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Original Article

Effect of ropivacaine and sufentanil in epidural labor analgesia

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Abstract: Objective: To investigate the application value of ropivacaine combined with sufentanil for epidural labor analgesia in painless labor. Methods: A total of 157 cases of pregnant female received painless labor in our hospital from January 2019 to December 2020 were randomly divided into observation group (n=81 cases) and control group (n=76 cases). The subjects in the observation group received 0.1% ropivacaine combined with sufentanil (0.25 μg/ml) 10 ml and added into the painless delivery pump, and the control group received 0.1% ropivacaine 10 ml into the painless delivery pump. The analgesic effect, lactation function, delivery outcomes and the labor course of the two groups were compared. Results: In the active stage of labor, the time of first labor process was shorter compared with the control group, those in the observation group were more active than the control group (P<0.05). The lactation initiation time of the observation group was shorter than that of the control group, and the effective rate of lactation was higher than that of the control group (P<0.05). The Visual analogue scale (VAS) score at 5 min, 30 min, 60 min, and 90 min after analgesia were improved in the observation group, the analgesic effect of ropivacaine combined with sufentanil for epidural labor analgesia was prior to ropivacaine alone. There were significant differences in the rates of conversion to cesarean section and usage rate of forceps between the two groups (P<0.05), while there had no significant differences in lateral episiotomy rate and Apgar scores at 1 and 5 min after birth between the two groups (P>0.05). Conclusion: Ropivacaine combined with sufentanil for epidural labor analgesia in painless labor can effectively relieve labor pain, improve lactation function, active the first stage of labor, shorten the time of labor, reduce the incidence of cesarean section and ensure the safety of mother and infant.

Keywords: Ropivacaine, sufentanil, labor analgesia, painless labor

Introduction

Delivery refers to the period and process in which the fetus is separated from the mother and becomes an independent individual. Due to the contraction of the uterus during delivery, most pregnant women will feel severe pain during delivery, resulting in maternal tension, anxiety, fear and other negative emotions. These negative emotions will lead to endocrine disorders, increased blood pressure, faster heart rate and serious complications. Patients with respiratory alkalosis and metabolic acidosis may have complications, which seriously threaten maternal health and affect the outcome of delivery [1, 2]. Painless delivery is a new delivery technology in recent years, which can reduce the pain of delivery, help to reduce the fear of delivery pain and postpartum fatigue. The parturient can get a full rest in the first stage of labor, and accumulate physical strength to shorten the process of labor and smooth delivery when the uterine orifice is fully opened [3-5]. In the process of painless delivery, the application of narcotic drugs can block the intraspinal nerves, reduce the delivery pain, effectively reduce the adverse pregnancy outcomes such as neonatal asphyxia and fetal distress induced by delivery pain, and improve the quality of life of mothers and infants [6].

Ropivacaine, as a new type of long-acting amide local anesthetic, has the characteristics of low toxicity to cardiovascular and central nervous system. When used in low concentration, it also has the characteristics of obvious sensory motor nerve separation, so it is specifically used in labor analgesia, and has no effect on the mother [7]. Sufentanil is a kind of opioid agonist, most of which are synthetic drugs. It

has the clinical advantages of long-term efficacy and fast onset, strong analgesic effect. At the same time, sufentanil has high fat solubility, which has selectively high affinity with opioid receptor, and has significant analgesic and anesthetic effect [8]. Ahirwar et al [9] found that sole ropivacaine was effective in decreasing labor pain compared with a combination of fentanyl or clonidine. However, a recent study showed that fentanyl and sufentanil in combination with bupivacaine have been found to provide comparable analgesic properties for labor pain relief, but the number of neonates with Apgar 7 was significantly greater [10]. Here, we investigate the application value of ropivacaine combined with sufentanil for epidural labor analgesia in painless labor.

Data and methods

Clinical data

157 pregnant women in our hospital from January 2019 to December 2020 met the inclusion and exclusion criteria and were randomized allocated into two group: the observation group (n=81 cases) and the control group (n=76 cases). The researchers systematically explained the role, purpose and process of the study to the patients and their families. The patients and their families voluntarily signed the informed consent form to participate in this study. This study was approved and recognized by the ethics committee of our hospital.

Inclusion and exclusion standard

Inclusive criteria: ① Pregnant women were full-term pregnancy (>37 weeks), and they required to painless delivery; ② The pelvic structure of the pregnant women was well, accorded with the indications of vaginal delivery; ③ age: ≥20 years; ④ No anesthesia contraindication; ⑤ The subjects were willing to cooperate and implement the experiment.

Exclusion criteria: ① Had a history of mental illness; ② Uterine atony; ③ had a history of nasal surgery; ④ Had serious cardiac *disorder*, *severe liver* malfunction or renal failure; ⑤ Coagulation dysfunction; ⑥ Had a history of cesarean section; ⑦ Unwilling to participate our research.

Method

All parturients received epidural anesthesia: When the parturients entered the first stage of labor or opened 2-3 cm at the uterine orifice, the medical staff timely and accurately established the venous channel, assisted the parturients to take the left lying position, and punctured the lumbar intervertebral space 3 and 4, epidural block was performed. After successful puncture, the catheter was inserted for 3 cm and indwelling. 10 ml of 45 mg of lidocaine (1.5%) in 3.0 mL containing 5 mg/mL epinephrine was injected to understand whether the puerpera had uterine contraction and lower limb motor sensation. The anesthesia plane was adjusted to T10. After confirmation, the painless delivery pump was connected.

The control group: Alone 0.1% ropivacaine (Yichang Renfu Pharmaceutical Co., Ltd) 10 ml was added into the painless delivery pump. The painless delivery was performed at 7 ml/h, and the locking time was 15 min.

The observation group: The subjects were received 0.1% ropivacaine (Yichang Renfu Pharmaceutical Co., Ltd) combined with sufentanil (0.25 μg/ml) (Yichang Renfu Pharmaceutical Co., Ltd) 10 ml was added into the painless delivery pump. The painless delivery was performed at 7 ml/h, and the locking time was 15 min.

Pain

Visual analogue scale (VAS) was used to evaluate the degree of pain before analgesia, 5 min, 30 min, 60 min and 90 min after analgesia, respectively [11]. The score range was 0-10, and the degree of pain increased with the increase of the score.

Lactation function

Record the two groups of maternal lactation start time and lactation efficiency, lactation efficiency criteria: good lactation for the number of maternal lactation within 24 hours postpartum ≥ 5 times, one lactation can make the newborn sleep more than 3 hours; lactation appropriate for the number of maternal lactation within 24 hours postpartum is 3~5 times, and need to add ≤ 30 ml infant formula to make

Table 1. Comparison of clinical data between the two groups

	Observation group (n=81)	Control group (n=76)	t/χ^2	*P*
Age (years)	28.5±1.32	28.35±1.49	1.15	0.74
Average gestational weeks	38.05±1.63	37.75±1.64	3.32	0 .57
BMI	22.85±1.24	22.45±1.02	1.39	0 .28
Smoking	5 (6.2%)	3 (3.9%)	5.26	0.13
Chronic Pain	8 (9.9%)	7 (9.2%)	6.29	0.29
Depression	3 (3.7%)	1 (1.3%)	3.19	0.18
Surgical history	15 (18.5%)	12 (15.8%)	4.38	0.22

Note: Compared with the control group, significant difference as P<0.05.

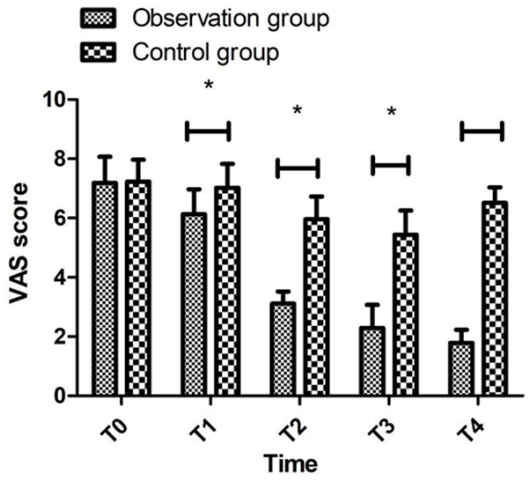

Figure 1. Comparison of *VAS score* between the two groups after labor analgesia. Note: Compared with control group, [a]*P<0.05.*

the newborn sleep; insufficient lactation for 24 hours postpartum If the times of breast-feeding of parturient women are less than 3 times, it is necessary to add >30 ml infant formula to make the newborn baby sleep safely [12]. Effective rate of lactation = good rate of lactation + appropriate rate of lactation.

The outcome of delivery

The conversion rate of cesarean section, forceps usage rate, episiotomy rate and Apgar score at 1 and 5 minutes after birth were recorded. Skin color, heart rate, muscle tension, respiration and response to external stimulation were evaluated. The total score was 10 points. 8-10 points were normal, 4-7 points were mild asphyxia, and 3 points and below were severe asphyxia [13].

Statistical analysis

All data were analyzed by SPSS 22.0. The statistical results are expressed by mean ± standard deviation (M ± s), the data comparison is conducted by t-test and the correlation analysis is conducted by person linear phase, P<0.05 was the difference with statistical significance. Analyses were performed using Graph Pad Prism 7 Software (Graph Pad Prism, San Diego, CA).

Results

Clinical data

Table 1 shown characteristics of the participants. The research included 157 patients after follow-up, involved 81 patients in the observation group, a mean age (28.5±1.32) years, while in the control group, a mean age (28.35±1.49) years. The BMI in the observation group was (22.85±1.24) kg/m^2, and in the control group was (22.45±1.02) kg/m^2, there was no statistical significance between two groups (P=0.28). The smoking people in the observation group were 5 (6.2%), and that in the control group was 3 (3.9%). The average gestational weeks in observation group was (38.05±1.63) weeks, and in control group was (37.75±1.64) weeks, there was no statistical significance between two groups (P=0.57). The number of patients who had a history of chronic pain in observation group was 8 (9.9%), and in control group was 7 (9.2%). The number of patients who had a history of depression in observation group was 3 (3.7%), and in control group was 1 (1.3%). The number of patients who had a history of surgical operation in observation group was 15 (18.5%), and in control group was 12 (15.8%). The two groups were similar in demographics, clinical characteristics, and there were no statistical significance between two groups.

Clinical relieve pain

As shown in **Figure 1**, the score of VAS before analgesia (T0) in the observation group was (7.19±0.88) points, and that in the control group was (7.23±0.74) points; while the score of VAS 10 min (T1), 30 min (T2) 60 min (T3) and 90 min (T4) after analgesia in the observation group respectively were (6.13±0.84) points, (3.11±0.41) points, (2.29±0.78) points and (1.79±0.44) points, and that in the control

Table 2. Comparison of lactation function between the two groups after labor analgesia

group	Number of cases	Onset time of lactation (h)	Good lactation	Moderate lactation	Insufficient lactation	Lactation effective rate
Observation group	81	25.57±4.43	33 (40.7%)	42 (51.9%)	6 (7.4%)	75 (92.6%)
Control group	76	33.98±6.41	25 (32.9%)	37 (48.7%)	14 (18.4%)	62 (81.6%)
t	-	8.193	7.138	8.147	5.261	6.628
P	-	0.0003	0.022	0.036	0.002	0.019

Note: Compared with the control group, significant difference as P<0.05.

Table 3. Comparison of the outcome of delivery between the two groups after labor analgesia

Group	Number of cases	Conversion to cesarean section	Forceps use	Episiotomy	Neonatal Apgar score	
					1 min after birth	5 min after birth
Observation group	81	1 (1.2%)	8 (9.9%)	15 (18.5%)	9.72±0.13	9.94±0.57
Control group	76	13 (17.1%)	21 (27.6%)	19 (25%)	9.41±0.29	9.74±0.63
t/χ^2	-	4.984	5.783	1.943	2.148	3.349
P	-	0.035	0.004	0.067	0.253	0.136

Note: Compared with the control group, significant difference as P<0.05.

group respectively were (7.02±0.81) points, (5.96±0.77) points, (5.44±0.81) points and (6.51±0.53) points, there had statistical significance between two groups after analgesia (P<0.05).

Lactation function

The lactation effective rate of the observation group was 92.6% (75/81), which was higher than that of the control group (81.6%), the differences were statistically significant (P<0.05). The onset time of lactation in the observation group was (25.57±4.43) h, and that in the control group was (33.98±6.41) h, the differences were statistically significant (P<0.05). In the experimental group, the good lactation rate was 40.7% (33 cases), the moderate lactation rate was 51.9% (42 cases), and the insufficient lactation rate was 7.4% (6 cases); in the control group, the good lactation rate was 32.9% (25 cases), the moderate lactation rate was 48.7% (37 cases), and the insufficient lactation rate was 18.4% (14 cases) (**Table 2**).

The outcome of delivery

The conversion rate of cesarean section in the observation group was 1.2% (1 case), and that in the control group was 17.1% (13 cases), the differences were statistically significant (P=0.035). The forceps use rate in the two groups were 9.9% (8 cases) and 27.6% (21 cases), respectively. The episiotomy rate in the observation group was 18.5% (15 cases), and that in the control group was 25% (19 cases), the differences had no statistically significant (P=0.067). The 1 min after birth of neonatal Apgar score in the observation group was (9.72±0.13) points, and that in the control group was (9.41±0.29) points, the differences had no statistically significant (P=0.253). The 5 min after birth of neonatal Apgar score in the two groups were (9.94±0.57) and (9.74±0.63) points, and there had no statistically significant (P=0.136) (**Table 3**).

The labor course

The time of first labor process in the observation group was (133.51±12.63) h, and that in the control group was (205.09±27.59) h, the differences were statistically significant (P<0.05). The time of second labor process in the two groups were (42.79±4.38) and (48.03±5.51) h, respectively. The time of third labor process in the observation group was (8.11±1.72) h, and that in the control group was (8.37±1.47) h, the differences had no statistically significant (P>0.05) (**Figure 2**).

Discussion

During natural childbirth, the parturient is in a state of stress, easy to produce fear and other bad emotions. The pain threshold of cerebral cortex decreases, and the pain sensitivity of parturient increases, which will cause uterine

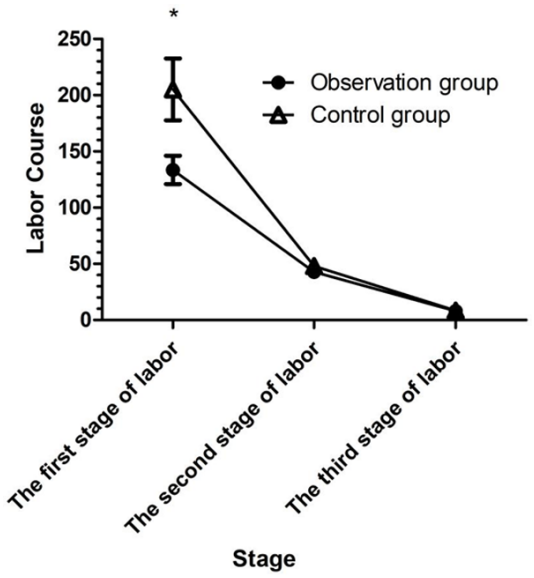

Figure 2. Comparison of the labor course between the two groups after labor analgesia. Note: Compared with control group, *$P<0.05$.

inertia and increase the probability of dystocia. Painless delivery is the delivery process of maternal anesthesia to achieve the maximum degree of painless, safe and smooth completion of natural childbirth [14].

Ropivacaine, as a new type of long-acting amide local anesthetic, has the characteristics of low toxicity to cardiovascular and central nervous system. When used in low concentration, it also has obvious characteristics of sensory motor nerve separation, so it is specifically used in labor analgesia, and has no effect on the mother [15]. Sufentanil, as a strong synthetic morphine like analgesic, has strong analgesic effect, long time effect and little side effect on hemodynamics [16]. In our study, the VAS scores of the observation group at 10, 30, 60 and 90 min after analgesia were significantly lower than those of the control group, indicating that the onset time of ropivacaine combined with sufentanil analgesia was faster and lasted for a longer time. Moreover, the first stage of labor in the observation group was shorter than that in the control group ($P<0.05$), this result indicated that ropivacaine combined with sufentanil could activate the first stage of labor, shorten the time of the first stage of labor, reduce maternal pain, and it has no effect on the second and third stages of labor.

The key to the success of painless delivery lies in the influence on puerpera and neonate. A study pointed out that ropivacaine combined with sufentanil and spinal epidural anesthesia can reduce the risk of total spinal anesthesia. In the application of painless delivery, it has little influence on postpartum lactation function and neonate, and is a safe and effective analgesia method [17]. We have found that the effective rate of lactation in the observation group was higher than that in the control group, and the onset time of lactation was shorter than that in the control group. There was no significant difference in Apgar score between the two groups, indicating that ropivacaine combined with sufentanil had less adverse effects on mother and infant. Furthermore, our results demonstrated that conversion to cesarean section and the forceps use rate in observation group decreased compared with the control group. The combination of ropivacaine hydrochloride and sufentanil can effectively relieve the labor pain of the puerpera, make the puerpera selection of the vaginal delivery mode as far as possible, reduce the incidence of cesarean section, have a certain positive impact on the postpartum rehabilitation of the puerpera, and also sfer for the newborn.

The therapeutic mechanism of ropivacaine combined with sufentanil for epidural labor analgesia in painless labor is unclear. We deduced that it related to pharmacological properties of narcotic drugs. Ropivacaine showed a more lasting analgesic effect, and the efficacy was faster, which would not cause greater adverse effects on maternal and neonatal. Sufentanil is a kind of fat soluble opioid anesthetics, which would have better analgesic effect. When sufentanil acts, it can be biotransformed through the liver, resulting in N-dealkylation and O-demethylation metabolites, which can be excreted through the urinary system; Its o-demethylated metabolite has certain pharmacological activity, about 1/10 of sufentanil, so it can make sufentanil last longer effect; In addition, sufentanil can effectively combine plasma protein with blood-brain barrier, so it can improve the analgesic effect to a large extent [18, 19]. The combination of the two drugs can not only prolong the duration, but also reduce the degree of motor nerve block [20, 21].

There had some weakness in our study. Firstly, the subjects of our study is limited, the reason maybe relate to the study period which is short and due to the strict inclusion and exclusion criteria. Secondly, we only included term parturient (gestational weeks >37 weeks), so other populations needed further study about its clinical effect. A larger, placebo-controlled, perspective study is still needed to explore the application value of ropivacaine combined with sufentanil for epidural labor analgesia in painless labor.

In conclusion, ropivacaine combined with sufentanil for epidurallabor analgesia in painless labor can effectively relieve labor pain, improve lactation function, active the first stage of labor, shorten the time of labor, reduce the incidence of cesarean section and ensure the safety of mother and infant.

Disclosure of conflict of interest

None.

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References

[1] Bozzuto L, Passarella M, Lorch S and Srinivas S. Effects of delivery volume and high-risk condition volume on maternal morbidity among high-risk obstetric patients. Obstet Gynecol 2019; 133: 261-268.

[2] Baskett TF. Evolution of operative obstetric delivery in Canada. J Obstet Gynaecol Can 2019; 9: S244-S250.

[3] Naser MA, van Dijk LV, He R, Wahid KA and Fuller CD. Application of ultrasound-guided epidural catheter indwelling in painless labour. J Pak Med Assoc 2020; 4: 45-50.

[4] Kwak EJ, Pang NS, Cho JH, Jung BY, Kim KD and Park W. Computer-controlled local anesthetic delivery for painless anesthesia: a literature review. J Dent Anesth Pain Med 2016; 16: 81-88.

[5] Aksoy M, Aksoy AN, Dostbil A, Celik MG and Ince I. The relationship between fear of childbirth and women's knowledge about painless childbirth. Obstet Gynecol Int 2014; 2014: 274303.

[6] Fung BK. Continuous epidural analgesia for painless labor does not increase the incidence of cesarean delivery. Acta Anaesthesiol Sin 2000; 38: 79-84.

[7] Cai S, Zheng J, Meng Q, Chai J, Ma R, Wang Y, Zhang W and Yang Z. Investigation of the minimum local analgesic concentration of epidural sufentanil combined with ropivacaine for labor analgesia. Clin Ther 2020; 42: 210-219.

[8] Cheng Q, Bi X, Zhang W, Lu Y and Tian H. Dexmedetomidine versus sufentanil with high- or low-concentration ropivacaine for labor epidural analgesia: a randomized trial. J Obstet Gynaecol Res 2019; 45: 2193-2201.

[9] Ahirwar A, Prakash R, Kushwaha BB, Gaurav A, Chaudhary AK, Verma R, Singh D and Singh V. Patient controlled epidural labour analgesia (PCEA): a comparison between ropivacaine, ropivacaine-fentanyl and ropivacaine-clonidine. J Clin Diagn Res 2014; 8: GC09-13.

[10] Li B, Wang HX and Gao CJ. Bupivacaine in combination with fentanyl or sufentanil in epidural/intrathecal analgesia for labor: a meta-analysis. J Clin Pharmacol 2015, 55: 584-91.

[11] Pratici E, Nebout S, Merbai N, Filippova J, Hajage D and Keita H. An observational study of agreement between percentage pain reduction calculated from visual analog or numerical rating scales versus that reported by parturients during labor epidural analgesia. Int J Obstet Anesth 2017; 30: 39-43.

[12] Orbach-Zinger S, Landau R, Davis A, Oved O, Caspi L, Fireman S, Fein S, Ioscovich A, Bracco D, Hoshen M and Eidelman LA. The effect of labor epidural analgesia on breastfeeding outcomes: a prospective observational cohort study in a mixed-parity cohort. Anesth Analg 2019; 129: 784-791.

[13] Ravelli ACJ, Eskes M, de Groot CJM, Abu-Hanna A and van der Post JAM. Intrapartum epidural analgesia and low Apgar score among singleton infants born at term: a propensity score matched study. Acta Obstet Gynecol Scand 2020, 99: 1155-1162.

[14] Aggarwal K, Lamba AK, Faraz F, Tandon S and Makker K. Comparison of anxiety and pain perceived with conventional and computerized local anesthesia delivery systems for different stages of anesthesia delivery in maxillary and mandibular nerve blocks. J Dent Anesth Pain Med 2018; 18: 367-373.

[15] Chen G, Gong M and Liu Y. Comparison of ropivacaine plus sufentanil and ropivacaine plus dexmedetomidine for labor epidural analgesia: a randomized controlled trial protocol. Medicine (Baltimore) 2020; 99: e22113.

[16] Costa-Martins JM, Dias CC, Pereira M and Tavares J. Effects of local anesthetic on the time between analgesic boluses and the duration of labor in patient-controlled epidural analgesia: prospective study of two ultra-low dose regi-

mens of ropivacaine and sufentanil. Acta Med Port 2015; 28: 70-6.
[17] Wang LZ, Chang XY, Liu X, Hu XX and Tang BL. Comparison of bupivacaine, ropivacaine and levobupivacaine with sufentanil for patient-controlled epidural analgesia during labor: a randomized clinical trial. Chin Med J (Engl) 2010; 123: 178-83.
[18] Zhang T, Yu Y, Zhang W and Zhu J. Comparison of dexmedetomidine and sufentanil as adjuvants to local anesthetic for epidural labor analgesia: a randomized controlled trial. Drug Des Devel Ther 2019; 13: 1171-1175.
[19] Roelants F and Lavand'homme P. Clonidine versus sufentanil as an adjuvant to ropivacaine in patient-controlled epidural labour analgesia: a randomised double-blind trial. Eur J Anaesthesiol 2015; 32: 805-11.
[20] Lin R, Tao Y, Yu Y, Xu Z, Su J and Liu Z. Intravenous remifentanil versus epidural ropivacaine with sufentanil for labour analgesia: a retrospective study. PLoS One 2014; 9: e112283.
[21] Dewandre PY, Decurninge V, Bonhomme V, Hans P and Brichant JF. Side effects of the addition of clonidine 75 microg or sufentanil 5 microg to 0.2% ropivacaine for labour epidural analgesia. Int J Obstet Anesth 2010; 19: 149-54.