, the two segment regression time was significant between all groups with a p value of 0.00. (Table 9 & Figure 6).

The mean time taken for regression to T12 level of sensory blockade was 145.80 ± 25.23 minutes in Group A, 126.25 ± 11.25 minutes in Group B and 118.50 ± 16.72 minutes in Group C. The regression time was longer in Group A indicating prolonged sensory block compared to Group B and Group C with p value of 0.000. There was statistically significant difference in the time required to regress to T12 level of sensory blockade when group A was compared to group B and Group C with a p value of 0.000 and 0.000 respectively. On comparison between Group B and Group C there was no difference in the time required to regress to T12 level of sensory blockade with a p value of 0.155. The duration of sensory blockade were similar between Group B and Group C. (Table10 & Figure7)

The mean time for regression to Bromage 0 was 269.38 ± 20.84 minutes in Group A, 294.98 ± 24.12 minutes in Group B and 185.3 ± 24.67 minutes in Group C with a p value of 0.00. The offset of motor blockade was faster in Group C when compared to Group A and Group B.On multiple comparison between the three groups using Tukey HSD test, the time to attain Bromage level 0 was significant between all groups with a p value of 0.00. Intergroup analysis has shown the regression of motor blockade was prolonged (294.98 ± 24.12 minutes) in Group B compared to Group A and Group C. The regression was quickest in Group C which was also statistically significant (185.3 ± 24.67 minutes).(Table 11 & Figure8)

19 patients had hypotension and was treated with intravenous ephedrine. When comparing the 3 groups Group A patients had more incidence of hypotension. Hemodynamical changes were similar in all the three groups. (Table 12-14 and figures 9-10)

IV. Discussion

Hyperbaric bupivacaine is the most frequently used intrathecal local anesthetic agent as it is reliable in producing predictable and effective sensorimotor blockade. Various studies have compared isobaric levobupivacaine to hyperbaric bupivacaine given intrathecally to assess the characteristics of blockade. The influence of additives has demonstrated dose sparing effect on both levobupivacaine and racemic bupivacaine. But there is limited research comparing plain levobupivacaine, levobupivacaine with adjuvants and hyperbaric bupivacaine. In our study we compared the characteristics of spinal blockade by analyzing the onset time for sensory and motor block, time taken for maximum level of sensorimotor blockade and their regression time after intrathecal injection of 0.5 % isobaric levobupivaine 2.5 ml, 0.5% isobaric levobupivacaine 2ml with fentanyl 25 mcg and 0.5 %hyperbaric bupivacaine 2.5 ml.

Bouvett et al[30] had shown the ED50 of Intrathecal Levobupivacaine as 6.2mgs and ED95 as 12.9 mgs in LSCS patients and suggested addition of additives or supplementation whenever smaller doses of levobupivacaine are given in intrathecal space. In our study we have chosen 12.5mgs (2.5 ml of 0.5 % Levobupivacaine) as a standard dose for hyperbaric and isobaric levobupivacaine group and a smaller dose of levobupivacaine (10mgs) in the levobupivcaine fentanyl group.

In our study, the onset of sensory blockade to T10 was quicker with hyperbaric bupivacaine than the group that received isobaric levobupivacaine with or without fentanyl. **D'Souza et al**[25] found the onset of T10 block with 3ml (15mg) of hyperbaric bupivacaine to be faster than same dose of isobaric levobupivacaine in their study. We found similar results in our study, with the mean onset time for sensory blockade to T10 level 3.38 ± 1.69 minutes for hyperbaric bupivacaine compared to 6 ± 1.17 minutes for isobaric levobupivacaine (p value 0.000). **Ozyilkan et al**[41] in their study observed the onset of sensory block to T10 dermatome longer with 11mgs of levobupivacaine compared to 11 mgs of levobupivacaine with 10mcgs of fentanyl given at a standard volume of 2.4ml.**Attri et al**[48]compared levobupivacaine 10mgs and levobupivacaine 10mgs with fentanyl 25mcgs in infra umbilical surgeries and reported faster onset of sensory block with levobupivacaine fentanyl combination than the plain group. We found similar results in our study where the time taken to achieve T10 level of sensory block was 6 ± 1.17minutes with 12.5mgs levobupivacaine and 4.13±2.51 minutes for 10mgs levobupivacaine –fentanyl(25mcg) combination with a significant p value of 0.000. This was achieved with a lower dose of levobupivacaine (10 mgs) compared to 12.5 mgs in the plain group. The synergistic effects of opioids on local anesthetics contributed to the dose sparing effect. Intergroup comparison showed no difference between hyperbaric bupivacaine and isobaric levobupivacaine with fentanyl. The addition of fentanyl 25mcgs to isobaric levobupivacaine (10mg) hastened the onset of blockade, which was equivalent to 2.5ml of hyperbaric bupivacaine.

In our study the peak level of sensory blockade achieved was T4, which was observed in 75%(30) of patients who received levobupivacaine alone and in 37.55% (15) of patients who received levobupivacaine with fentanyl. Only 22.5% (9) of patients who received hyperbaric bupivacaine achieved T4 level in our study. Similar findings were observed by **Vanna et al**[35], where the peak level of blockade was higher(T4) with 2.5ml of 0.5% levobupivacaine which was statistically significant compared to the same dose of hyperbaric bupivacaine. **Sahin et al**[27] reported peak sensory blockade at T6 dermatome level with3 ml of 0.5% isobaric levobupivacaine compared to 3 ml of 0.5% racemic bupivacaine given intrathecally inpatients who underwent lumbar disc surgery in prone position.

Ozyilkan et al[41] reported statistically significant rapid onset of maximal level of sensory blockade, with 11 mgs of levobupivacaine in combination with fentanyl compared to plain levobupivacaine. In our study also, the onset of maximal sensory blockade was decreased for levobupivacaine fentanyl group (17.6 ± 3.88minutes) compared to plain levobupivacaine group(21.08± 4.95 minutes)with a pvalue of 0.000.Though the time taken to achieve peak level was fastest with hyperbaric bupivacaine(15.75± 3.31 minutes), intergroup comparison showed no difference between hyperbaric bupivacaine 12.5mgs and 10mgs of levobupivacaine with 25mcgs fentanyl due to the augmenting effects of opioids on the local anesthetics.

Glaser et al[37] observed mean time for onset of motor blockade at 10 ± 7 minutes for 3.5ml of intrathecal levobupivacaine. **Ozyilkan et al**[41] reported that onset of motor blockade was shortened by adding fentanyl to levobupivacaine than plain levobupivacaine in their study. The mean onset time was 10± 4 minutes with plain levobupivacaine and 3± 1.75 minutes after addition of fentanyl to levobupivacaine. Similarly, in our study, we observed reduction in the time needed for the onset of motor blockade time by addition of fentanyl to levobupivacaine (4.96±1.45 minutes) compared to (6.07±0.47) minutes with plain levobupivacaine. However, the onset of Bromage score 1 was fastest in the group that received hyperbaric bupivacaine than the other groups which correlated to the findings of **Gulec et al**[28]**.** In their study, intrathecal injection of isobaric levobupivacaine (15mgs) resulted in prolonged time for the onset of motor blockade and maximum Bromage scores compared to hyperbaric bupivacaine which correlated to our findings.

Guler et al[42] found the onset of maximal motor blockade at 11.36 ± 2.35minutes after intrathecal dose of 10mgs of levobupivacaine with 15mcgs of fentanyl. In our study, the mean time taken for onset of maximum motor blockade was achieved at 10.28 ± 3.98 minutes in the levobupivacaine with fentanyl group which was similar to the onset time observed by Guler et al.

The mean time taken for two segment regression in our study was quicker (77.43±17.92 minutes) in the levobupivacaine fentanyl group, followed by hyperbaric bupivacaine (109.70 ± 23.870 minutes). The sensory regression with plain levobupivacaine lasted longer than all the other groups (129.38 ± 26.75minutes). **Vanna et al**[35] observed regression time similar for levobupivacaine and hyperbaric bupivacaine given at a dose of 12.5mg whereas **Guler et al**[42] observed prolonged sensory block with levobupivacaine compared to hyperbaric bupivacaine with fentanyl as adjuvant in both the groups. In our study, the two segment regression time and regression to T12 were increased with 12.5mg of levobupivacaine compared to hyperbaric bupivacaine. **Ozyilkan et al**[41] in their study found two segment regression time similar between 11mgs of levobupivacaine and11mgs of levobupivacaine with fentanyl 10mcgs. In our study, the two segment regression time and regression to T12 level of sensory blockade were prolonged with plain levobupivacaine compared to levobupivacaine with fentanyl combination. The difference in dosage of levobupivacaine (10mg versus 12.5mg) in the fentanyl versus plain group given in our study probably was the reason for prolonged sensory block in our study.

Cuvas et al[45] in their study found quicker regression of motor blockade in patients who received levobupivacaine along with fentanyl than levobupivacaine alone. Similarly in our study, motor power was regained first in patients who received levobupivacaine-fentanyl (185.30±24.67 minutes) which was followed by plain isobaric levobupivacaine (269.38 ±20minutes). **Guler et al**[42]in their study observed that the time taken for recovery of motor power was prolonged with hyperbaric bupivacaine compared to isobaric levobupivacaine given at similar doses(10mg). We also observed that the recovery of motor blockade was prolonged (294.98±24.1 minutes) in the hyperbaric bupivacaine group compared to isobaric levobupivacaine (269.38 ±20minutes) with a dose of 12.5mgs.

The small dose of fentanyl added to 10mgs of levobupivacaine produced effective sensory and motor blockade with rapid recovery of motor power unlike the hyperbaric or the plain levobupivacaine group. The maximum time taken for regression of motor block was observed with hyperbaric bupivacaine in our study was similar to the observation by **Sahin et al**[27]**and Guler et al**[42]**.**

There were no significant differences in the mean arterial pressure changes between the three groups, although more number of patients in levobupivacaine group received ephedrine. There were more number of patients with T4 level of blockade which could be the reason for ephedrine usage in this group. There was no incidence of bradycardia and/or pruritus in our study.

No data was collected regarding surgeon satisfaction scores in the intraoperative period, which was a limitation in our study. The duration of analgesia which was measured as pain score higher than 3, was not included in our study protocol, since all sub umbilical surgeries were included in our study and pain score is a subjective sign.

In our study, intrathecal administration of 0.5% levobupivacaine 12.5 mgs resulted in prolonged onset time of sensory and motor blockade with increased sensory regression time compared to hyperbaric bupivacaine and levobupivacaine with fentanyl. The addition of fentanyl to levobupivacaine decreased the onset time of sensory and motor blockade along with the quicker regression of motor power compared to all other

groups. Hyperbaric bupivacaine was associated with prolonged motor blockade in spite of quick onset time of sensory and motor blockade.

V. Conclusion

In our study comparing 0.5% isobaric levobupivacaine 12.5 mgs to that of 0.5 % hyperbaric bupivacaine 12.5 mgs and isobaric levobupivacaine 10 mgs with fentanyl 25 mcg showed

- The onset of sensory, motor, maximum level of blockade, were prolonged with 0.5 % isobaric levobupivacaine alone.
- Rapid onset of sensory, motor and maximum level of blockade with delayed recovery of motor power was noted with hyperbaric bupivacaine.
- Addition of fentanyl 25 mcgs to 10 mgs of isobaric levobupivacaine produced blockade equivalent to 12.5 mg of hyperbaric bupivacaine in terms of onset of sensory block, maximum level of blockade, sensory regression to T12, but with quick recovery of motor power.

Conflict of Interest

There is no conflict of interest

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