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Original Article

Preventive and therapeutic effects of dezocine and butorphanol combined with midazolam on shivering during and after cesarean section

Baojun Fang[1*], Qinzheng Zhao[1*], Qingfeng Zeng[2*], Changting Yan[1], Qingjuan Wang[1], Shuai Zhang[3], Chunhua Li[3], Junhong Guo[4], Guan Wang[5], Chengbao Li[6]

Departments of [1]Anesthesiology, [3]Nursing, Liaocheng Dongchangfu District Maternal and Child Health Hospital, Liaocheng, Shandong Province, China; [2]Department of Anesthesiology, Gongan County Traditional Chinese Medicine Hospital, Gongan County, Hubei Province, China; [4]Department of Nursing, Dongchangfu People's Hospital, Liaocheng, Shandong Province, China; [5]Department of Anesthesiology, The Second Hospital of Dalian Medical University, Dalian, Liaoning Province, China; [6]Department of Critical Care Medicine, Shanghai Tenth People's Hospital, Tongji University School of Medicine, Shanghai City, China. [*]Equal contributors and co-first authors.

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Abstract: Objective: The aim of this study was to compare preventive and therapeutic effects of dezocine and butorphanol combined with midazolam on shivering, during and after cesarean section, and to select a safe and effective strategy for prevention and treatment of this condition. Methods: From July 2015 to July 2016, 200 patients undergoing cesarean section in Liaocheng Dongchangfu District Maternal and Child Health Hospital were monitored. Patients were randomly divided into a prevention group (n=100, drugs administered intravenously immediately after delivery) and treatment group (n=100, drugs administered intravenously immediately when shivering occurred after delivery). The prevention group was randomly divided into two subgroups: subgroup I (n=50) receiving dezocine (0.1 mg/kg) + midazolam (0.03 mg/kg) and subgroup II (n=50) receiving butorphanol (0.01 mg/kg) + midazolam (0.03 mg/kg). The treatment group was also randomly divided into two subgroups: subgroup III (n=50) receiving dezocine (0.1 mg/kg) + midazolam (0.03 mg/kg) and subgroup IV (n=50) receiving butorphanol (0.01 mg/kg) + midazolam (0.03 mg/kg). Mean arterial pressure (MAP), heart rate (HR), respiratory rate (RR), shiver grading, shiver treatment efficacy, Ramsay sedation score, traction reaction grading, and other adverse reactions (such as nausea and vomiting, respiratory depression, uterine contractions pain, etc.) of patients were recorded at each time point: entering room (T0), before medication (T1), 3 minutes after medication (T2), 5 minutes after medication (T3), 10 minutes after medication (T4), 30 minutes after medication (T5), and 1 hour after surgery (T6). Results: MAP of patients in subgroup I of the prevention group decreased slightly at T4 ($P<0.05$) but no significant differences were seen at other time points in the prevention group and at any time point in treatment group (all $P>0.05$). Similarly, no significant differences were seen in HR and RR values in the two groups at any time point (all $P>0.05$). There were no significant differences in shiver grading between the subgroups in the prevention group ($P>0.05$). Time of elimination of shivering in the treatment group was significantly shorter in subgroup IV compared to subgroup III ($P<0.01$), but there were no significant differences in effective rate of shiver treatment ($P>0.05$). Ramsay sedation score of patients increased at T3 and T5 (both $P<0.05$) and increased significantly at T4 ($P<0.01$) in subgroup II in the prevention group, while increasing at T2 in subgroup IV in the treatment group ($P<0.05$). In the prevention group, traction reaction of subgroup I was significantly better than that of subgroup II ($P<0.05$), while no significant differences were seen between subgroups in the treatment group ($P>0.05$). Conclusion: Dezocine and midazolam are recommended for prevention of shivering while butorphanol and midazolam are recommended for treatment of shivering.

Keywords: Dezocine, butorphanol, midazolam, cesarean section, shiver

Introduction

With continuous improvement in medical technology and quality of life, the rate of cesarean sections (C-sections) has increased annually, worldwide. Due to the special physiological state of parturients, intravertebral anesthesia has been widely used during C-sections [1, 2].

Combined spinal-epidural anesthesia (CSEA) has been widely used in this type of surgery due to rapid effectiveness, complete analgesia during surgery, definite muscle relaxation, and less adverse reactions [3, 4].

Shivering, a common complication of intravertebral anesthesia, occurs in 5%-65% of cases [5]. Onset of shivering during surgery can lead to pain and discomfort for parturients and increase metabolism and other adverse reactions [6]. Although underlying mechanisms are not yet fully understood, shivering may be the result of the combination of anesthesia and decreased body temperature during surgery. After CSEA, some sensory and motor nerves of the body are blocked. The body temporarily loses control of skeletal muscle and skeletal muscle temporarily loses contractile function. Some sympathetic nerves are also blocked, weakening the contraction response of peripheral blood vessels to cold. Dilated vessels of body surface leading to dissipation of heat from the core to the periphery. Due to this constant loss of heat in the anesthetized area, average temperature of the body gradually drops [7-9]. Since patients cannot quickly re-establish heat balance between the core and periphery, core body temperature decreases and, after falling below a threshold, causes shivering and vasoconstriction in unblocked areas. Shivering during surgery increases intraocular pressure and intracranial pressure while significantly affecting heart rate, blood pressure, blood glucose, and heart rhythm. Shivering-induced increase in O_2 consumption and CO_2 generation results in hypoxia in the heart, brain, lungs, and kidneys, causing serious discomfort and stress for patients. Furthermore, hypoxemia results in intrauterine hypoxia and even intrauterine distress [10, 11]. Therefore, prevention and treatment of shivering, during and after C-section, has received extensive attention in recent years.

Dezocine is a novel opioid with receptor agonist-antagonist roles, acting as a κ receptor agonist and μ receptor antagonist. It can produce anti-shivering effects through agonistic action on spinal cord κ receptors, quickly relieving post-anesthetic shivering. It simultaneously acts on μ receptors in an antagonistic manner and inhibits nausea and vomiting, with low dependency and addiction. In contrast, dezocine has little activity on δ receptors and, thus, rarely produces dysphoria, anxiety, and other discomforts routinely caused by opioid agonists [8].

Butorphanol, also known as Stadol, is another novel opioid with agonist-antagonist roles. The drug and its metabolites can exert spinal analgesia, sedation, and anti-shivering by activating κ receptors. It acts on μ receptors, both agonistically and antagonistically, with low incidence of respiratory depression and addiction. It has little activity on δ receptors, thus, rarely producing dysphoria and other discomfort [12, 13]. The anti-shivering action of butorphanol may be related to its inhibition of synaptic 5-hydroxytryptamine (5-HT) and norepinephrine (NE) reuptake in spinal cord segments. 5-HT and NE neurotransmitters play a role in temperature regulation, belonging to pain pathways under the dorsal raphe nucleus and locus coeruleus and exerting anti-shivering action as neurotransmitters [14]. Through the abovementioned summaries, it has been theorized that dezocine and butorphanol can better treat intraoperative and postoperative shivering.

Midazolam is the only water-soluble benzodiazepine in common clinical use. A central nervous system (CNS) inhibitor, it results in sedation, anterograde amnesia, and partial indirect muscle relaxation by binding to benzodiazepine receptors, GABA receptors, and ion channels (chloride ion). Combination of anesthetic analgesics has a synergistic effect on CNS inhibition and the quality and comfort of obstetric anesthesia [15, 16]. It has been shown that benzodiazepines drugs can significantly attenuate the response of murine spinal cord to depolarization by stimuli of peripheral receptors. The most likely mechanism is inhibition of nerve impulse transmission to the CNS, thereby inhibiting shivering. Honarmand et al. have shown that intravenous midazolam administration prevents shivering, either due to its sedative effects, by improving patient tolerance to stimulation, or by lowering the body's stress response [17]. Qiu et al. found that combination of dezocine and midazolam and fentanyl and midazolam could achieve good analgesia sedation, inhibit traction reaction, and reduce adverse reactions and poor memory. Incidence of side effects is lower with the dezocine and midazolam combination [18].

In conclusion, various factors can lead to surgery-related shivering in parturients after anesthesia. This causes discomfort for parturients and affects the surgical operation and accuracy of physiological indicators during surgery. In addition, it also can easily lead to various complications during and after surgery. It is especially important to avert drop of core body temperature to prevent shivering. No single drug therapy is effective in preventing and treating chills. By combining dezocine, butorphanol, and midazolam, their anti-shivering effects can be theoretically synergized, reducing respective side effects by minimizing amounts of each drug. The optimal combination of drugs depends on various factors and should consider the safety of the mother and fetus. In addition, to be considered for use during C-section, the combination should be easy and comfortable to administer. This is of great guiding significance for future operations involving cesarean section.

The aim of this study was to compare the safety and efficacy of different drug combinations, such as dezocine combined with midazolam and butorphanol combined with midazolam for prevention and treatment of C-section-related shivering. In addition, this study also compared the advantages and disadvantages of prophylactic and therapeutic regimens to guide clinical medication.

Materials and methods

Patient data

This study was approved by the Ethics Committee of Liaocheng Dongchangfu District Maternal and Child Health Hospital. Detailed notifications (including intraoperative and postoperative shivering treatment methods and signature of informed consent) were completed during preoperative visits. Patients receiving C-section in Liaocheng Dongchangfu District Maternal and Child Health Hospital, from July 2015 to July 2016, were selected for the study.

Inclusion criteria: C-section performed with CSEA; ASA I or II grade; Aged between 20 to 45 years; Full-term pregnancy with single fetus; Patients agreed to participate and signed informed consent.

Exclusion criteria: Patients with hypertension, coronary heart disease, and other cardiovascular diseases; Patients with diabetes, hyperthyroidism, and other diseases of the endocrine system; Patients with disorders of the respiratory system and CNS; Patients with coagulation dysfunction; Patients with placental abnormalities such as placenta previa and placental abruption; Patients with fetal abnormalities such as macrosomia, fetal distress, and fetal malformation; Pre-delivery shivers; Contraindication to intra-spinal anesthesia; Patients with history of opioid allergies or opioid usage within one month.

Experimental grouping

After following all inclusion and exclusion criteria, 200 full-term pregnant women preparing to undergo C-section were selected and randomly divided into a prevention group (n=100, drugs administered intravenously immediately after delivery) and treatment group (n=100, drugs administered intravenously immediately when shiver occurred after delivery). Each group was further randomly divided into two subgroups based on drug combinations. The prevention group was randomly divided into subgroup I (n=50, 0.1 mg/kg dezocine + 0.03 mg/kg midazolam) and subgroup II (n=50, 0.01 mg/kg butorphanol + 0.03 mg/kg midazolam). Treatment group was randomly divided into two groups: subgroup III (n=50, 0.1 mg/kg dezocine + 0.03 mg/kg midazolam) and subgroup IV (n=50, 0.01 mg/kg butorphanol + 0.03 mg/kg midazolam).

Anesthetization

All patients had fasted for 12 hours, not drinking any liquids for 6 hours before surgery. After admitting patients into the operating room, electrocardiogram (ECG), blood pressure, heart rate (HR), and pulse oxygen saturation (SpO_2) were routinely monitored. In addition, peripheral venous access was opened and nasal catheter oxygen inhalation was performed. Temperature and humidity of the operating room were maintained at 25°C and 55%, respectively. None of the patients received any preoperative medication. Before starting anesthesia, 500 mL hydroxyethyl starch (130/0.4) was infused rapidly within 30 minutes and then maintained with lactated Ringer's injection. Patients were brought to left lateral position, disinfected, towels were spread, and epidural puncture was performed in the L3-4 interspinal interstice. The success of puncture was judged through negative pressure attraction. Lumbar puncture was then performed and the pumpback of cere-

Table 1. Comparison of general information ($\bar{x}$ ± sd)

		Age (year old)	Height (cm)	Weight (kg)	Gestational age (week)
Prevention group	Subgroup I (n=50)	29.2±5.0	159.7±4.5	74.7±8.0	37.3±0.9
	Subgroup II (n=50)	28.0±4.3	160.6±5.3	75.7±9.8	37.4±1.1
	t	1.29	0.96	0.55	0.30
	P	0.20	0.34	0.59	0.77
Treatment group	Subgroup III (n=50)	28.6±5.1	160.1±5.0	74.6±7.8	37.5±1.0
	Subgroup IV (n=50)	28.5±4.8	159.6±4.4	71.2±10.9	37.0±1.1
	t	0.16	0.55	1.78	0.15
	P	0.87	0.58	0.08	0.88

Note: There were no significant differences between the groups.

brospinal fluid was unobstructed. A total of 0.5% hyperbaric ropivacaine (2 mL) was slowly injected. If cerebrospinal fluid was unobstructed during withdrawal of the lumbar puncture needle, the epidural catheter was implanted. Patients were brought to a supine position, the operating bed was tilted slightly to the left by 30 degrees, and anesthesia plane was adjusted below the T6. When systolic blood pressure was lower than 30% of the basic value, 5-10 mg ephedrine was intravenously administered. Atropine was administered when the heart rate was lower than 60 beats/min. Atropine was given as needed. During the operation, if anesthetic effects decreased, 2% lidocaine (5 mL) was pre-administered to epidural after the anesthesia plane had been determined. After determining the anesthetic plane, whether to increase lidocaine was determined according to the situation. Ondansetron (4 mg) was intravenously administered 20 minutes before the end of the surgery. At the end of surgery, the anesthetic plane was determined again so that it did not exceed T6.

Observation indices

Mean arterial pressure (MAP), HR, respiratory rate (RR), shiver grading, shiver treatment efficacy, Ramsay sedation score, traction reaction grading, and other adverse reactions (such as nausea and vomiting, respiratory depression, contractions pain, etc.) of patients were recorded at different time points (entering room - T0, before medication - T1, 3 minutes after medication - T2, 5 minutes after medication - T3, 10 minutes after medication - T4, 30 minutes after medication - T5, 1 hour after surgery - T6).

Shivering was graded using Dewitte grading standards: grade 0 - no shivering; grade 1 - slight muscle fasciculation in the face or neck and ECG interference without upper limb random movement; grade 2 - obvious twitching of more than one muscle group; grade 3 - muscle shaking of the whole body [19, 20].

Efficacy criteria for treatment of shivering were as follows: elimination of shivers (no sign of muscle tremors), significantly reduced (no muscle tremors but presence of hair erection and peripheral vascular contraction), partially reduced (tremors in only one muscle group), invalid (tremors in two or more muscle groups affecting surgery).

Ramsay sedative scores were graded as follows: 1 - anxious; 2 - sedated and cooperative; 3 - somnolent but able to follow instructions; 4 - asleep and can be awakened; 5 - unresponsive to arousal; and 6 - in deep slumber and cannot be awakened [21, 22].

Grading of traction reaction, during peritoneum pulling and abdominal cavity cleaning, was as follows: grade 0 - no nausea, vomiting, and bulging of the intestines and no traction pain or stomach discomfort; grade 1 - mild stomach discomfort or nausea but no vomiting and traction pain; and grade 2 - traction pain with stomach discomfort or nausea and vomiting, with visibly bulging of the intestines and dysphoria.

Statistical analysis

All data were analyzed using SPSS 17.0 statistical software. Measurement data are presented as mean ± standard deviation ($\bar{x}$ ± sd) and t-test was used to compare two groups. Count data are expressed as the number of cases and percentages (%). Chi-square test or Fisher's exact test was used for comparison. Differences

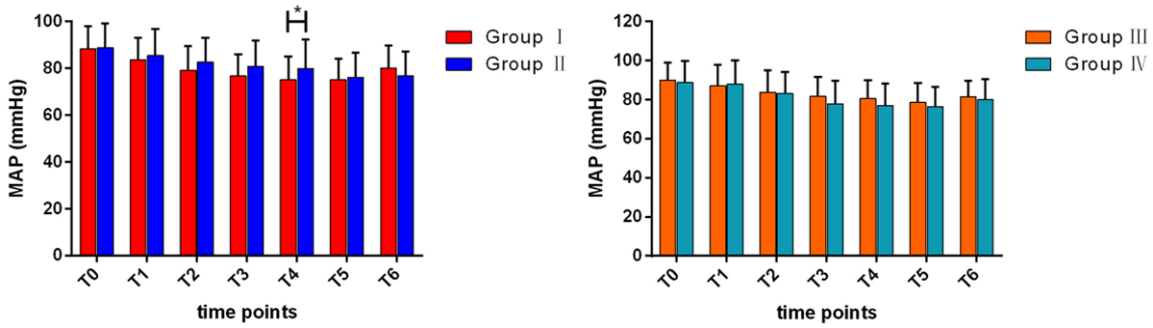

Figure 1. Comparison of MAP at different time points. MAP, mean arterial pressure; *P<0.05.

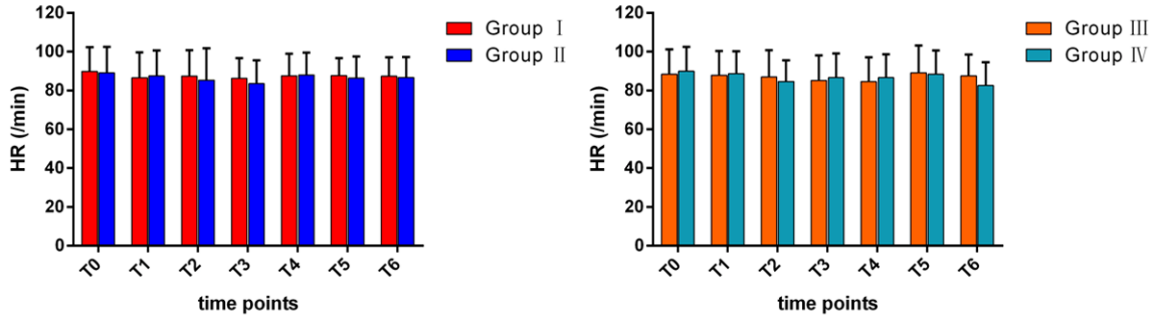

Figure 2. Comparison of HR at different time points. HR, heart rate.

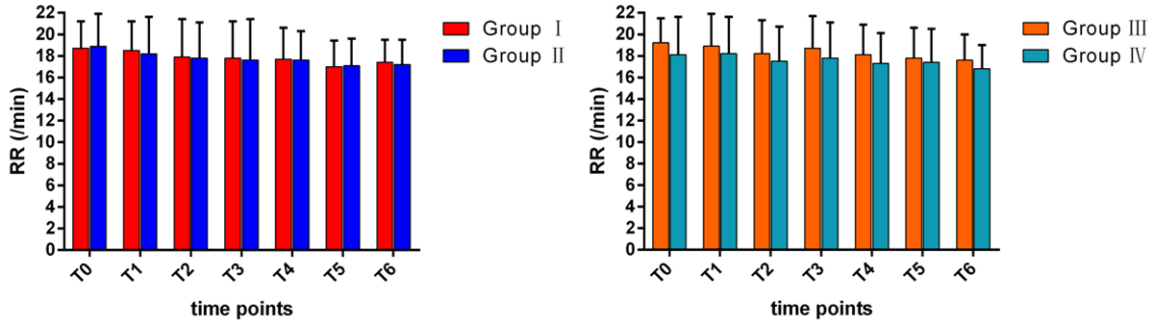

Figure 3. Comparison of RR at different time points. RR, respiratory rate.

were considered statistically significant when P<0.05.

Results

General patient data

There were no significant differences between the prevention group and the treatment group in terms of age, height, weight, gestational age, and other clinically relevant parameters (all P> 0.05). See **Table 1**.

Comparison of MAP, HR, and RR at each time point

In the prevention group, MAP was significantly reduced in subgroup I at T4 compared to subgroup II (t=2.15, P=0.03), while there were no significant differences between the two groups at other time points (all P>0.05). In the treatment group, MAP was always within the normal range in both subgroups and there were no significant differences at all points (all P>0.05). See **Figure 1**. No significant differences were

Table 2. Conditions of shivering in prevention group (case)

	Zero level	One level	Two level	Three level	Incidence (%)
Subgroup I (n=50)	48	2	0	0	4
Subgroup II (n=50)	45	5	0	0	10

Note: There were no significant differences between the groups.

Table 3. Effective rates for eliminating shivering in treatment group

	Subgroup III (n=50)	Subgroup IV (n=50)
Eliminating time (min)	4.04±1.46	2.85±0.69**
Elimination	30	39
Significant relief	14	6
Partial relief	5	3
Invalidation	1	2
Total effective rate	49 (98%)	48 (96%)

Note: Compared to subgroup III, **P<0.01.

seen in HR or RR between the prevention group and treatment group at all points (all P>0.05). See **Figures 2** and **3**.

Comparison of shivering grading and therapeutic efficacy

In the prevention group, the number of parturient women with shivering grades 0/1/2/3 in subgroups I and II were 48/2/0/0 and 45/5/0/0, respectively. Total incidence rates of the two subgroups were 4% and 10%, respectively, and were not significantly different (χ^2=1.38, P=0.24). See **Table 2**. In the treatment group, regression time of shivering using medication was significantly shorter in subgroup IV compared to subgroup III (t=5.21, P=0.002). In terms of efficacy of shivering treatment, the number of patients in subgroups III and IV at each grade was 30/14/5/1 and 39/6/3/2, respectively. Total effective rates of treatment were 98% and 96%, respectively, and were not significantly different (χ^2=0.34, P=0.56). See **Table 3**.

Comparison of Ramsay sedation scores in each group

As is shown in **Figure 4**. Combination of butorphanol and midazolam in the prevention groups lightly increased Ramsay sedation scores of patients at T3 and T5 (t=3.07, P=0.02; t=2.91, P=0.04) and significantly increased Ramsay sedation scores at T4 (t=4.21, P=0.004). In the treatment group, combination of butorphanol and midazolam at T2 increased Ramsay sedation scores of patients (t=3.79, P=0.01).

Comparison of traction reaction grading and incidence of adverse reactions

In the prevention group, the number of patients at each traction reaction grade in subgroup I and II were 46/4/0 and 37/10/3, respectively, and total incidence rates were 8% and 26%, respectively. Combination of dezocine and midazolam could significantly reduce the incidence of traction reaction during surgery (χ^2=5.74, P=0.02). However, in the treatment group, the number of patients at each traction reaction grade in subgroup III and IV were 45/5/0 and 48/1/1, respectively, with total incidence rates of 10% and 4%, respectively. There were no significant differences in occurrence of traction reaction between the two subgroups (χ^2=1.38, P=0.24). See **Table 4**. No adverse reactions, such as nausea, vomiting, respiratory depression, and uterine contraction pain were observed in either group.

Discussion

The number of pregnant women has steadily increased in China since introduction of the two-child policy. With constant improvements in C-section technology and relaxed surgical indications, the rate of C-sections in China has increased annually [23, 24]. C-section is a safe and convenient method of delivery which can reduce pain associated with childbirth. However, due to special physiological characteristics of parturient women and presence of the fetus, several adverse reactions can occur during surgery. Shivering, during and after the C-section, is a major problem [25].

Shivering seriously affects the physiological state of parturient women. It leads to significant increase in the metabolic rate, leading to more oxygen consumption. The oxygen consumption rate is almost 4-8 times higher than resting state due to the irregular tetanic contraction of skeletal muscles. Furthermore, decrease in core body temperature contracts peripheral blood vessels leading to a doubling of the car-

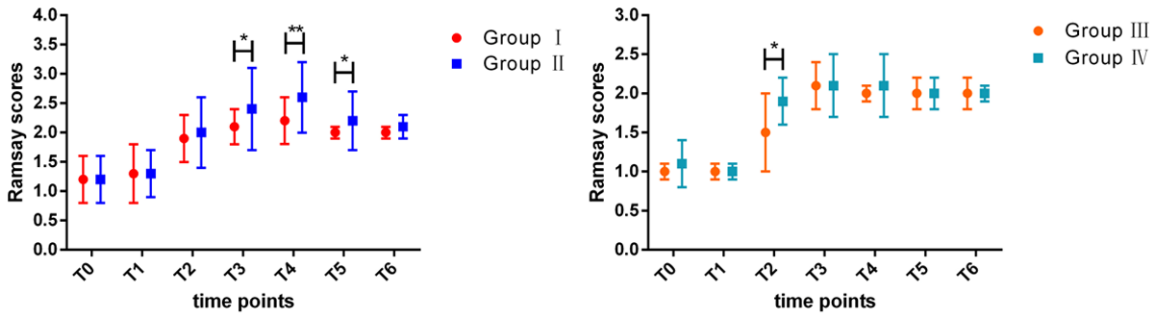

Figure 4. Comparison of Ramsay scores at different time points. *P<0.05, **P<0.01.

Table 4. Incidence of draw reaction in prevention and treatment groups

Draw reaction	Prevention group		Treatment group	
	Subgroup I (n=50)	Subgroup II (n=50)	Subgroup III (n=50)	Subgroup IV (n=50)
Zero level	46	37	45	48
One level	4	10	5	1
Two level	0	3	0	1
Incidence (%)	8	26*	10	4

Note: Compared to subgroup I, *P<0.05.

diac afterload. The heart load of parturients is increased in late pregnancy. This is a great challenge to heart function and increases risk of cardiovascular accidents [26, 27]. Shivering can also redistribute blood flow throughout the whole body, directing it to vital organs such as the heart and brain, while decreasing blood flow to organs such as the liver and kidneys. In addition, it slows down the metabolism of anesthetic drugs, prolongs their retention in the body, and increases incidence rate of adverse reactions such as nausea, vomiting, and respiratory depression. Changes in vascularity result in long-term hypoxia which increases risk of cell injury or even necrosis [28, 29]. Occurrence of shivering also affects the maternal immune system. Function of white blood cells in the body is damaged, increasing incidence of infection [30].

Occurrence of shivering has a great influence on management of anesthesia and the normal process of the operation. Shivering during the operation also influences the interpretation of physiological indices by the anesthesiologist. An inaccurate reading can significantly increase the ratio of ventilation and blood flow in patients, as well as the amount of invalid pulmonary shunt. This, in turn, results in respiratory dysfunction and hypoxemia during surgery, increasing the management of anesthesia during surgery. Furthermore, irregular tremors of multiple skeletal muscle groups affects the accuracy of the operation and increases probability of surgical errors, compromising the safety of parturients. Therefore, prevention and treatment of shivering, during and after C-section, is crucial.

In clinical work, treatment of shivering is mainly through drug therapy, except for basic methods of heat preservation. At present, the following drugs are typically used: Cholinergic inhibitors (physostigmine); Opioids (especially opioid receptor agonists (morphine, pethidine etc.) have a therapeutic effect on shivering in clinical application; Dizocine and butorphanol also belong to opioid receptor agonists, but specific efficacy and combination effects of the drugs are described in detail in this study [31, 32]; and Biogenic amines (tramadol). The above medications for treatment of shivering all have certain effects. However, due to various reasons such as severe adverse reactions, the particularity of maternal pregnancy, and impact on the fetus, these medications have not fully satisfied patient needs regarding cesarean section intraoperative and postoperative shivering. This present study focused on dezocine, butorphanol, and midazolam. Two different combinations of the drugs were tested for prevention and treatment of shivering and clinical outcomes were evaluated.

MAP, HR, and RR were recorded at different time points after medication. In the prevention

group, the MAPs of parturients that received midazolam with dezocine/butorphanol, immediately after delivery, were within the normal range and did not lead to a significant decrease in MAP, except at T4 (10 min after medication) when MAP decreased significantly in the dezocine + midazolam subgroup without any obvious effects on the body. In the treatment group, there were no significant differences in MAP between the two groups and all were within normal range. This demonstrates that the two combinations of drugs, whether in prevention or treatment of shivering, will not have much effect on body MAP.

Monitoring the HR of each time point, it was found that HR of the prevention group and treatment group were within the normal range and there were no statistical differences between the two groups. Therefore, this study concludes that neither combination of the two drugs significantly affect the heart rate of patients and can be used normally.

Dezocine and butorphanol have been reported to result in slight respiratory depression, while midazolam results in considerable respiratory depression [33, 34]. The results demonstrate that the two combinations of drugs did not significantly change breathing, as RR was within normal range. There were no significant differences in comparisons within groups. Therefore, neither of the two medication regimens significantly affect patient respiratory conditions.

The extent of shivering in the prevention group and the treatment group were graded by Dewitte scale. For prevention of shivering drugs, medicine was given to patients at the birth of the fetus. The highest shivering level was taken as experiment data. Incidence of shivering in the prevention group was low, overall, and most parturients exhibited grade I shivers. There were no significant differences between the two drug-combination subgroups, indicating that both medication regiments had considerable anti-shivering effects (**Table 2**).

Treatment of shivering drugs refers to patients that have had shivers after the birth of the fetus. When shivering occurred, they were given medicine immediately. The highest shivering level was recorded as experiment data. During shivering, the state of parturients and the operation are affected. Therefore, shivering should be quickly eliminated to carry out the later work. When drugs were administered immediately after shivering occurred (treatment group), time to eliminate shivering was significantly shorter with butorphanol + midazolam than with dezocine + midazolam (**Table 3**). In terms of total effective rate of shiver treatment, the number of patients with completely eliminated shivers was significantly more in subgroup IV, compared to subgroup III. Therefore, the combination of butorphanol and midazolam was more effective in treatment of shivering.

Ramsay sedation scores evaluate patient consciousness and can indirectly show whether the patient has a somnolent response. High Ramsay sedation scores indicate a poor chance of postoperative resuscitation. Ramsay scores in subgroup II of the preventive medication group were elevated compared to that in subgroup I, at T3 and T5, and were significantly increased at T4, indicating that butorphanol + midazolam could cause significant somnolence in patients. In the treatment group, although Ramsay scores in the subgroup IV were significantly higher than that in subgroup III at T2, they were still within the range of sobriety and did not significantly affect maternal consciousness. Therefore, each drug combination resulted in similar Ramsay sedative scores during treatment.

Traction reaction is a common complication during C-section. Pulling the peritoneum and cleaning the abdominal cavity can lead to an obvious traction reaction, causing nausea and vomiting. This not only affects surgery but also increases risk of reflux and aspiration. Therefore, it is very important to minimize traction reaction during C-section. This present study excluded any traction occurring before the drugs were administered. In the prevention group, combination of dezocine and midazolam significantly reduced incidence of traction reaction, whereas the butorphanol + midazolam group had a higher rate of traction reaction, indicating that the former had a better therapeutic effect during shiver prevention. In the treatment group, however, incidence of traction reaction was very low in both medication subgroups. There were no significant differences between the two groups, indicating that both drug regimens equally managed traction reaction during surgery.

In conclusion, there were no significant differences in cardiovascular and respiratory indices, such as MAP, HR, and RR, at each time point in both prevention and treatment groups. In the preventive medication group, both drug combinations significantly reduced incidence of shivering. The combination of dezocine and midazolam significantly reduced incidence of traction reaction and combination of butorphanol and midazolam aggravated somnolence. In the therapeutic medication group, combination of butorphanol and midazolam quickly eliminated shivers, while both combinations significantly reduced the incidence of traction reaction and did not differ in terms of Ramsay sedative scores. Therefore, this study recommends the combination of dezocine and midazolam to prevent shivering and combination of butorphanol and midazolam to treat shivering.

Address correspondence to: Guan Wang, Department of Anesthesiology, The Second Hospital of Dalian Medical University, No.467 Zhongshan Road, Shahekou District, Dalian 116027, Liaoning Province, China. Tel: +86-0411-84671291; E-mail: wangguan259@163.com

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