Epidural analgesia for labor pain: what has changed in the last 1 year? Literature review and clinical results our experience in labor analgesia

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Labor analgesia effectiveness

Abstract
Aim: The technique of epidural analgesia is the most accepted method of labor analgesia in the contemporary world because it allows the mother to participate both in the physical and emotional aspects of the delivery as well as eliminating the pain that occurs during labor. The aim of our study is to investigate the effects of epidural analgesia on mother, fetus, and labor. Material and Method: Files of pregnancies underwent epidural labor analgesia were reviewed retrospectively. Demographic data, hemodynamic parameters, Activity, Pulse, Grimace, Appearance, Respiration scores (APGAR scores), durations of first and second stages of labor, side effects, drug doses and amounts, VAS and VRS scores, maternal satisfaction ratings were examined. Results: In the primiparous group there is a moderate positive correlation between the total dose and Verbal Rating Scale 2 (VRS 2) and Visual Analog Scale 2 (VAS 2), (p-values are \( p<0.001 \), \( p<0.001 \) respectively). In the multiparous group, there is a strong positive correlation between VRS 2 and VAS 2 (p-values are \( p<0.001 \), \( p<0.001 \) respectively). There is also a moderate positive correlation between the total dose and VRS 2 and VAS 2 when all pregnant women are examined (p-values are \( p<0.001 \), \( p<0.001 \) respectively). It was observed that epidural analgesia had no effect on the 1st and 5th minute APGAR scores. There was a significant moderate positive correlation between total dose and duration of labor (p<0.001). Discussion: The use of epidural analgesia, during labor that generates intensive maternal pain and stress, when done by specialists, allows a highly satisfactory and comfortable labor by reducing pain of the mother.

Keywords
Labor Pain; Epidural Analgesia; Maternal Satisfaction Level; Bupivacaine; Fentanyl

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Introduction

Labor pain is a cause of stress and anxiety that exhausts the mother mechanically increases the need for hyperventilation and oxygen. Labor pain causes maternal metabolic acidosis and decrease in uteroplacental blood flow in the result of sympathetic stimulation and changes it causes in response to stress and anxiety. This condition disrupts fetal oxygenation [1]. Pain leads to changes similar to stress response that occurs during surgery. Although anxiety plays a role, pain is a more important factor. Gastrin hormone secretion has been stimulated during painful labors. It is also suggested that excessive sympathetic activity is responsible for the increased uterine contractility and prolongation of labor. It is important to eliminate labor pain in these conditions [2]. Although labor analgesia is technically quite easy, the most important difficulty seems to be that application is not becoming widespread. In this respect, perhaps one of the underdeveloped subjects in our country is obstetric analgesia/anesthesia. The effects of this are very important for those young mothers who are afraid of pain and directed to cesarean section because the labor pain cannot be remedied adequately. In recent years, cesarean section has been perceived as practically a normal form of delivery rather than an operation performed only in cases with indications in our country [3]. The risk of maternal mortality and morbidity form general anesthesia which is widely used with cesarean section in our country is sixteen times higher than from regional anesthesia [3]. In addition, since fluid in the lungs couldn’t be ejected by pressure on the chest wall, the risk of the newborn transient tachypnea is high in these babies [4]. It shows the importance of normal vaginal delivery and therefore the importance of painless labor. In our study, we aimed to compare the combination of bupivacaine and fentanyl by intermittent bolus application, for the epidural method for painless labor, in terms of pain relief, drug consumption, maternal and neonatal side effects.

Material and Method

The approval of the Ordu University Faculty of Medicine Clinical Research Ethics Committee dated 12.07.2018 and numbered 2018/15 was granted for retrospective examination of the painless labor practices between the dates of 1 August 2017 and 1 August 2018 at the Maternity Department, Ordu University Faculty of Medicine Education and Research Hospital. The files of patients, who were administered electively for labor by the Gynecology and Obstetrics Department and admitted to the painless labor protocol that is routinely performed in our clinic, were retrospectively examined. Demographic information of the pregnancies appropriate for inclusion criteria (protocol, age, weight, height, gravidity, parity, gestational week) was recorded. Patients taken into the study were divided into two groups as a primiparous and a multiparous group. Our painless delivery protocol routinely applied in our clinic was as follows: after the patients were taken to the labor room, fetal heart rate reactivity was monitored by intermittent cardiotocography as fetal heart rate monitoring by the obstetrics team. When the cervical span ≥ 4 cm, detected by an intermittent vaginal examination also performed by the obstetrics team, our anesthesia team is also informed about it. The patients are monitored (electrocardiography (ECG), sPO2 (pulse oximetry), noninvasive blood pressure (NIBP), peripheral vascular access is created with 20 Gauge catheter, and fluid replacement is performed with 15 ml.kg-1 5% dextrose 0.45% NaCl solution for all the patients. Patients are taken to sitting position or left lateral position and procedure is performed for epidural anesthesia according to the required asepsis and antisepsis rules. Skin and subcutaneous anesthesia is produced by 2 ml of lidocaine 2% solution (Jetmonal 2% ampule, Adeka pharmaceutical, Turkey) by determining (Lumbar) L3-L4, L4-L5 intervertebral disc spaces in the physical examination with reference to the iliac crest. Using the Tuohy 18 Gauge needle, entry of the needle into the epidural space was identified by the loss of resistance technique and the catheter was advanced 3-4 cm in length in the cranial direction. Lidocaine 40 mg (2%) was injected into the catheter as a bolus test dose. When it was confirmed that there was no motor block, the portion of the catheter outside the skin was fixed from the waist to the shoulder. All hemodynamic data of the mother during the procedure were recorded at each step of the procedure. After the epidural catheterization procedure, patients were brought into left lateral recumbent position to prevent the compression of the inferior vena cava by the weight of the uterus. Hemodynamic values at this stage were recorded. A 20% decrease in blood pressure or 90 mmHg of systolic arterial pressure was assessed as hypotension and an intravenous administration of ephedrine 5 mg/ml was planned if necessary. The mixture prepared for analgesia was 5 ml (0.5%) bupivacaine and 50 μg (micrograms) fentanyl, diluted with 5cc 0.9% NaCl solution completed to 10 ml was used. Bupivacaine solution (10 ml) 0.25% was used. All patients were evaluated with Visual Analogue Scale (VAS) and Verbal Rating Scale (VRS) after catheterization, and if VAS ≥ 4, 5cc solution was applied as a second bolus through the epidural catheter. Thus, a total of 25 mcg fentanyl and 10 mg (milligrams) bupivacaine were administered as the second dose. Hemodynamic parameters were recorded, at intervals of 5 to 15 minutes after the application, at intervals of 15 minutes to 1 hour after the application, and at intervals of 30 minutes to 1 hour after the insertion of the catheter and until the completion of the delivery. Throughout the whole labor, labor data (cervix dilation) acquired from gynecology and obstetrics specialists were added to the follow-up form. Correlation between the duration of regional block data and stages of labor, of the patients whom epidural analgesia follow-ups were performed, was investigated. Motor block (Bromage scale), sensory block (Pinprick test) and pain (VAS, VRS) assessments were recorded as regional block data, simultaneously with the hemodynamic parameters.

Bromage Scale:
0: No block.
1: With foot flexion, with knee flexion or without.
2: No knee flexion, foot flexion is minimal.
3: The leg and foot were not able to make any movements (full paralysis).

The type of delivery was recorded as normal birth, assisted delivery (forceps and vacuum) or cesarean section. The 1st and 5th minute APGAR scoring system (Activity, Pulse, Grimace, Appearance, Respiration score) was used for the evaluation of...
the newborn. The total dose and the number of boluses of the epidural analgesia applied were recorded. The cases with interventional delivery and cesarean section were excluded from the study.

The total dose of ephedrine administered for all cases was recorded. Adverse reactions (itching, sedation, nausea, vomiting, hypotension, tremor, back pain) during and after the application of regional epidural analgesia in all patients were planned to be recorded.

The patients were informed about the VAS score where 0 = no pain, 1 = very mild pain, 2 = mild pain, and 10 was said to be the most severe pain that is possible; pain scores were recorded. VRS was described as following: 0 = no pain, 1 = mild pain, 2 = tolerable pain, 3 = severe pain, and pain scores were recorded as VAS 1, VRS 1 when the first epidural was administered through the catheter; as VAS 2, VRS 2 at the time when the second dose was administered; and as VAS end, VRS end at the time when the episiotomy suture is done.

The time for cervix to open from 3-4 cm to 10 cm was recorded as the 1st stage, and the time from the full opening to the birth of the baby was recorded as the 2nd stage. Patients that were to undergo cesarean section were administered 15 ml (2%) lidocaine and 5 ml (0.5%) bupivacaine through epidural catheter and were taken to the operation. The patients were asked about their satisfaction level after the removal of the catheter. Satisfaction level was evaluated as poor, moderate and good.

Statistical Analysis of Data

The data were analyzed with IBM SPSS v23. Normal distribution fitness was examined with Shapiro-Wilk test. Mann-Whitney U test was used for comparison of data with non-normal distribution. The relationship between variables was examined by Spearman's rank correlation. Chi-square test was used for the comparison of the categorical data. Data showing normal distribution were presented as mean ± standard deviation while data not matching normal distribution were presented as median (min-max). Categorical data were presented as frequency (percent). The significance level was taken as p < 0.05.

Results

The median values of maternal age differ from group to group (p < 0.001). The median value in the primiparous group was 22 while it was 28 in the multiparous group. The mean values of maternal weight differ from group to group (p = 0.010). The mean value in the primiparous group was 69.9, while it was 77.3 in the multiparous group. The mean values of maternal height do not differ from group to group (p = 0.905). The mean value in the primiparous group was 160.5, while in the multiparous group it was 160.6. The median values of the first cervical opening (cm) do not differ from group to group (p = 0.990). The median value in the primiparous group as well as in the multiparous group was 5. The median values of the second cervical opening (cm) do not differ from group to group (p = 0.466). The median value in the primiparous group as well as in the multiparous group was 0. The median values of the first dose (ml) do not differ from group to group (p = 0.005). The median value in the primiparous group as well as in the multiparous group was 10. In the primiparous group, the first dose values ranged from 5 to 10, while all values in the multiparous group were 10. The median values of internmission (minute) do not differ from group to group (p = 0.504). The median value in the primiparous group as well as in the multiparous group was 0. The median values of the second dose (ml, milliliter) do not differ from group to group (p = 0.483). The median value in the primiparous group as well as in the multiparous group was 0. The median values of total dose (ml) do not differ from group to group (p = 0.196). The median value in the primiparous group as well as in the multiparous group was 50. The mean values of the baby’s head circumference (cm) do not differ from group to group (p = 0.028). The mean value in the primiparous group was 3191.9, while it was 3483.9 in the multiparous group. The median values of the baby’s head circumference (cm, centimeter) do not differ from group to group (p = 0.053). The median value in the primiparous group was 36 while it was 35 in the multiparous group. Demographic data of cases and mean values of infant height, weight, head circumference, duration of labor, cervical opening are presented in Table 1.

Table 1. Demographic data and mean values of infant’s height, weight, head circumference, duration of labor, cervical opening

<table>
<thead>
<tr>
<th></th>
<th>Primiparous (n = 26)</th>
<th>Multiparous (n = 22)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mother’s age</td>
<td>22 (18 - 28)</td>
<td>28 (24 - 40)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maternal weight</td>
<td>69.9 ± 10</td>
<td>77.3 ± 8.8</td>
<td>0.010</td>
</tr>
<tr>
<td>Maternal height</td>
<td>160.5 ± 5</td>
<td>160.6 ± 5.1</td>
<td>0.905</td>
</tr>
<tr>
<td>First cervical opening (cm)</td>
<td>5 (4 - 6)</td>
<td>5 (4 - 6)</td>
<td>0.990</td>
</tr>
<tr>
<td>Second cervical opening (cm)</td>
<td>0 (0 - 10)</td>
<td>0 (0 - 9)</td>
<td>0.466</td>
</tr>
<tr>
<td>The first dose (ml)</td>
<td>10 (5 - 15)</td>
<td>10 (10 - 20)</td>
<td>0.005</td>
</tr>
<tr>
<td>Intermission (min)</td>
<td>0 (0 - 330)</td>
<td>0 (0 - 200)</td>
<td>0.504</td>
</tr>
<tr>
<td>The second dose (ml)</td>
<td>0 (0 - 10)</td>
<td>0 (0 - 10)</td>
<td>0.953</td>
</tr>
<tr>
<td>Total Dose (ml)</td>
<td>10 (5 - 20)</td>
<td>10 (20 - 20)</td>
<td>0.483</td>
</tr>
<tr>
<td>Duration of Labor (min)</td>
<td>107.5 (50 - 420)</td>
<td>125 (0 - 280)</td>
<td>0.909</td>
</tr>
<tr>
<td>Infant height</td>
<td>50 (48 - 51)</td>
<td>50 (47 - 51)</td>
<td>0.196</td>
</tr>
<tr>
<td>Infant weight</td>
<td>3191.9 ± 440.8</td>
<td>3483.9 ± 445.1</td>
<td>0.028</td>
</tr>
<tr>
<td>Infant head circumference (cm)</td>
<td>36 (34 - 50)</td>
<td>35 (33 - 37)</td>
<td>0.053</td>
</tr>
</tbody>
</table>

In the primiparous group, there is a significant moderate positive relationship between total dose and duration of labor (r = 0.681, p < 0.001). As the dose increases, the duration of labor increases. In the multiparous group, there was no significant relationship between total dose and duration of labor (r = 0.360, p = 0.100). When the results were examined without group discrimination, there was a significant moderate positive relationship between total dose amount and duration of labor (r = 0.540, p < 0.001). The correlation coefficients and the level of significance between the total amount of local anesthetic (ml) administered from the epidural catheter and the duration of labor are shown in Table 2.
There is a moderate positive correlation between the total dose and the second VRS and the second VAS in the primiparous group (R-values are 0.694 and 0.758 respectively; P-values are p < 0.001, p < 0.001 respectively). In the multiparous group, there is a strong positive correlation between the second VRS and the second VAS (R-values are 0.847 and 0.890 respectively, P-values are p<0.001, p<0.001 respectively). When all patients were examined, there was a moderate positive correlation between the total dose and the second VRS and the second VAS (R-values are 0.767 and 0.783 respectively, P-values are p < 0.001, p<0.001 respectively). Table 3 shows the correlation relationship and significance levels between the total dose that was administered through epidural catheter and VAS 1, VRS 1, VAS 2, VRS 2, VAS end, VRS end scores in both groups and for all patients.

VRS 1 and VRS 2 distributions do not differ from group to group (P-values are 0.069 and 0.603, respectively). According to the VRS end scores, 54.5% of patients in the multiparous group had mild pain while 23.1% of the patients in the primiparous group had mild pain. In Table 4, the VRS scores of the groups are presented.
Only for 2 of all cases decision was made to perform cesarean section due to prolonged labor action, and cases were left out of the study. No intervention technique was performed for patients who underwent labor analgesia (forceps, vacuum). No statistically significant correlation was found between the total dose and the infant head circumference, infant height, maternal height, maternal weight, and infant weight, for both primiparous and multiparous group and when all patients examined without group discrimination. When 1st and 5th minute APGAR scores of infants were examined, there was no baby born with a low APGAR score. All APGAR scores are above 6. The 1st minute APGAR scores of infants were distributed as 7 for 1 (2.08%) infant, 8 for 1 (2.08%) infant and 9 for 46 (95.83%) infants. The 5th minute APGAR scores of infants were distributed as 8 for 1 (2.08%) infant, 9 for 2 (4.16%) infants and 10 for 45 (93.75%) infants. No complications, such as nausea, vomiting, back pain, itching, tremor, were observed in any of the patients.

Discussion

The maternal satisfaction levels were quite high in the patients in which we performed labor analgesia. No infant with low APGAR score was detected and no intervention during labor did occur. VAS scores in both primiparous and multiparous groups, especially VAS 1 and VAS end scores were very low. Especially VAS 2 and VRS 2 values decreased as the total dose (ml) administered through the epidural catheter increased. We did not find side effects due to epidural analgesia. We found a statistically significant and moderately positive correlation between the second cervical opening and the total dose (ml) administered through the epidural catheter and duration of labor. These results suggest that epidural labor analgesia mildly prolongs the 1st stage of the labor.

It has been reported that labor analgesia decreases both maternal and perinatal morbidity rates [5]. The epidural analgesia is the most widely used pharmacological method in the alleviation of labor pain. The technique of epidural analgesia is the most accepted method of labor analgesia in the contemporary world because it allows mother to participate both in the physical and emotional aspects of the labor as well as eliminating the pain that occurs during labor [2,6]. The concept of modern pain therapy in labor argues that the ongoing severe pain and the stress it creates must be effectively removed for its harmful effects to the mother and possibly to the fetus. Clinical trials have shown that well-performed analgesia reduces maternal mortality and morbidity [7,8]. There were no interventions during labor in the cases included in our study, and the infants’ 1st and 5th minute APGAR scores were quite good. Our results are consistent with the findings in the literature. Does epidural analgesia actually increase the rates of intervention during labor? Numerous studies have investigated the effects of epidural analgesia on the incidence of intervention during labor. Halpern et al. in their meta-analysis, found no difference in terms of assisted delivery between the ropivacaine and bupivacaine groups [9]. Atienzar et al. investigated the effects of levobupivacaine, bupivacaine, and ropivacaine, and found that there was no difference in the frequency of instrumental delivery among the groups [10]. Likewise, in our study, we found that there was no increase in the frequency of assisted labor in patients who had undergone epidural labor analgesia. None of our cases had any intervention during labor.

Several opinions argue that epidural analgesia, along with side effects, sensory and motor block it creates, prolongs or shortens the stages of labor. For this reason, many studies have been conducted to investigate the effects of epidural analgesia on labor. Among these studies, 2369 patients were analyzed in the meta-analysis by Halpern et al. and it was shown that the first and second stages of labor prolonged [11]. There are similar studies supporting this [12-14]. Gomer et al. and Leighton et al. have reported that prolongation of the second stage was observed when there was no change in the first stage of labor [15-17]. Lurie et al. have also found prolongation in the first and second stages of labor [18]. Contrary to all these, there are some studies that say the duration of the labor is not affected [19]. We also concluded in our study that it prolongs the first stage of labor. The results of our study partially overlap with the findings in the literature.

Epidural opioids alone have not been able to provide adequate analgesia in a variety of painful conditions [20]. For this reason, they are widely used in combination with local anesthetics to reduce motor block risk and to provide adequate analgesia. Genc et al. found in their study that the duration of the first stage of labor was significantly shortened in patients undergoing epidural analgesia with low doses of bupivacaine and fentanyl compared with patients without epidural analgesia [21]. Although fentanyl is thought to play a role in the shortening of the first stage, we have observed in the literature that it is not possible to distinguish the effects of fentanyl from the effects of bupivacaine, and also our own view is that the effects of fentanyl and bupivacaine cannot be separated from each other. In addition, the investigators reported that with labor analgesia there is shortening in the first stage, and also superior analgesia, higher quality analgesia, reduced catecholamine release and inhibition of uterine contractility by this reduction, faster cervical dilation and progression of labor in epidural groups compared to patients that were not epidural catheterized [22]. In our study, bupivacaine and fentanyl were combined and used for labor analgesia.

Nowadays, maternal and fetal side effects due to the epidural local anesthetic drugs, motor block that causes mother to be unable to participate in active labor, possible necessity of assistant methods for progress of labor (instrumental delivery, forceps etc.) and concern that it may prolong the stages of labor causes the Gynecology and Obstetrics specialists to move away from the epidural analgesia. Therefore, many studies have been carried out in order to find the lowest analgesic doses of the medicines used in the epidural analgesia that have the least side effects and cause the least motor block. Burke et al. used bupivacaine at 0.25% concentration and levobupivacaine in the
same concentration for labor analgesia; as a result, they found that the analgesic activities of the two local anesthetics are similar. There was no difference found between the groups in terms of sensory, motor block and side effects [23]. Belin et al. applied epidural analgesia to 238 pregnant women. They compared the same concentrations of bupivacaine, ropivacaine, and levobupivacaine in terms of labor types with sensory and motor block formation, and neonatal effects. They administered 15 ml of medication containing 0.0625% concentration of local anesthetics and 2 μg/ml of fentanyl. There was no difference detected between the groups in terms of the actual duration of labor and the type of labor. Motor block development in the levobupivacaine group was less common than in the ropivacaine and bupivacaine groups [20]. A study by Lacassie et al. also compared motor blocking potentials levobupivacaine and bupivacaine, and their effects on the duration of labor. In the study conducted with 60 pregnant women, local anesthetics were applied at 0.25% concentration. As a result of the study, the minimum local anesthetic dose that develops motor block was found to be 0.31% for levobupivacaine and 0.27% for bupivacaine. As a result, levobupivacaine was found to be less potent in terms of motor block formation compared to bupivacaine [24]. We used 0.25% bupivacaine for labor analgesia in our study. The drug and concentration we selected are consistent with the literature.

In a retrospective study by Staikou C. et al., data from obstetric clinics of 50 hospitals in Greece were examined. The study included 9475 cesarean and 8155 vaginal delivery cases. It was reported that single-shot spinal anesthesia was preferred in cesarean sections, and epidural analgesia is rarely used in normal spontaneous vaginal delivery in all clinics, especially in peripheral hospitals. Writers have emphasized that the epidural labor analgesia is not widely recognized and should be utilized more frequently in clinical practice [25]. Although the labor analgesia is technically quite easy, the most important difficulty seems to be that application is not becoming widespread. In this respect, perhaps one of the underdeveloped subjects in our country is obstetric analgesia/anesthesia. The effects of this fact are very important for young mothers who are afraid of pain and directed to the cesarean section because the labor pain cannot be remedied adequately. In recent years, caesarean section in our country has been perceived as a nearly normal type of labor rather than an operation performed only in cases with indications [1]. A study by Sahin S et al. reflects the facts of our country. Low recognition and low rates of utilization of labor analgesia in clinical practice may cause an increase in cesarean section frequency [1,25].

Many studies use VAS in assessing pain. VAS can be assessed using 10 or 100 cm rulers. We used a 10-cm ruler. Boutros et al. in their study have compared intermittent epidural bolus, continuous epidural infusion, and patient-controlled analgesia using a mixture of bupivacaine and sufentanil for painless labor, and found that VAS scores at 6th hour were higher in patient-controlled analgesia groups compared to continuous epidural infusion and intermittent epidural bolus groups [26]. However, at all times measured after epidural analgesia, VAS scores were found to be less than 30% in all three groups [26]. Ledin et al. found VAS scores similar in both groups at all times measured in their studies, comparing patient-controlled analgesia (PCA) and continuous epidural infusion methods for painless labor with epidural analgesia [27]. Manuel et al. also found similar VAS scores in all three groups, in their study they have compared continuous infusion, patient-controlled analgesia, and patient-controlled analgesia with basal infusion for painless labor with epidural method [28]. In our study, we preferred intermittent epidural bolus method because by means of this method, the patients who have undergone labor analgesia can be controlled frequently, VAS scores are being asked or it can be followed if any complication develops. VAS, VRS scores, especially VAS 2, VRS 2 and VAS end, VRS end scores were found to be very low. Epidural labor analgesia provides an effective analgesia, regardless of which method is used. This reflects the same fact in the literature and in our study results.

As a result, epidural analgesia for painless labor provides a safe and comfortable delivery to mother who is experiencing intense pain and stress, by reducing pain. Minimizing complications during epidural analgesia requires careful obstetric and anesthetic follow-up. Intermittent bolus administration through the epidural catheter may be preferred for this purpose. Obstetricians, family physicians, and anesthesiologists should give detailed information to pregnant mothers and encourage them to labor analgesia. The epidural labor analgesia can be applied safely to all pregnancies. We believe that there may be a significant reduction in cesarean section rates if labor analgesia is utilized more frequently in clinical practice.

Scientific Responsibility Statement
The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest
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