Original Article
Effects of remifentanil PCIA with multiple acupoint stimulation on labor analgesia and maternal and infant outcomes

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Abstract: Objective: This study aimed to observe the effect of remifentanil PCIA with multiple acupoint stimulation on labor analgesia and maternal and infant outcomes. Method: A total of 177 parturients from March 2017 to May 2019 were selected and grouped according to the analgesic method. The control group (CG) (81 cases) received no labor analgesia, and the research group (RG) (96 cases) received remifentanil PCIA with multiple acupoint stimulation. The labor process, postpartum hemorrhage and hospital stay in the two groups were observed. The VAS score, Ramsay score, stress-related hormone levels before analgesia (T0), 30 min after analgesia (T1), 1 h after analgesia (T2), at the opening of the birth canal (T3) and at delivery (T4), and the adverse events were compared between the CG and the RG. Apgar score and NBNA score were compared between the CG and the RG. Results: The duration of the first stage of labor, the second stage of labor and total labor, as well as postpartum hemorrhage and hospital stay in the RG were all lower than those in the CG (P<0.05). The VAS scores of the RG were lower than those of the CG at T1, T2, T3 and T4, and the Ramsay scores of the RG were higher than those of the CG. The incidence of maternal adverse events and maternal and infant outcomes in the RG were better than those in the CG, while there was no evident difference in Apgar score and NBNA score between the two groups. The levels of ACTH, Cor, NE and E in the RG were lower than those in the CG after delivery. Conclusion: Remifentanil PCIA combined with multiple acupoint stimulation can reduce maternal pain, shorten labor time, reduce stress reactions and improve maternal and infant outcomes.

Keywords: Remifentanil PCIA, multiple acupoints stimulation, labor analgesia, maternal and infant outcome

Introduction

Childbirth is an important physiological activity, and it allows humans to seed future generations and continue life, and it is a process that many women may go through [1]. Labor pain is a physiological pain that occurs during labor, and the intensity of pain is second only to burn pain, ranking second in the world [2]. The main causes of labor pain are visceral pain and body pain, which are related to uterine contraction, cervical dilatation, local tissue ischemia, traction and extrusion caused by severe uterine contractions during labor [3]. Severe pain during childbirth can trigger a series of physiological and psychological stress reactions [4]. Excessive stress reactions can lead to sympa-

thetic nerve excitement, and the secretion of stress hormones such as catecholamine, adrenocorticotropic hormone and endorphins in the body, which can eventually lead to abnormal labor process, fetal distress and other adverse maternal and infant outcomes [5]. With the improvement of people's quality of life and the popularization of the medical concepts of humanistic care, people's awareness and demand for labor analgesia are constantly improving [6]. Labor analgesia may have a protective effect on children's intellectual development and can effectively reduce the incidence of labor pain and postpartum depression, and also reduce the rate of cesarean section [7]. Therefore, labor analgesia is conducive to improving obstetric quality, ensuring the health

and safety of mothers and infants, and improving the quality of life.

At present, labor analgesia methods can be divided into drug-induced labor analgesia and non-drug-induced labor analgesia [8]. Drug-induced labor analgesia can have an analgesic effect by using anesthetic or sedative drugs [9], and it has the advantages of quick onset and exact analgesic effects, but its side effects are also inevitable, such as an influence on the labor process, motor nerve block, and the suppression of the maternal and infant respiratory system. At present, the most commonly used methods of labor analgesia are intrathecal analgesia, such as spinal-epidural analgesia and continuous epidural analgesia, but their long onset time, complicated operations and many contraindications, limit their application [11]. Patient controlled intravenous analgesia (PCIA) is widely used in clinics as a new labor analgesia technique [12]. However, related studies have found that the intravenous administration of remifentanil in small doses does not achieve satisfactory analgesic effects, while large doses can lead to adverse reactions such as respiratory depression and decreased fetal heart rate [13]. Non-drug labor analgesia includes prenatal education during pregnancy, training, midwifery, guidance, spiritual encouragement and support during various labor stages [14]. It also includes acupuncture anesthesia analgesia, transcutaneous electrical nerve stimulation, water births, intradermal water injection or Chinese medicine physiotherapy [15]. Auricular point magnetic bead plaster therapy is a new non-drug assisted analgesia method, which stimulates the uterus; with the Shenmen point and other sympathetic and endocrine acupoints of the ear, it generates stimulation signals, activates analgesic mechanisms, increases the pain threshold, and inhibits sympathetic nerve activity and pain stress responses to achieve the purpose of analgesia [16]. Non-drug labor analgesia is relatively safe for labor and the fetus, but the clinical analgesic effect is often unsatisfactory, which results in instability and uncertainty [17]. Therefore, it is of great clinical significance to explore a safe, effective, reasonable, easy and less traumatic labor analgesia method.

At present, there are few studies on remifentanil PCIA combined with multiple acupoint stimulation in labor analgesia. In this study, we applied remifentanil PCIA combined with multiple acupoint stimulation in labor analgesia, and discussed its influence on labor analgesia and maternal and infant outcomes.

Materials and methods

General data

A total of 177 parturients from March 2017 to May 2019 were selected and divided into two groups according to the analgesic methods. The control group (CG) (81 cases) received no labor analgesia, and the research group (RG) (96 cases) received remifentanil PCIA combined with multiple acupoint stimulation. The patients in the RG were aged 22-38 years, with an average age of (28.21±2.86) years, and the gestational period was 37-42 weeks, with an average of (40.21±1.06) weeks. The patients in the CG were aged 21-39 years, with an average age of (28.63±2.78) years, and the gestational period was 38-41 weeks, with an average of (40.31±1.14) weeks.

Inclusion and exclusion criteria

Inclusion criteria: (1) All parturients were single cephalic term pregnancies; (2) The anesthesia was regarded as grade I-II by American Society of Anesthesiologists (ASA) [18]; (3) The dilatation of the cervix was ≥ 3 cm, and there were regular contractions; (4) There were no pregnancy complications during the whole pregnancy; (5) This study has been approved by the Ethics Committee of our hospital, and patients have signed a completely informed consent form.

Exclusion criteria: (1) Patients with contraindications for anesthesia; (2) Patients with fetal distress; (3) Patients who had a history of opioid addiction; (4) Patients who were allergic to the drugs used in this study; (5) Patients with severe primary organ diseases, such as cardiovascular diseases, respiratory diseases, liver and kidney insufficiency; (6) Patients with coagulation dysfunction and immune system diseases; (7) Patients with incomplete clinical data; (8) Patients who had a family history of mental illness in the past; (9) Patients who dropped out the experiment halfway.

Analgesic methods

After all parturients entered the delivery room with regular contractions, the upper limb veins were routinely monitor for blood pressure, electrocardiogram, oxygen saturation, respiration and fetal heart rate. In the CG, the parturients were given routine obstetric delivery without analgesia. The puerpera in the RG received remifentanil PCIA combined with multiple acupoint stimulation for labor analgesia. The specific methods are as follows:

First, PCIA of remifentanil hydrochloride (Yichang Humanwell Pharmaceutical Co., Ltd., Yichang, China, H 20030199) was implemented with self-controlled analgesia pump. The parameters were set as follows: the first dose was 0.25 µg/kg, the background infusion volume was 0.05 µg/(kg min), the single dose was 0.25 µg/kg, and the locking time was 2 min, and the analgesia was stopped at the end of the third labor stage. In order to achieve rapid analgesia and reduce the dosage of remifentanil, the patient-controlled analgesia was used reasonably when the midwife's guidance was insufficient. At the same time, a Chinese medicine doctor used Huatuo auricular point magnetic bead plaster therapy (Suzhou Medical Products Factory Co., Ltd., Suzhou, China, YZB/0903-2013) to apply magnetic beads to press the auricular points. Shenmen, internal genitalia (uterus), endocrine and sympathetic points were applied, and one more bead was applied on the back of the corresponding each acupoint of each ear. After finding the point, it was pressed with thumb and index finger until the puerpera had numbness and slight pain. Massage of the auricular points was performed once every 15 min for 1 min until the contractions entered the active stage.

Outcome measures

(1) The duration of each labor stage, postpartum hemorrhage and length of hospitalization time of the two groups were recorded. (2) VAS score [19]: The VAS scores before analgesia (T0), 30 min after analgesia (T1), 1 h after analgesia (T2), at the opening of the birth canal (T3) and at delivery (T4) of the two groups were recorded; with a total score of 10 points, 0 was painless, 1-3 was mild pain, 4-6 was moderate pain. (3) Ramsay score [20]: The Ramsay scores before analgesia (T0), 30 min after analgesia (T1), 1 h after analgesia (T2), at the opening of the birth canal (T3) and at delivery (T4) of the two groups were recorded. With a total score of 6 points; 1 point indicates restless and irritable; 2 points indicates quiet and cooperative; 3 points indicates drowsiness, and patients can follow instructions; 4 points indicates patients are in sleep state and can be woken up; 5 points indicates patients are falling asleep, and the response is slow; 6 points indicates patients are in deep sleep state, and it is difficult to wake up. A high score indicates patients are more calm. (4) Apgar score of newborn [21]: After delivery, Apgar scores of newborn at 1 min and 5 min after birth was recorded; 8-10 is normal, 4-7 is mild asphyxia, and 0-3 is severe asphyxia. (5) NBNA score of newborn [22]: After delivery, the NBNA scores of the newborn at 15 min and 24 h after birth were recorded, with a total of 40 points, and ≥ 35 points indicates normal. (6) Stress hormones: 5 mL of venous blood was collected before and 30 min after delivery. ELISA was used to detect the levels of adrenocorticotropic hormone (ACTH), cortisol (Cor), norepinephrine (NE) and epinephrine (E) in the two groups. Measurements were performed according to the instructions of human ACTH ELISA, human Cor ELISA, human NE ELISA and human E ELISA (Shanghai Jingkang Bioengineering Co., Ltd., Shanghai, China, JK-(e)-A905, JKSW-E15000, JK-(a)-5709 and JK-(a)-4989). (7) The incidence of adverse events in the two groups was recorded.

Statistical methods

SPSS 20.0 (IBM Corp, Armonk, NY, USA) was used for statistical analysis, and GraphPad Prism 7 for illustrating the figures. Counting data was represented by [n (%)] and compared by chi-square test. Measurement data were represented as (x ± SD) and compared by t test of independent samples. Paired t test was used for comparison before and after treatment. One way ANOVA was used to analyze the data at different time points in the group, and SNK-q method was used for pairwise comparison at different time points in the group. When $P < 0.05$, the difference was statistically significant.

Table 1. Comparison of general data of parturients between two groups [n (%)] (x ± sd)

Classification	RG (n=96)	CG (n=81)	t/χ^2 value	P value
Age (years)	28.21±2.86	28.63±2.78	0.985	0.325
Pregnancy cycle (weeks)	40.21±1.06	40.31±1.14	0.604	0.546
BMI (kg/m^2)	24.35±3.14	24.12±3.01	0.494	0.621
ASA grade			0.042	0.837
I	71 (73.96)	61 (75.31)		
II	25 (26.04)	20 (24.69)		
Residence			0.084	0.771
Urban	62 (64.58)	54 (66.67)		
Rural	34 (35.42)	27 (33.33)		
Nationality			0.028	0.866
Han	78 (81.25)	65 (80.25)		
Minorities	18 (18.75)	16 (19.75)		
Educational level			0.734	0.391
≥ high school	68 (70.83)	62 (76.54)		
< high school	28 (29.17)	19 (23.46)		
Smoking history			0.012	0.913
Yes	16 (16.67)	14 (17.28)		
No	80 (83.33)	67 (82.72)		
Drinking history			0.306	0.580
Yes	26 (27.08)	25 (30.86)		
No	70 (72.92)	56 (69.14)		

Result

General data

There was no significant difference in clinical baseline data such as the age of parturient, pregnancy cycle, body mass index (BMI), ASA grade, residence, nationality, educational background, smoking history and drinking history between the CG and the RG (P>0.05). See **Table 1**.

Comparison of labor process time, postpartum hemorrhage and length of hospitalization between the CG and the RG

The duration of labor, postpartum hemorrhage and length of hospital stay in the RG were evidently lower than those in the CG (P<0.05). See **Figure 1**.

Comparison of VAS scores between two groups of parturients

There was no significant difference in VAS scores between the CG and the RG before analgesia (P>0.05). The VAS scores of the RG at T1, T2, T3 and T4 were evidently lower than those of the CG, while the VAS scores of the CG at T1, T2, T3 and T4 were evidently higher than those at T0 (P<0.05). See **Figure 2**.

Comparison of Ramsay score between two groups of parturients

There was no significant difference in Ramsay scores between the CG and the RG before analgesia (P>0.05). The VAS scores of the RG at T1, T2, T3 and T4 were evidently higher than those of the CG (P<0.05), while the VAS scores of the CG at T0, T1, T2, T3 and T4 had no significant difference (P>0.05). See **Figure 3**.

Comparison of Apgar score between two groups

There was no significant difference in Apgar scores between the CG and the RG at 1 min and 5 min after delivery (P>0.05). See **Figure 4**.

Comparison of NBNA scores between two groups of newborns

There was no significant difference in NBNA scores between the CG and the RG at 15 min and 24 h after delivery (P>0.05). See **Figure 5**.

Comparison of stress hormones between two groups of parturients

The levels of ACTH, Cor, NE, E before delivery were not evidently different between the CG and the RG (P>0.05). The levels of ACTH, Cor, NE, E in the two groups decreased evidently after 30 min after delivery, and the levels in the RG were evidently lower than the CG (P<0.05). See **Figure 6**.

Incidence of maternal adverse events in two groups

The incidence of adverse events in the RG (5.20%) was evidently lower than that in the CG (18.52%) (P<0.05). See **Table 2**.
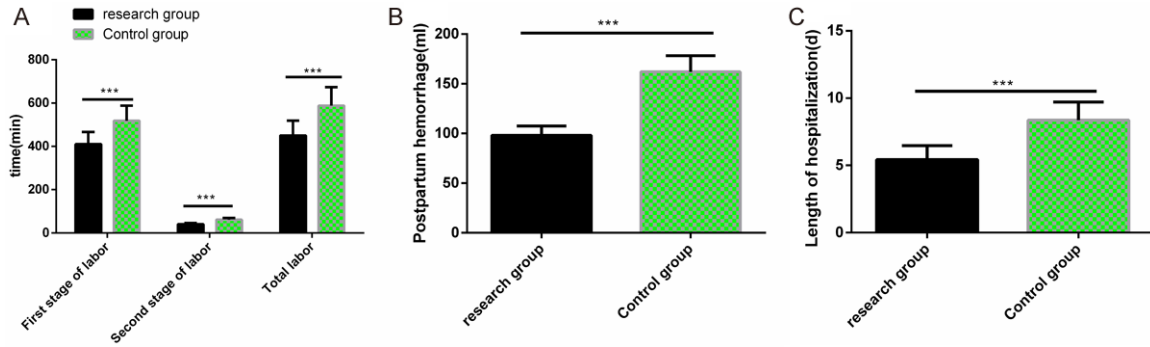
Figure 1. Comparison of labor process time, postpartum hemorrhage and hospitalization time between two groups. A: The duration of the first stage of labor, the second stage of labor and the total labor in the RG were evidently lower than those in the CG. B: The postpartum hemorrhage in the RG was evidently lower than that in the CG. C: The hospital stay of the RG was evidently lower than that of the CG. Note: *** indicates P<0.001.
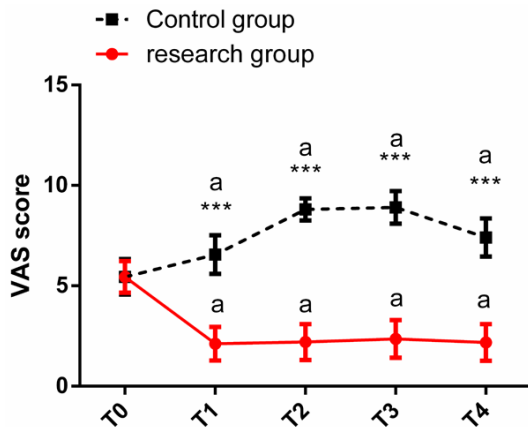

Figure 2. Comparison of VAS scores between two groups of parturients. There was no significant difference in VAS scores between the CG and the RG before analgesia. The VAS scores of the RG at T1, T2, T3 and T4 were evidently lower than those of the CG. The VAS scores of the CG at T1, T2, T3 and T4 are evidently higher than those at T0. Note: *** indicates P<0.001; a indicates compared with T0, P<0.05.
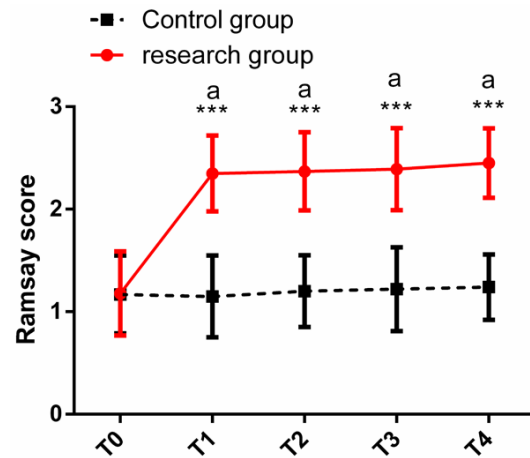

Figure 3. Comparison of Ramsay scores between two groups of parturients. There was no significant difference in Ramsay scores between the CG and the RG before analgesia. Ramsay scores of the r at T1, T2, T3 and T4 were evidently higher than those at T0 and were evidently higher than those of the CG at the same time. Note: *** indicates P<0.001; a indicates compared with T0, P<0.05.

Discussion

Labor pain is an unbearable pain accompanied by regular contractions of the uterus while the fetal head descends during labor [23]. Labor pain is a main factor affecting maternal labor and perinatal outcome [24]. With the development of society and the progress of perinatal medicine, how to relieve the pain in childbirth, relieve bad psychological moods of parturients and improve the quality of perinatal medicine is the focus of perinatal workers at present [25]. The ideal labor analgesia is to provide satisfactory analgesia for pregnant women without affecting the safety of the mother and infant

[26]. According to relevant research reports, non-drug acupuncture assisted analgesia has been widely used, and it has a good effect in controlling common back pain, headaches, cancer pain and labor pain [27]. In this study, remifentanil PCIA combined with multiple acupoint stimulation was used in puerpera to explore the effects on labor analgesia and maternal and infant outcomes.

Related studies have found that remifentanil PCIA can accelerate various labor processes and reduce postpartum hemorrhage [28]. In this study, we found that the duration of the
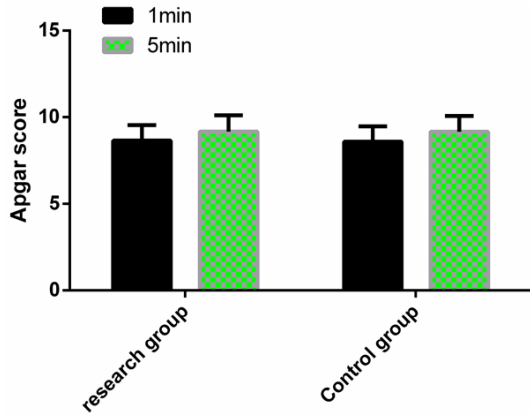
Figure 4. Comparison of Apgar scores between two groups. There was no significant difference in Apgar scores between the CG and the RG at 1 min and 5 min after delivery.
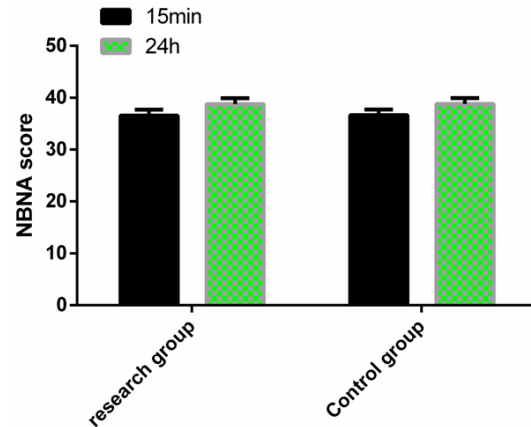

Figure 5. Comparison of NBNA scores between two groups. There was no significant difference in NBNA scores between the CG and the RG at 15 min and 24 h after delivery.

first stage of labor, the second stage of labor, the total labor, the amount of postpartum hemorrhage and the length of hospital stay in the RG were evidently lower than those in the CG, indicating that remifentanil PCIA combined with multiple acupoint stimulation can accelerate the labor process, reduce the amount of postpartum hemorrhage and promote postpartum recovery. In the research of Van de Velde M et al. [29], it was suggested that remifentanil PCIA has definite analgesic effects in parturient, which can evidently relieve the pain during childbirth, but it can inhibit the respiration of parturient, which needs close monitoring. In the research of Liu X et al. [30], it was found that the application of multiple acupoint electroacupuncture stimulation after anesthesia in tumor resection patients could evidently reduce the pain during and after operation, without adverse side effects, and can also improve the postoperative recovery. Chinese medicine promotes that ear is a gathering of assembled channels, and choosing corresponding acupoint massage in the ear can promote the dredging of meridians, the regulating of Qi and blood, and achieve the purpose of relieving pain [31]. Ear acupoint pressing is an analgesic technique similar to acupuncture. In the research of Alimoradi Z et al. [32], it was considered that ear acupoint pressing could evidently reduce the stress response in childbirth, promote the secretion of analgesic substances, block the introduction of pain impulse and increase the pain threshold. The results of this study showed that the VAS scores of the RG

after analgesia were evidently lower than those before analgesia, and evidently lower than those of the CG at the same time, indicating that remifentanil PCIA combined with multiple acupoint stimulation can evidently reduce the pain of parturient. At the same time, the Ramsay scores of parturients in the RG were evidently higher than those in the CG before and at the same time after analgesia, which indicated that remifentanil PCIA combined with multiple acupoint stimulation could alleviate the restlessness of parturients during childbirth and help them to better cooperate with doctors. It may be that multi-acupoint stimulation can enhance the analgesic effect of remifentanil and plays a synergistic role. Finally, the combination of the two has a significant effect on analgesia and sedation of parturient. Previous studies suggested that remifentanil PCIA has no adverse effects on the fetus in labor analgesia, and the drug use is safe [33]. According to the research of Heesen M [34], remifentanil PCIA has no obvious effects on Apgar score of newborns, and has no adverse effect on newborns. The results of this study showed that there was no significant difference in Apgar scores at 1 min and 5 min and NBNA scores at 15 min and 24 h between the RG and the CG, which indicated that remifentanil PCIA combined with multiple acupoint stimulation was safe and effective for newborns, which was similar to the results of Heesen M. This is supported by relieving pain during childbirth, protecting both mother and fetus, and improving the nutritional status of the fetus within
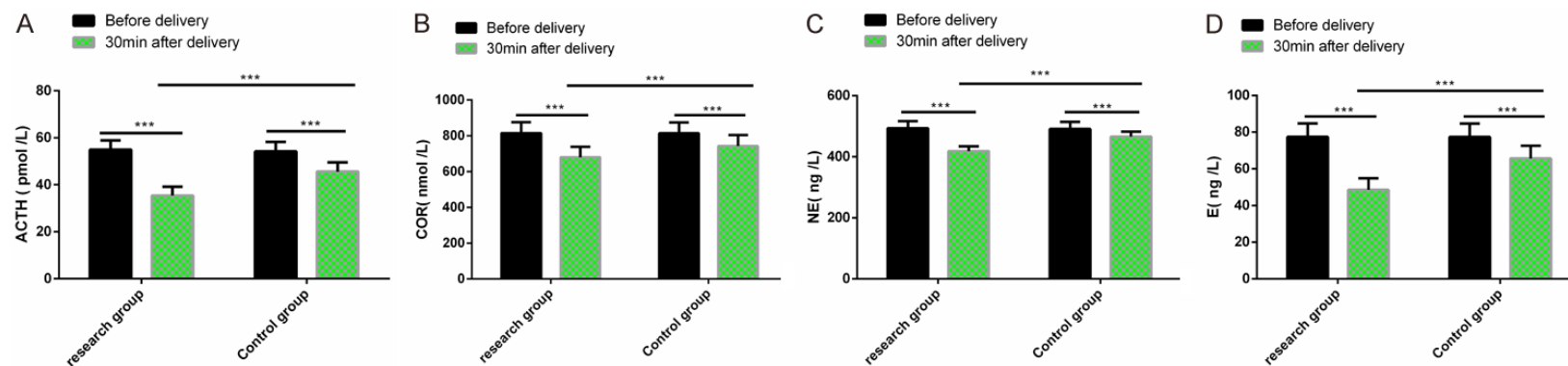
Figure 6. Comparison of stress hormones between two groups. A: There was no significant difference in the level of ACTH between the CG and the RG before delivery, but the level of ACTH between the CG and the RG after 30 min after delivery was evidently reduced, and the RG was evidently lower than the CG. B: There was no significant difference in Cor levels between the CG and the RG before delivery, but the Cor levels of the two groups decreased evidently after 30 min after delivery, and the RG was evidently lower than the CG. C: There was no significant difference RG before delivery, but the NE levels of the two groups decreased evidently 30 min after delivery, and the RG was evidently lower than the CG. D: There was no significant difference in E level between the CG and the RG before delivery, but the E level of the two groups after 30 min after delivery decreased evidently, and the RG was evidently lower than the CG.

Table 2. Comparison of incidence of maternal adverse events between two groups [n (%)]

Group	Urinary retention	Fetal distress	Postpartum hemorrhage	Total incidence rate
RG (n=96)	2 (2.08)	1 (1.04)	2 (2.08)	5 (5.20)
CG (n=81)	5 (6.17)	4 (4.94)	6 (7.41)	15 (18.52)
χ^2	-	-	-	7.765
P	-	-	-	0.005

mother. At the same time, the adverse events such as postpartum hemorrhage and fetal distress in the delivery process in the RG were evidently lower than those in the CG, which indicated that this analgesic method was safe for the maternal and infant delivery outcomes. Finally, we also measured the stress hormones of the two groups before and after delivery. The results showed that there was no significant difference in the levels of ACTH, Cor, NE and E between the CG and the RG before delivery, and the level of the RG was evidently lower than that of the CG 30 min after delivery, indicating that remifentanil PCIA combined with multiple acupoint stimulation can effectively relieve stress reactions and relieve labor pain. According to the research results of Czech I et al. [35], epidural anesthesia combined with non-drug analgesia methods such as aromatherapy, massage techniques, acupuncture, music therapy and yoga can effectively relieve labor analgesia and reduce the secretion of stress hormones such as ACTH and Cor, which is similar to our research results.

Although this study confirmed that remifentanil PCIA combined with multiple acupoint stimulation can bring better clinical efficacy to parturient, there is still room for improvement in this study. For example, we can further analyze the risk factors that affect puerpera's recovery after delivery and provide clinical basis for the puerpera's recovery. We can also analyze the interaction mechanism of the two, and provide theoretical basis for combination application. In the future, we will gradually conduct supplementary research from the above perspectives.

To sum up, remifentanil PCIA combined with multiple acupoint stimulation can alleviate the pain degree of parturient, shorten the labor process time, reduce the incidence of adverse events of parturient, reduce the stress hor-mone levels, improve the maternal and infant outcomes, and the analgesic effect is safe and effective.

Disclosure of conflict of interest

None.

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References

[1] Chau A, Bibbo C, Huang CC, Elterman KG, Cappiello EC, Robinson JN and Tsen LC. Dural puncture epidural technique improves labor analgesia quality with fewer side effects compared with epidural and combined spinal epidural techniques: a randomized clinical trial. Anesth Analg 2017; 124: 560-569.

[2] Wilson SH, Wolf BJ, Bingham K, Scotland QS, Fox JM, Woltz EM and Hebbar L. Labor analgesia onset with dural puncture epidural versus traditional epidural using a 26-gauge whitacre needle and 0.125% bupivacaine bolus: a randomized clinical trial. Anesth Analg 2018; 126: 545-551.

[3] Epsztein Kanczuk M, Barrett NM, Arzola C, Downey K, Ye XY and Carvalho JC. Programmed intermittent epidural bolus for labor analgesia during first stage of labor: a biased-coin up-and-down sequential allocation trial to determine the optimum interval time between boluses of a fixed volume of 10 ml of bupivacaine 0.0625% with fentanyl 2 μg/mL. Anesth Analg 2017; 124: 537-541.

[4] Nunes J, Nunes S, Veiga M, Cortez M and Seifert I. A prospective, randomized, blinded-end-point, controlled study - continuous epidural infusion versus programmed intermittent epidural bolus in labor analgesia. Braz J Anesthesiol 2016; 66: 439-444.

[5] Lim G, Farrell LM, Facco FL, Gold MS and Wasan AD. Labor analgesia as a predictor for reduced postpartum depression scores: a retrospective observational study. Anesth Analg 2018; 126: 1598-1605.

[6] Mankowitz SK, Gonzalez Fiol A and Smiley R. Failure to extend epidural labor analgesia for cesarean delivery anesthesia: a focused review. Anesth Analg 2016; 123: 1174-1180.

[7] Rehberg B, Wickboldt N, Juillet C and Savoldelli G. Can remifentanil use in obstetrics be improved by optimal patient-controlled analgesia bolus timing? Br J Anaesth 2015; 114: 281-289.

[8] Aaronson J, Abramovitz S, Smiley R, Tangel V and Landau R. A survey of intravenous remifentanil use for labor analgesia at academic medical centers in the United States. Anesth Analg 2017; 124: 1208-1210.

[9] De Lipsis L, Belmonte R, Cusano M, Giannetti MA, Muccio CF and Mancinelli M. Subdural hematoma as a consequence of labor epidural analgesia. Asian J Neurosurg 2018; 13: 931-934.

[10] Haller G, Pichon I, Gay FO and Savoldelli G. Risk factors for peripheral nerve injuries following neuraxial labour analgesia: a nested case-control study. Acta Anaesthesiol Scand 2017; 61: 1203-1214.

[11] Deshmukh VL, Ghosh SS, Yelikar KA and Gadappa SN. Effects of epidural labour analgesia in mother and foetus. J Obstet Gynaecol India 2018; 68: 111-116.

[12] Hwang BY, Kwon JY, Jeon SE, Kim ES, Kim HJ, Lee HJ and An J. Comparison of patient-controlled epidural analgesia with patient-controlled intravenous analgesia for laparoscopic radical prostatectomy. Korean J Pain 2018; 31: 191-198.

[13] Bushuven S, Kreuer S and Kranke P. Remifentanil update - Part 2. Anasthesiol Intensivmed Notfallmed Schmerzther 2017; 52: 630-639.

[14] Liu Y, Xu M, Che X, He J, Guo D, Zhao G, Zhang G, Zhang S, Kang K, Zhang C, Wang Y, Li S, Zhang Q, Xu L, Zhang M, Han B, Jing Y and Zhang N. Effect of direct current pulse stimulating acupoints of JiaJi (T10-13) and Ciliao (BL 32) with Han's Acupoint Nerve Stimulator on labour pain in women: a randomized controlled clinical study. J Tradit Chin Med 2015; 35: 620-625.

[15] Koyyalamudi V, Sidhu G, Cornett EM, Nguyen V, Labrie-Brown C, Fox CJ and Kaye AD. New labor pain treatment options. Curr Pain Headache Rep 2016; 20: 11.

[16] Hou PW, Hsu HC, Lin YW, Tang NY, Cheng CY and Hsieh CL. The history, mechanism, and clinical application of auricular therapy in traditional chinese medicine. Evid Based Complement Alternat Med 2015; 2015: 495684.

[17] Zhong Q, Wang D, Bai YM, Du SZ, Song YL and Zhu J. Effectiveness of auricular acupressure for acute postoperative pain after surgery: a systematic review and meta-analysis. Chin J Integr Med 2019; 25: 225-232.

[18] Doyle DJ, Goyal A, Bansal P and Garmon EH. American society of anesthesiologists classification (ASA Class). StatPearls: Treasure Island (FL); 2020.

[19] Tashjian RZ, Hung M, Keener JD, Bowen RC, McAllister J, Chen W, Ebersole G, Granger EK and Chamberlain AM. Determining the minimal clinically important difference for the American shoulder and elbow surgeons score, simple shoulder test, and visual analog scale (VAS) measuring pain after shoulder arthroplasty. J Shoulder Elbow Surg 2017; 26: 144-148.

[20] Rasheed AM, Amirah MF, Abdallah M, P J P, Issa M and Alharthy A. Ramsay sedation scale and richmond agitation sedation scale: a cross-sectional study. Dimens Crit Care Nurs 2019; 38: 90-95.

[21] Cnattingius S, Norman M, Granath F, Petersson G, Stephansson O and Frisell T. Apgar score components at 5 minutes: risks and prediction of neonatal mortality. Paediatr Perinat Epidemiol 2017; 31: 328-337.

[22] Su Q, Zhang H, Zhang Y, Zhang H, Ding D, Zeng J, Zhu Z and Li H. Maternal stress in gestation: birth outcomes and stress-related hormone response of the neonates. Pediatr Neonatol 2015; 56: 376-381.

[23] Dehcheshmeh FS and Rafiei H. Complementary and alternative therapies to relieve labor pain: a comparative study between music therapy and Hoku point ice massage. Complement Ther Clin Pract 2015; 21: 229-232.

[24] Jahdi F, Sheikhan F, Haghani H, Sharifi B, Ghaseminejad A, Khodarahmian M and Rouhana N. Yoga during pregnancy: the effects on labor pain and delivery outcomes (a randomized controlled trial). Complement Ther Clin Pract 2017; 27: 1-4.

[25] Moghimi-Hanjani S, Mehdizadeh-Tourzani Z and Shoghi M. The effect of foot reflexology on anxiety, pain, and outcomes of the labor in primigravida women. Acta Med Iran 2015; 53: 507-511.

[26] Dong C, Hu L, Liang F and Zhang S. Effects of electro-acupuncture on labor pain management. Arch Gynecol Obstet 2015; 291: 531-536.

[27] Sriasih NGK, Hadi MC, Suindri NN, Surati GA and Mahayati NMD. The effect of massage therapy using frangipani aromatherapy oil to reduce the childbirth pain intensity. Int J Ther Massage Bodywork 2019; 12: 18-24.

[28] Myers ER, Sanders GD, Coeytaux RR, McElligott KA, Moorman PG, Hicklin K, Grotegut C,

Villers M, Goode A, Campbell H, Befus D, McBroom AJ, Davis JK, Lallinger K, Fortman R and Kosinski A. Labor Dystocia [Internet]. Rockville (MD) 2020.

[29] Van de Velde M and Carvalho B. Remifentanil for labor analgesia: an evidence-based narrative review. Int J Obstet Anesth 2016; 25: 66-74.

[30] Liu X, Li S, Wang B, An L, Ren X and Wu H. Intraoperative and postoperative anaesthetic and analgesic effect of multipoint transcutaneous electrical acupuncture stimulation combined with sufentanil anaesthesia in patients undergoing supratentorial craniotomy. Acupunct Med 2015; 33: 270-276.

[31] He Q, Yang YF and Wu CL. A clinical trial of treatment of primary insomnia of patients with qi-stagnation constitution by shallow acupuncture combined with ear-acupoint pellet-pressing. Zhen Ci Yan Jiu 2019; 44: 293-296.

[32] Alimoradi Z, Kazemi F, Valiani M and Gorji M. Comparing the effect of auricular acupressure and body acupressure on pain and duration of the first stage of labor: study protocol for a randomized controlled trial. Trials 2019; 20: 766.

[33] Van de Velde M. Remifentanil patient-controlled intravenous analgesia for labor pain relief: is it really an option to consider? Anesth Analg 2017; 124: 1029-1031.

[34] Heesen M, Klohr S, Hofmann T, Rossaint R, Devroe S, Straube S and Van de Velde M. Maternal and foetal effects of remifentanil for general anaesthesia in parturients undergoing caesarean section: a systematic review and meta-analysis. Acta Anaesthesiol Scand 2013; 57: 29-36.

[35] Czech I, Fuchs P, Fuchs A, Lorek M, Tobolska-Lorek D, Drosdzol-Cop A and Sikora J. Pharmacological and non-pharmacological methods of labour pain relief-establishment of effectiveness and comparison. Int J Environ Res Public Health 2018; 15: 2792.