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Study on the Effect of Dexmedetomidine Combined with Sufentanil in Post-Operative Epidural Analgesia after Cesarean Section

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Abstract

Objective: The aim was to provide a reliable trial of the application of sufentanil combined with dexmedetomidine for epidural analgesia after cesarean section in terms of clinical efficacy and safety.

Methods: The study population was selected from 80 cases of primiparous women who underwent elective caesarean section in Jiangyin People's Hospital from March 2019 to March 2021, and they were equally divided into two groups, with 40 cases in each group. In the control group (Group C), sufentanil citrate 50 ug + 0.9% saline, 120 ml in total; in the study group (Group D), sufentanil citrate 50 ug + dexmedetomidine hydrochloride 1 ug/kg + 0.9% saline, 120 ml in total. Observation indexes: VAS analgesia scores for contraction pain and incisional pain and OAA/S modified sedation scores in the two groups of pregnant women after surgery; determination of the time to first lactation in both groups; adverse events during postoperative analgesia.

Results: The control group had significantly higher VAS scores for incisional pain and contraction pain at 4 h, 8 h, 12 h and 24 h postoperatively than the study group (P<0.05); the control group had significantly higher OAA/S scores for sedation at 4 h, 8 h, 12 h and 24 h postoperatively than the study group (P<0.05); the study group had less time to first lactation than the control group (P<0.05). In terms of time to first lactation, the study group had less time than the control group (P<0.05); in terms of lactogen levels at 24 h and 48 h postoperatively, the study group had significantly higher levels than the control group (P<0.05); in terms of adrenocorticotropic hormone levels at 24 h postoperatively, the study group had significantly lower levels than the control group (P<0.05); in terms of prostaglandin hormone levels at 24 h postoperatively, the study group had significantly lower levels than the control group (P<0.05); in terms of maternal adverse effects in both groups, the control group had significantly higher levels of nausea and vomiting. The number of nausea and vomiting in the control group was significantly higher than that in the study group (P<0.05).

Conclusion: The combination of the two drugs for post-operative epidural analgesia after cesarean section is more effective in relieving maternal tension and anxiety without excessive sedation, with fewer adverse effects and reduced postoperative stress.

Keywords: Caesarean section; Dexmedetomidine; Sufentanil; Epidural analgesia

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Background

Postoperative pain management has always been a hot topic in the field of anesthesiology. The pain after caesarean section is of greater concern to the anesthetist, as the woman experiences different types of pain, mainly postoperative incisional pain and contraction pain. Post-operative pain can cause stress and anxiety and even depression, and these negative effects can greatly interfere with the woman's sleep and diet, thus greatly affecting her recovery and breastfeeding of her newborn [1]. Postoperative pain relief is always a challenge for doctors, and if pain is not managed properly after a caesarean section, it can affect not only the recovery and lactation of the mother but also the health of the newborn. It is therefore important to ensure that a safe and effective analgesia program is in place for the acute post-caesarean period. Several key factors (including pain relief, reduction of stress, reduction of adverse effects, prevention of delayed recovery of gastrointestinal motility and no disruption to lactation) determine how analgesia is administered [2]. In the present study, dexmedetomidine combined with sufentanil was used to provide epidural analgesia after caesarean section to observe the efficacy of analgesia and its effect on the postoperative stress state of the mother.

General information and methods

General information: The study population was selected from 80 primiparous women who underwent elective caesarean section and received postoperative epidural analgesia at Jiangyin People's Hospital from March 2019 to March 2021. The trial design was approved by the Ethics Committee of Zhongshan Hospital, Dalian University, and informed consent was signed with the patients and their families.

Inclusion criteria: Full-term, singleton primigravida; American Society of Anesthesiologists (ASA) class I-II; age 23 to 35 years; weight 65 kg to 85 kg; gestational week 37 to 40 weeks. Exclusion criteria: Known maternal allergy to the drugs used in the study; previous history of endocrinopathies, allergic immune diseases and psychiatric disorders; patients with blood coagulation abnormalities; lumbar spine abnormalities.

Grouping: The women were divided into two groups according to the order of admission, with 40 cases in each group. Control group (Group C): Sufentanil citrate 50 ug + 0.9% saline 120 ml; Study group (Group D): Sufentanil citrate 50 ug + dexmedetomidine hydrochloride 1 ug/kg + 0.9% saline 120 ml.

In both groups, the maternal self-administered epidural analgesia pump was set to a background dose of 2.0 ml/h, with each additional dose of 0.5 ml and a lock-in time of 15 min.

Anesthesia method: After admission to the operating room, the basic vital signs were monitored and recorded, oxygen was administered continuously *via* venturi (3 L/min to 4 L/min), the venous access to the upper extremities was opened, and sodium ringer acetate was administered. The patient was placed in the left lateral position, punctured in the L3-4 intervertebral space, and local anesthesia was performed with 1% lidocaine. 2.5 ml of 0.375% bupivacaine (1.5 mL of bupivacaine diluted to 3 ml with 10% dextrose) was injected into the subarachnoid space. Place an epidural catheter 4 cm to 5 cm to the side of the maternal head, and finally fix it. Wait for the block level to reach the T6 level before operating. It should be added that if the level does not reach T6 or if the procedure takes longer, additional injections of 1.5% lidocaine 3 mL at a time can be given through the epidural catheter to bring the maternal block level to T6. Intravenous ramosetron 0.3 mg is routinely given at the time of suturing to prevent postoperative nausea and vomiting. At the end of the operation, when the block level dropped below T10, the epidural self-administered analgesic pump was connected and turned on.

Observation indexes: (1) Visual Analogue Scoring (VAS) was used to assess postoperative pain and modified alertness/sedation (OAA/S) was used to assess postoperative sedation, and the observation time points were 4 h, 8 h, 12 h, 24 h and 48 h postoperatively; (2) The time of first lactation after surgery was recorded: The time from cesarean section to the first lactation; (3) Lactogen, adrenal stimulating hormone and prostaglandin were measured. Corticotropin and prostaglandin: 3 ml/time of maternal peripheral venous blood was collected 24 h before, 24 h after and 48 h after surgery, respectively, and then centrifuged, and the supernatant was taken and stored in a refrigerator. The Enzyme-Linked Immunoassay (ELISA) method was applied for determination; (6) the number of adverse reactions, including dizziness, respiratory depression and nausea and vomiting, was recorded.

Statistical analysis: SPSS 19.0 Software was applied for statistical processing, and the measurement data were expressed by mean ± standard deviation (x ± s). Among them, the count data were expressed by applying the rate (%), and the chi-square test was used for comparison between groups; the t-test was applied for comparison between groups of measurement data, and if the data did not meet the normality test, the non-parametric test was applied, and P<0.05 was considered to be statistically different.

Results

Comparison of the general maternal conditions between the two groups

There was no significant difference between the two groups in terms of age, height, weight, gestational week, and operative elapsed time, (p>0.05) (Table 1).

Comparison of VAS scores of incisional pain and contraction pain at different time points between the two groups

We observed the postoperative pain aspects in both groups on a follow-up basis and found that patients in the control (Beijing Aegean Lezhi Technology Co., Ltd, 2018) group would be more painful in terms of incisional pain and contraction pain at 4 h, 8 h, 12 h and 24 h postoperatively compared to patients in the study group at the following time points and there was a statistical difference between the data of the two groups (p<0.05) (Table 2, 3).

Comparison of maternal OAA/S scores at different time points between the two groups

In terms of sedation OAA/S scores at 4 h, 8 h, 12 h and 24 h postoperatively, the control group scores were significantly higher than the study group (P<0.05) (Table 4).

Comparison of the time to first lactation between the two groups

In terms of time to the onset of first lactation, both study groups (24.35 ± 4.33 h) were less than the control group (27.22 ± 5.34 h), and the difference was statistically significant (P<0.05).

Comparison of maternal serum lactogen levels between the two groups

At 24 h and 48 h postoperatively, prolactin levels were significantly

Table 1: Comparison of general maternal conditions between the two groups.

Group	Age (y)	Height (cm)	Weight (kg)	Gestational Cycle (w)	Surgery time (min)
Group C	26.21 ± 3.41	165.23 ± 3.89	69.26 ± 6.41	38.21 ± 1.21	47.62 ± 8.51
Group D	27.52 ± 2.92	164.91 ± 4.11	72.3 ± 4.54	37.98 ± 1.36	48.11 ± 7.65

Table 2: VAS scores of maternal incisional pain in both groups.

Group	Postoperative 4 h	Postoperative 8 h	Postoperative 12 h	Postoperative 24 h	Postoperative 48 h
Group C	3.19 ± 0.98	3.24 ± 0.78	3.27 ± 0.88	2.91 ± 0.65	2.41 ± 0.45
Group D	2.43 ± 0.85*	2.49 ± 0.45*	2.42 ± 0.43*	2.39 ± 0.48*	2.16 ± 0.56

*P<0.05, compared with the control group

Table 3: Maternal contraction pain VAS scores in both groups.

Group	Postoperative 4 h	Postoperative 8 h	Postoperative 12 h	Postoperative 24 h	Postoperative 48 h
Group C	3.15 ± 0.99	3.20 ± 1.01	3.11 ± 0.98	2.89 ± 0.68	2.39 ± 0.48
Group D	2.38 ± 0.89*	2.31 ± 0.96*	2.11 ± 0.78*	2.15 ± 0.77*	2.13 ± 0.61

*P<0.05, compared with the control group

Table 4: Comparison of maternal OAA/S scores at different time points between the two groups.

Group	Postoperative 4 h	Postoperative 8 h	Postoperative 12 h	Postoperative 24 h	Postoperative 48 h
Group C	4.72 ± 0.26	4.81 ± 0.11	4.88 ± 0.10	4.75 ± 0.18	4.51 ± 0.29
Group D	4.21 ± 0.29*	4.37 ± 0.29*	4.48 ± 0.17*	4.51 ± 0.19*	4.42 ± 0.32

*P<0.05, compared with the control group

Table 5: Comparison of serum maternal lactogen in the two groups.

Group	Preoperative 24 h (μg/L)	Postoperative 24 h (μg/L)	Postoperative 48 h (μg/L)
Group C	256.72 ± 43.21	337.45 ± 41.23	359.73± 37.11
Group D	245.87 ± 38.93	378.17 ± 39.22*	389.46 ± 40.02*

*P<0.05, compared with the control group

Table 6: Comparison of maternal adrenocorticotropic hormone levels between the two groups.

Group	Preoperative 24 h (μg/L)	Postoperative 24 h (μg/L)	Postoperative 48 h (μg/L)
Group C	9.34 ± 3.14	17.55 ± 4.20	11.73 ± 3.41
Group D	9.17 ± 3.03	13.17 ± 3.32*	10.96 ± 3.08

Note: *P < 0.05, compared with the control group

Table 7: Comparison of maternal serum prostaglandin levels between the two groups.

Group	Preoperative 24 h (pg/mL)	Postoperative 24 h (pg/mL)	Postoperative 48 h (pg/mL)
Group C	124.56 ± 37.24	167.55 ± 34.27	129.38 ± 36.42
Group D	123.87 ± 36.83	144.87 ± 37.35*	126.76 ± 37.02

Note: *P < 0.05, compared with the control group

Table 8: Comparison of maternal adverse reactions between the two groups.

Group	Vomiting	Dizziness	Respiratory inhibition	Itchy skin
Group C	4	1	0	1
Group D	1	2	0	1

higher in the study group than in the control group (P<0.05) (Table 5).

Comparison of maternal serum adrenocorticotropic hormone levels between the two groups

In the 24 h postoperative adrenocorticotropic hormone level, the study group was significantly lower than the control group (P<0.05) (Table 6).

Comparison of maternal serum prostaglandin levels between the two groups

At 24 h postoperative prostaglandin hormone level, the study group was significantly lower than the control group (P<0.05) (Table 7).

Comparison of maternal adverse reactions between the two groups

In terms of maternal adverse reactions between the two groups, the number of nausea and vomiting in the control group was significantly higher than that in the study group, and there was a statistical difference (P<0.05) (Table 8).

Discussion

Modern medicine considers pain as an unpleasant emotion caused by damaged tissues in the organism or tissues that are potentially damaged [3]. At the same time the body tissues produce a nociceptive response to these damaging stimuli, so the body tissues are able to produce a corresponding defensive response. Postoperative analgesia for cesarean delivery in these special groups of pregnant women is of even greater concern to anesthesiologists.

(1) Surgical incision: The incision of cesarean section will cause damage to the body tissues, so that the body will produce a series of defensive measures when it is adversely stimulated, so the damaged tissues or cells can secrete a series of inflammatory substances including nociceptive substances, which can trigger the body receptors to make nociceptive responses, and at the same time stimulate. Therefore, the surgical incision of cesarean section can produce corresponding mechanical injury to the nerve endings of the body, and at the same time lead to the increase of pain sensitivity of peripheral and central nerve cell functions to adverse stimuli, which is the main factor triggering postoperative pain.

(2) Uterine contraction: After delivery, the secretion of prostaglandin and oxytocin in the body is greatly increased, and the uterus is affected by the action of these two hormones, which will lead to strong contraction of the uterus, causing the phenomenon of uterine smooth muscle hypoxia, and the accumulation of too much acid in the smooth muscle of the uterus, which makes severe pain symptoms occur after the birth of the mother. In addition, when the mother is breastfeeding the baby, the baby's sucking stimulation will also cause strong contraction of the uterus to produce pain.

(3) Mental factors: Because most first-time mothers do not have experience in childbirth, mental tension and even anxiety

can occur before and after cesarean delivery, so hormones such as catecholamine's, cortisol and adrenocorticotropic hormones are secreted in large amounts, and mothers are more sensitive to pain [4].

Sufentanil citrate (Sufentanil), a fentanyl N-4 thiophene derivative, is a potent analgesic opioid, which mainly agonizes the mu receptor, and sufentanil for postoperative analgesia is divided into peripheral and central analgesia [5]. It is more effective and longer lasting. However, sufentanil applied epidurally can block the impulse transmission of sympathetic preganglionic fibers, which can cause vagal excitation of the gastrointestinal system and eventually lead to nausea and vomiting [6].

Dexmedetomidine hydrochloride belongs to a derivative of the imidazolin class of highly selective adrenergic receptor α2 agonists [7]. Dexmedetomidine inhibits neuronal transmission and thus sympathetic nerve activity mainly by agonizing α2 receptors in the spinal cord and brain, thus producing analgesic, sedative, and anxiolytic functions. In addition to this, dexmedetomidine prevents postoperative chills and reduces the occurrence of postoperative nausea and vomiting. Compared to opioids, the occurrence of respiratory depression is lower. Zhang et al. showed that in addition to inhibiting sympathetic nerve activity, dexmedetomidine can also slow down apoptosis, reduce oxidative stress and inflammation in the body, and therefore protect vital organs (heart, kidney, brain, liver, and lungs). It has also been reported that the α2 receptor is a subtype that is found in the central nervous system, peripheral nervous system, and autonomic nervous system, and that it produces the corresponding functions: Maintenance of endocrine homeostasis, control of the respiratory system, control of the circulatory system, and regulation of the hematological system. α2 receptors have four subtype structures: A, B, C, and D. All four subtype structures can react with the G-protein coupling system and can cause calcium ionization. All four subtypes can react with the G-protein coupling system to induce calcium inward flow, which then inhibits neurotransmitter secretion, resulting in presynaptic inhibition. Li et al. experiment also found that dexmedetomidine leads to excitation of the vagus nerve and inhibition of sympathetic excitation, thus the activity of the central sympathetic nervous system is inhibited, while agonizing the presynaptic membrane α2 receptors in sympathetic nerve terminals and inhibiting the secretion of catecholamine's and NE, and its organism manifests as a decrease in heart rate and blood pressure, so that the organism is more hemodynamically smooth when it is subjected to injurious stimuli [8-10].

In this experiment, dexmedetomidine combined with fentanyl was applied to the epidural analgesic pump for postoperative analgesia after cesarean delivery according to the mechanism of multimodal analgesia, and the results showed that the control group was significantly higher than the study group in terms of incisional pain and contraction pain VAS scores at 4 h, 8 h, 12 h and 24 h postoperatively ($P<0.05$), indicating that dexmedetomidine combined with sufentanil administered through the epidural analgesic pump could enhance the In terms of sedation OAA/S scores, the control group had significantly higher scores than the study group at 4 h, 8 h, 12 h and 24 h postoperatively, indicating that the combination of sufentanil and dexmedetomidine through epidural analgesia could better relieve postoperative pain and anxiety and irritability, and dexmedetomidine had good sedative effects; in terms of maternal adverse reactions in both groups, the number of nausea and vomiting in the control group was significantly higher than that in the study group. The number of nausea and vomiting in the control group was significantly higher than that in the study group, so it is possible that dexmedetomidine can alleviate the side effects produced by opioids.

Cesarean delivery is not only painful, but also causes a number of stress reactions that can adversely affect postoperative recovery and breastfeeding [11]. Two of these stress hormones are prostaglandins and adrenocorticotropic hormones, which are widely distributed in the nervous system and are involved in the regulation of neurotransmission and transmitter secretion as well as in the diastole and contraction of uterine muscle cells. They are released in large amounts when the body is injured. The results showed that prostaglandin and adrenocorticotropic hormone levels increased significantly in both groups at 24 h postoperatively, but the levels of both hormones were significantly lower in the study group than in the control group, indicating that the combination of the two drugs was more effective in suppressing prostaglandin secretion, reducing the postoperative stress response, and thus more effective in relieving incisional and contraction pains. The relevant literature reported [12] that the timing of first lactation can be greatly influenced by postoperative pain after cesarean section. The reason for this is that nervousness and pain lead to sympathetic arousal through neurological reflexes and therefore to a high secretion of catecholamine's, which leads to a decrease in the release of serum lactogen and finally to a decrease in maternal milk production [13,14]. The single postoperative application of opioid pain medication, although it can alleviate the pain after cesarean section, does not alleviate the symptoms of maternal anxiety and thus the secretion of milk is also affected to some extent. In terms of the time of first lactation onset, both study groups were smaller than the control group; comparing maternal lactogen levels in both groups, the study group was significantly higher than the control group at 24 h and 48 h postoperatively, probably because the combined application of the two drugs could improve the pain tolerance threshold of patients and reduce a variety of adverse stimuli such as pain, tension, and irritability, thus facilitating the release of lactogen and the secretion of lactation after cesarean section.

Conclusion

Sufentanil combined with dexmedetomidine hydrochloride has better epidural analgesia after cesarean section than sufentanil alone, more effective in relieving maternal tension and anxiety without excessive sedation, less adverse effects, and lower postoperative stress.

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