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ORIGINAL RESEARCH ARTICLE

EPIDURAL TRAMADOL IMPROVES THE QUALITY OF PAIN RELIEF DURING LABOR

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ABSTRACT

To study the analgesic efficacy and side effects of Tramadol for painless labor in combination with Bupivacaine. Randomized, controlled, double blind, open prospective study conducted at Department of Obstetrics and Gynaecology, Chitwan Medical College from July 1st 2015 to June 30th 2016. 100 patients of ASA Grade I and II, aged between 20-35 years willing for epidural analgesia for labor pain were included in the study. They were divided into two groups: Group A- Control group and Group B- Study group. Subjects of Group A received 10 ml of 0.25% Bupivacaine and that of Group B received 10ml of 0.25% Bupivacaine with 1mg/kg body weight of tramadol. Analgesic efficacy was assessed by Visual Analogue Scale (VAS) and other vital parameters (Blood Pressure, Heart Rate and Respiratory Rate) before the administration of the drug and at different time intervals of 0, 5 min, 10 min, 15 min, 30 min, 45 min, 60 min and every hourly up to maximum of 5 hrs. Neonatal out comes were assessed by the use of APGAR scores and the side effects of the drugs in two groups were also evaluated. Total number of patients was 100, of ASA Grade I and II, aged between 20-35 years. The mean age of patients in Group A was 23.54 ± 3.74 years and 24.22 ± 3.64 years in Group B. Mode of delivery was spontaneous vaginal in 42 patients (84%) in group A and 45 patients (90%) in group B. Instrumental vaginal delivery was done in 1 patient (2%) of group A and none of group B. Cesarean section was done in 7 patients (14%) of group A and 5 patients (10%) of group B. There was no significant difference in heart rate, blood pressure and respiratory rate at various time intervals. Pain score of Group B was significantly less at 60th min and had lower values than Group A at various time intervals. Time for first top up was significantly delayed and the total dose of bupivacaine was significantly lower in Group B patients but the incidence of nausea and vomiting was significantly high among Group B patients. At one minute majority of the babies of group A had mean APGAR score 6.98 ± 0.55 versus 7.18 ± 0.60 in group B. At 5 minute, Group A had mean score of 8.02 ± 0.47 versus 8.22 ± 0.58 in Group B. There were no significant differences in 2 groups. In both the groups there was no significant effect on duration of second stage of labor and it wasn't prolonged in any of the patients. Epidural anesthesia with bupivacaine and tramadol provided better pain relief and reduced the total dose of bupivacaine in majority of the patients with no adverse effects on mother and fetus. As tramadol is cheap, safe and effective, it can be considered as a better option to improve quality of pain relief during labor.

Key words: *Bupivacaine, Epidural analgesia, Painless labor, Tramadol.*

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INTRODUCTION

Labor pain is as old as man and one of the worst pains experienced by women. Pain in itself is a protective biological mechanism but the physiological and psychosocial issues associated with it, can harm the individuals so some form of analgesia should be offered to all parturients to reduce harmful effects on mother and fetus[1]. Maternal respiration increases by 75–150% during the first stage of unmodified labor. At the same time, maternal anxiety is associated with increased plasma catecholamines and cortisol which activates the stress response. This leads to release of ACTH and cortisol which in turn may lead to incoordinate uterine action and reduced uteroplacental perfusion[2-3]. Labor pain relief is one of the important aspects related to women health that has long been neglected. Effective epidural analgesia reduces maternal plasma concentration of the catecholamine. Decreased alpha and beta receptor stimulation may result in improved uteroplacental perfusion and more effective uterine

activity[4]. Epidural anesthesia along with a skilled anesthetist, a faithful obstetrician and a trained midwife can convert the painful labor into a less stressful event [5].Delivery of the infant into the arms of conscious and pain free mother is one of the most rewarding feelings in medicine[6].

Currently different modalities, pharmacological and non-pharmacological, are being tried for alleviation of labor pain. The only consistent effective method of labor pain relief, epidural analgesia, has undergone substantial improvement addressing concerns of both parturients and care providers. The term 'Epidural' refers to the space where local anesthetic is injected which is bounded anteriorly by posterior longitudinal ligament, posteriorly by ligamentum flavum and vertebral lamina, laterally by the vertebral pedicles and caudally by sacrococcygeal ligament covering sacral hiatus.

Epidural anaesthesia is generally associated with prolonged labor which in turn leads to increased assisted vaginal delivery. Blockade of sympathetic tone may lead to fall in blood pressure due to vasodilation. Bupivacaine is most suitable drug due to its prolonged action and has been extensively studied for analgesia for both obstetric and non-obstetric purpose. Bupivacaine 0.125%- 0.5% has been extensively used for labor analgesia. Tramadol, on the other hand, is a synthetic analgesic with weak μ receptor agonist and non-opoid spinal and CNS effect via norepinephric and serotoninergic pathway[7]. Tramadol is therefore both an opoid and non-opoid analgesic with minimal sedation, respiratory depression, gastrointestinal stasis and abuse potential. There is low incidence of respiratory and cardiac depression in neonates and also produces effective analgesia in laboring mother with minimum adverse effects[8].

MATERIALS AND METHODS

This case controlled, randomized, double blind, open prospective study was conducted in the labor ward of Chitwan Medical College and Teaching Hospital. The study protocol was approved by the Institutional Ethics Committee. 100 patients of ASA Grade I and II, aged between 20-35 years, willing for epidural analgesia were selected. Women with mal presentation, multiple pregnancy, ante-partum haemorrage, uncorrected hypovolemia, coagulopathy, infection at local site/generalized sepsis, acute fetal distress, known allergy to local anaesthetics, uncontrolled cardiac/neurological disease and severe systemic disease were excluded from the study. All enrolled women provided written informed consent for participation. Women were allocated to one of two groups using a computer-generated randomization sheet. Group A (control group) received 10 ml of 0.25% bupivacaine through epidural catheter and Group B (study group) received 10 ml of 0.25% bupivacaine with 1mg/kg body wt of tramadol. The obstetrician was consulted to confirm that the patients were in active labor and fetal well being was assessed in consultation with obstetrician. Pre-anaesthetic evaluations were performed to all patients including all relevant past history. An IV access was secured with 16G cannula and all necessary monitors were attached like NIBP, ECG and SpO2. All patients were preloaded with 20ml/kg body weight of Ringer's lactate solution to diminish the incidence of maternal hypotension and fetal heart rate troubles. Under complete aseptic condition; 18 gauge Tuohy's epidural needle was placed in L2/3 or L3/4 interspace with patient either in sitting or lateral decubitus position by midline approach. Epidural space was recognized by loss of resistance to air injection using LOC glass syringe. Intravascular or subarachnoid placement was excluded by absence of CSF and blood during aspiration test. Epidural catheter was threaded to the depth of 3-5 cm in the epidural space. A test dose of 3ml of 2% xylocaine with adrenaline (1:200000) was given after careful aspiration. When effect of test dose was negative, 10 ml of 0.25% bupivacaine or 0.25% bupivacaine with 1mg/kg body wt of tramadol was injected to achieve cephalad-sensory level of approximately T10. The initial dose of drug was administered once the labor was well established with strong uterine contraction lasting about 1 min each and occurring every 3 mins apart and dilatation of cervix 3-4cm. After 15 mins, the block was assessed using loss of sensation to gentle pinprick. Top-ups were given whenever the patient stated that they were not comfortable or feeling pain. Tramadol was not included in the top-ups. 8ml of 0.25% bupivacaine was given as top-ups. Before the placement of epidural catheter, the patient were asked to quantify the pain that they had been experiencing on a verbal analogue scale

(VAS) of 0-10 with 0=no pain and 10=the worst imaginable pain. Injections into the epidural space were evaded during contractions and were given in between contractions to avoid the risk of increased spread. Pain was assessed by VAS. Assessment was done before and after the administration of the drug and till full dilatation at (0) then after 5, 10, 15, 30, 45 minutes then at 1 h, 2 h, 3h, 4h and 5 h. All the participants were haemodynamically observed prior to the conduct of analgesia and every 5 minutes following injection. Non-invasive blood pressure

(NIBP), five leads electrocardiogram (ECG), pulse oximetry, heart rate, oxygen saturation and respiratory rate were recorded. Side effects like sedation, vomiting, drowsiness, tachycardia, and fetal distress were noted following the administration of the drug. Maternal sedation was assessed [11]. Intrapartum monitoring was done according to the standard labor ward protocol using the partogram. The time interval between drug administration and delivery was recorded. Labor progress, mode of delivery and side effects of analgesia either maternal or fetal were recorded. Neonatal evaluation was done by the neonatologist using APGAR score. The data were collected from each patient, compiled in a chart and analysed statistically at the end of the study. Results were expressed as mean ± standard deviation (SD). Parametric data was compared using Student's *t*-test. Nonparametric data were compared with Mann-Whitney *U* test. . Proportionate data was compared with Chi-square test. A *P* value of <0.05 was considered significant.

RESULTS

One hundred cases were taken in the study, having ASA physical status Grade I and II, aged between 20-35 years willing for epidural analgesia for labor pain in the duration from 1st July 2015 to 30th June 2016 in Department of Obstetrics and Gynecology, Chitwan Medical College and Teaching Hospital. They were divided into 2 equal groups. All 100 parturients enrolled completed the study. No technical difficulty or inadvertent dural puncture was encountered. Maternal characteristics like age, height, weight and body mass index (BMI) were mentioned in (Table 1). No significant differences were found between both groups. Table 2 showed that Group B had significantly lower heart rate than that of Group A at 45th, 60th and 120th minutes after the block. There were no statistical differences in both groups regarding blood pressure and respiratory rate as p value was >0.05 at various time intervals.

Table 1

Parameters	Group A (n = 50)	Group B (n = 50)	P Value
Age in years (Mean ± SD)	23.54 ± 3.74	24.22 ± 3.65	0.36
Weight in kg (Mean ± SD)	58.86 ± 7.24	57.90 ± 5.14	0.45
Height in cm (Mean ± SD)	163.05 ± 5.30	161.04 ± 6.35	0.78
BMI (Mean ± SD)	23.60 ± 1.39	23.47 ± 1.09	0.58

Table 2

Heart Rate (beats/min)	Group A (n = 50)	Group B (n = 50)	P value
0 min	88.62 ± 13.01	92.00 ± 14.94	0.146
5 min	90.70 ± 13.48	88.86 ± 11.54	0.465
10 min	85.16 ± 10.12	84.88 ± 11.00	0.895
15 min	82.94 ± 15.16	83.74 ± 8.37	0.745
30 min	86.57 ± 11.77	84.30 ± 7.18	0.248
45 min	87.29 ± 8.96	83.60 ± 7.98	0.033
60 min	88.22 ± 8.87	84.10 ± 9.08	0.024
120 min	87.92 ± 9.90	84.66 ± 9.93	0.151
180 min	86.46 ± 24.58	87.10 ± 12.13	0.902
240 min	87.20 ± 9.89	85.00 ± 12.25	0.713

Pain score of patients in Group B was significantly higher at 5th minute but it was significantly less at 60th minute than Group A (Table 3). Table 4 revealed that there was no significant difference between the patients who needed various mode of delivery between two groups. 42 patients in Group A and 45 patients in group B had normal vaginal delivery. Likewise LSCS was done in 7 and 5 patients of Group

A and Group B respectively. There was only one patient in Group A who requires forceps delivery but none in Group B. Table 5 showed that 2 and 10 patients of Group A and B respectively had developed nausea which was found to be statistically significant (p=0.01). 6 patients in Group A had vomiting whereas in Group B, 16 patients developed vomiting which was also statistically significant (p=0.02).

Table 3

Pain Score (Mean ± SD)	Group A (n = 50)	Group B (n = 50)	P value
0 min	94.20 ± 7.85	94.20 ± 8.59	0.92
5 min	26.60 ± 24.71	39.20 ± 24.31	0.012
10 min	4.00 ± 11.43	4.60 ± 13.09	0.80
15 min	1.84 ± 6.67	0.96 ± 4.51	0.348
30 min	1.43 ± 5.77	0.80 ± 3.96	0.528
45 min	2.48 ± 8.92	1.20 ± 6.84	0.240
60 min	7.80 ± 22.79	2.45 ± 9.02	0.01
120 min	11.35 ± 23.23	7.13 ± 22.41	0.419
180 min	23.79 ± 27.05	13.81 ± 28.19	0.212
240 min	20.00 ± 27.39	3.00 ± 9.49	0.093

Table 4

Mode of delivery	Group A (n = 50)	Group B (n = 50)	P value
Normal vaginal delivery	42	45	0.7
Forceps	1	0	-
Ventouse	0	0	-
LSCS	7	5	0.6
Total	50	50	-

Table 5

Side effect	Group A (n = 50)	Group B (n = 50)	P value
Pt who developed nausea	2	10	0.01
Pt who developed vomiting	6	16	0.02

Requirement of 1st top-up was significantly delayed for the patients of Group B (p=0.001) but difference between the time intervals of 2nd, 3rd and 4th top-ups was not significant between two groups. Similarly the total dose of Bupivacaine required for Group B was significantly lower than Group A (p <0.05).There was no significant difference between two groups in the duration of 2nd stage of labor. The second stage was not prolonged in any of the groups. The mean APGAR score of babies at one minute in group(A) was 6.98± 0.55 and at 5 minutes was 8.02± 0.47. While mean APGAR score at one minute in group (B) was 7.18± 0.60 and at 5 minutes was 8.22± 0.58 with no significant difference (Table 6).

Table 6

Parameters	Group A (n = 50)	Group B (n = 50)	P value
Top-up 0- 1st dose in mins (Mean ± SD)	109.97 ± 65.23	165.37 ± 63.00	0.001
Top-up 1st – 2nd dose in mins (Mean ± SD)	88.19 ± 32.76	106.67 ± 63.51	0.423
Top-up 2nd – 3rd dose in mins (Mean ± SD)	86.64 ± 38.24	80.00 ± 00.00	0.667
Total dose of Bupivacaine (mg) (Mean ± SD)	54.20 ± 22.93	37.00 ± 14.57	<0.05
Duration of 2nd stage in mins (Mean ± SD)	29.88 ± 29.31	24.70 ± 18.03	0.290
APGAR score at 1 min (Mean ± SD)	6.98 ± 0.55	7.18 ± 0.60	0.085
APGAR score at 5 min (Mean ± SD)	8.02 ± 0.47	8.22 ± 0.58	0.062
APGAR score at 10 min (Mean ± SD)	9.16 ± 0.51	9.18 ± 0.52	0.847

DISCUSSION

Various pharmacological and non-pharmacological modalities have been tried to alleviate the labor pain. The ideal technique should be safe, effective, easy to administer and should have no adverse effect on mother and fetus. Neuraxial blockade in the form of lumbar epidural comes to ideal[1]. The use of this technique allows the patient to be awake and share the various aspects of birthing process [9]. The purpose of this study was to explore the efficacy of analgesia as well as side effects of Tramadol given for labor pain in combination with bupivacaine. There were two groups of 50 patients each. One

group received 10ml of 0.25% Bupivacaine whereas the other group received 10ml of 0.25% Bupivacaine with 1 mg/kg of Tramadol through epidural catheter. The results of the present study showed that there was better pain control in patients who received combination of tramadol and bupivacaine as shown by VAS score. The higher VAS at 5th minute in tramadol group is most probably because of randomization as pain perception varies between individuals and it is unlikely that epidural block was active within 5 minutes of administration. Lower pain score of patients receiving tramadol at 60th minute which was statistically significant , a trend of low VAS starting from 15th minutes up to 240th minute, and delayed requirement of top-ups also signify that pain control was better with addition of tramadol. Patient receiving tramadol also showed lower heart rate at 45th, 60th and 120th minute after the block signifying better pain control with tramadol. The results of present study also showed that there were no significant changes among fetal heart rate at various time intervals between two groups. The fetal outcome of all the babies was good in both the groups. APGAR scores were favorable at 1 minute, 5 minutes and 10 minutes. These results show that Tramadol does not have any detrimental effect on fetus. . The results are in accordance with previous trials that have documented no statistically significant changes in APGAR score[10-12]. In the present study, there was no statistically significant difference between various modes of delivery between two groups. Zhang et al also showed similar results[13]. Among the patients receiving tramadol, 10 patients had nausea and 16 patients developed vomiting which was found to be statistically significant. Major side effect in the patients receiving tramadol was nausea and vomiting which is attributable to its action through 5-hydroxytryptamine receptor[14, 15].The present study is comparable to study of Long et al[10] and Chatrath et al[12] which also showed similar results. Tramadol is known to cause higher incidence of nausea and vomiting[16]. So drugs to control nausea and vomiting should be given when tramadol is used. The requirement of first top-up was significantly delayed and the total amount of Bupivacaine requirement was also significantly low in patients receiving tramadol. This may be due to the superior analgesic effect and prolonged duration of action of Tramadol added to Bupivacaine[17].

There are some obvious limitations of our study. First, although epidural administration of tramadol has been extensively used for analgesia by numerous investigators in clinical studies, more studies are needed to assess the safety of its intrathecal administration for labor analgesia. Second, 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.

CONCLUSION

Bupivacaine separately and Tramadol in combination with bupivacaine can be used safely for pain relief in labor without any adverse effects on mother and baby. Addition of Tramadol significantly improves the quality of pain relief and also decreases requirement of total dose of drug by delaying top-ups but the problem of nausea and vomiting needs to be addressed. However, these results need to be confirmed with larger prospective trials.

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