

Timing of Initiating Epidural Analgesia and Mode of Delivery in Nulliparas: A Retrospective Experience Using Ropivacaine

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Background: The timing of initiation of epidural analgesia and its causal relationship with mode of delivery is controversial. This retrospective investigation reviews and determines whether early initiation of epidural analgesia in nulliparous women influences the rate of cesarean sections as well as other obstetric outcome measures.

Methods: The nursing records of 1623 parturients who received epidural analgesia were retrospectively reviewed. Of these, 704 nulliparous parturients who presented in spontaneous labor or had spontaneous rupture of the membranes and received epidural analgesia with a regimen of ropivacaine and fentanyl were included in this study. All parturients received the epidural protocol following their first request. Parturients were divided into early (n = 457) and late (n = 247) groups according to cervical dilatation <3 cm and ≥ 3 cm, respectively, when epidural analgesia was initiated. The mean primary cesarean section rate during the research period was calculated from the monthly report of the department of obstetrics and gynecology.

Results: The mean primary cesarean section rate in the institution was 23.6% during the research period. The overall cesarean section rate was 13.4% (n = 704) in the studied groups. The early group required more top-up epidural anesthetic boluses, and had a higher cesarean section rate than the late group (16.4% vs. 7.7%, $p = 0.002$). However, the cesarean section rates of both groups were lower than the mean primary cesarean section rate. No difference was observed between groups in the percentage of arrested labor as the primary indication for cesarean section. Early epidural analgesia shortened the duration of the active phase of the first stage of vaginal delivery. No difference was observed between groups in the duration of the second stage or the instrumental vaginal delivery rate.

Conclusions: The administration of epidural analgesia with a regimen of ropivacaine and fentanyl should not be delayed until cervical dilatation reaches 3 cm in nulliparas who are in spontaneous labor or have spontaneous rupture of the membranes. The timing of epidural analgesia should be determined on an individualized basis.

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Key words: epidural analgesia, ropivacaine, cesarean section rate, nulliparas

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Epidural analgesia provides effective pain relief during labor and delivery, but has side effects. The effects of epidural analgesia on the progress and outcomes of labor are controversial.⁽¹⁻⁹⁾ The timing of initiation of epidural analgesia and its associated cesarean section rate have been debated.⁽¹⁻⁷⁾ Previously it was recommended that physicians delay administration of epidural analgesia in nulliparous parturients until cervical dilatation reaches 4-5 cm to avoid prolonged labor and reduce the risk of a required cesarean section.⁽¹⁰⁾ However, the updated *Practice Guidelines for Obstetric Anesthesia*⁽¹¹⁾ states that epidural analgesia should not be withheld on the basis of achieving an arbitrary cervical dilation, and should be offered on an individualized basis. Most clinical reports on this issue concern analgesia with bupivacaine.⁽¹⁻⁹⁾ Epidural bupivacaine provides highly effective pain relief, but limitations to its utility include motor blockade and cardiovascular toxicity.⁽¹²⁾ Studies conflict on whether the choice of local anesthetic influences the mode of delivery.⁽¹³⁻¹⁵⁾

Ropivacaine, which is a long-acting amide local anesthetic agent, is almost identical to bupivacaine in onset, quality and duration of sensory block.⁽¹⁶⁾ Ropivacaine has been reported to decrease the potential of central nervous system toxicity, cardiotoxicity and neonatal depression, and it also produces less motor block than bupivacaine. Motor block may influence pelvic floor tone and maternal expulsive efforts.^(14,15) These properties suggest that ropivacaine could be superior to bupivacaine in obstetric analgesia. Eddleston et al. reported that ropivacaine may increase the likelihood of spontaneous delivery, and decrease the rate of instrumental vaginal delivery.⁽¹³⁾ However, some investigations demonstrated no difference in the mode of delivery between ropivacaine and bupivacaine for labor epidural analgesia.^(14,15)

In the past few years, epidural analgesia had been administered to nulliparous parturients with a regimen of ropivacaine and fentanyl. Many of these patients had not reached 3-4 cm of cervical dilatation. The purpose of this retrospective study was to review and determine whether early initiation of epidural analgesia with ropivacaine in nulliparous women influences the rate of cesarean sections and other obstetric outcome measures.

METHODS

The study was approved by the Ethics

Committee of our hospital. The nursing records of 1623 parturients who received epidural analgesia from August 2003 to July 2005 were retrospectively reviewed. We sequentially excluded parturients with incomplete data records (7), a regimen other than ropivacaine (260), preterm labor or termination (26), failed or replaced epidural catheterization during epidural analgesia (9), admission for induction of labor (252), a seizure history (1), pregnancy induced hypertension (13), and gestational diabetes mellitus (22), and those who were not nulliparas (329). Finally, 704 nulliparous parturients who presented in spontaneous labor or with spontaneous rupture of the membranes and received epidural analgesia with ropivacaine and fentanyl were included in this study.

The epidural insertion followed intravenous prehydration with 500-1,000 ml of lactated Ringer's solution. The lower lumbar epidural space was identified by the loss-of-resistance technique with a 18-gauge Tuohy needle with the parturient in the lateral position. An epidural catheter was inserted into the epidural space. If no signs of an intravascular or subarachnoid puncture were observed, the catheter was secured and the parturient was placed in the supine position with left uterine displacement. All parturients received a standardized epidural protocol when requiring analgesia which consisted of a 10 ml initial loading dose of ropivacaine (0.75 mg/ml) and fentanyl (7.5 µg/ml), and a continuous maintenance dose of ropivacaine (0.75 mg/ml) combined with fentanyl (2 µg/ml) given at a rate of 10 ml/hour after 15 minutes of normal recordings (electrocardiography, automated noninvasive blood pressure and fetal heart rate monitoring). An additional 1.5-2 mg/ml ropivacaine 10 ml was given as a top-up bolus to achieve adequate pain relief at the request of the patient. Epidural analgesia was continued through the second stage of labor. Decisions concerning obstetrical management were made by the obstetricians.

Maternal age, body height and body weight were recorded as pre-labor characteristics. The durations from admission to delivery, and from initiation of epidural analgesia to delivery, the durations of the active phase of the first stage and of the second stage, the frequency of top-up boluses and parturients' complaints after epidural anesthesia (including nausea, vomiting, backache and dizziness) were recorded as labor characteristics. The mode of deliv-

ery, primary indication for cesarean section, Apgar scores of the newborn, and postpartum hemorrhage were recorded as labor outcomes. The extent of cervical dilatation when initiating epidural analgesia was also recorded. Parturients were divided into early and late groups based on the extent of cervical dilatation <3 cm and ≥ 3 cm, respectively, when initiating epidural analgesia.

There was a total 4046 parturients in our hospital during this study period. The mean primary cesarean section rate during the research period was calculated from the monthly report of the department of obstetrics and gynecology. Data were presented as mean \pm standard deviation. Differences in continuous variables were analyzed with Student's *t* test. Differences in categorical variables were analyzed with the chi-square test with Yates' correction, or with Fisher's exact test. A value of $p < 0.05$ was viewed as statistically significant.

RESULTS

Data were obtained from 704 parturients, of whom 457 were in the early group and 247 were in the late group. The sample size of 704 had an 85% power to detect differences. The alpha was equal to 0.05.

No differences were observed in pre-labor characteristics between the two groups. The mean values for maternal age, height, and weight were 30 years, 160 cm, and 67 kg, respectively. Parturients in the early group had more complaints of discomfort after epidural analgesia; the most common complaints were nausea and vomiting. The early group required more top-up boluses of local anesthetic to achieve adequate pain relief, had a longer mean duration from admission to delivery (957 ± 538 min vs. 642 ± 409 min, $p < 0.0001$) and a longer mean duration from initiation of epidural analgesia to delivery (596 ± 369 min vs. 394 ± 237 min, $p < 0.0001$). The duration of the active phase of the first stage in vaginal delivery with early epidural analgesia was shorter than that with late analgesia. (246 ± 197 min vs. 368 ± 221 min, $p < 0.0001$). No difference was observed for the duration of the second stage (93 ± 57 min vs. 102 ± 70 min, $p = 0.113$) (Table 1). The early group had a higher cesarean section rate than the late group (16.4% vs. 7.7%, $p = 0.002$). Arrested labor was the primary indication for cesarean section in 80.0%

Table 1. Labor Characteristics

| Descriptor | Early group (n = 457) | Late group (n = 247) | p value |
|--|--------------------------|-------------------------|----------|
| Frequency of discomfort complaints | 54 (11.8%) | 10 (4.0%) | 0.001* |
| Frequency of top-up boluses | 0.8 \pm 1.3 | 0.3 \pm 0.6 | <0.0001* |
| Duration from admission to delivery (min) | 957 \pm 538 | 642 \pm 409 | <0.0001* |
| Duration from initiation of epidural analgesia to delivery (min) | 596 \pm 369 | 394 \pm 237 | <0.0001* |
| Duration of active phase of first stage (min) | 246 \pm 197 | 368 \pm 221 | <0.0001* |
| Duration of second stage (min) | 93 \pm 57 | 102 \pm 70 | 0.113 |

*: Statistical significance.

(60/75) and 84.2% (16/19) in the early and late groups, respectively ($p > 0.99$). Therefore the higher cesarean section rate in the early group was not a result of an increase in arrested labor. Other reasons for cesarean section included fetal distress (13/704, 1.8%), fever in the parturient or suspected chorioamnionitis (4/704, 0.6%) and instrumental delivery failure (1/704, 0.1%). No difference was observed between early and late groups in the instrumental delivery rate, Apgar score of the newborn, or number of postpartum hemorrhages (Table 2).

The overall cesarean section rate in our studied group (13.4%) was lower than the mean primary cesarean section rate for all parturients (23.6%) during the research period.

Table 2. Labor Outcome

| Descriptor | Early group (n = 457) | Late group (n = 247) | p value |
|-----------------------------|--------------------------|-------------------------|---------|
| Vaginal delivery | 307 (67.2%) | 185 (74.9%) | 0.041* |
| Instrumental delivery | 75 (16.4%) | 43 (17.4%) | 0.816 |
| Cesarean delivery | 75 (16.4%) | 19 (7.7%) | 0.002* |
| Cesarean for arrested labor | 60 (80.0%) | 16 (84.2%) | > 0.99 |
| Cesarean for fetal distress | 12 (16.0%) | 1 (5.3%) | 0.455 |
| Cesarean for other reasons | 3 (4.0%) | 2 (10.5%) | 0.265 |
| Apgar score < 7 at 1 min | 10 (2.2%) | 3 (1.2%) | 0.559 |
| PPH | 1 (0.2%) | 1 (0.4%) | > 0.99 |

Abbreviations: PPH: postpartum hemorrhage; *: Statistical significance.

DISCUSSION

This study had four major findings: (1) Epidural analgesia in nulliparas did not raise the incidence of primary cesarean sections. (2) The early group required more top-up epidural anesthetic boluses, and had a higher cesarean section rate than the late group. (3) The duration of the second stage, the instrumental delivery rate, and the percentage of patients with arrested labor as a primary indications for cesarean section were irrelevant to the timing of initiating epidural analgesia. (4) Early epidural analgesia accelerated the active phase of the first stage for parturients who delivered vaginally. These facts should always be discussed with parturients, to allow them to make informed decisions.

The increased availability of epidural analgesia has not been accompanied by a higher cesarean section rate.^(17,18) Additionally, the primary cesarean section rate can be influenced by the institution.⁽¹⁷⁾ According to the Taiwan Quality Indicator Project, the primary cesarean section rate is an important indicator of medical quality. These data indicate that epidural analgesia does not raise the risk of primary cesarean section in nulliparous parturients who present in spontaneous labor or with spontaneous rupture of the membranes. Our data are consistent with current advice, and patients should be reassured that the application of epidural analgesia does not increase the incidence of cesarean delivery.⁽¹¹⁾ The studied group did not include parturients who had induction of labor, which is a well-known risk factor for cesarean delivery.⁽¹⁹⁾ This may explain why the studied group had a lower than average cesarean section rate.

Some observational studies have reported that early administration of epidural analgesia raises the rate of cesarean delivery.^(2,7) However, other studies have found no difference.^(1,3,4,6) This study found that early epidural analgesia led to a significantly higher cesarean section rate than late epidural analgesia, but found no difference in the percentage of arrested labor between the early and late groups.

This study found that patients in the early group had more pain in the labor course than those in the late group, since they required more top-up boluses. Requests for analgesia early in labor has been reported as a sign of dysfunctional labor.⁽²⁰⁻²²⁾ The intensity

of labor pain may be associated with an increased risk of cesarean delivery.⁽²⁰⁻²²⁾ Our data demonstrated that the cesarean section group required more top-up boluses than the vaginal delivery group (1.3 ± 2.0 vs. 0.5 ± 0.9 , not shown in the table). The need for epidural local anesthetics was higher among women who underwent cesarean delivery for dystocia than in women who delivered vaginally.⁽²³⁾ If parturients with severe labor pain were more likely to request epidural analgesia, then the association between early epidural analgesia and cesarean delivery would be logical, but not causative.⁽²¹⁾ This finding provides one explanation why the early group had a higher cesarean section rate than the late group.

The early group had longer mean durations from admission to delivery, and from initiation of epidural analgesia to delivery. Conversely, early epidural analgesia was found to shorten the duration of the active phase of the first stage in vaginal delivery. Factors influencing the progress of labor are not well understood. Autonomic imbalance has been proposed as an explanation for the association between epidural analgesia and prolonged labor.⁽²⁴⁾ Epidural analgesia theoretically attenuates the maternal response to stress and decreases the pain of parturition and plasma epinephrine levels, but has no influence on oxytocin secretion or the frequency of uterine contractions, and therefore facilitates cervical dilatation.^(24,25) Most studies did not differentiate between the latent and active phases in the first stage. The duration of the latent phase is poorly defined and the effects of epidural analgesia on it are hard to evaluate. The active phase of the first stage has been widely studied, but no definite conclusions have been drawn.⁽²⁶⁾

Prolonged infusion of an epidural anesthetic may lead to motor blockade, and raise the risk of instrumental delivery.⁽²⁷⁾ Our data indicate that the early group had a longer epidural anesthetic infusion than late group, but the rates of instrumental vaginal delivery were not increased and the second stage was not prolonged compared to the late group. This is consistent with previous studies.^(1,3-6) We conclude that our regimen with a low-concentration of ropivacaine and fentanyl does not generally lead to motor blockade.

Administration of epidural analgesia with a regimen of ropivacaine and fentanyl does not need to be delayed until cervical dilatation reaches 3 cm in nul-

liparas who are in spontaneous labor or have spontaneous rupture of the membranes. While it is true that this study demonstrated a higher cesarean section rate in the early group, it was still a much lower absolute percentage compared to the mean primary cesarean section rate in our institution.

Limitations

This study had some limitations. First, oxytocin usage was not recorded, so it could not be compared. Second, most of our parturients accepted epidural analgesia in early labor, thus leading to different parturient numbers between groups. A prospective study with adequate control on potential confounders should be designed for future study.

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初產婦硬脊膜外止痛之施行時機與生產方式： 耐樂品 (Ropivacaine) 之回溯性經驗

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- 背景：**硬脊膜外止痛之施行時機與生產方式的因果關係仍有爭議，此一回溯性研究旨在探討初產婦早期施打硬脊膜外止痛對剖腹產率及各項產科因子的影響。
- 方法：**回溯性分析 1623 位接受硬脊膜外止痛產婦之護理紀錄，選出 704 位自發性陣痛或破水且施打以耐樂品 (ropivacaine) 及吩坦尼 (fentanyl) 為止痛劑之硬脊膜外止痛的初產婦為研究群組，根據施打時子宮頸開的程度分為兩組：小於 3 公分者為早打組，大於或等於 3 公分者為晚打組。從婦產科之每月報表計算研究期間內之平均初次剖腹產率與研究群組作比較。
- 結果：**研究期間，機構內之平均初次剖腹產率為 23.6%，研究群組之剖腹產率為 13.4%。早打組需要較多次數的止痛加強劑，且剖腹產率較晚打組高，但以產程遲滯為主要剖腹產原因的比例，兩組則沒有差異。早打組第一產程活動期的時間比晚打組短。第二產程及以器械輔助之經陰道生產率兩組則沒有差異。
- 結論：**在自發性陣痛或破水的初產婦，不應等子宮頸開到 3 公分才能施行以耐樂品 (ropivacaine) 及吩坦尼 (fentanyl) 為止痛劑之硬脊膜外止痛，施行時機應以個別產婦需要作決定。
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關鍵詞：硬脊膜外止痛，耐樂品 (ropivacaine)，剖腹產率，初產婦