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FENTANYL VERSUS TRAMADOL WITH LEVOBUPIVACAINE IN LABOUR ANALGESIA

Anaesthesiology

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ABSTRACT

BACKGROUND: Labor analgesia using epidural levobupivacaine has become very popular by virtue of its safety and lesser motor blockade. Adding opioids to local anesthetic drugs provide rapid onset and prolonged analgesia but may be associated with several maternal and fetal adverse effects. The purpose of this study is to compare fentanyl and tramadol used in epidural in terms of duration of analgesia and frequency of the adverse fetomaternal outcome.

MATERIALS AND METHODS: A total of 60 primipara patients with a singleton pregnancy in active labor were given epidural analgesia after randomly allocating them in two groups of 30 each. Group I received 10 ml 0.125% solution of levobupivacaine + 50 µg fentanyl. Group II received 50 mg tramadol instead of fentanyl. Epidural top ups were given when parturient complained of two painful contractions (visual analogue scale ≥ 4) with 3 ml of respective solution to each group. Data collected were demographic profile of the patients, analgesic qualities, side- effects and the fetomaternal outcome.

RESULTS: Patients in Group II had significantly prolonged analgesia (145 ± 9 minutes) than in Group I (95 ± 7 minutes). Patients receiving fentanyl showed rapid onset of analgesia, but there were more incidence of side-effects like shivering, pruritus, transient fetal bradycardia, hypotension, nausea and vomiting. Only side-effect in the tramadol group was nausea and vomiting. During labor, maternal satisfaction was excellent.

CONCLUSIONS: Adding tramadol to local anesthetic provides prolonged analgesia with minimal side effects. Fentanyl, when used as adjuvant to local anesthetic, has a rapid onset of analgesia but has certain fetomaternal side-effects.

KEYWORDS

epidural, fentanyl, labor analgesia, levobupivacaine, tramadol

INTRODUCTION:

Labor is a painful process of childbirth, which can be the most agonizing event experienced by the majority of women. This distress may harm the mother and fetus. Painful labor often results in excessive maternal stress, mechanical workload, increased oxygen demand and hyperventilation resulting in increased catecholamines secretion leading to uterine vasoconstriction, increased uterine contractility, hypoperfusion of the fetoplacental unit, fetal hypoxia and acidosis. These responses can easily be obtunded by providing analgesia during labor. Epidural nerve block is widely used for labor analgesia because of its effective pain relief, reduced maternal stress response, improved parturient satisfaction, and potential ability to provide anesthesia. [1]The addition of lipophilic opioids to local anesthetic for neuraxial analgesia increases the duration of sensory block.[2] Levobupivacaine is a newer local anesthetic agent, which is found to have lesser motor blockade and toxic effects, making it a preferred local anesthetic for walking labor analgesia. [3]

The present study was designed to compare fentanyl and tramadol used in epidural analgesia in labor. The following parameters were noted : the onset and duration of analgesia, motor block, maternal and fetal outcomes, incidence of side-effects like pruritus, nausea, vomiting, headache, shivering and fetal heart rate changes.

MATERIAL AND METHODS:

This was prospective, randomized, double-blind study conducted in our hospital after ethics committee approval on 60 primiparous, American Society of Anesthesiologist (ASA) grade I and II parturient consenting for labor analgesia. The study design was developed in association with the obstetrician of our hospital. The women included in the study had singleton pregnancy with vertex presentation, cervical dilatation of 3-5 cm and had no contraindication for labor analgesia, were randomly allocated in two groups of 30 each using sealed envelopes:

Group I received 10 ml 0.125% solution of levobupivacaine with 50 µg fentanyl.

Group II received 10 ml 0.125% solution of levobupivacaine with 50 mg tramadol.

Double blinding in any clinical trial is used to remove any possibility of bias by keeping both the experimenter and the subject from knowing what is being tested. In our study, the patient as well as the anesthesiologist administering the drug did not know which drug was used. The drug was prepared by another anesthesiologist who was not directly involved in the study.

Exclusion criteria consisted of patients of ASA grade III and IV, patients having bleeding diathesis and on anticoagulant therapy, raised intracranial tension, cephalopelvic disproportion, preterm gestation, deformity of vertebral column, e.g., scoliosis and kyphosis, preexisting neurological deficits in the lower extremities, any sign of infection at puncture site, history of cardiac arrhythmias, hypertension, history of anaphylaxis to local anesthetic and drugs to be used, gestational age <35 weeks, nonsingleton pregnancy, nonvertex presentation and body mass index of 35 or more.

Before the initiation of analgesia, the following parameters: Maternal age, height, weight, gestational age, cervical dilatation, use of oxytocin and parity were recorded. Baseline pain score was assessed using visual analogue scale (VAS) (VAS; 10 cm; 0 = no pain and 10 = worst imaginable pain) before the epidural analgesia. An intravenous (i.v.) access was achieved in every parturient and preloading was done with 10 ml/kg body weight of lactated Ringer's solution. The epidural analgesia was performed with parturients in left lateral position, under all aseptic precautions at L2-L3 or L3-L4 level. Epidural space was sought with the help of 18-gauge Tuohy's needle using loss of resistance technique. Epidural catheter was threaded through the needle, aspirated to confirm the absence of blood or CSF, but test dose was not administered because administration of traditional epidural test dose causes unwanted loss of proprioceptive and motor functions, the preservation of which are necessary to permit safe ambulation in labor. The study drug was given to each patient as per group allocation. The parturient was turned supine, and a wedge was placed under the right buttock to prevent aortocaval compression.

Maternal blood pressure, heart rate, respiratory rate, oxygen saturation were measured noninvasively by a blinded observer every 2 minutes for 10 minutes, then every 5 minutes for 30 minutes, every 15 minutes for 120 minutes, every 20 minutes from 120 to 300 minutes or delivery of fetus whichever was early. Maternal hypotension was defined as a fall in systolic blood pressure of >20% from the baseline and was treated by giving i.v. fluid boluses and if necessary, giving i.v. ephedrine. Fetal heart rate was also monitored with continuous cardiotocography throughout the study. At any evidence of fetal

bradycardia, obstetrician was consulted when necessary.

Time of onset was taken as the time between epidural injection till the time when parturient became pain-free (VAS = 0). Duration of analgesia was taken from epidural injection to the time of request of additional analgesia for painful contractions (VAS ≥ 4). Highest dermatome level, degree of motor block using modified Bromage scale and side effects were assessed and documented. The highest dermatome sensory block was tested in each dermatome bilaterally for the loss of pinprick sensation using 26-gauge needle. Patients satisfaction score was noted at follow-up visit after 24 h of delivery with a scale; 5 – excellent, 4 – very good, 3-good, 2-fair, 1-poor.

Modified Bromage Scale :
Grade 0 Able to raise the whole lower limb at the hip
Grade 1 Able to flex the knee but unable to raise the leg at hip
Grade 3 Able to planter flex the ankle but unable to flex the knee
Grade 3 No movement of lower limb

Statistical analysis:
The data was analyzed using "Statistical Package for the Social Sciences" version 17.0 (SPSS Inc., Chicago, USA). Patient and obstetric data are presented as the mean ± SD or % or number of patients, as appropriate. Analysis was carried out using Chi-square test and Student's unpaired *t*-test for nonparametric and parametric data respectively. The *P*-value was set as the level of significance, if <0.05 = significant at 5% significance level; if $P < 0.01$ = significant at 1% significance level and a $P < 0.001$= highly significant. The sample size of this study was computed by difference in duration of analgesia between the two groups with a power >95% and α = 0.05.

RESULTS:

Among 60 parturients enrolled in the study, none of them were excluded out of the study for any reason. There were no technical problems in inserting the epidural catheters. There was no incidence of any cesarean section or instrumental delivery.

Patients in both the groups were comparable in their demographic profile.

Table 1: Demographic Data and Obstetric Parameters

Parameters	Group I (n=30)	Group II (n=30)	P value	Significance
Age (in years)	23.73±2.97	24.37±3.42	0.447	NS
Height (in cm)	154.43±4.72	152.3±2.58	0.059	NS
Weight (in kg)	59.8±6.5	58.7±6.2	0.505	NS
Cervical dilatation (in cm)	4.47±0.5	4.57±0.5	0.447	NS
Pain score on VAS(preblock)	9.23±0.57	9.77±0.63	0.274	NS

NS: Nonsignificant; VAS: Visual Analog Scale

Table2 : Parturient analgesic quality

Analgesic Quality	Group I (n=30)	Group II (n=30)	P value
Onset of analgesia (in mins)	10.85±0.49	14.57±0.5	0.000*
Duration of epidural analgesia (in mins)	95.67±7.96	145.8±9.11	0.000*
Highest dermatome of epidural analgesia (median)	T6	T6	1.000
Time to reach highest dermatome (in mins)	10.48±1.09	14.7±2.27	0.000*
Motor block (median Bromage score)	0	0	0.150
Duration of labour (in mins)	713.8±105.11	753.1±79.83	0.108
Duration of first stage of labour (in mins)	574.97±103.4	604.17±77.9	0.222
Duration of second stage of labour (in mins)	132.53±18.35	141.2±16.75	0.061
Epidural to delivery interval (in mins)	215±37.03	231±35.38	0.090
Number of Patients that required epidural top up (%)	30(100)	29(96.7)	1.000
Patient satisfaction score	4.8±0.01	4.83±0.01	0.744

*Significant

Table 3 : The APGAR score of newborn and maternal side-effects.

PARAMETERS	GROUP I (n=30)(%)	GROUP II (n=30)(%)	P value
APGAR score (≥8) 1 minutes 5 minutes 10 minutes	28(93.3) 30(100) 30(100)	30(100) 30(100) 30(100)	0.521 0.061 0.105
Hypotesion	1(3.3)	0(0)	0.508
Pruritis	7(23.3)	0(0)	0.005*
Nausea/ vomiting	5(16.7)	11(36.7)	0.000*
Respiratory depression	0(0)	0(0)	NA
Shivering	7(23.3)	0(0)	0.005*
Headache	0(0)	0(0)	NA
Urinary retention	0(0)	0(0)	NA
Transient foetal bradycardia	5(16.7)	0(0)	0.020*

*Significant; NA: Not available

DISCUSSION

The epidural analgesia technique is gaining popularity because of its rapid and reliable onset of analgesia with lower dose of anesthetic, minimal motor blockade [4,5] and the flexibility to prolong the duration of analgesia as per the duration of labor. Although neuraxial techniques provides excellent pain relief during parturition but may affect the progress and outcome of labor. Obstetricians and anesthetists have always feared the increased incidence of instrumental deliveries in women receiving labor analgesia as compared to those who do not receive it. [6] Factors contributing to instrumental delivery include diminished pain and sensation from uterine contraction leading to diminished Fergusson's reflex, the perception of the need to push at full dilatation, reduced motor force due to weakened abdominal musculature and inadequate rotation of the presenting part due to weakened pelvic floor musculature.[7]

"Walking epidural" is preferred for labor analgesia as ambulation in labor increases the intensity of uterine contractions and may, therefore, result in more effective progression of labor. [8] Levobupivacaine causes lesser motor blockade as compared with bupivacaine and is therefore preferred.

Cervical dilatation at the time of initiation of labor analgesia has an impact on the outcome of labor. Most observational studies showed a higher rate of caesarean delivery when labor analgesia was initiated early in labor (≤2 cm). The American College of Obstetricians and Gynaecologists statement had suggested that EA may be delayed until a cervical dilatation of 4-5 cm is reached based on the study published by Pandya. [9] However, a recent report by the ASA task force on Obstetric Anesthesia concluded that cervical dilatation at the time of epidural administration does not impact the outcome of labor. [10] In our study, we appropriately timed the initiation of analgesia at cervical dilatation between 3 cm and 5 cm.

The mean onset of analgesia of patients in Group I was 10.85 ± 0.49 minutes and Group II was 14.57 ± 0.50 minutes. Onset of sensory block in Group I was found to be earlier than in Group II. Frikha *et al*., [11] in their study comparing sufentanil 2.5 mg and tramadol 25 mg concluded that sufentanil group had a rapid onset of analgesia than tramadol combined to intrathecal bupivacaine.

The mean duration of epidural analgesia was significantly greater with Group II 145.83 ± 9.11 minutes than Group I which was 95.67 ± 7.96 minutes with a $P = 0.001$. In a study done by Chan and Chiu [12] using 2.5 mg levobupivacaine and 25 µg fentanyl intrathecally, the duration of analgesia was 101.4 ± 26.64 minutes. Hepner *etal*., [13] in their study comparing CSEA and epidural analgesia (EA) showed the duration of epidural component of CSE group to be 91.1 ± 32.6 minutes. Pascual-Ramirez *et al*., [14] compared CSEA and EA on labor and delivery durations and found the average duration of epidural analgesia to be 113 ± 93 minutes.

Continuous search for balanced labor analgesia that provides relief from pain, while preserving motor function, has led to the development of an ambulatory labor analgesia technique. In our study grade of motor blockade was measured using Bromage scale. 93% patients had grade 0 motor blockade, and none of the patients had grade 2 and 3

blockade in both the groups with $P = 0.067$. Vercauteren *et al*., [15] comparing bupivacaine and levobupivacaine found bromage 1 motor block in 34% patients in the bupivacaine group and no motor impairment in levobupivacaine group.

The most common side effect experienced by our patients in fentanyl group was pruritus in 7 patients; hypotension in 1 patient; nausea and vomiting in 5 patients; shivering in 7 patients and transient fetal bradycardia in 5 patients. The only side-effect noticed in the tramadol group was nausea and vomiting seen in 11 patients. The fetal outcome of all the babies was good in both the groups. APGAR scores were favorable at 1 minutes, 5 minutes and 10 minutes. Palmer *et al*., [16] in a retrospective study compared the incidence of fetal heart rate abnormalities after institution of two techniques of labor analgesia (either subarachnoid fentanyl or conventional epidural labor analgesia). Both techniques were associated with 6-12% incidence of fetal heart abnormalities and no difference in neonatal outcome was found.

Our study demonstrated that fentanyl group provides rapid onset of analgesia compared to tramadol group, but tramadol gives longer duration of analgesia. Major side effect in the tramadol group was nausea and vomiting which is attributable to its action through 5-hydroxytryptamine receptors. [17,18] whereas shivering, pruritus, transient fetal bradycardia were seen predominantly in the fentanyl group. Patient satisfaction score was also better in the tramadol group.

The obvious limitation of our study, cord blood pH, which is an objective retrospective measure of the fetal exposure and response to hypoxia during labor and the timing of cord blood clamping, is critical for the interpretations of cord blood gases. All these could not be done effectively in our setup due to some technical issues. The result of our study could have been more precise if the sample size of study group would have been large, but the patients willing for labor analgesia were limited in our institution. Also, we had no control group of patients who received either i.v. labor analgesia or who did not receive any analgesia, so we could not comment on prolongation of the second stage of labor or overall duration of labor.

CONCLUSIONS

We concluded that epidural fentanyl combined with levobupivacaine provides rapid onset and profound analgesia with some maternal and fetal side-effects, whereas epidural tramadol with levobupivacaine provides longer-lasting analgesia. The major side-effect is vomiting. Labor analgesia in both the groups was effective and patients were hemodynamically stable throughout the labor. Although both drugs could be used to provide pain relief during labor, epidural tramadol was better with respect to prolonged analgesia and lesser side-effects.

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