

# Effects of dexmedetomidine hydrochloride on hemodynamics, postoperative analgesia and cognition in cesarean section

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**Abstract.** The present study aims to investigate the effects of dexmedetomidine hydrochloride (Dex) on hemodynamics, postoperative analgesia and cognition in cesarean section. One hundred and two pregnant women who underwent cesarean section were selected from August 2016 to July 2017 in People's Hospital of Zhangqiu District and randomly divided into control group and observation group. Control group was anesthetized with bupivacaine hydrochloride, and morphine + ropivacaine hydrochloride were given postoperatively. Observation group received intraoperative anesthesia with bupivacaine hydrochloride and Dex, and Dex + ropivacaine hydrochloride were given for postoperative analgesia. Hemodynamic factors were compared between the two groups. Postoperative Ramsay sedation score, the incidence of adverse reactions and the incidence of transient neurological syndrome (TNS) were compared between the two groups. Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE) scoring were performed to evaluate the cognitive function of the two groups. The mean arterial pressure (MAP) and visual analogue scale (VAS) scores of the observation group after anesthesia were significantly lower than those of control group ( $P < 0.05$ ). The Ramsay sedation score of the observation group was significantly better than that of control group at different time-points after surgery ( $P < 0.05$ ). Incidence of postoperative agitation in observation group was significantly lower than that in control group ( $P < 0.05$ ). Incidence of TNS in observation group was significantly lower than that in control group during 1 week after surgery ( $P < 0.05$ ). MoCA and MMSE scores of the observation group were better than that of control group at

1 day after operation ( $P < 0.05$ ). The use of Dex anesthesia in cesarean section can achieve more stable hemodynamic conditions during perioperative period and more obvious analgesic effect after operation. It also reduced the incidence of postoperative TNS and cognitive dysfunction, and had important clinical significance.

## Introduction

Cesarean section refers to the surgical procedure of fetal removal by opening the lower abdominal cavity and uterus. This surgery is usually performed for high-risk pregnant women or those with abnormal delivery (1). Cesarean section operation is performed under anesthesia, and the main method is combined spinal-epidural anesthesia, which does not affect spontaneous breathing and cognition (2). Analgesic assistance is needed intraoperatively and postoperatively, and attentions should be paid on both analgesic effect and selection of drugs to protect the fetus (3). Intraoperative and postoperative pain should be carefully controlled after local anesthesia to relieve pain, achieve analgesic effect and facilitate the rapid recovery of pregnant women. However, postoperative complications, including transient neurological syndrome (TNS), agitation, delirium, anxiety and confusion, may happen (4,5). In this study, dexmedetomidine hydrochloride (Dex) was used in cesarean section to investigate its effects on hemodynamic factors, postoperative analgesia and cognition.

## Materials and methods

**Clinical data.** A total of 102 pregnant women who underwent cesarean section were selected from August 2016 to July 2017 in People's Hospital of Zhangqiu District (Jinan, China). Inclusion criteria: i) patients who underwent cesarean section; ii) single cephalic term pregnant women; and iii) patients who signed the written informed consent. Exclusion criteria: i) patients with serious drug allergy; ii) patients with obstetric complications and surgical complications; and iii) patients with severe mental illness. Patients were randomly divided into control group and observation group, with 51 cases in each group. There was no significant difference in general information between the two groups ( $P > 0.05$ ) (Table I). The

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Table I. Comparison of general information between the two groups.

Items	Observation group (n=51)	Control group (n=51)	t/ $\chi^2$ test	P-value
Age (years)	20-38	20-40		
Average age (years)	28.46±5.63	28.82±5.13	0.338	0.736
BMI (kg/m <sup>2</sup> )	23.03±1.15	23.16±1.29	0.537	0.592
Average gestational age (weeks)	38.74±1.18	38.49±1.23	1.047	0.298
Education (n, %)				
Junior high school and below	8 (15.69)	6 (11.76)		
Secondary and high school	20 (39.21)	23 (45.10)	0.517	0.772
College or above	23 (45.10)	22 (43.14)		

study was approved by the Ethics Committee of People's Hospital of Zhangqiu District (Jinan, China).

**Methods.** Both groups received combined spinal-epidural anesthesia. Patients were fixed in left lateral position. After conventional disinfection, L2-L3 intervertebral space was punctured. Epidural space was localized by using the resistance viscosity method. Arachnoid was punctured by using a spine needle. When cerebrospinal fluid reflux became smooth, 10 ml bupivacaine hydrochloride (state approval no. H50020012; Southwest Pharmaceutical Co., Ltd., Chongqing, China) were injected into patients in each group. After that, 0.9% sodium chloride was injected into control group through a spine needle, while 4  $\mu$ g of Dex in the same volume of 0.9% sodium chloride was used in the observation group. Spine needle was removed after injection. Patients were adjusted to supine position and T6 plane. After the onset of anesthesia, cesarean section was performed to remove the baby from the mother.

Patients were given epidural continuous controlled analgesia after operation. In control group, morphine (5 mg) + ropivacaine hydrochloride (0.15%) (state approval no. H20050325; Guangdong Huarun Shunfeng Pharmaceutical Co., Ltd., Guangdong, China) in 100 ml 0.9% sodium chloride solution was used. In control group, Dex (1  $\mu$ g/kg) + ropivacaine hydrochloride (0.15%) in 100 ml 0.9% sodium chloride solution was used. A loading dose (2 mg morphine in control group and Dex at a dose of 0.1  $\mu$ g/kg in observation group) + a background dose (2 ml/h) + PCA (0.5 ml each time with an interval of 15 min) was performed for 48 h.

#### Evaluation method

Heart rate (HR), mean arterial pressure (MAP), mean oxygen saturation (SpO<sub>2</sub>), and visual analogue scale (VAS) scores were compared between the two groups before anesthesia (T1), 10 min after anesthesia (T2), when the baby was born (T3) and immediately after surgery (T4).

Ramsay sedation scoring was performed at 6, 12, 24 and 48 h after surgery: i) 1 point, irritability or anxiety; ii) 2 points, good directive force and cooperation ability; iii) 3 points, drowsiness, but can respond to instructions; iv) 4 points, can respond to strong sound stimuli or eyebrows reaction; v) 5 points, slow response to strong sound stimuli or eyebrows reaction; and vi) 6 points, no response to strong sound stimulation or light eyebrows (6).

Postoperative adverse reactions, including nausea, vomiting, hypoxemia, delayed recovery and postoperative agitation were observed in the two groups of patients. Postoperative TNS determination and grading: patients with dysfunction of the lower extremity on one or both sides; sensory disturbances and obvious pain, and the nature of pain is burning-like, press-like or radioactive pain. While electrophysiological examination results were normal. i) Grade I, single or bilateral dyskinesia and sensory disturbances were obvious, dyskinesia score <26 points, sensory disturbance score <16 points; ii) grade II, unilateral or bilateral motor impairment was not obvious, score  $\geq$ 26 points, but there was obvious sensory disturbance, sensory disturbance score <16 points; iii) grade III, unilateral or bilateral dyskinesia and sensory disturbances were not very obvious, only numbness and pain were observed (7).

Montreal Cognitive Assessment (MoCA) was used to evaluate the condition of patients at 1 day before and after operation through 8 aspects including executive ability, memory, attention, nomenclature, language, delayed recall, abstract thinking and directionality (8). Mini-Mental State Examination (MMSE) was used to evaluate the orientation force, language, memory, attention and computational power of patients (9). Both scores were negatively associated with the degree of cognitive impairment.

**Statistical analysis.** Data were processed by using SPSS 19.0 (IBM Corp., Armonk, NY, USA) software. Measurement data were expressed as mean  $\pm$  standard deviation (mean  $\pm$  SD); t-test was used for the comparisons between groups. Count data were expressed as rate and processed by  $\chi^2$  test. P<0.05 was considered to be statistically significant.

## Results

**Comparison of hemodynamic factors between the two groups.** There was no significant difference in HR and SpO<sub>2</sub> between the two groups during perioperative period (P>0.05). The MAP score of the observation group after anesthesia was significantly lower than that of control group (P<0.05) (Tables II-IV).

**Comparison of VAS scores during perioperative period.** After anesthesia, patients in observation group showed significantly reduced pain score compared with those in control group (P<0.05) (Table V).

Table II. Comparison of HR between the two groups at different time-points (mean  $\pm$  SD, bpm).

Groups	Cases	T1	T2	T3	T4
Observation	51	84.83 $\pm$ 8.14	74.53 $\pm$ 7.48	68.26 $\pm$ 6.15	74.86 $\pm$ 5.52
Control	51	85.46 $\pm$ 8.15	75.05 $\pm$ 7.53	67.87 $\pm$ 6.27	75.14 $\pm$ 5.63
t-test		0.391	0.350	0.317	0.254
P-value		0.697	0.727	0.752	0.800

HR, heart rate.

Table III. Comparison of SpO<sub>2</sub> between the two groups at different time-points (mean  $\pm$  SD, %).

Groups	Cases	T1	T2	T3	T4
Observation	51	97.47 $\pm$ 0.44	98.62 $\pm$ 0.34	97.42 $\pm$ 0.38	99.55 $\pm$ 0.17
Control	51	97.52 $\pm$ 0.31	98.57 $\pm$ 0.26	97.35 $\pm$ 0.45	99.58 $\pm$ 0.28
t-test		0.663	0.834	0.849	0.654
P-value		0.509	0.406	0.398	0.515

SpO<sub>2</sub>, oxygen saturation.

Table IV. Comparison of MAP between the two groups at different time-points (mean  $\pm$  SD, mmHg).

Groups	Cases	T1	T2	T3	T4
Observation	51	66.67 $\pm$ 3.52	67.24 $\pm$ 4.46	65.27 $\pm$ 3.28	62.62 $\pm$ 3.47
Control	51	67.12 $\pm$ 3.64	79.67 $\pm$ 4.63	75.58 $\pm$ 3.54	69.35 $\pm$ 3.35
t-test		0.635	13.808	15.257	2.562
P-value		0.527	<0.001	<.001	0.012

MAP, mean arterial pressure.

Table V. Comparison of VAS score at different time-points (mean  $\pm$  SD, points).

Groups	Cases	T1	T2	T3	T4
Observation	51	6.95 $\pm$ 1.14	0.36 $\pm$ 0.13	1.13 $\pm$ 0.32	2.13 $\pm$ 1.12
Control	51	7.16 $\pm$ 1.23	0.73 $\pm$ 0.25	1.86 $\pm$ 0.27	3.56 $\pm$ 1.17
t-test		0.894	9.377	12.451	6.305
P-value		0.373	<0.001	<0.001	<0.001

VAS, visual analogue scale.

*Comparison of analgesic conditions between the two groups.* Ramsay sedation scores in observation group were significantly better than those in control group at different time-points (P<0.05) (Table VI).

*Comparison of adverse reactions between the two groups.* There was no significant difference in incidence of nausea and vomiting, hypoxemia and delayed recovery between the two

groups (P>0.05). The incidence of postoperative agitation in observation group was significantly lower than that in control group (P<0.05) (Table VII).

*Comparison of incidence of TNS between the two groups within 1 week after operation.* The incidence of TNS was significantly lower in observation group than in control group (P<0.05) (Table VIII).

Table VI. Comparison of postoperative Ramsay sedation scores between the two groups.

Groups	Cases	6 h after operation	12 h after operation	24 h after operation	48 h after operation
Observation	51	2.95±0.14	4.76±0.23	2.98±0.26	2.63±0.22
Control	51	2.16±0.23	3.42±0.25	2.65±0.26	2.36±0.27
t-test		20.953	7.148	4.467	5.536
P-value		<0.001	<0.001	<0.001	<0.001

Table VII. Comparison of adverse reactions between the two groups (n, %).

Groups	Cases	Nausea and vomiting	Hypoxemia	Postoperative agitation	Delayed recovery
Observation	51	3 (5.88)	1 (1.96)	0 (0.00)	2 (3.92)
Control	51	5 (9.80)	3 (5.88)	6 (11.76)	4 (7.84)
$\chi^2$ test		0.136	0.260	4.427	0.177
P-value		0.713	0.610	0.035	0.674

Table VIII. Comparison of incidence of TNS between the two groups (n, %).

Groups	Cases	I	II	III	Incidence of TNS
Observation	51	1 (1.96)	2 (3.92)	3 (5.88)	6 (11.76)
Control	51	4 (7.84)	5 (9.80)	7 (13.73)	16 (31.37)
$\chi^2$ test					4.694
P-value					0.030

TNS, transient neurological syndrome.

Table IX. Comparison of MoCA and MMSE scores between the two groups (mean ± SD, points).

Groups	MoCA				MMSE			
	1 day before	1 day after	t-test	P-value	1 day before	1 day after	t-test	P-value
Observation	28.14±1.23	26.65±1.09	6.475	<0.001	30.12±1.12	26.12±1.23	17.172	<0.001
Control	28.13±1.14	25.37±1.08	12.552	<0.001	29.78±1.13	23.06±1.24	28.606	<0.001
t-test	0.043	5.957			1.526	12.512		
P-value	0.966	<0.001			0.130	<0.001		

MoCA, Montreal Cognitive Assessment; MMSE, Mini-Mental State Examination.

*Comparison of MoCA and MMSE scores between the two groups.* Postoperative MoCA and MMSE scores of both groups were lower than those before surgery, and the decreases in control group were more significant than that in observation group ( $P<0.05$ ) (Table IX).

## Discussion

With the development of human society, the maternal delivery method has undergone significant changes. With the advantages of good muscle relaxation effects, exact analgesic effects and satisfactory postoperative analgesic effects, cesarean section has been more and more applied in clinical

practices (10). Primiparas are usually affected by bad mood, resulting in longer labor course and uterine contractions and severe physical pain than those of multipara. Severe physical pain, anxiety, fear, tension and other adverse emotions can induce secretion of adrenal cortex hormones, endorphins, catecholamines and pain-causing substances, resulting in increased sensitivity to pain (11). Therefore, primiparas are usually treated with cesarean section to end delivery.

During perioperative period of cesarean section, surgical procedures can cause changes in heart rate and blood pressure (12). Dex is a highly selective  $\alpha_2$ -adrenergic receptor agonist that can suppress various surgical stress responses and maintain hemodynamic stability (13). Results of this study

showed no significant difference in perioperative HR and SpO<sub>2</sub> between the two groups ( $P>0.05$ ). MAP and VAS scores in observation group after anesthesia were significantly lower than those in control group ( $P<0.05$ ). This is because Dex can reduce the intraoperative hypertension reaction and activate the  $\alpha_2$  receptor in the motor neuron complex on the dorsal medulla oblongata, so as to effectively reduce blood pressure. In addition, Dex can inhibit the release of adrenaline, so that the tension of the sympathetic nervous system will be reduced, resulting in analgesic and antiemetic effects.

Pain is severe with 48 h after cesarean section, and this pain can reduce uterine contractility and cause postpartum hemorrhage, leading to reduced uterine contractility, postpartum hemorrhage, reduced oxytocin secretion, reduced milk production and failure of breastfeeding (14). Without proper control, postoperative severe pain of cesarean section may lead to chronic pain. In Western countries, the incidence of chronic pain after caesarean section shows a continuous increasing trend (15). Therefore, proper postoperative analgesia is essential. Results of this study showed that the Ramsay sedation score of the observation group was significantly higher than that of the control group at 6, 12, 24 and 24 h after operation ( $P<0.05$ ). This is because Dex can activate maternal K<sup>+</sup> channels and promote K<sup>+</sup> conduction, thereby activating an endogenous sleep-promoting pathway, resulting in a hypnotic effect. Dex can also enter cerebrospinal fluid to bind to  $\alpha_2$  receptor to inhibit the release of histamine in the cortical and subcortical projection systems, thereby mediating conscious sedation. Dex can reduce sympathetic tone while enhancing vagal activity, thereby reducing excessive catecholamine and norepinephrine release, resulting in long-term analgesic effects (16).

Results of this study showed no significant difference in the incidence of adverse reactions such as nausea and vomiting, hypoxemia and delayed recovery between the two groups ( $P>0.05$ ). The incidence of postoperative agitation was significantly lower in observation group than in control group, and the incidence of TNS in observation group was significantly lower than that in control group ( $P<0.05$ ). This is because Dex can inhibit Ca<sup>2+</sup> influx in nerve endings, reduce excitability of the postsynaptic membrane, inhibit vasoconstriction and reduce temperature threshold of chills, resulting in anti-chills effects and inhibit the occurrence of postoperative agitation (17). Combined spinal-epidural anesthesia may cause damage to the nerve root, and narcotic drugs can easily deposit in spinal nerve root to block nerves. Intrathecal vulnerable area is posterior spinal nerve root, and nerve fibers have no myelination. Besides that, excessive air or saline may be injected to increase pressure within the spinal canal to cause damage to this area (18). Synergistic effects of Dex and local anesthetics can enhance the analgesic effect and reduce the use of local anesthetic, reduce the mild toxicity of narcotic drugs, thereby reducing the incidence of TNS.

Various discomforts during the postoperative recovery of cesarean section may cause sympathetic nervousness and central nervous system sensitization, resulting in various stress reactions. Activated inflammatory factors may cause inflammatory reactions. With the release of excessive inflammatory cytokines, they may migrate through the blood-brain barrier and cause inflammation in the hippocampus of the brain, resulting in cognitive dysfunction (19). Results of this

study showed that postoperative MoCA and MMSE scores of both groups were lower than preoperative scores, and the decreases were more significant in control group than in observation group ( $P<0.05$ ). This is because Dex has a certain anti-inflammatory effect, can inhibit the production of inflammatory cytokines, so as to reduce the damage to nervous system and protect brain. Dex is not harmful to central cholinergic neurons and fibers, and can improve the level of acetylcholine to participate in cognitive function, such as feeling, awakening, learning and judgment, so as to reduce cognitive impairment (20).

In conclusion, the use of Dex anesthesia in cesarean section can achieve stable hemodynamic conditions during perioperative period and obvious analgesic effect after operation. It also reduced the incidence of postoperative TNS and cognitive dysfunction.

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### Availability of data and materials

All data generated or analyzed during this study are included in this published article.

### Authors' contributions

DK and JB designed the study. SM and CL collected the patients' data. LY and XK analyzed the patients' data. All authors read and approved the final manuscript.

### Ethics approval and consent to participate

The present study was approved by the Ethics Committee of People's Hospital of Zhangqiu District (Jinan, China). Written informed consents were obtained from all patients.

### Patient consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

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