Sedative effect of dexmedetomidine in spinal-epidural anesthesia on hysteromyomectomy

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Abstract: To investigate the sedative effect of dexmedetomidine in spinal-epidural anesthesia on hysteromyomectomy a total of 100 hysteromyomectomy patients were randomly divided into the control group and the observation group with 50 in each group. Patients in the control group received the general anesthesia, while those in the observation group received spinal-epidural anesthesia, and intravenous injection of dexmedetomidine. For maintenance of anesthesia, ropivacaine was adopted for both groups. Before anesthesia, at 30 min and 60 min after anesthesia, we measured the heart rate (HR), bispectral index (BIS) and sedative effect. Before anesthesia, HR, BIS and Ramsay scores were compared between two groups, and the results showed that differences had no statistical significance ($p>0.05$); but at 30 min after anesthesia, HR and BIS of patients in the observation group were significantly lower than those in the control group ($p<0.05$), and Ramsay score was higher than the control group ($p<0.05$). No statistical significance was found in differences of the incidence rate of adverse reactions between two groups ($p>0.05$). Application of dexmedetomidine in spinal-epidural anesthesia gains promising sedative effect and safety in hysteromyomectomy, which is worthy of being promoted in clinical treatment.

Keywords: Dexmedetomidine; hysteromyomectomy; sedative effect.

INTRODUCTION

Uterine leiomyoma, a common benign tumor in gynecological department, is mainly treated with hysteromyomectomy. However, tremendous injury in hysteromyomectomy tortures patients severely, and in addition to the worries on the fertility function after surgery, patients usually are anxious, nervous or scared, which, in turn, increases the risk of surgeries. Thus, it is necessary for use of sedative in surgery for patients (An *et al.*, 2014; Bekker *et al.*, 2013). As a kind of α^2 receptor agonist, dexmedetomidine has a significant effect in sedation that can effectively relieve patients from the severe stress response of surgery (Choi *et al*., 2015). In this study, 100 patients who planned to undergo hysteromyomectomy were enrolled as subjects, 50 of which received the spinal-epidural anesthesia through intravenous injection of dexmedetomidine, and promising outcomes were obtained.

MATERIALS AND METHODS

Clinical data

Between January 2017 and January 2018, a total of 100 patients who were diagnosed as uterine leiomyoma according to the diagnostic criteria in *Obstetrics and Gynecology* (7^{th} edition) and the ultrasound B and computed tomography examinations, and planned to undergo hysteromyomectomy were enrolled as subjects. All patients had no allergic history of anesthetics, and had the surgical indications of hysteromyomectomy without any severe complications. Using the random digit table, subjects were divided into the control group and the observation group with 50 in each group. In the control group, patients ranged from 31 to 45 years old with an average of (36.2±3.3) years old; there were 25 patients with single onset, and 25 with multiple onset; diameters of uterine leiomyoma ranged from 7 to 14 cm with an average of (8.8±1.4) cm. In the observation group, patients ranged from 32 to 44 years old with an average of (35.8±3.1) years old; there were 26 patients with single onset, and 24 with multiple onset; diameters of uterine leiomyoma ranged from 8 to 15 cm with an average of (9.1±1.6) cm. Comparisons of the general data, including the age and diameter of tumor, showed that the difference had no statistical significance ($p>0.05$), suggesting that data were comparable.

Anesthetic methods

Heart rate (HR), blood pressure (BP), average arterial pressure, oxyhemoglobin saturation and bispectral index (BIS) were monitored before anesthesia. At 20 min before anesthesia, patients underwent intravenous injection of Compound Sodium Lactate Injection (500 mL). Under general anesthesia, patients in the control group received intravenous injection of propofol at 60μg /(kg·min) (Libang Pharmaceutical, Lot No.: MC486), and injection was withdrawn at 5 min before the end of surgery. Patients in the observation group underwent spinal-epidural anesthesia: Briefly, in lateral position, puncture was carried out in L2-3 space to deliver 3 mL 2% lidocaine (Tianyuan Pharmaceutical, 2 mL: 4 mg, SFDA Approval No.: H14022773) for anesthesia, during which changes in HR and oxyhemoglobin saturation were measured to exclude the suppression on autonomous

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respiration. Then, 15 mL lidocaine was injected at 1 mL/s, and dexmedetomidine was intravenously injected (Jiangsu Hengrui Medicine Co., Ltd; Lot No.: 16062532) at 0.4 g/(kg·h). Drug withdrawal was performed before abdominal closure. For maintenance of anesthesia, 6 to 8 mL of 0.75% ropivacaine (Pude Pharmaceutical, Lot No.: LAYD) was administrated for both groups.

Observation index

Before anesthesia, at 30 min and 60 min after administration, HR, BIS and sedative effect of patients were compared. (1) BIS: Covidien BIS monitor (BISTA, USA) was used to monitor the anesthetic depth (ranged from 0 to 100). Patients with higher BIS are more conscious, and lower BIS suggests more severe suppression on the cortex. For evaluation, patients with BIS between 85 and 100 are deemed normal; between 65 and 84, sedative; between 40 and 64, anesthesia; less than 40, burst suppression. (2) Ramsay criteria for sedation (An *et al.,* 2014) were also adopted for evaluating the sedative effect: 1 point for agitated or intolerance to anesthesia; 2 points for silence and cooperative to operation; 3 points for patients in sleep state but responsive to external stimuli; 4 points for patients in shallow sleep but were able to be aroused; 5 points for patients in moderate sleep, able to be aroused but slow in response; 6 points for patients in deep sleep and not able to response to external stimuli. (3) Patients were closely monitored to observe the adverse reactions, including cardiac arrhythmia, hypotension and respiratory suppression.

Ethical approval

This protocol had been approved by the Ethic Committee of the Taizhou People's Hospital of Jiangsu and all subjects had agreed to participate in the study.

STATISTICAL ANALYSIS

SPSS 19.0 was used for data analysis. Measurement data in normal distribution were presented as mean ± standard deviation ($\bar{}$±), and analysis of variance of repeated measurement was adopted. Measurement data in skewed distribution were presented as median, and non-parameter rank sum test was performed for intergroup comparison of independent samples. Enumeration data were compared by chi-square test. $p<0.05$ suggested that difference had statistical significance.

RESULTS

Comparison of the general data between two groups

Comparisons of the age and diameter of tumor between two groups showed no statistically significant difference ($p>0.05$), suggesting that data were comparable (table 1).

Comparison of HR, BIS and Ramsay scores at different time points between two groups Before anesthesia, comparisons of HR, BIS and Ramsay scores between two groups showed no statistically significant difference (HR: F=1.266, p=0.465; BIS: F=1.069, p= 0.836 ;Ramsay: F=1.000, p=1.000); 30 min after administration, HR and BIS in the observation group were lower than those in the control group (HR: F=3.325, $p<0.001$; BIS: F=2.804, p=0.002); and the Ramsay score was higher than that in the control group (F=4.000, $p<0.01$; table 2).

Comparisons of the hemodynamic variations between two groups

No statistically significant difference was figured out in comparison of the incidence rates of bradycardia and hypotension between two groups ($p>0.05$), and intergroup comparison showed no statistically significant difference (table 3).

Comparison of the adverse reactions between two groups

During and after surgery, no severe complications were observed in two groups, and most of patients suffered from agitation, hypoxemia, nausea and vomiting, hypotension and bradycardia. In the observation group, there were 5 patients with adverse reaction (12.5%, 5/40); in the control group, there were 7 patients with adverse reaction (17.5%, 7/40). Comparisons between two groups showed no statistically significant difference (χ^2=0.399; p=0.528).

DISCUSSION

Uterine leiomyoma, a common benign tumor in reproductive system of females, is usually treated through conservative therapy for patients with tumor in small diameter, but hysteromyomectomy is considered for tumor in diameter larger than 5 cm (Choi *et al*., 2015; Gil *et al*., 2009). Most of the patients suffer from psychological pressure in varying degrees in perioperative period, emerging anxiety, worry or tension, which result in a decrease in tolerance to surgery and the risks of hemorrhage during surgery. Therefore, sedatives with evident sedative and analgesic effects in anesthesia are quite important for surgeries.

Dexmedetomidine, an agonist commonly applied in clinical practice in recent years, is specific for the adrenergic receptor with promising sedative, analgesic and spasmolytic effects (Gornall *et al.,* 2013; Grosu *et al.,* 2011). It is believed that dexmedetomidine can bind to the α^2-A channel to inhibit the synthesis and release of norepinephrine and block the delivery of pain signal (Gupta *et al.,* 2013), so as to achieving the analgesic effect. α^2 adrenergic receptor, distributed widely in organs, central nervous system, vessels and peripheral nerves of human beings, can bind to the dexmedetomidine to inhibit the sympathetic nerve, to exert the sedative effect. In addition, half-time of dexmedetomidine is as short as 2 h, which means that patients can recover from

Table 1: Comparison of the general data between two groups

Group	Case (n)	Age (years)	Uterine leiomyoma		
			Type (one/multi)	Diameter (cm)	
Control group	50	31～45 (36.2±3.3)	25/25	7～14	(8.8±1.4)
Observation group	50	32～44 (35.8±3.1)	26/24	8～15	(9.1±1.6)

Table 2: Comparisons HR, BIS and Ramsay scores at different time points between two groups (±)

Indicator	Case (n)	Group	Before anesthesia	30 min after administration	60 min after administration
HR	50	Control group	72.3±6.3	69.1±5.0	71.3±6.0
(beat/time)	50	Observation group	71.7±7.1	60.1±9.2	70.4±5.7
BIS	50	Control group	94.2±6.0	92.3±4.2	93.1±5.5
	50	Observation group	93.9±5.8	65.3±7.1	92.4±6.3
Ramsay score	50	Control group	2.1±0.3	3.1±0.5	2.4±0.4
(point)	50	Observation group	2.0±0.3	4.8±1.0	2.5±0.5

Table 3: Comparisons of the hemodynamic variations between two groups [n(%)]

Group	Case (n)	Bradycardia	Hypotension	Total
Control group	50	4 (8.00)	2 (4.00)	6 (12.00)
Observation group	50	3 (6.00)	3 (2.00)	6 (12.00)

anesthesia immediately after drug withdrawal, thereby decreasing the incidence of adverse reaction. Since dexmedetomidine acts on the nucleus coeruleus, it induces fewer adverse reactions of respiratory suppression after medication than other sedatives. Combination with other anesthetics can effectively reduce the dose of drugs, which is conducive to the recovery of consciousness and reduction of complications (Little *et al.*, 2010; Lambert *et al.*, 2014).Short surgical duration of hysteromyomectomy ameliorates the stimuli to patients, and adverse reaction is mainly caused by the cardiovascular reactions induced by skin incision and pneumoperitoneum. Thus, it is suitable for treatment of uterine leiomyoma. For elder patients, or those with cardiovascular diseases or bradycardia, large-dose administration of dexmedetomidine is not applicable. With slow onset caused by its pharmacokinetic features, dexmedetomidine works poorly on dose control in comparison with the propofol. Literature (McQueen-Shadfar *et al.*, 2011) has reported that calm status can only be attained at 20 min after intravenous injection of dexmedetomidine. High-dose intravenous injection of dexmedetomidine induces the evident contraction of peripheral vessels, further giving rise to an acute increase of blood pressure. Thus, in anesthesia, it is preferably that continuous intravenous injection should be initiated after the a low-dose injection for 5 min, and one-time injection should be avoided. Dexmedetomidine can decrease the heart rate of patients through blocking the activity of sympathetic nerves and is not applicable for patients with cardiac conduction block or sinus arrhythmia (Wanchoo *et al.*, 2011).

In this study, Ramsay score of patients in the observation group was higher than that in the control group, and no severe adverse reactions were observed, which are consistent with the reports of Yaman *et al*. (2012); thus, application of dexmedetomidine in spinal-epidural anesthesia gains promising sedative effect and is safe in hysteromyomectomy. BIS refers to a mixed digital form of frequency and power of brain wave, which can be directly reflected in the electroencephalogram (EEG) of cortex, thus displaying the suppression status of cortex. In this study, we found that BIS was lower in the dexmedetomidine-assisted spinal-epidural anesthesia in comparison with the levels before anesthesia and of the control group, suggestive a minor suppressive effect on brain.

CONCLUSION

Application of dexmedetomidine in spinal-epidural anesthesia for hysteromyomectomy gains promising sedative effect with a high safety and little effect on respiration. However, special caution should be taken for elder patients, or those with cardiac conduction block, sinus arrhythmia or hypotension.

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