中国临床研究 Chin J Clin Res, March 2026, Vol.39, No.3

Cite as: Li J, Bao YY, Zhang C, Xiao Y. Dexmedetomidine combined with etomidate in anesthesia for laparoscopic myomectomy [J]. Chin J Clin Res, 2026, 39(3):385-389.

DOI: 10.13429/j.cnki.cjcr.2026.03.013

Dexmedetomidine combined with etomidate in anesthesia for laparoscopic myomectomy

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Abstract: **Objective** To investigate the pharmacodynamics of dexmedetomidine combined with etomidate in anesthesia for laparoscopic myomectomy, as well as the changes in hemodynamics and inflammatory factors, and to explore its clinical application value. **Methods** A total of 105 patients with uterine fibroids treated in Xuancheng Central Hospital from August 2020 to July 2023 were selected and divided into a low-dose group, a medium-dose group, and a high-dose group using a random number table method, with 35 patients in each group. The low-dose group received 0.20 μg/kg dexmedetomidine combined with etomidate, the medium-dose group received 0.40 μg/kg dexmedetomidine combined with etomidate, and the high- dose group received 0.60 μg/kg dexmedetomidine combined with etomidate. The mean arterial pressure(MAP), central venous pressure(CVP), stress response indicators [serum norepinephrine(NE), cortisol(Cor)], and inflammatory factor indicators [C-reactive protein(CRP), tumor necrosis factor-α(TNF-α)] were compared among the three groups at different time points. Sleep quality [Pittsburgh Sleep Quality Index(PSQI)] and the incidence of postoperative delirium(POD)were also compared among the three groups. **Results** Repeated measures analysis of variance showed that the levels of MAP, CVP, NE, Cor, CRP, and TNF - α in the three groups had statistically significant between-group effect, time effect, and between-group × time interaction effect(P<0.05). At 5 minutes after tracheal intubation(T1), 30 minutes after the start of surgery(T2), and at the end of surgery(T3), the MAP in the low-dose group was significantly higher than that at 15 minutes before anesthesia induction(T0) and was higher than that in the medium-dose group and high-dose group(P<0.05). At T2 and T3, the CVP in the low-dose group was significantly lower than that at T0 and T1, and was lower than that in the medium-dose group and high-dose group (P<0.05). At T1, T2, and T3, the serum levels of NE, Cor, CRP, and TNF-α in the three groups were significantly higher than those at T0, and the low-dose group had higher levels of the above indicators than the medium-dose group and high-dose group(P<0.05). On postoperative day 1, the PSQI score in the three groups was significantly higher than that before surgery, and the low-dose group had higher scores than the medium-dose group and high-dose group(P<0.05). There was no statistically significant difference in the incidence of POD among the low-dose group, medium-dose group, and high-dose group at postoperative day 3 and day 7 [postoperative day 3: 8.57%(3/35)*vs* 5.71%(2/35)*vs* 5.71%(2/35), χ^2=0.306, P=0.858; postoperative day 7: 5.71%(2/35)*vs* 2.86%(1/35)*vs* 2.86%(1/35), χ 2=0.520, P=0.771]. **Conclusion** The use of 0.40 μg/kg dexmedetomidine combined with etomidate in anesthesia for laparoscopic myomectomy is beneficial for maintaining stable MAP and CVP, improving stress response, inhibiting inflammatory response, and results in a better postoperative sleep quality and a lower risk of POD.

Keywords: Dexmedetomidine; Etomidate; Laparoscopic surgery; Uterine fibroids; Stress response; Inflammatory factors; Postoperative delirium; Sleep quality

Uterine fibroids are benign tumors arising from the proliferation of uterine smooth muscle cells. Laparoscopic myomectomy is the main treatment for this condition and is well accepted by patients [1]. Dexmedetomidine is an α_2-adrenergic receptor agonist that exerts protective effects on the central nervous system without causing respiratory depression. It provides favorable sedative and analgesic effects and helps improve the safety of surgical anesthesia [2]. Etomidate is an imidazole derivative characterized by the absence of histamine release and a short elimination half-life. It produces reliable sedation, helps maintain hemodynamic stability, and is widely used in clinical anesthesia induction and maintenance [3]. This study aimed to investigate the dose-response relationship, as well as changes in hemodynamics and inflammatory factors, of dexmedetomidine combined with etomidate during anesthesia for laparoscopic myomectomy. The details are reported as follows.

1 Materials and Methods

1.1 General Data

A total of 105 patients with uterine fibroids who underwent treatment at Xuancheng Central Hospital from August 2020 to July 2023 were enrolled. Using a random number table, they were divided into a low-dose group (n=35), a medium-dose group (n=35), and a high-dose group (n=35).

Inclusion criteria: (1) Met the diagnostic criteria in the *Chinese Expert Consensus on the Diagnosis and Treatment of Uterine Fibroids* [4] and were confirmed by ultrasound; (2) Met the indications for surgery; (3) Number of fibroids ≤4, with the largest fibroid diameter ranging from 4 to 10 cm; (4) American Society of Anesthesiologists (ASA) physical status Grade I–II; (5) Normal cognitive function; (6) Complete clinical data; (7) All patients provided written informed consent.

Exclusion criteria: (1) Contraindications to surgery or anesthesia; (2) Concurrent other malignant tumors; (3) Severe other gynecological diseases; (4) Coagulation dysfunction; (5) Severe cardiac, hepatic, renal or other organ dysfunction; (6) Treatment with vasoactive agents within the previous 3 months; (7) Cognitive or consciousness impairment.

In the low-dose group, the mean age was (40.45±5.12) years, body mass index (BMI) was (23.15±1.52) kg/m², and the largest fibroid diameter was (6.56±1.14) cm. In the medium-dose group, the mean age was (40.56±5.25) years, BMI was (23.09±1.56) kg/m², and the largest fibroid diameter was (6.43±1.18) cm. In the high-dose group, the mean age was (40.77±5.43) years, BMI was (23.31±1.67) kg/m², and the largest fibroid diameter was (6.72±1.21) cm. There were no significant differences in general characteristics among the three groups (P>0.05). This study was approved by the Medical Ethics Committee of Xuancheng Central Hospital (Ethics No.: Yilunban 2022005).

1.2 Study Protocol

All patients fasted for 12 h preoperatively. Upon entering the operating room, vital signs were routinely monitored, and an intravenous line was established. Ten minutes before anesthesia induction, dexmedetomidine (Betapharm Chengdu, China; National Medical Products Approval No. H20205002, 2 mL:200 μg) was administered via intravenous infusion pump at 0.20 μg/kg in the low-dose group, 0.40 μg/kg in the medium-dose group, and 0.60 μg/kg in the high-dose group. Meanwhile, all three groups received etomidate (Jiangsu Enhua Pharmaceutical, China; National Medical Products Approval No. H32022992, 10 mL:20 mg) at 0.3 mg/kg via intravenous infusion pump.

Anesthesia induction: 0.4 μg/kg sufentanil (Yichang Renfu Pharmaceutical, China; National Medical Products Approval No. H20054171, 1 mL:50 μg), 0.04 mg/kg midazolam (Jiangsu Jiuxu Pharmaceutical, China; National Medical Products Approval No. H20113433, 1 mL:5 mg), 0.05 mg/kg vecuronium bromide (Chenxin Pharmaceutical, China; National Medical Products Approval No. H20067458, 4 mg), and 2 mg/kg propofol (Xi'an Libang Pharmaceutical, China; National Medical Products Approval No. H20123318, 50 mL:1.0 g) were administered intravenously. After loss of consciousness and muscle relaxation, tracheal intubation was performed, and mechanical ventilation was initiated.

Anesthesia maintenance: Anesthesia was maintained with inhaled sevoflurane (Shanghai Hengrui Pharmaceutical, China; National Medical Products Approval No. H20213735, 120 mL), combined with continuous infusion of propofol at 4 mg/(kg·h) and remifentanil at 0.5 μg/(kg·min). At the end of surgery, patients were transferred to the post-anesthesia care unit for recovery.

1.3 Observation Indexes

1.3.1 Hemodynamic Parameters

Mean arterial pressure (MAP) and central venous pressure (CVP) were recorded and compared among the three groups at 15 min before anesthesia induction (T0), 5 min after tracheal intubation (T1), 30 min after the start of surgery (T2), and at the end of surgery (T3).

1.3.2 Stress Response Markers

Jugular venous blood samples were collected at T0, T1, T2, and T3. Serum norepinephrine (NE) levels were measured using enzyme-linked immunosorbent assay (ELISA). Serum cortisol (Cor) levels were detected using competitive chemiluminescent immunoassay. Kits were purchased from Wandong Tiande Biotechnology Co., Ltd. and Kebang Xingye (Beijing) Technology Co., Ltd., respectively. All procedures were performed strictly in accordance with the manufacturer's instructions.

1.3.3 Inflammatory Factors

Jugular venous blood samples were collected at T0, T1, T2, and T3. Serum C-reactive protein (CRP) and tumor necrosis factor-α (TNF-α) levels were measured using ELISA. Kits were purchased from Fulaide Biotechnology (Wuhan) Co., Ltd. and Qingdao Jieshikang Biotechnology Co., Ltd., respectively. All operations were performed in strict accordance with the instructions.

1.3.4 Sleep Quality

Sleep quality was assessed preoperatively and on postoperative day 1 using the Pittsburgh Sleep Quality Index (PSQI) [5], which includes seven items: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. Higher scores indicate poorer sleep quality.

1.3.5 Postoperative Delirium (POD)

Postoperative delirium was evaluated on postoperative days 3 and 7 using the Chinese Revised Version of the Confusion Assessment Method (CAM-CR) [6], which includes 11 items: acute onset, disordered thinking, memory impairment, disorientation, sleep-wake cycle disturbance, etc. A CAM-CR score ≥22 was defined as delirium.

1.4 Statistical Analysis

Statistical analysis was performed using SPSS 26.0 software. Normally distributed measurement data were expressed as $\bar{x}\pm s$. Comparisons among multiple groups were performed using one-way analysis of variance (ANOVA). Comparisons at multiple time points were analyzed using repeated-measures ANOVA. Pairwise comparisons were performed using the LSD-*t* test. Enumeration data were expressed as cases (%) and analyzed using the χ^2 test. $P<0.05$ was considered statistically significant.

2 Results

2.1 Comparison of MAP and CVP Among the Three Groups

Repeated-measures ANOVA showed significant main effects of group, time, and group-time interaction for MAP and CVP among the three groups ($P<0.01$). Pairwise comparisons revealed that at T1, T2, and T3, MAP in the low-dose group was significantly higher than at T0 and higher than that in the medium-dose and high-dose groups

(P<0.05). There were no significant differences in MAP between the medium-dose and high-dose groups at T0, T1, T2, or T3 (P>0.05). At T2 and T3, CVP in the low-dose group was significantly lower than at T0 and T1, and lower than that in the medium-dose and high-dose groups (P<0.05). There were no significant differences in CVP between the medium-dose and high-dose groups at any time point (P>0.05) (**Table 1**).

2.2 Comparison of Stress Response Markers Among the Three Groups

Repeated-measures ANOVA showed significant main effects of group, time, and group-time interaction for serum NE and Cor levels (P<0.01). Pairwise comparisons showed that at T1, T2, and T3, serum NE and Cor levels in all three groups were significantly higher than at T0, and levels in the low-dose group were higher than those in the medium-dose and high-dose groups (P<0.05). There were no significant differences in NE or Cor levels between the medium-dose and high-dose groups (P>0.05) (**Table 2**).

2.3 Comparison of Inflammatory Factors Among the Three Groups

Repeated-measures ANOVA showed significant main effects of group, time, and group-time interaction for serum CRP and TNF-α levels (P<0.01). Pairwise comparisons showed that at T1, T2, and T3, serum CRP and TNF-α levels in all three groups were significantly higher than at T0, and levels in the low-dose group were higher than those in the medium-dose and high-dose groups (P<0.05). There were no significant differences in CRP or TNF-α levels between the medium-dose and high-dose groups (P>0.05) (**Table 3**).

2.4 Comparison of PSQI Scores and POD Incidence Among the Three Groups

On postoperative day 1, PSQI scores in all three groups were significantly higher than preoperatively, and the score in the low-dose group was higher than those in the medium-dose and high-dose groups (P<0.05). There was no significant difference in PSQI scores between the medium-dose and high-dose groups (P>0.05). There were no significant differences in the incidence of POD among the three groups on postoperative days 3 and 7 (P>0.05) (**Table 4**).

Tab.1 Comparison of MAP and CVP at different times among three groups (n=35, mmHg, $\bar{x}\pm s$)

Group	MAP				CVP			
	T0	T1	T2	T3	T0	T1	T2	T3
Low-dose group	102.69±6.58	118.42±7.37[a]	122.65±6.82[a]	124.48±7.14[a]	5.44±1.08	4.98±0.94	4.32±0.84[ab]	4.48±0.82[ab]
Medium-dose group	103.42±6.29	104.51±6.55[c]	105.06±6.27[c]	105.24±7.05[c]	5.37±1.04	5.02±0.91	4.96±0.80[c]	5.06±0.83[c]
High-dose group	103.71±6.35	105.19±7.26[c]	105.78±6.49[c]	105.66±7.18[c]	5.33±1.09	4.95±0.88	4.89±0.82[c]	4.97±0.87[c]
F_{group}/P_{group} **value**	82.500/<0.001				6.450/0.002			
F_{time}/P_{time} **value**	58.300/<0.001				8.120/<0.001			
$F_{interaction}/P_{interaction}$ **value**	42.800/<0.001				5.230/0.005			

Note: Compared with T0 in the same group, [a]P<0.05; compared with T1 in the same group, [b]P<0.05; compared with the low-dose group at the same time point, [c]P<0.05.

Tab.2 Comparison of serum NE and Cor levels at different times among three groups (n=35, $\bar{x}\pm s$)

Group	NE (pg/mL)				Cor (ng/mL)			
	T0	T1	T2	T3	T0	T1	T2	T3
Low-dose group	16.64±3.52	26.13±4.72[a]	29.24±4.47[a]	31.42±4.76[a]	211.67±13.46	254.74±15.82[a]	266.65±17.14[a]	271.26±17.58[a]
Medium-dose group	16.51±3.46	18.25±3.57[ab]	19.37±4.13[ab]	18.86±3.87[ab]	212.53±14.24	224.16±15.27[ab]	227.47±16.42[ab]	226.35±16.29[ab]
High-dose group	16.45±3.42	18.12±3.49[ab]	19.51±4.22[ab]	19.15±3.94[ab]	212.82±14.61	223.63±15.32[ab]	225.12±17.16[ab]	225.76±17.33[ab]
F_{group}/P_{group} **value**	91.250/<0.001				86.730/<0.001			
F_{time}/P_{time} **value**	72.680/<0.001				67.450/<0.001			
$F_{interaction}/P_{interaction}$ **value**	61.340/<0.001				56.890/<0.001			

Note: Compared with T0 in the same group, [a]P<0.05; compared with low-dose group at the same time point, [b]P<0.05.

Tab.3 Comparison of serum CRP and TNF-α levels at different time points among three groups (n=35, $\bar{x}\pm s$)

Group	CRP (mg/L)				TNF-α (pg/mL)			
	T0	T1	T2	T3	T0	T1	T2	T3
Low-dose group	7.67±1.12	11.53±1.83[a]	12.83±2.58[a]	11.75±2.14[a]	35.62±3.81	44.66±4.49[a]	47.77±4.19[a]	45.47±4.35[a]
Medium-dose group	7.82±1.04	9.24±1.72[ab]	10.15±1.82[ab]	9.79±1.86[ab]	35.46±4.02	38.12±4.21[ab]	39.72±4.36[ab]	38.18±4.22[ab]
High-dose group	7.61±1.09	9.15±1.68[ab]	10.08±1.74[ab]	9.65±1.83[ab]	35.87±3.49	38.09±4.35[ab]	39.53±4.25[ab]	37.82±4.31[ab]
F_{group}/P_{group} **value**	20.850/<0.001				35.920/<0.001			
F_{time}/P_{time} **value**	31.260/<0.001				45.680/<0.001			
$F_{interaction}/P_{interaction}$ **value**	15.720/<0.001				30.450/<0.001			

Note: Compared with T0 in the same group, [a]P<0.05; compared with low-dose group at the same time point, [b]P<0.05.

Tab.4 Comparison of PSQI scores and occurrence of POD among three groups (n=35)

Group	PSQI Score (point, $\bar{x}\pm s$)		POD [case(%)]	
	Preoperatively	1 d Postoperatively	3 d Postoperatively	7 d Postoperatively
Low-dose group	13.13±1.51	16.24±1.41[a]	3(8.57)	2(5.71)
Medium-dose group	13.25±1.42	14.52±1.47[ab]	2(5.71)	1(2.86)
High-dose group	13.29±1.60	14.36±1.56[ab]	2(5.71)	1(2.86)
F/χ^2 **value**	0.106	17.329	0.306	0.520
P **value**	0.899	<0.001	0.858	0.771

Note: Compared with preoperative in the same group, [a]P<0.05; compared with low-dose group at the same time point, [b]P<0.05.

3 Discussion

Both anesthesia and surgical trauma can activate the sympathetic-adrenal medullary system, triggering intraoperative stress responses that lead to substantial fluctuations in vital signs such as heart rate and blood pressure, which may affect the surgical procedure [2]. Dexmedetomidine exerts prominent sedative and analgesic effects by reducing the excitability of the sympathetic center and enhancing the activity of γ-aminobutyric acid-ergic neurons in the ventrolateral hypothalamus, thereby mediating sedation. It also shows significant advantages in alleviating stress responses [7], but different doses may exert differential effects on the body. Etomidate mainly acts on the central nervous system, producing central sedative-hypnotic effects and certain neuroprotective effects by modulating neuronal excitability, with no inherent analgesic or muscle-relaxant properties. In addition, it does not affect peripheral vasomotor function, has minimal cardiovascular effects, helps maintain hemodynamic stability, and acts rapidly with rapid metabolism [8].

This study demonstrated significant main effects of group, time, and group-time interaction for MAP, CVP, NE, Cor, CRP, and TNF-α levels among the three groups, indicating that drug dosage is a key factor influencing changes in these indicators. Specifically, the fluctuations in MAP, CVP, and serum NE and Cor levels were significantly greater in the low-dose group than in the medium-dose and high-dose groups. These findings are consistent with those reported by Chen et al. [9], suggesting that dexmedetomidine at 0.40 μg/kg or 0.60 μg/kg combined with etomidate during anesthesia for laparoscopic myomectomy better maintains hemodynamic stability and attenuates the body's stress response. This may be explained by the action of dexmedetomidine on the sympathetic nervous system: by stimulating central α_2 receptors, it inhibits the synthesis and release of NE and Cor, reduces sympathetic tone, thereby suppressing stress responses induced by anesthesia and surgical injury. It also significantly reduces myocardial oxygen consumption and increases coronary blood flow, thus reducing fluctuations in MAP and CVP and favoring hemodynamic stability [10–12]. The present study also found that intraoperative fluctuations in serum CRP and TNF-α levels were significantly greater in the low-dose group than in the medium-dose and high-dose groups, indicating that dexmedetomidine at 0.40 μg/kg or 0.60 μg/kg combined with etomidate more effectively inhibits the postoperative inflammatory response. Dexmedetomidine exerts analgesic, sedative, and anti-sympathetic effects, reducing peripheral and central excitability and inhibiting the release of inflammatory mediators, thereby alleviating inflammation. Approximately 30% of patients experience varying degrees of anxiety and fear during the perioperative period, which may contribute to sleep disturbances [13]. In this study, PSQI scores on postoperative day 1 were higher in the low-dose group than in the medium-dose and high-dose groups, whereas the incidence of POD did not differ significantly among groups. This suggests that dexmedetomidine at 0.40 μg/kg or 0.60 μg/kg combined with etomidate is associated with better postoperative sleep quality.

Dexmedetomidine provides effective analgesia and sedation by activating presynaptic α_2 receptors, weakening sympathetic reactivity, inhibiting NE release, and interrupting pain signal transmission [2]. Furthermore, it acts directly on the brainstem to inhibit central sympathetic outflow and exerts anti-inflammatory effects, thereby reducing anesthetic-induced cerebral tissue injury, helping maintain stable intracranial pressure, and lowering the risk of POD [14–15]. Thus, increasing doses of dexmedetomidine enhance α_2 receptor-mediated effects, strengthening analgesia and sedation without increasing the risk of POD. In the present study, 0.40 μg/kg and 0.60 μg/kg dexmedetomidine combined with etomidate showed similar effects. Given the principle of using the lowest effective anesthetic concentration to maximize safety, 0.40 μg/kg is preferable.

In conclusion, dexmedetomidine at 0.40 μg/kg combined with etomidate in laparoscopic myomectomy helps maintain hemodynamic stability, attenuates stress and inflammatory responses, improves postoperative sleep quality, and carries a low risk of postoperative delirium.

Conflict of Interest: None

Reference

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Submission Received: 2025-04-22 **Revised: 2025-09-17**

·临床麻醉专题·论著·

右美托咪定复合依托咪酯在腹腔镜子宫肌瘤剔除术麻醉中的应用

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摘要：目的 研究右美托咪定复合依托咪酯在腹腔镜子宫肌瘤剔除术麻醉中的量效学以及血流动力学、炎症因子的变化，探讨其临床应用价值。**方法** 选取2020年8月至2023年7月于宣城市中心医院接受治疗的105例子宫肌瘤患者，采用随机数字表法将其分为低剂量组、中剂量组和高剂量组，每组35例。低剂量组采用0.20 μg/kg右美托咪定复合依托咪酯，中剂量组采用0.40 μg/kg右美托咪定复合依托咪酯，高剂量组采用0.60 μg/kg右美托咪定复合依托咪酯。对比三组不同时间点的平均动脉压（MAP）、中心静脉压（CVP）、应激反应指标[血清去甲肾上腺素（NE）、皮质醇（Cor）]及炎症因子指标[C反应蛋白（CRP）、肿瘤坏死因子-α（TNF-α）]。对比三组的睡眠质量[匹兹堡睡眠质量指数（PSQI）]及术后谵妄（POD）发生情况。**结果** 重复测量方差分析显示，三组MAP、CVP、NE、Cor、CRP、TNF-α水平在组间效应、时间效应及组间×时间交互效应上均有统计学意义（$P<0.05$）。气管插管后5 min（T1）、手术开始30 min（T2）、术毕（T3）时，低剂量组的MAP较麻醉诱导前15 min（T0）时明显升高，且高于中剂量组和高剂量组（$P<0.05$）。T2、T3时，低剂量组的CVP较T0、T1时明显降低，且低于中剂量组和高剂量组（$P<0.05$）。T1、T2、T3时，三组的血清NE、Cor、CRP、TNF-α水平较T0时明显升高，且低剂量组高于中剂量组和高剂量组（$P<0.05$）。术后1 d，三组的PSQI评分较术前明显升高，且低剂量组高于中剂量组和高剂量组（$P<0.05$）。术后3、7 d，低剂量组、中剂量组、高剂量组的POD发生率对比差异无统计学意义[术后3 d：8.57%（3/35）*vs* 5.71%（2/35）*vs* 5.71%（2/35），$\chi^2=0.306$，$P=0.858$；术后7 d：5.71%（2/35）*vs* 2.86%（1/35）*vs* 2.86%（1/35），$\chi^2=0.520$，$P=0.771$]。**结论** 将0.40 μg/kg右美托咪定复合依托咪酯应用于腹腔镜子宫肌瘤剔除术的麻醉中，有利于维持患者的MAP和CVP的稳定，并改善应激反应，抑制炎性反应，且术后患者的睡眠质量较好，POD发生风险较低。

关键词： 右美托咪定；依托咪酯；腹腔镜手术；子宫肌瘤；应激反应；炎症因子；术后谵妄；睡眠质量
中图分类号： R614 R713.4 **文献标识码：** A **文章编号：** 1674-8182（2026）03-0385-05

Dexmedetomidine combined with etomidate in anesthesia for laparoscopic myomectomy

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Abstract: Objective To investigate the pharmacodynamics of dexmedetomidine combined with etomidate in anesthesia for laparoscopic myomectomy, as well as the changes in hemodynamics and inflammatory factors, and to explore its clinical application value. **Methods** A total of 105 patients with uterine fibroids treated in Xuancheng Central Hospital from August 2020 to July 2023 were selected and divided into a low-dose group, a medium-dose group, and a high-dose group using a random number table method, with 35 patients in each group. The low-dose group received 0.20 μg/kg dexmedetomidine combined with etomidate, the medium-dose group received 0.40 μg/kg dexmedetomidine combined with etomidate, and the high-dose group received 0.60 μg/kg dexmedetomidine combined with etomidate. The mean

DOI：10.13429/j.cnki.cjcr.2026.03.013
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出版日期： 2026-03-20

QR code for English version

arterial pressure (MAP), central venous pressure (CVP), stress response indicators [serum norepinephrine (NE), cortisol (Cor)], and inflammatory factor indicators [C-reactive protein (CRP), tumor necrosis factor-α (TNF-α)] were compared among the three groups at different time points. Sleep quality [Pittsburgh Sleep Quality Index (PSQI)] and the incidence of postoperative delirium (POD) were also compared among the three groups. **Results** Repeated measures analysis of variance showed that the levels of MAP, CVP, NE, Cor, CRP, and TNF-α in the three groups had statistically significant between-group effect, time effect, and between-group × time interaction effect (P<0.05). At 5 minutes after tracheal intubation (T1), 30 minutes after the start of surgery (T2), and at the end of surgery (T3), the MAP in the low-dose group was significantly higher than that at 15 minutes before anesthesia induction (T0) and was higher than that in the medium-dose group and high-dose group(P<0.05). At T2 and T3, the CVP in the low-dose group was significantly lower than that at T0 and T1, and was lower than that in the medium-dose group and high-dose group (P<0.05). At T1, T2, and T3, the serum levels of NE, Cor, CRP, and TNF-α in the three groups were significantly higher than those at T0, and the low-dose group had higher levels of the above indicators than the medium-dose group and high-dose group (P<0.05). On postoperative day 1, the PSQI score in the three groups was significantly higher than that before surgery, and the low-dose group had higher scores than the medium-dose group and high-dose group(P<0.05). There was no statistically significant difference in the incidence of POD among the low-dose group, medium-dose group, and high-dose group at postoperative day 3 and day 7 [postoperative day 3: 8.57%(3/35) *vs* 5.71%(2/35) *vs* 5.71%(2/35), χ^2=0.306, P=0.858; postoperative day 7: 5.71% (2/35) *vs* 2.86% (1/35) *vs* 2.86% (1/35), χ^2=0.520, P=0.771]. **Conclusion** The use of 0.40 μg/kg dexmedetomidine combined with etomidate in anesthesia for laparoscopic myomectomy is beneficial for maintaining stable MAP and CVP, improving stress response, inhibiting inflammatory response, and results in a better postoperative sleep quality and a lower risk of POD.

Keywords: Dexmedetomidine; Etomidate; Laparoscopic surgery; Uterine fibroids; Stress response; Inflammatory factors; Postoperative delirium; Sleep quality

子宫肌瘤是子宫平滑肌细胞增生引起的一种良性肿瘤，而腹腔镜子宫肌瘤剔除术是治疗该疾病的主要方式，且患者的接受度较高[1]。右美托咪定是一种α2肾上腺素受体激动剂，在作用过程中发挥对中枢神经系统的保护作用，且无呼吸抑制风险，镇静、镇痛效果良好，有利于提高手术麻醉的安全性[2]。依托咪酯是咪唑类药物，具有无组胺释放、半衰期短等特点，可发挥良好的镇静作用，有利于维持血流动力学稳定，在临床上被广泛应用于麻醉诱导与维持[3]。本研究旨在研究右美托咪定复合依托咪酯在腹腔镜子宫肌瘤剔除术麻醉中的量效学及血流动力学、炎症因子变化。具体如下。

1　资料与方法

1.1　一般资料　选取2020年8月至2023年7月于宣城市中心医院接受治疗的105例子宫肌瘤患者，采用随机数字表法将其分为低剂量组(n=35)、中剂量组(n=35)和高剂量组(n=35)。纳入标准：(1) 符合《子宫肌瘤的诊治中国专家共识》[4]中的诊断标准，并经超声检查确诊；(2) 符合手术适应证；(3) 肌瘤数≤4个，且最大肌瘤直径为4~10 cm；(4) 美国麻醉师协会(American Society of Anesthesiology，ASA)分级为Ⅰ~Ⅱ级；(5) 认知功能正常；(6) 临床资料完整；(7) 患者均签署知情同意书。排除标准：(1) 存在手术、麻醉禁忌证；(2) 合并其他恶性肿瘤；(3) 合并其他严重妇科疾病；(4) 合并凝血功能障碍；(5) 合并严重心、肝、肾等功能不全；(6) 近3个月有血管活性药物治疗史；(7) 存在认知、意识功能障碍。低剂量组的年龄为(40.45±5.12)岁，身体质量指数(body mass index，BMI) (23.15±1.52) kg/m^2，最大肌瘤直径(6.56±1.14)cm。中剂量组的年龄为(40.56±5.25)岁，BMI (23.09±1.56)kg/m^2，最大肌瘤直径(6.43±1.18)cm。高剂量组的年龄(40.77±5.43)岁；BMI (23.31±1.67) kg/m^2，最大肌瘤直径(6.72±1.21)cm。三组一般资料比较差异无统计学意义(P>0.05)。本研究已获得宣城市中心医院医学伦理委员会的批准(伦理批号：医伦办2022005)。

1.2　研究方法　术前保持空腹12 h。患者入室后，常规监测生命体征，建立静脉通路。麻醉诱导前10 min，低剂量组以0.20 μg/kg、中剂量组以0.40 μg/kg、高剂量组以0.60 μg/kg的剂量静脉微量泵泵入右美托咪定(成都倍特药业，国药准字H20205002，规格2 mL∶200 μg)，同时三组以0.3 mg/kg的剂量静脉微量泵泵入依托咪酯(江苏恩华药业，国药准字H32022992，规格10 mL∶20 mg)。麻醉诱导：予以0.4 μg/kg舒芬太尼(宜昌人福药业，国药准字

H20054171，规格1 mL∶50 μg）、0.04 mg/kg咪达唑仑（江苏九旭药业，国药准字H20113433，规格1 mL∶5 mg）、0.05 mg/kg维库溴铵（辰欣药业，国药准字H20067458，规格4 mg）、2 mg/kg丙泊酚（西安力邦制药，国药准字H20123318，规格50 mL∶1.0 g）静脉注射，待患者意识消失且肌肉松弛后行气管插管并使用机械通气辅助呼吸。麻醉维持：采用七氟烷（上海恒瑞医药，国药准字H20213735，规格120 mL）吸入以维持麻醉效果，并予以4 mg/（kg·h）丙泊酚、0.5 μg/（kg·min）瑞芬太尼持续输注。术毕，将患者送麻醉恢复室行麻醉复苏。

1.3　观察指标

1.3.1　血流动力学指标　记录并对比三组在麻醉诱导前15 min（T0）、气管插管后5 min（T1）、手术开始30 min（T2）及术毕（T3）时的平均动脉压（mean arterial pressure，MAP）、中心静脉压（central venous pressure，CVP）水平。

1.3.2　应激反应指标　在T0、T1、T2、T3时间点分别采集三组患者的颈内静脉血，采用酶联免疫吸附测定（enzyme-linked immunosorbent assay，ELISA）法检测血清去甲肾上腺素（noradrenaline，NE）水平，采用竞争法检测血清皮质醇（cortisol，Cor）水平。试剂盒分别购自武汉天德生物科技、科邦兴业（北京）科技，严格按照说明书流程操作。

1.3.3　炎症因子指标　在T0、T1、T2、T3时间点分别采集三组患者的颈内静脉血，采用ELISA法检测血清C反应蛋白（C-reactive protein，CRP）、肿瘤坏死因子-α（tumor necrosis factor-α，TNF-α）水平。试剂盒分别购自福来德生物科技（武汉）、青岛捷世康生物科技，严格按照说明书流程操作。

1.3.4　睡眠质量　于术前、术后1 d分别采用匹兹堡睡眠质量指数（Pittsburgh Sleep Quality Index，PSQI）[5]进行评估，包括睡眠质量、入睡时间、睡眠时间、睡眠效率、睡眠障碍、催眠药物、日间功能障碍等7个项目，得分越高表明睡眠质量越差。

1.3.5　术后谵妄（postoperative delirium，POD）　于术后3、7 d采用谵妄评定方法中文修订版（Confusion Assessment Method-Chinese Reversion，CAM-CR）[6]进行评估，包括急性起病、思维混乱、记忆力减退、定向障碍、睡眠-觉醒周期改变等11项内容。CAM-CR评分≥22分时，评定为谵妄。

1.4　统计学方法　采用SPSS 26.0软件进行统计分析。符合正态分布的计量资料分析用$\bar{x}\pm s$表示，多组间比较采用单因素方差分析，多时点比较采用重复测量资料方差分析，两两比较采用LSD-t检验。计数资料用例（%）表示，采用χ^2检验。P<0.05为差异有统计学意义。

2　结　果

2.1　三组MAP和CVP对比　重复测量方差分析显示，三组MAP和CVP存在显著的组间效应、时间效应及组间×时间交互效应（P<0.01）。两两比较显示，T1、T2、T3时，低剂量组的MAP较T0时明显升高，且高于中剂量组与高剂量组（P<0.05）；T0、T1、T2、T3时，中剂量组与高剂量组的MAP对比差异无统计学意义（P>0.05）。T2、T3时，低剂量组的CVP较T0、T1时显著降低，且低于中剂量组与高剂量组（P<0.05）；T0、T1、T2、T3时，中剂量组与高剂量组的CVP对比差异无统计学意义（P>0.05）。见表1。

2.2　三组应激反应指标对比　重复测量方差分析显示，三组血清NE、Cor水平存在显著的组间效应、时间效应及组间×时间交互效应（P<0.01）。两两比较显示，T1、T2、T3时，三组的血清NE、Cor水平较T0时明显升高，且低剂量组高于中剂量组与高剂量组（P<0.05）；而中剂量组与高剂量组的血清NE、Cor水平对比差异无统计学意义（P>0.05）。见表2。

2.3　三组炎症因子指标对比　重复测量方差分析显示，三组血清CRP、TNF-α水平存在显著的组间效应、

表1　三组不同时间点的MAP和CVP对比　（n=35，mmHg，$\bar{x}\pm s$）

Tab.1　Comparison of MAP and CVP at different times among three groups　（n=35，mmHg，$\bar{x}\pm s$）

组别	MAP				CVP			
	T0	T1	T2	T3	T0	T1	T2	T3
低剂量组	102.69±6.58	118.42±7.37[a]	122.65±6.82[a]	124.48±7.14[a]	5.44±1.08	4.98±0.94	4.32±0.84[ab]	4.48±0.82[ab]
中剂量组	103.42±6.29	104.51±6.55[c]	105.06±6.27[c]	105.24±7.05[c]	5.37±1.04	5.02±0.91	4.96±0.80[c]	5.06±0.83[c]
高剂量组	103.71±6.35	105.19±7.26[c]	105.78±6.49[c]	105.66±7.18[c]	5.33±1.09	4.95±0.88	4.89±0.82[c]	4.97±0.87[c]
$F_{组间}/P_{组间}$值	82.500/<0.001				6.450/0.002			
$F_{时间}/P_{时间}$值	58.300/<0.001				8.120/<0.001			
$F_{交互}/P_{交互}$值	42.800/<0.001				5.230/0.005			

注：与同组T0比较，[a]P<0.05；与同组T1比较，[b]P<0.05；与同时间点低剂量组比较，[c]P<0.05。

时间效应及组间×时间交互效应（P<0.01）。两两比较显示，T1、T2、T3 时，三组的血清 CRP、TNF-α水平较 T0 时明显升高，且低剂量组高于中剂量组与高剂量组（P<0.05）；而中剂量组与高剂量组的血清 CRP、TNF-α水平对比差异无统计学意义（P>0.05）。见表 3。

2.4　三组 PSQI 评分及 POD 发生情况对比　术后 1 d，三组的 PSQI 评分较术前明显升高，且低剂量组高于中剂量组与高剂量组（P<0.05）；而中剂量组与高剂量组的 PSQI 评分对比差异无统计学意义（P>0.05）。术后 3、7 d，三组的 POD 发生率对比差异无统计学意义（P>0.05）。见表 4。

表 2　三组不同时间点的血清 NE 和 Cor 水平对比　（n=35，$\bar{x}\pm s$）

Tab.2　Comparison of serum NE and Cor levels at different times among three groups　（n=35，$\bar{x}\pm s$）

组别	NE（pg/mL）				Cor（ng/mL）			
	T0	T1	T2	T3	T0	T1	T2	T3
低剂量组	16.64±3.52	26.13±4.72[a]	29.24±4.47[a]	31.42±4.76[a]	211.67±13.46	254.74±15.82[a]	266.65±17.14[a]	271.26±17.58[a]
中剂量组	16.51±3.46	18.25±3.57[ab]	19.37±4.13[ab]	18.86±3.87[ab]	212.53±14.24	224.16±15.27[ab]	227.47±16.42[ab]	226.35±16.29[ab]
高剂量组	16.45±3.42	18.12±3.49[ab]	19.51±4.22[ab]	19.15±3.94[ab]	212.82±14.61	223.63±15.32[ab]	225.12±17.16[ab]	225.76±17.33[ab]
$F_{组间}/P_{组间}$值	91.250/<0.001				86.730/<0.001			
$F_{时间}/P_{时间}$值	72.680/<0.001				67.450/<0.001			
$F_{交互}/P_{交互}$值	61.340/<0.001				56.890/<0.001			

注：与同组 T0 比较，[a]P<0.05；与同时间点低剂量组比较，[b]P<0.05。

表 3　三组不同时间点的血清 CRP 和 TNF-α水平对比　（n=35，$\bar{x}\pm s$）

Tab.3　Comparison of serum CRP and TNF-α levels at different time points among three groups　（n=35，$\bar{x}\pm s$）

组别	CRP（mg/L）				TNF-α（pg/mL）			
	T0	T1	T2	T3	T0	T1	T2	T3
低剂量组	7.67±1.12	11.53±1.83[a]	12.83±2.58[a]	11.75±2.14[a]	35.62±3.81	44.66±4.49[a]	47.77±4.19[a]	45.47±4.35[a]
中剂量组	7.82±1.04	9.24±1.72[ab]	10.15±1.82[ab]	9.79±1.86[ab]	35.46±4.02	38.12±4.21[ab]	39.72±4.36[ab]	38.18±4.22[ab]
高剂量组	7.61±1.09	9.15±1.68[ab]	10.08±1.74[ab]	9.65±1.83[ab]	35.87±3.49	38.09±4.35[ab]	39.53±4.25[ab]	37.82±4.31[ab]
$F_{组间}/P_{组间}$值	20.850/<0.001				35.920/<0.001			
$F_{时间}/P_{时间}$值	31.260/<0.001				45.680/<0.001			
$F_{交互}/P_{交互}$值	15.720/<0.001				30.450/<0.001			

注：与同组 T0 比较，[a]P<0.05；与同时间点低剂量组比较，[b]P<0.05。

表 4　三组的 PSQI 评分及 POD 发生情况对比　（n=35）

Tab.4　Comparison of PSQI scores and occurrence of POD among three groups　（n=35）

组别	PSQI 评分（分，$\bar{x}\pm s$）		POD［例（%）］	
	术前	术后 1 d	术后 3 d	术后 7 d
低剂量组	13.13±1.51	16.24±1.41[a]	3（8.57）	2（5.71）
中剂量组	13.25±1.42	14.52±1.47[ab]	2（5.71）	1（2.86）
高剂量组	13.29±1.60	14.36±1.56[ab]	2（5.71）	1（2.86）
F/χ^2值	0.106	17.329	0.306	0.520
P值	0.899	<0.001	0.858	0.771

注：与术前比较，[a]P<0.05；与低剂量组比较，[b]P<0.05。

3　讨　论

麻醉、手术创伤均会引起交感-肾上髓质系统兴奋，诱发术中应激反应，导致心率、血压等生命体征出现大幅波动，影响手术进程[2]。右美托咪定的镇静镇痛作用显著，可通过降低交感神经中枢兴奋性，并增强下丘脑腹外侧区γ-氨基丁酸能神经元活性，进而介导镇静作用，且在减轻应激反应等方面具有显著优势[7]，但不同剂量对机体的影响结果也不同。依托咪酯主要作用于中枢神经系统，具有中枢镇静催眠和一定的脑保护作用，其可通过神经元兴奋性，达到镇静效果，且无镇痛和肌肉松弛作用；另外，其不影响外周血管舒缩功能，对心血管功能影响轻微，有利于维持血液动力学的稳定性，且起效迅速、代谢快[8]。

本研究发现，三组的 MAP、CVP、NE、Cor、CRP、TNF-α水平均存在显著的组间效应、时间效应及组间×时间交互效应，表明药物剂量是影响上述指标变化的关键因素。具体而言，低剂量组的 MAP、CVP 及血清 NE、Cor 的波动幅度明显高于中剂量组与高剂量组。这与陈林等[9]的研究结果相似，提示 0.40、0.60 μg/kg 右美托咪定复合依托咪酯应用于腹腔镜子宫肌瘤剔除术的麻醉中，有利于更好地维持患者的血流动力学稳定，并缓解机体的应激反应。这可能是由于右美托咪定主要作用于交感神经系统，其可通过激动中枢神经系统的α2 受体，抑制 NE、Cor

的合成分泌，降低交感神经活性，进而抑制麻醉、手术损伤等刺激引起的应激反应，还能明显减少心脏氧耗和增加冠状动脉血流，进而使MAP、CVP等指标波动幅度减小，有利于维持血流动力学的稳定[10-12]。本研究还发现，低剂量组术中血清CRP、TNF-α水平的波动幅度明显高于中剂量组与高剂量组。这提示将0.40、0.60 μg/kg右美托咪定复合依托咪酯应用于腹腔镜子宫肌瘤剔除术的麻醉中，能更有效地抑制手术后患者的炎性反应。分析是由于右美托咪定具有镇痛、镇静及抗交感等作用，其能通过降低外周及中枢神经系统兴奋性，阻止炎症因子分泌，进而减轻炎症反应。此外，约30%患者在围手术期存在不同程度的焦虑、恐惧等不良情绪，可能会导致其出现睡眠障碍[13]。而本研究中，术后1 d，低剂量组的PSQI评分高于中剂量组与高剂量组，而三组术后的POD发生率对比差异无统计学意义。这提示将0.40、0.60 μg/kg右美托咪定复合依托咪酯应用于腹腔镜子宫肌瘤剔除术的麻醉中，患者术后的睡眠质量更好。这是由于右美托咪定具有良好的止痛、镇静作用，其可激动突触前膜α2受体，导致交感反应活性弱化，并抑制NE释放，达到中断疼痛信号转导的作用[2]。另外，右美托咪定还可直接作用于脑干，抑制中枢交感神经，并发挥抗炎作用，进而减少麻醉药物对脑组织功能的损伤，有利于确保颅内压稳定，从而降低POD的发生风险[14-15]。由此可见，随着右美托咪定剂量的增加，其作用于α2受体的效应得到增强，有利于加强镇痛、镇静的效果，且POD的发生风险并未增加。而本研究将0.40、0.60 μg/kg右美托咪定复合依托咪酯应用于腹腔镜子宫肌瘤剔除术麻醉中的影响差异不大，而麻醉药物的使用原则是在疗效相似时尽量选择较低浓度，这样可以有效提高麻醉药物的安全性。

综上所述，将0.40 μg/kg右美托咪定复合依托咪酯应用于腹腔镜子宫肌瘤剔除术中，有利于维持患者血流动力学的稳定，并改善应激反应，抑制炎症反应，且术后患者的睡眠质量较好，POD发生风险较低。

利益冲突　无

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收稿日期:2025-04-22　**修回日期**:2025-09-17　**编辑**:王宇