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Original Research Article

Comparison of Minimum Volume and Dose of Epidural Levobupivacaine 0.125%W/V and 0.25%W/V with Fentanyl for Labor Analgesia

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Abstract

Background: The pain of childbirth is arguably the most severe pain women will endure in their lifetime. Since pain relief in labor has always been surrounded with myths and controversies, providing effective and safe analgesia during labor have remained an ongoing challenge. In our study we did the comparison of minimum volume and dose of epidural levobupivacaine 0.125%w/v and 0.25%w/v with fentanyl for labor analgesia.

Objectives: To assess the minimum volume and dose of epidural levobupivacaine 0.125% & 0.25% with fentanyl for labor analgesia, to compare maternal analgesia, progress of labor, mode of delivery, neonatal outcome and maternal side effects in both groups.

Methods: After obtaining institutional ethics committee approval a prospective observational study was performed on 48 parturients consenting for labor analgesia and receiving continous doses of formulated drug. Parturients were divided into two groups. Group 1 received 0.125% levobupivacaine with 2 microgram/ml fentanyl and group 2 received 0.25% levobupivacaine with 2 microgram/ml fentanyl. For analysis purpose, data collected from 24 parturients who received 0.125% levobupivacaine with fentanyl were listed in group 1 and 0.25% levobupivacaine with fentanyl in group 2 respectively.

Statistical analysis was done using computer software SPSS version-18. Student's t-test and Chi-square test were used and $p < 0.05$ was considered as significant.

Results: The total volume of drug required in group 1 was more compared to group 2. The total dose of drug used in group 1 was less compared to group 2. Motor blockade was more in group 2 parturients and were associated with assisted delivery. Number of top-up boluses given were more in group 1 compared to group 2. Maternal satisfaction, heart rate, foetal heart rate, progress of labor, neonatal outcome, maternal side effects were comparable in both groups and was not statistically significant.

Conclusion: In our study 0.125% levobupivacaine can produce same analgesia with a 24% increase in volume and 45 % reduction in dose when compared with 0.25 % levobupivacaine.

Keywords: Labor Analgesia, Epidural, Continous Infusion, Levobupivacaine.

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Introduction

The pain experienced during delivering a child is beyond words can explain. Neuraxial analgesic technique is the gold standard for pain relief during labor and delivery; it provides complete analgesia via blocking pain sensation from both stages of labor. Continuous lumbar epidural analgesia with local anaesthetic drugs has been the mainstay of neuraxial labor analgesia. Levobupivacaine is a single-enantiomer local anaesthetic and a levorotatory stereoisomer of bupivacaine. It is less cardiotoxic than bupivacaine. Adjuvant administration of local amide anaesthetics in combination with opioids is routinely used for relief of labor pain. Synthetic opioids such as lipid-soluble sufentanil and fentanyl can increase the potency of local amide anaesthetics. Clonidine, dexmedetomidine, neostigmine, epinephrine and dexamethasone are the other adjuvants used.[1]

Objectives

Primary objective

To assess the minimum volume and dose of epidural levobupivacaine 0.125% & 0.25% with fentanyl for labor analgesia.

Secondary objective

- To compare maternal analgesia in both concentrations using visual analogue scale.
- To study progress of labor
- To study mode of delivery.
- To study the neonatal outcome: APGAR.
- To study the incidence of maternal side effects in both groups till two hours postpartum.

Materials and Methods

This is an observational study conducted among parturients consenting for labor analgesia and receiving continuous doses of formulated drug. Parturients admitted to labour room for safe confinement in Government T. D. Medical College Alappuzha were included in the study. The study was carried out over a period of 18 months from January 2018 to June 2019 after obtaining institutional ethics committee clearance. Informed written consent was taken from all patients in the study. Confidentiality of patient details was strictly maintained.

Sampling Sample Size

$n= (Z\alpha+Z\beta)^2 SD^2 \times 2 \div d^2$

SD =5.51, d =4.4 from the study conducted by Lyons Gordan [2]

$= (1.96+0.84)^2 \times 5.51^2 \times 2 \div 4.4^2$

=24 parturients in each group

Inclusion Criteria

- Parturients–primigravida between 18-40 yrs. who was willing to receive labor analgesia
- Height between 145 cm & 170 cm
- Weight less than 100kg
- Uncomplicated vertex presentation
- Singleton gestation
- Gestational age > 36 weeks
- 4 cm cervical dilatation

Exclusion Criteria

- ASA 3 and above
- History of allergy to local anesthetic
- Cardiac disease or other major medical comorbidities
- Patients who received parenteral opioids within previous 2 hrs.
- Skin and soft tissue infection at the site of needle puncture
- suspected coagulopathy
- Recent pharmacological anticoagulation

Sampling Procedure

Data was collected from all patients who received either 0.125% levobupivacaine with fentanyl and 0.25% levobupivacaine with fentanyl. For analysis purpose, data collected from those patients who were given 0.125% levobupivacaine with

fentanyl was listed in group 1 and 0.25% levobupivacaine with fentanyl was listed in group 2. The parturient with odd serial numbers were included in group 1 and even numbers in group 2.

Study Procedure

After getting clearance from the institutional research and ethics committees, parturients were selected as per the inclusion and exclusion criteria. The drugs were prepared by the researcher and administered by the concerned duty anesthesia Medical Officer who was not involved in the study. Researcher continued parturient monitoring and care.

Detailed preanesthetic evaluation was done including obstetric, surgical, medical and allergic history. Physical examination including vitals, airway assessment, respiratory system, cardiovascular system, nervous system, and spine was done. Routine blood investigations, ABO blood grouping, Rh typing and screening was done. Parturients were instructed to use visual analogue scale (VAS). Marks are from 0- 100, 0 means no pain and 100 means worst pain possible.

After obtaining an informed written consent peripheral intravenous access was obtained with 18 G cannula. 500 ml of Ringer Lactate was co-loaded. Maternal pulse rate, blood pressure, ECG, SpO2, respiration was noted. Foetal heart rate and degree of uterine contractions was monitored using cardiotocograph. Resuscitation equipments and drugs were kept ready.

Parturients were positioned in lateral decubitus position for insertion of epidural catheter. Procedure was done under strict asepsis, local anaesthetics infiltration given, the epidural space was identified using the loss of resistance to the injection of saline technique, with an 18 G Tuohy needle inserted at the second -third lumbar interspace via midline approach. With the bevel directed cephalad, a three side-hole catheter was advanced 3–4 cm through the needle into the epidural space. A 3 ml test dose of 1.5% lignocaine with adrenaline 15 mcg was injected after negative aspiration to rule out intrathecal or intravascular placement.

Epidural catheter was secured in place. Parturients were positioned supine and wedge was placed under right buttock to prevent aortocaval compression. An initial bolus dose of 5ml of 0.125% or 0.25% Levobupivacaine with fentanyl 2 microgram/ml was injected at 4-5 cm cervical dilatation or patient complaints of pain. Increment of 3ml of injection levobupivacaine was given every 5 minutes till a sensory level of T10 was achieved. Assessment of the level of epidural block was done by absence of pin prick sensation with a short-beveled 27-gauge hypodermic needle every 5 minutes. If sensory block had not been achieved bilaterally at the T10 level after 20 min, and the parturient still in pain, an additional 3 ml dose of injection levobupivacaine with fentanyl was administered. If at 30 min a bilateral sensory block to T10 has not been produced despite this additional bolus, the parturient was withdrawn from the study and systemic analgesia was given. The time at which the T10 level was achieved (or the parturient become pain free) was defined as ‘time zero’. Once T10 level sensory blockade was achieved and parturient started on continuous infusion of formulated drug at 4ml/hour.

Parturient can be placed in lateral position or supine position with a wedge under the right buttock. Sensory block was assessed bilaterally in the mid-clavicular line using a short- beveled 27 G hypodermic needle. After achieving T10 level, labor pain was assessed using VAS at 30 min interval. If (and only if) pain relief was requested by the patient, sensory level was checked and additional 3 ml of the study mixture was given (maximum number rescue doses 3 in 1-hour, minimum interval between doses 15 min), and the time of the rescue bolus was noted. If still pain was not controlled,

previous base line infusion rate, was increased by 2ml/hr. Levels of sensory and motor block assessments, maternal heart rate, blood pressure and respiration were done at the same time as pain assessment. Foetal heart rate and degree of uterine contraction were monitored continuously by cardiotocograph. Patient was motivated to bear down during active contractions. Pain during episiotomy incision was controlled with epidural drug administration in the propped-up position. Hypotension (defined as 30% decrease in initial systolic blood pressure or a systolic blood pressure less than 100 mm Hg) was treated with Ringer Lactate/ Normal Saline and/or intra venous boluses of ephedrine 3 mg. Side effects like pruritus, urinary retention, nausea, vomiting, shivering and maternal pyrexia were observed in both groups. Postpartum evaluation for complete placental removal, contracted uterus, postpartum haemorrhage was done. Total dose and volume of the drug was calculated from 4cm cervical dilatation to delivery of foetus. Parturient were monitored throughout labor by the researcher

Methods of Data Collection

The study variables recorded included volume & dose of Levobupivacaine and dose of fentanyl used, quality of analgesia as assessed by VAS, attainment of time zero, duration of labor, progress of labor, mode of delivery, neonatal outcome assessed by APGAR score and incidence of NICU admission, degree of motor block as assessed by Modified Bromage score and maternal side effects like hypotension, nausea, vomiting, pruritus, urinary retention, shivering, respiratory depression, fever, bradycardia, tachycardia &seizures.

Statistical Analysis

Data was entered in excel sheet. Analysis was done using computer softwāre SPSS version-18. All quantitative variables were summarized using mean and standard deviation and qualitative variables was expressed percentage or proportion. Student's t-test and Chi-square test were used and $p < 0.05$ was considered as significant.

Results

Twenty-four parturients each in group 1 and group 2 were selected as per inclusion and exclusion criteria and none of the parturients were excluded from enrolled. Group 1 received 0.125% levobupivacaine with 2microgram/ml fentanyl and group 2-received 0.25% levobupivacaine with 2microgram/ml fentanyl.

Baseline Variables

Patient demographics

The mean age in years in group 1 was 23.58 ± 3.438 and group 2 was 23.58 ± 2.977. The mean height in centimeters in group 1 was 158.75 ± 2.541 and group 2 was 158.29 (3.747). The mean weight in kilogram of parturient in group1 was 69.21±4.520 and group 2 was 69.08 ±7.144. The mean completed gestational age in weeks with group 1 was 38.04 ± 0.954 and with group 2 was 38.41 ± 0.717. Both groups were comparable in view of their age, height, weight, and gestational age. Epidural administration of drug combination started at 4 cm dilatation in parturients in both groups.

Table 1: Patient demographics

n=24	Group 1 mean (SD)	Group 2 mean (SD)	P value
Age(years)	23.58 (3.438)	23.58 (2.977)	1.000
Height(cm)	158.75 (2.541)	158.29 (3.747)	0.622
Weight(kg)	69.21 (4.520)	69.08 (7.144)	0.943
Gestational age(wks.)	38.04 (0.954)	38.41 (0.717)	0.131
Cervical dilatation(cm)	4	4	-

Group 1 - received 0.125% levobupivacaine with 2microgram /ml fentanyl. Group 2 received 0.25% levobupivacaine with 2microgram/ml fentanyl. p value < 0.05 significant.

Outcome variables

Table 2: Attainment of time zero

n=24	Group 1 mean (SD)	Group 2 mean (SD)	P value
Time zero (min)	12.08(2.518)	11.04(2.074)	0.125

There is no statistically significant difference in duration for attainment of time zero between group 1 (12.08±2.518) and group 2 (11.04±2.074). (p valve 0.125)

Table 3: VAS score (median with IQR)

Time at (min)	n of group 1	n of group 2	Group 1	Group 2	P value
30	24	24	0(0)	0(0)	0.317
60	23	23	0(0)	0(10)	0.485
90	23	23	0(10)	0(0)	0.99
120	21	21	0(15)	0(0)	0.57
150	18	17	0(0)	0(0)	1
180	11	7	10(20)	1(10)	0.167
210	11	7	0(0)	0(0)	0.780
240	8	6	0(15)	0(5)	0.717
270	6	5	a	0(5)	0.273
300	5	5	10(20)	1(10)	0.078
330	4	3	5(10)	a	0.317
360	3	3	a	0(-)	0.564
390	1	3	a	a	1

Percentage%

In every 30 minutes patient delivered were omitted for analysis of VAS. ‘a’ is VAS at that particular time is constant in one or more split file. It has been omitted. Good pain relief was noticed, and sensory level was maintained at T 10 in both groups and there was no statistically significant difference in VAS score comparing both the groups using Mann Whitney test.

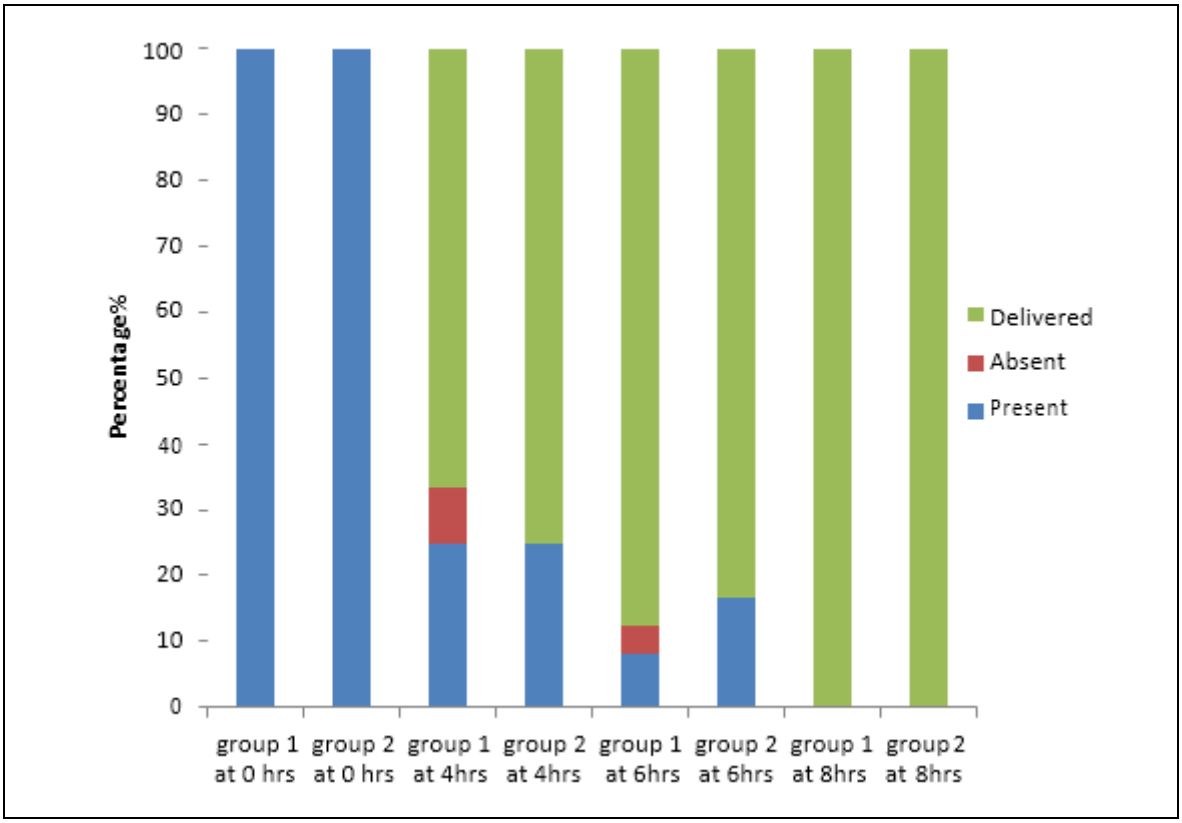

Figure 1: Progress of Labor

Both groups had progress of labor at 'o' hour, so not statistically significant. Progress of labor at 4 hours is not statistically significant (p value 0.650). Progress of labor at 6 hours is not statistically significant (p value 0.666). At 8 hours all parturients in both groups were delivered.

Table 4: Duration of labor

Time (min)	Group 1 Mean (SD) n= 24	Group 2 Mean (SD) n= 24	P value
Duration of labor	05.21(95.661)	89.79(110.340)	0.312

Group 1 (205.21 ± 95.661mins) was found to have longer duration of labor compared to group 2 (189.79 ± 110.340mins) but the difference is not statistically significant.

Table 5: Total volume& dose of Levobupivacaine

Levobupivacaine	Group 1 mean (SD) n=24	Group 2 mean (SD) n=24	P value
Total Volume (ml)	27.04(12.85)	21.96(16.35)	0.208
Total Dose(mg)	35.83(16.06)	65.39(40.84)	0.000

To find out the mean volume of drug required, both groups who receive a volume >60 ml were excluded (considered them as outliers).

Table 6: Total volume in parturients who received a volume <60 ml

Levobupivacaine	Group 1 mean (SD) n=23	Group 2 mean (SD) n=21	P value
Total Volume (ml)	27.17(10.811)	20.33(4.127)	0 .009

We had 1 parturient in group 1 and 3 parturients in group 2 who required a total volume >60 ml, probably because of increased duration of labor. Group 1 received a mean volume of 27.17ml and group 2 20.33 ml. p value < 0.009 significant.

Table 7: Fentanyl dose

Group, n = 24	Group 1 mean (SD)	Group 2 mean (SD)	P value
Fentanyl (microgram)	57.33(25.712)	51.58(33.310)	0.507

Fentanyl dose required is more in group 1 (57.33 ± 25.712 microgram), when compared to group 2 (51.58 ± 33.310 microgram) but the difference is not statistically significant. (p value 0.507)

Table 8: Number of top-up boluses given

	0 dose	1 dose	2 doses	3 doses	4 doses
Group 1	14(58.3%)	5(20.8%)	0(0%)	4(16.7%)	1(4.2%)
Group 2	19(79.2%)	1(4.2%)	3(12.5%)	0(0%)	1(4.2%)

p value is 0.016. Number of top up boluses given in both groups is found to be statistically significant. (p value 0.016).

Table 9: Motor block

Parturients		Bromage 0	Bromage 1	Bromage 2	Total
Group 1	n	15	9	0	24
	Percentage	62.5%	37.5%	0%	100.0%
Group 2	n	1	19	4	24
	Percentage	4.2%	79.2%	16.7%	100.0%

No: of parturients= n, (p value 0.000)

Bromage score 0 was noted in 15 parturients of group 1 and 1 parturient of group 2. Bromage score 1 was noted in 19 parturients of group 1 and 9 parturient of group 2. None of the parturients in group 1 had Bromage score 2 but 4 in group 2 had Bromage score 2. Degree of motor blockade is statistically significant between 2 groups. (p value 0.000).

Table 10: Mode of delivery

Mode	Normal vaginal delivery	Assisted	LSCS
Group 1 n & (%)	16(66.7%)	2(8.3%)	6(25%)
Group 2 n & (%)	14(58.3%)	6 (25%)	4(16.7%)

Sixteen parturients in group 1 and fourteen parturients of group 2 had normal vaginal delivery. Two parturients in group 1 and six parturients in group 2 had assisted delivery. Six parturients in group 1 and four parturients in group 2 delivered by LSCS. There is statistically no significant difference between the two groups (p value 0.332).

Table 11: APGAR score in 1 minute & 5 minute

	APGAR score in 1minute			APGAR score in 5minutes	
	<9	**9**	**p**	**<9**	**9**
Group 1	16	8	1.000	0	24
Group 2	16	8		0	24

In both groups at one minute, 16 neonates had APGAR score < 9 and 8 neonates had score 9; p value is 1 which is not statistically significant. APGAR score in 5 minutes was 9 in all 24(100%) newborns of both groups. Therefore, p value could not be calculated

Table 12: Maternal side effects

Side effects	Group 1	Group 2	p
Hypotension	2(8.3%)	1(4.2%)	1.000
Sedation	0(0%)	0(0%)	-
Vomiting	0(0%)	0(0%)	-
Pruritis	1(4.2%)	0(0%)	1.000
Urinary retention	24(100%)	24(100%)	-
Shivering	0(0%)	0(0%)	-
Respiratory depression	0(0%)	0(0%)	-
Maternal fever	0(0%)	1(4.2%)	1.000

There is no statistically significant difference in side effects in both the groups but hypotension was found to be higher in group 1 compared to group 2. All parturients in both group had urinary retention. In both groups vomiting, shivering, respiratory depression was absent

Discussion

In our study the mean time for attainment of time zero are 12.08 minutes with group 1 and 11.04 minutes with group 2 which is statistically not significant. Wahdan AS et al did a study comparing epidural levobupivacaine (0.125%) versus a combination of levobupivacaine (0.125%) and dexamethasone.[3] The mean attainment of time zero with levobupivacaine 0.125% was 10.8 minutes. In a study done by D. Burke et al, the mean attainment of time zero with epidural infusion of 0.25 % levo-bupivacaine was 12 minutes,[4] which is comparable with our study.

Maternal analgesia was compared using VAS. In our study every 30 minutes VAS score was assessed and compared with both groups and scored between(0 -100). Good pain relief was noticed and sensory level was maintained at T10 in both groups and there was no statistically significant difference in VAS score between both the groups. In the study by Wahdan A S, the median VAS score in both groups was 2. VAS scored between (0 - 10), which is not statistically significant (p 0.22).[3]

Progress of labor in group 1 and 2 are not statistically significant which can be compared with the study done by Ahmed Mostafa et al, in which three different concentrations of levobupivacaine (0.0625%, 0.125% and 0.25 %) were compared.[5]

The mean total duration of labor in group 1 and 2 in our study are 205.21 minutes and 189.79 minutes respectively. Burke et al did a study with 0.25 % levobupivacaine in which the mean total duration of labor was 649.80 minutes.[4]

In our study, group 1 required a mean total volume of 27.04 ml and group 2 required 21.96 ml in (p value 0.208). Among the parturients, 4 patients required a volume > 60 ml and their duration of labor was also

>6 hours. Increased volume required in this parturients may be because of increased duration of labor. Considering the parturients who required volume > 60 ml as outliers, the mean total volume required in our study was 27.17 ml in group 1 and 20.33 ml in group 2 (p value - 0.009), which is statistically significant. In our study the total dose required with group 1 and 2 are 35.83 mg and 65.39 mg. This was statistically significant (p value 0.000). In our study 0.125% levobupivacaine group produced same analgesia with a 24% increase in volume and 45% reduction in dose when compared with 0.25% levobupivacaine group.

Lyons Gordon et al in a study on bupivacaine 0.125% when compared with 0.25% produced equivalent analgesia with a 50% increase in volume, and a 25% reduction in dose[2]. In our study 0.125% levobupivacaine group obtained same analgesia as 0.25% levobupivacaine group with only a 24 % increase in volume whereas in the study done by Lyons Gordon it is 50 % increase. In the same study by Lyons Gordon 0.125% levobupivacaine group got equivalent analgesia as 0.25% levobupivacaine group with 25% decrease in dose of drug, whereas in our study, with 50% reduction in total dose 0.125% levobupivacaine group could attain equivalent analgesia as 0.25% levobupivacaine group.

Uma Srivatsava et al did a study on 'Patient Controlled Epidural Analgesia' (PCEA) and 'Patient Controlled Epidural Analgesia' (PCEA) with continous background infusion during labor using 0.125% bupivacaine with 2 microgram/ml fentanyl. The mean total volume of drug with PCEA group was 50 ml and patient controlled epidural analgesia with continous background infusion was 55ml[6]. In our study, volume in group 1 is 27.17 ml which is very much less.

In our study the total dose required with group 1 and 2 are 35.83 mg and 65.39 mg. This was statistically significant (p value 0.000). Rodriguez Campoo et al did a study comparing the total dose required with 0.125% levobupivacine in Patient Intermittent Epidural Boluses (PIEB) plus very low Continuous Epidural Infusion (CEI) versus Patient-Controlled Epidural Analgesia (PCEA) plus continuous epidural infusion (CEI) and were 62.04mg and 52.97 mg respectively[7]. These were statistically significant. Wahdan AS et al did a study in which the total dose required with 0.125% levobupivacaine was 130 mg[2]. Group 1 in our study required a less total amount of drug compared to above study, it may be because of addition of fentanyl to levobupivacaine.

The mean dose of fentanyl used in our study are 57.33 microgram in group 1 and 51.58 microgram in group 2, which is not statistically significant (p0.507). Robinson Andrew et al did a study on levobupivacaine for epidural analgesia in labor in which they compared levobupivacaine (control group), levobupivacaine with 2 microgram/ml fentanyl and levobupivacaine with 3 microgram/ml fentanyl. Parturients who received levobupivacaine with 2 microgram/ml fentanyl had a 0.047% decrease in volume whereas parturients who received levobupivacaine with 3 microgram/ml fentanyl had a 0.05% decrease in volume when compared with the control group.[8]

In our study degree of motor blockade is assessed using Bromage scale. Bromage score 0 was noted in 15 parturients of group 1 and 1 parturient of group 2. Bromage score 1 was noted in 19 parturients of group 1 and 9 parturients of group 2. None of the parturients had Bromage score 2 in group 1, but 4 parturients in group 2 had Bromage score 2. Degree of motor blockade was statistically significant between 2 groups (p value 0.000). Ahmed Mostafa et al did a comparison of three different concentrations of levobupivacaine (0.25%,

0.125%, 0.0625%) for epidural labor analgesia. No motor block was observed in (0.125%, 0.0625%) groups, as all parturients could freely move the lower limbs, but in 0.25% group, motor block occurred in (39% of parturients) in the form of Bromage score 1. Bromage score of 2 or 3 was not observed in any of the groups.[5]

In our study sixteen parturients (66.7%) in group 1 and fourteen parturients (58.3%) of group 2 had normal vaginal delivery. Two parturients (8.3%) in group 1 and six parturients (25%) in group 2 had assisted delivery. Six parturients (25%) in group 1 and four parturients (16.7%) in group 2 delivered by LSCS. There is statistically no significant difference between the two groups (p value 0.332) but increased number of assisted deliveries seen in group 2, may be because of motor blockade with 0.25% levobupivacaine. Ahmed Mostafa et al in their study found no assisted delivery with 0.125% levobupivacaine with fentanyl[5]. Burke et al in a study find 47% of parturients with assisted delivery in receiving 0.25% levobupivacaine.[4]

There is no statistically significant difference in maternal heart rate in group 1 and group 2. This is similar to the study done by Ahmed Mostafa et al where there was no difference in maternal heart rate.[5]

Foetal heart rate was monitored throughout the labor and recorded every 30 minutes. Statistically significant difference in foetal heart rate was seen in group 1 and group 2 at 180 min. only, p value 0.018.

Foetal outcome is monitored using APGAR score at 1 and 5 minutes. There is no statistically significant difference in APGAR score between the groups. This finding is similar to the study done by Wahdan A S et al using same drug formulation.[3]

Incidence of maternal hypotension is more in group 1 compared to group 2 but it is not statistically significant. In the study done by Amr Samir Wahdan et al using the same drug formulation there was no hypotension in both groups.[3]

Catheterisation was done in all parturients in both groups for urinary retention. One parturient in group 1 had pruritus; one parturient in group 2 had maternal fever which are not statistically significant. None of the parturients in both groups had vomiting, sedation, shivering and respiratory depression.

Conclusion

In our study, group 1 (0.125% levobupivacaine group) produce same analgesia with a 24% increase in volume and 45 % reduction in dose when compared with group 2 (0.25 % levobupivacaine group). Addition of fentanyl decreased the total dose requirement of levobupivacaine. Number of top-up boluses required was less in group 2 compared to group 1. Attainment of time zero, visual analogue scale score, progress of labor, duration of labor, maternal heart rate, foetal heart rate, neonatal outcome and maternal side effects were comparable in both groups and were not statistically significant.

With the technique of continuous infusion, a stable level of analgesia, less maternal hypotension, less chance of local anaesthetic systemic toxicity was noted. Continuous infusion with 0.125% levobupivacaine with fentanyl can be considered as the good drug formulation compared with 0.25% levobupivacaine with fentanyl group.

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