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Research Article

Does Early Initiation of Labor Epidural Analgesia Affect Labor Outcomes? A Randomized Clinical Trial

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ABSTRACT

Background: Although epidural analgesia (EA) is a popular and effective method for pain relief during labor, significant controversy exists in terms of the impact of EA on labor outcomes and the best time for initiation of EA. Here, we aim to explore the effects of early initiation EA on the labor process in nulliparous at-term pregnant women.

Methods: A total of 240 nulliparous women enrolled in this study. The early epidural (EE) group (n=120) consisted of women in the latent phase of labor and the late epidural (LE) group (n=120) were in the active phase of labor. Each group received 16 ml of 0.125% preservative-free isobaric bupivacaine with 50 µg fentanyl (total: 17 ml) as a primary bolus dose in the epidural space for labor analgesia and an intermittent bolus of 5-10 ml of the primary solution was administered via a catheter. The length of labor, rate of cesarean section (CS), neonatal well-being, and infant Apgar scores were recorded.

Results: There were no statistically significant differences between the two groups regarding the duration of the first (p=.43) and second (p=.54) phases of labor. No statistically significant differences were observed between the two groups in terms of the rate of CS (p=.21), causes for CS (p=.24), and neonatal Apgar scores (p=0.84).

Conclusion: Initiation of EA during early labor did not result in increased CS or instrumental vaginal deliveries, and did not prolong labor duration.

Introduction

Epidural analgesia (EA), a common method for alleviating labor pain, operates by delivering local anesthetics near the pain-transmitting nerves located in the epidural space. Epidural solutions are delivered through a bolus injection (a large, rapid injection), continuous infusion, or a patient-controlled pump [1].

The optimal timing for the placement of EA remains a topic of debate, and the potential benefits of EA for women in early labor are a matter of ongoing discussion. Previously, it was recommended that physicians should delay administration of EA in nulliparous parturient until cervical dilatation reaches 4-5 cm in order to avoid prolonged labor and reduce the risk for cesarean section (CS) [2]. Although observational data indicates a potential increase in the risk of cesarean section (CS) with early initiation of an epidural, recent randomized controlled trials have not reported the same findings. On the other hand, there is discussion as to whether the choice of local anesthetic influences the mode of delivery [3].

According to a 2014 Cochrane systematic review, there were no observed differences in the risk of CS and instrumental birth between early and late initiation of EA for labor pain relief. However, the patient selection in these evaluated studies was not homogenous [4].

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The purpose of this prospective study is to determine whether early initiation of EA with bupivacaine plus fentanyl in nulliparous women could influence the rate of CS and other obstetric outcome measures.

Methods

The study received approval from the Investigational Review Board at Tehran University's Faculty of Medicine and all participants provided written consent. It was registered with the Clinical Trial Registry under the identifier IRCT20140111016161N6 on March 4, 2018. In total, 240 healthy women who were American Society of Anesthesiology Physical status (ASA) classes I and II, 18-40 years of age, nulliparous at term (≥37 weeks) with labor pain, and stated a preference for an epidural were enrolled in this study. Primary outcomes included the length of the labor and the rate of CS. Secondary outcomes were neonatal well-being and infant Apgar score.

The study participants were divided into two groups of 120 patients per group. Women in group 1 were in the latent phase of labor (early epidural group) and those in group 2 were in the active phase of labor (late epidural group). The inclusion criteria consisted of women who were 37-42 weeks of gestation, planned a vaginal birth, and had a viable single fetus with a vertex presentation. Women were excluded if they had any of the following: preterm labor (<37 weeks of gestation); diagnosed with antenatal conditions such as pre-eclampsia, severe bronchial asthma, history of pelvic trauma, glaucoma, or heart or liver problems; diabetics ,pre-existing hypertension that necessitated treatment; hepatorenal or other end organ disease; treated with opioid agonist or agonist/antagonist in the preceding six hours or within one hour if given intravenously before study enrollment ; or morbid obesity (BMI >40 kg/m2). Patients with coagulation or neurological disorders, spinal deformities, or skin infections were also excluded.

We used the random allocation process with the block method and six blocks to assign the study participants to one of two intervention groups. Random group assignments were made by the epidemiologist and placed in sealed envelopes.

First, patients were placed in the sitting position for administration of intravenous pre hydration with 500-1000 ml of lactated Ringer's solution. Next, an 18-gauge Tuohy needle (Medikit, Gurgaon, India) was used to identify the epidural space in the interspace below L2, by the loss of air resistance. The patients subsequently received a test dose of 3 mL of an intravascular injection of 1.5% lidocaine with 1:200 000 epinephrine. If this test dose was negative (20% increase in maternal heart rate within 20 seconds of the test dose) and intrathecal injection (no signs of motor block after three minutes of monitoring), then 16 ml of preservative-free 0.125% isobaric bupivacaine in 50 µg fentanyl (17 ml) was injected for labor analgesia.

Next, a clear catheter with 20 gauge and closed Tip-3 lateral eyes (Medikit, Gurgaon, India) was inserted in the patient's epidural space while the patient remained in the sitting position. The catheter was secured in place with tape, leaving a length of 3-4 cm in the epidural space. Following the block, patients were positioned supine with left uterine displacement. Throughout labor, patients were closely monitored using electrocardiogram, pulse oximeter, and non-invasive blood pressure readings taken every 5 minutes for the first 30 minutes, and then every 15 minutes thereafter. Additionally, a fetal heart monitor was attached to the patient.

Midwives documented the following parameters: maternal heart rate and blood pressure, sensory level using the pinprick method, pain score assessed via the verbal analogue scale, motor block evaluated using the Bromage scale, fetal heart rate monitored with a fetal Doppler, labor progression tracked using a partograph, and any occurrence of adverse events.

Patients in both groups who experienced pain greater than four (VAS) and requested additional medications, received an intermittent bolus of 5-16 ml of the primary solution (administered via the epidural catheter), provided the delivery was not imminent.

The patients were allowed to ambulate provided there was no detectable motor block and the fetal heart rate pattern was normal. All of women were asked to immediately state the onset of their relief from pain.

We recorded and analyzed the time of the active phase of labor, phases 1 and 2, and analyzed the rate of CS and normal spontaneous delivery (NSD), as the predefined primary study outcomes.

Apgar scores at one and five minutes were recorded. The tip of catheter was also checked once the catheter was removed from the patient.

Statistical Analysis

We referred to the Naik et al. study where they reported effacement at the start of the epidural in the EE and LE groups (89.40 ± 3.73 and 87.20 ± 4.53, respectively) [2]. We took into consideration a 0.05 type I error, power of 0.8, and the possibility of 20% attrition in each group to derive a total sample size of 140 patients with 70 per group.

To maintain random allocation, the intention-to-treat method was generally employed for data analysis. The data from the study were analyzed using STATA statistical software (version 13). Qualitative data analysis utilized the chi-square and Fisher's exact tests, while quantitative data analysis employed the independent t-test or Mann-Whitney non-parametric test based on the data distribution in the statistical population. Statistical significance was set at a p-value of less than 0.05.

Results

A total of 240 pregnant women (120 per group) were enrolled in this study, and all of them were included at final analyses. The mean ± SD age of participants was

significantly higher in the EEA group compared to LEA group (25.27 ± 4.85 vs 23.25 ± 3.88 respectively; P-value: 0.0001). The other baseline characteristics including the weight, height, and gestation age were similar between the groups. Demographic and baseline characteristics of participants are showed at (Table 1).

As we presented at table 2, duration of the first phase of labor was slightly shorter in LEA group (156.75 ± 79.46 minutes) in comparison to EEA group (185.60 ± 112.47 minutes), however this difference was not statistically significant (P value: 0.43). Results were reversed for the second stage of labor, as the LEA group had a non-significant longer second phase compared to EEA group (59.07 ± 33.56 minutes, vs 50.16 ± 28.95 minutes, P value: 0.54).

CS rate were 29 (24.4%) in the EEA group and 23 (19.2%) in the LEA group; however, this difference was not statistically significant (p=0.21). The causes for CS are also showed at (Table 2). There was no statistically significant difference between the two groups for the causes of CS. The mean Apgar scores at one minutes after birth for the EEA and LEA groups were 8.67 ± 1.16 and 8.71 ± 0.82, and at five minutes after birth were 9.85 ± 0.39 and 9.85 ± 0.42, respectively. There were no statistical differences in terms of neonatal Apgar scores at one and five minutes between the two groups (p= 0.84 and p=0.18, respectively).

Table 1- Demographic and baseline characteristics of two groups

	EEA group	LEA group	P value
Maternal age (years) [a]	25.27 ± 4.85	23.25 ± 3.88	0.0001
Weight (kg) [a]	65.51 ± 11.17	65.53 ± 11.98	0.59
Height (cm) [a]	160.45 ± 5.3	160.73 ± 6.43	0.79
Gestational age (weeks) [a]	39.4 ± 1.08	39.1 ± 1.1	0.16

a: Data Presented as mean ± standard deviation and analyzed by T-test; EEA: Early epidural analgesia; LEA: Late epidural analgesia

Table 2- Comparison of labor properties and mood of delivery between the two groups

	EEA group	LEA group	P value
First phase of labor [a]	185.60 ± 112.47	156.75 ± 79.46	0.43
Second phase of labor [a]	50.16 ± 28.95	59.07 ± 33.56	0.54
C/S rate [b]	29 (24.2)	23 (19.2)	0.21
Indication of C/S [b]			
Labor arrest I	12 (41.4)	4 (17.4)	0.10
Labor arrest II	4 (13.8)	2 (8.7)	
Fetal Distress	13 (44.8)	17 (73.9)	
Apgar I * [a]	8.67 ± 1.16	8.71 ± 0.82	0.84
Apgar II * [a]	9.85 ± 0.39	9.85 ± 0.42	0.18

a: Data Presented as mean ± standard deviation and analyzed by T-test; b: Data Presented as n (%) and analyzed by chi-square test; EEA: Early epidural analgesia; LEA: Late epidural analgesia; CS: Cesarean section; Labor arrest I: Labor arrest at first stage of active phase (6 cm to full 10 cm cervical dilation); Labor arrest II: Labor arrest at second sage of active phase (full dilation to delivery); Apgar I: Apgar Score 1 minutes after birth; Apgar II: Apgar Score 5 minutes after birth.

Discussion

The best time for initiation of EA in labor is under debate. Most believe that early onset labor epidural analgesia doesn't lead to ideal result and may increase the cesarean rate. Our findings in this study suggest that early EA in nulliparous women is not associated with a high incidence of CS. Early analgesia administration during labor did not have any negative effect on labor progression and fetal well-being during labor, in our study. Although these results support previously reported findings [5-6], others have reported different results [7]. The use of a high concentration of local anesthetic (0.2%-0.25% bupivacaine) to maintain EA during labor may explain the observed difference. Recent trends towards the use of a less concentrated local anesthetic (0.0625%-0.1%) in conjunction with lipophilic opioids like fentanyl or sufentanil have led to improved labor results and a decrease in adverse effects, including motor blockage.

Some clinicians suggest that EA may decrease the CS rate in nulliparous women by alleviating pain and elevating the threshold of a mother's tolerance for pain [8].

In this study the duration of the latent phase and second stage of labor were not higher in the EE group, which was similar to the outcomes of other studies [9]. However, Zha reported a longer labor time in their early group of patients [10]. According to Lipschuetz M. research, although EA increased the labor time, they observed no differences between early and late timing of the epidural [11]. According to a study by Naik and colleagues, the active phase of the first stage in a vaginal birth was found to be shorter when EA was administered early, as compared to later administration. This difference might be due to administration of ropivacaine as the local anesthetic for EA or their patient selection, and they included multiparous patients [2].

A Cochrane systematic review published prior to 12 February, 2014 summarized the best available evidence

in terms of the effectiveness and safety of early initiation versus late initiation of EA in spontaneous and augmented labor. There was considerable variation in the study results concerning the length of labor's first stage. This inconsistency may be attributed to differences in the studies' definitions of early and late EA initiation, as well as variations in EA's dosage, concentration, and application method. [4].

We found the timing of initiation of EA also did not influence Apgar score and fetal well-being, which supported the findings of other studies [12-13]. According to some meta analyses, EA did not negatively impact neonatal outcome [14].

In this study we focused on primi parous mothers, because due to the longer labor time in this group, it is possible to study the latent and active phase time more accurately.

Limitations

Our study had some limitations, including refusal from some obstetricians for early EA administration and their concern about its probably adverse effects on labor progression. Furthermore, there was a decreased tendency for an instrumental delivery in our obstetricians, which might influence the CS rate. We used the intermittent bolus method for administration of EA. In the future, continuous epidural infusions and precise control of potential confounders should be assessed to verify the outcomes of this study.

Conclusion

Early initiation of EA in labor doesn't have any effect on cesarean section rate and dosent increase labor duration, and other labor outcome like instrumental delivery, full arrest, neonatal apgar score are not affected by the EA start time and we can do EA in any mothers who is in pain with any cervical dilatation.

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