Comparison of the analgesic effects of dezocine, tramadol and butorphanol after cesarean section

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Abstract: At present, the drugs used in the field of postoperative analgesia are mainly opioids. The three analgesics selected in this study are opioid receptor agonists, but opioids are easy to produce adverse reactions. In this study, the visual analogue score of resting pain and dynamic pain at two time points of 4 hours and 12 hours was observed in group B and group C were higher than that in group A ($P<0.05$), indicating that the analgesic effect of dezocine was better. Follow up observation of adverse reactions, dezocine group patients had fewer adverse reactions ($P<0.05$). It can be seen that although there are certain differences in the mechanism of these three drugs, there are some relevant evidence that all three drugs can be used safely and effectively for postoperative obstetric analgesia.

Keywords: Dezocin, inflammatory mediator, tramadol, VAS score, adverse reaction.

INTRODUCTION

Postoperative pain is a nociceptive acute pain, but recent studies have shown that acute pain also has the possibility of peripheral and central sensitization (Brown *et al.*, 2014). Therefore, the prevention of peripheral and central hyperalgesia during postoperative analgesia has become the focus of attention of anesthesiologists in the treatment of acute pain (Cahill *et al.*, 2015). Postoperative pain is from the nature of pain. It is acute pain that occurs immediately after the operation, usually lasting for no more than 7 days (Dindo *et al.*, 2004). The operation itself is a traumatic injury that can cause damage to the nerve endings or nerve fibers. This nociceptive signal sends a specific nerve impulse to the nerve center (Chen *et al.* 2009). The signal passes through the peripheral afferent fibers of the peripheral pain receptor to the dorsal horn of the spinal cord, and after this replacement of the neurons through the spinal cord and thalamus (Faezeh *et al.*, 2017). The ascending bundle is transmitted to the central nervous system of the thalamus and limbic system, and the pain signal is perceived and integrated. With the development of tissue damage, the brain and spinal cord will release peptides and amine media, such as AD, 5-HT, NE, and P, which can prevent the signal transduction of pain. This is the four stage of the acute pain neurotransmission pathway (Fanny *et al.*, 2016). With the complete healing of the wound and the disappearance of abnormal excitability, the conduction function of nerve will then return to normal. Therefore, postoperative pain is caused by the stimulation of normal physiological pathway, which is a reversible pain. Furthermore, as a nociceptive stimulus, surgery will also cause changes in the system and metabolism of the body, resulting in the reduction of the body's immunity and mental and psychological changes (Ghoneum *et al.*, 2015).

With the improvement of the safety of cesarean section and the rapid development of perinatal medicine, the rate of cesarean section in China is increasing. More and more women are facing the problem of knife edge pain and uterine contraction after cesarean section (Balmadrid *et al.*, 2015). Abdominal incision injury is the main cause of postoperative pain. Surgery can cause damage to the body caused by local tissue trauma, and the tissue that is injured by injurious stimulation produces a large number of inflammatory mediators, and some of the inflammatory mediators (PGE2, bradykinin) can cause pain. In addition, cesarean section women often need intravenous injection of oxytocin, promote uterine contraction, reduce bleeding, and the use of oxytocin can cause a strong law of contraction pain, often make it difficult for women to endure (Betrán *et al.*, 2016). The negative emotions such as anxiety and irritability will aggravate the subjective feelings of the pain. Postoperative pain will aggravate the psychological burden of the parturient and postpone the healing of the incision, and the perfect postoperative analgesia can reduce the release of catecholamine and other stress hormones, reduce heart rate, reduce heart work and myocardial oxygen consumption, which is especially beneficial to the parturient with cardiac dysfunction.

Good postoperative analgesia should be individualized. As a special group of patients, parturient women have special physiological and psychological aspects. At present, the drugs used in the field of postoperative analgesia are mainly opioids. The three analgesics selected in this study are opioid receptor agonists. However, opioids are often accompanied by adverse

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reactions, such as respiratory depression, vomiting, dizziness, lethargy, retention of urine, and the occurrence of adverse reactions. Furthermore, according to the related theory of pain sensitization, the mechanism of drug analgesia is very complex and there are many paths, and no one of them can play a role at every site. Multimodal analgesia with multiple stages, multiple routes and multiple drugs is undoubtedly the best choice for future postoperative pain management.

MATERIALS AND METHODS

Case selection

We selected a single full term parturient for cesarean section in Ji'nan Center Hospital from January 2016 to December 2017, strictly enforced the inclusion and exclusion criteria, strictly implemented the inclusion and exclusion criteria, and finally selected 180 delivery women as the research object. The total samples were randomly divided into 60 cases (group A), tramadol group (group B) and butorphanol tartrate group (group C) with random numbers. All patients were approved by ethics committee of our hospital, ethical approval number as 2015JCHPT2 and all patients signed on the informed consent.

Inclusion criteria: (1) whether single term full term parturient is not limited to primipara. (2) Age at the age of 20~38.(3) the height is from 155 to 178cm. (4) The weight was 60~80 kg. (5) The gestational weeks were from 38 to 41W. (6) ASA was graded from I to II. (7) The results of liver and kidney work before operation were normal. (8) The results of blood routine and hemagglutination were normal. (9) No hypertension and diabetes. (10) A history of no drug allergy. (11) Contraindications of combined spinal and hard anesthesia. (12) Those are willing to cooperate with the informed consent.

Exclusion criteria: (1) A person with a history of mental illness. (2) A history of opioid dependence. (3) The person who is not willing to cooperate with himself or his family. (4) The anesthetic effect was unsatisfactory in the operation. (5) The high level of anaesthesia at the end of the operation.

Elimination standard: (1) The use of other analgesics after the operation. (2) The VAS scorer was not completed. (3) Other reasons are required to withdraw.

Ethical principles

The maternal and family members were informed and willing to participate in the study and were fully aware of the purpose and process of the study, as well as the possible risks and accidents involved in the study. Patients' right to privacy has been respected throughout the research process, and all data and information obtained in the study are strictly confidential.

Anesthetic method

The patients in each group had no preoperatively. After entering the operation room, oxygen inhalation, open venous access and rapid infusion of colloid fluid were carried out. All groups were monitored by non-invasive blood pressure, electrocardiogram, heart rate and arterial oxygen saturation. The patients in each group were treated with combined spinal and epidural anesthesia (CSEA). The patients were routinely sterilize the napkin, and the patient's height and weight were diluted to 2 ~ 2.5ml by 1.5 ~ 1.7ml of 1% ropivacaine and saline to 2 ~ 2.5ml. The puncture space was selected and the L3-4 space was selected for puncture. After the anesthesia was completed, the patient was supine and the tilt of the left side of the operating table was 15-30°. Oxygen uptake was observed and the control block level was above T6. If the systolic blood pressure of the patient is less than 100mmHg or the decrease of blood pressure is more than 20% of the patient's basic blood pressure, the intravenous injection of methoxin is 2 ~ 3mg, and the change of blood pressure is closely observed. If the blood pressure drops again during the operation, it should be given to methoxin again. The patients in each group were given the same caesarean section, and other sedative and analgesic drugs were not given during the operation, such as the abdominal organs of the patients, such as nausea and vomiting, were pulled and pulled, the operation was suspended, and the antiemetic agent was given. At the end of operation, the patient again tested the block level before transshipment back to the ward, and the patients with a block level above T4 excluded the study.

Analgesic scheme

Immediately after the operation, the analgesia pump was delivered to the pregnant woman. The pump was pumped at constant speed into the venous access 2ml/h, and a single additional dose of 0.5ml was injected continuously for 48 hours. The combination of three groups of analgesic pumps: group A was gezocine 50 mg; group B was tramadol 1000mg; C group was butorphanol tartrate 10mg; the three groups were all add tocoxanetron 5mg, and diluted to 100ml with saline.

Observation project

The anesthetic effect, operative time, fluid volume and bleeding volume were observed and recorded during the operation. After the operation, the uninformed nurses were interviewed and the visual analogue score (VAS) was used to evaluate the pain of resting and dynamic pain at 4, 12, 24, 36 and 48 hours after the parturient women, and the adverse reaction of each group of parturient women was counted.

It includes nausea and vomiting, dizziness, headache, drowsiness, itching, dizziness, headache, dysuria and respiratory depression. The pain level was graded as follows: Pain free pain score was 0 points; mild pain score

was 1~4; moderate pain score was 5~7; severe pain score was 8~9; severe pain and pain score was 10. The night time visits were completed by the nurses in the class. The sleeping patients were graded according to the quality of sleep (less than 4 points), and the sober patients were graded according to the actual pain relief.

STATISTICAL ANALYSIS

The data were analyzed by SPSS17.0 software package, and the data were measured by means of mean (X±s). Measurement data were analyzed by one-way ANOVA, counting data usage and percentage, and $\chi 2$ test was used to test the level of alpha =0.05.

RESULTS

General data and comparison of intraoperative conditions

There was no significant difference in the general data, operative time, fluid volume and bleeding volume between the three groups (P>0.05). As shown in table 1 and 2.

Comparison of VAS scores in three groups of parturients

VAS score of resting pain: 4 hours, 12 hours, 12 hours after operation, group C was higher than group A, the difference was statistically significant (P<0.05), there was no statistical difference between group B and group C in each time point group (P>0.05). As shown in table 3. VAS score of dynamic pain: 4 hours, 12 hours, 24 hours, B and C were higher in group A than in group A (P<0.05), and there was no statistical difference between group B and C group at each time point group (P>0.05). As shown in table 4

Comparison of the occurrence of adverse reactions

No adverse reactions such as respiratory depression and dysuria were found in all groups. The incidence of adverse reactions: the difference between the three groups was statistically significant, X2 =6.127, P=0.041. Group A and C group, X2 =5.183, P=0.021, the difference has statistical significance, A group and B group, X2 =1.469, P=0.079, the difference is not statistically significant; B group compared with C group, there is no statistical significance.

DISCUSSION

Injury induced by surgical trauma can cause a series of complex physiological and psychological changes, accompanied by high cesarean section rate followed by postoperative analgesia (Gunaldi *et al.,* 2015). How to relieve postoperative pain and ensure patient safety, while not having adverse effects on newborns, has become a prominent problem faced by anesthesiologists (Inzucchi *et al.*, 2015). An ideal analgesic drug should have the following conditions: (1) the effect is fast and the effect is smooth. (2) There was no significant effect on the respiratory and circulatory cycles when the treatment window was wide. (3) The metabolites were inactive and no accumulation (Jean *et al.,* 2017).

At present, none of these drugs can me*et al*l the above criteria. Opioid receptor agonist antagonist is an agonist antagonist that has an agonizing effect on a type of opioid receptor and has an antagonistic effect on other receptors (Liu *et al.,* 2013; Kearney *et al.,* 2016). The drug is characterized by better analgesic effects, less addiction and weaker respiratory inhibition, but a quasi mental side effect. Dezocin, tramadol and Bhutto enphol as opioid analgesics are the most commonly used analgesic drugs in clinical (Kargulewicz *et al.,* 2016). There are certain differences in the mechanism of drug action between the three, but there are some relevant evidence that all three drugs can be used safely and effectively for postoperative analgesia in obstetrics (Li *et al.,* 2012). In this study, the selected subjects were similar in weight (P<0.05). In this study, the visual analogue scores of resting pain and dynamic pain at two time points of 4 hours and 12 hours were followed up in group B and group C were higher than those in group A (P<0.05), indicating that the analgesic effect of gezocin was better. Follow up observation of adverse reactions, dezocine group patients had fewer adverse reactions (P<0.05).

The standard PCIA (patient controlled intravenous analgesia) is an early set of doses of analgesic drugs by adding a button to the intravenous pump when the patient is conscious of pain (Mellotte *et al.,* 2015). It is necessary to adjust the infusion of drugs to meet the patient's analgesic needs of personalized analgesia (Qin *et al.,* 2015). PCIA allows patients to control their own pain according to the extent of their subjective pain, and PCIA turns the traditional one - time oral, intramuscular, or intravenous injection into small doses and many times (Zhu *et al.,* 2015). This method adapts the individualized demand of different individuals to analgesics, makes the effect of postoperative pain more perfect, and overcomes the shortcomings of traditional analgesic methods, such as time lag, slow effect, poor effect and many adverse reactions (Rosenthal *et al.,* 2015). In addition, it can reduce the anxiety, depression and other bad emotions of the patient, and can effectively reduce the aggravation of the feeling of pain caused by emotional factors (Salhotra *et al.,* 2016). After operation, patients often have nausea and vomiting, which are associated with many causes, such as anesthesia, the use of postoperative analgesics, the sex of the patient, the negative emotion of the patient, and so on (Shim *et al.,* 2010). The body will generate some excitatory peripheral and vomiting centers such as ACh, DA, AD, AE and 5-HT, resulting in nausea and vomiting. 5-HT plays an important role in the pathogenesis of vomiting (Yoshio *et al.,* 2013).

Table 1: General comparison of patients

Index	Experimental group (n=120)	Control group (n=120)	P value
Sex (male / female)	67/53	62/58	0.014
Age (age)	42.3±7.15	43.5±6.14	0.582
Course of disease (year)	6.13±2.65	7.04±3.17	0.16

Table 2: Score comparison

Group	Cough score		Dyspnea score	
	Before treatment	After treatment	Before treatment	After treatment
Experience group	1.82±0.72	0.71±0.66	2.01±1.24	0.63±0.71
Control group	1.79±0.4	0.88±0.4	2.35±1.12	0.91±0.86

Table 3: Pulmonary function index

Group	FEV1%		PEF%	
	Before treatment	After treatment	Before treatment	After treatment
Experience group	55.27±2.83	61.56±3.12	59.14±2.13	72.64±3.56
Control group	57.13±1.92	68.34±3.24	62.27±2.61	79.61±4.12

Table 4: Comparison of experimental indexes

Group	IL-6(ng/l)		BNP(pg/ml)		CRP(mg/l)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Experience group	314.2±50.13	139.4±45.62	573.2±61.7	341.2±51.6	4.75±1.22	2.13±1.05
Control group	320.7±49.7	151.7±52.61	572.6±54.3	457.8±61.7	4.83±1.31	2.54±1.13

Table 5: Comparison of WBC and EOS

Group	WBC(10*9/L)		EOS(10*9/L)	
	Before treatment	After treatment	Before treatment	After treatment
Experience group	7.56±1.12	6.24±0.91	0.65±0.11	0.15±0.14
Control group	7.59±1.26	5.91±0.83	0.64±0.10	0.22±0.15

Table 6: Adverse reaction

Group	Flustered	Pharynx discomfort	Finger flutter	Fungal infection
Experience group	2	8	0	0
Control group	4	11	1	1

The 5-HT receptor is denser in the brain stem center. The receptor plays an important role in the production of vomiting (Sutton *et al.,* 2017). When the secretion of the gastrointestinal tract produces a large number of 5-HT, the transmitter can stimulate the 5-HT receptor located in the gastrointestinal mucosa and the brain stem center, thus producing vomit reflex. The drugs used for postoperatively emetic are DA receptor antagonists, droperidol, etc. However, these drugs play an antiemetic effect while their side effects are also obvious, such as dizziness, sleepiness, orientation disorder, and external vertebrae reaction, and so on (Tokioka *et al.,* 2012). It has high selective competitive antagonism in both peripheral and central 5-HT3 receptors, but the principle of its pharmacodynamics is to weaken the vomiting reflex by competitive inhibition of the 5-HT3 receptor in the presynaptic membrane of peripheral neurons (Xuan, 2015). In this study, nausea and vomiting were rare in all groups, indicating that it was necessary to add PCIA in the patients. In addition, under the premise of not violating the principle of the premise of reducing the patient's fasting, drinking time, keeping the patient's environment stable as far as possible and giving benzene two azo drugs and PPI acid suppressant before the start of the operation, it is also an effective measure to prevent postoperative nausea and vomiting.

CONCLUSION

The three drugs of dezococine, tramadol and Bhutto tartaric acid are ideal for postoperatively, and the effect of PCIA is better than that of tramadol and Bhutto, and the incidence of adverse reactions is less. With the development and application of new analgesic drugs to

clinical, postoperative analgesia and new vitality, and the development of patient controlled analgesia, it is possible to provide individualized analgesic solutions for different patients. However, the satisfactory postoperative analgesia depends on our anesthesiologist's mastery of the substance of the pain and the mechanism of drug action and the full and informed understanding of the patient. The best analgesic effect can be achieved with no or little adverse reactions, and the patient's satisfaction is improved.

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