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Effect of Remifentanil on Active Phase Duration of Labor in Nulliparous Pregnant Women: A Cross-sectional Study

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Abstract

Objectives: Due to the increase in elective cesarean section and its high complications, epidural analgesia is the gold standard for reducing the pain of vaginal delivery. In contraindication cases, other effective and safe analgesic methods such as remifentanil are suggested. The present study aimed to compare the duration of active phase of labor at stages I and II, as well as neonatal Apgar score following the use of remifentanil analgesia.

Materials and Methods: In this study, 120 healthy primiparous women who were candidates for vaginal delivery were selected. After matching for age and body mass index (BMI), the participants were assigned into two equal groups (n=60 each) of intervention (receiving remifentanil) and control. We compared the duration of active phase of labor at stages I and II, neonatal Apgar scores, and the cesarean section rate between the groups. Statistical analysis was performed using SPSS software (version 23).

Results: There was no statistically significant difference between the two groups in terms of the duration of active phase in the first and second stages of labor ($P=0.84$ and $P=0.78$, respectively), 1-minute Apgar score ($P=0.95$), 5-min Apgar score ($P=0.92$), and the rate of cesarean section ($P=0.067$). Moreover, we observed no maternal complications with remifentanil.

Conclusions: According to our results, remifentanil did not increase the duration of labor, rate of cesarean section, and maternal complications. Hence, it can be a good alternative in cases where epidural analgesia is contraindicated.

Keywords: Delivery analgesia, Injectable opioids, Remifentanil, Delivery stages

Introduction

Pain during childbirth may have detrimental effects on the health of mother and baby due to the secretion of catecholamines (1). To reduce labor pain, systemic opioids are widely used as analgesics in obstetric anesthesia (2). Currently, epidural anesthesia is the gold standard for relieving labor pain. However, some studies have shown that epidural analgesia may cause complications such as prolonged labor, spinal hematoma, etc (3). Also, the use of this method may be contraindicated in such cases as infection, bleeding disorders, spinal abnormalities, some neuropathies, use of anticoagulants, etc (2,4). Therefore, in these cases, effective alternatives such as parenteral opioids should be used for labor analgesia to make the delivery process safe for mother and child (5).

Remifentanil, with its agonist effect on opioid receptors, has been recognized as a relatively effective and popular analgesic for labor and an alternative to epidural analgesia in the past two decades. It has unique pharmacokinetic properties, such as rapid onset of action and very short half-life, as well as a rapid and organ-independent metabolism (2,3,6,7). However, some cases of maternal pulmonary cardiac arrest due to remifentanil administration as a pregnancy anesthetic have been reported (8). Also, several studies have shown that remifentanil crosses the placenta, causing respiratory distress and suffocation in infants and problems for maternal and fetal safety (8,9). Therefore, further research is required to evaluate the effects, advantages, and disadvantages of using remifentanil as the labor analgesia.

Given the limited evidence on the efficacy and side effects of remifentanil, contradictory findings about this analgesic technique, and the polarization of the obstetric and gynecological anesthesia community, the use of this analgesic technique is very controversial. Accordingly, this study aimed to compare the effect of using remifentanil on the duration of active phase of labor at stages I and II in healthy nulliparous pregnant women.

In nulliparous parturients, the mean duration of active phase of labor at first stage is about 4.9 hours and the maximum duration is 11.7 hours. However, the duration is shorter in multiparous parturients (minimum rate: 1.5 cm/h). Regarding the mean duration of active phase of labor at stage II, the mean and maximum durations are 50 minutes and 2 hours in nulliparous parturients, and 20 minutes and 1 hour in multiparous parturients, respectively (10).

Materials and Methods

Participants and Study Protocol

In this cross-sectional study, we included 120 healthy primiparous parturient women referred to Taleghani

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and Alzahra hospitals in Tabriz, Iran from 22 May 2019 to 26 May 2020. After matching for age and body mass index (BMI), the participants were assigned into two equal groups (n=60 each) of intervention (receiving remifentanil) and control by convenience sampling method. The intervention group received intravenous remifentanil (Repaxir from EXIR company) with bolus dose 1-2 μ/kg and maintenance dose 0.04-0.06 μ/kg/h.

The inclusion criteria were nulliparous women aged 15-49 years with gestational age ≥37 weeks that underwent vaginal delivery. All women with epidural anesthesia, history of anesthesia complications, fetal distress, cardiovascular disease, contraindications to remifentanil, hemodynamic disorders, and incomplete data were excluded.

The participants' information, including mother's age, height, and weight, gestational age, dilatation and effacement at onset, dilatation and effacement at the beginning of analgesia, the duration of active phase of labor at stages I and II (dilatation 6-10 cm of the cervix and complete dilatation to fetal born, respectively), 1-minute and 5-minute Apgar scores, final delivery type (cesarean section or vaginal delivery), and analgesia complications (such as fetal heart rate [FHR] changes, hypotension, respiratory depression due to opioids, and pruritus) were extracted from the participants' files and recorded.

Considering a significance level of 95% and the power of 80%, the sample size was estimated as 120 participants (60 in each group) based on the study by Blair et al (7), and using the following formula:

$$n = \frac{\left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}\right)(\delta_1^2 + \delta_2^2)}{(\mu_1 - \mu_2)^2}$$

Statistical Analysis

For statistical analysis, the Statistical Package for the Social Sciences software, version 23 (USA, III., Chicago, SPSS Inc.) was used. Quantitative variables were presented as mean±standard deviation and qualitative variables as number (percentage). The data were analyzed by chi-square and independent *t* test. Normal distribution of data was analyzed by Kolmogorov-Smirnov test. A *P* value ≤0.05 was considered as statistically significant.

Results

In this study, 120 healthy primiparous women were assigned into two equal groups of intervention (receiving remifentanil) and control. There were no significant differences between the two groups in terms of age, weight, height, number of cesarean sections, and BMI (Table 1). The results of 1-minute and 5-minute Apgar scores indicated no statistically significant between the two groups. Also, there was no statistically significant difference between the two groups regarding the duration of active phase of labor at first ($P = 0.84$) and second stages ($P = 0.78$) (Table 2).

Discussion

In this study, we compared the effect of using remifentanil on the duration of active phase of labor at stages I and II, neonatal Apgar scores, and cesarean section rate in healthy nulliparous pregnant women. The results showed no statistically significant difference between the two groups in terms of the mentioned variables. Although the duration of active phase of labor in both stages was shorter in the remifentanil group, the difference was not statistically significant. Therefore, remifentanil could effectively replace the usual methods of analgesia during childbirth. In addition, no side effects were observed in the mother or fetus.

Some findings of this study were consistent with several previous studies. A study conducted in 2005 showed that the duration of stage I and II, neonatal Apgar score, and umbilical cord pH were similar in the remifentanil and pethidine groups (7). In another study, there was no significant difference between bupivacaine and sufentanil in terms of duration of labor, pain intensity, and patient satisfaction between the two groups receiving remifentanil and epidural analgesia (11). The results of another study performed on 254 pregnant women showed that the duration of the fetal expulsion phase in primiparous women was the same in all groups, while the duration of this ectopic phase was longer in women with fentanyl epidural anesthesia group than control group. Also, neonatal Apgar score, umbilical artery pH, and neonatal acidosis were the same between the two groups (12).

However, several studies report that using intravenous remifentanil analgesia caused adequate pain relief and

Table 1. Demographic Characteristics of the Participants in Two Study Groups

Variables	Intervention (n=60)	Control (n=60)	*P* Value
Age (y), Mean ± SD	23.70±6.91	24.13±4.46	0.71[a]
Weight (kg), Mean ± SD	86.76±6.78	85.67±5.6	0.14[a]
Height (cm), Mean ± SD	165.44±7.4	164.45±8.2	0.29[a]
BMI (kg/m²), Mean ± SD	31.76±4.8	30.95±4.3	0.14[a]
Cesarean section, No. (%)			
Cesarean section	3(5)	9 (15)	0.067[b]
Vaginal delivery	57 (95)	51 (85)	

[a] Independent *t* test, [b] Chi-square test.

Table 2. The Comparison of Apgar Scores and Duration of Labor Between the Two Groups

Variables	Intervention (n=60)	Control (n=60)	*P* Value
1-minute Apgar score	9.00±0.00	9.00±0.19	0.95[a]
5-minute Apgar score	10.00±0.00	9.98±0.13	0.92[a]
Active phase duration of stage I	86.25±33.92	87.60±36.92	0.84[a]
Duration of stage II	28.05±14.09	29.27±15.12	0.78[a]

[a] Independent *t* test.

high maternal satisfaction in both stages of labor (2). The results of a meta-analysis showed that remifentanil patient-controlled analgesia (PCA) had excellent analgesia and greater patient satisfaction during delivery than pethidine; on the other hand, epidural analgesia offered better pain relief than remifentanil (13). Another study on 401 women in the active phase of term pregnancy found that the use of remifentanil reduced the need for epidural anesthesia by half and could be used as an alternative method (14). Douma et al reported that epidural pain relief with bupivacaine/sufentanil was more effective than intravenous remifentanil analgesia in 20 women (15). Some studies suggested remifentanil as an effective alternative to epidural analgesia over other drugs (14,16,17). This is because women taking remifentanil can easily control their painkillers, which stimulates labor progress by reducing stress and increasing the secretion of the oxytocin hormone (3).

Limitations

The main limitation of this study was the small sample size. Further studies with larger sample size and stronger design are recommended to consider the effects of confounding factors, neonatal complications, and other factors such as breastfeeding.

Conclusions

The findings of this study showed that the clinical use of remifentanil provided adequate analgesia for labor due to its optimal efficacy. Due to the positive effects of remifentanil on both mother and fetus, it can be a good alternative for women whom epidural administration is contraindicated. However, when choosing the appropriate method of analgesia during childbirth, all the side effects, advantages, and disadvantages of analgesic drugs should be considered, and the most appropriate drug should be used.

Authors' Contribution

NM, FM, and HP designed the study and conducted the research. NM and FM monitored, evaluated, and analyzed the results of the study. NM participated in the preliminary drafting of the manuscript and FM and HP critically revised it for important intellectual content. All authors approved the final manuscript and take responsibility for the integrity of the data.

Conflict of Interests

Authors have no conflict of interest.

Ethical Issues

This study was in accordance with the principles of the Helsinki Declaration. Also, the Ethics Committee of Tabriz University of Medical Sciences and Health Services, Tabriz, Iran approved the study protocol (Code: IR.TBZMED.REC.1398.859).

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