Cite as: Sun WN, Xiang Z, Li X, Wang M, Wang Q. Effect of esketamine combined with remimazolam in hysteroscopic surgery [J]. Chin J Clin Res, 2025, 38(12): 1813-1816.

DOI: 10.13429/j.cnki.cjcr.2025.12.005

Effect of esketamine combined with remimazolam in hysteroscopic surgery

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Abstract: **Objective** To investigate the anesthetic effects and safety of esketamine combined with remimazolam in hysteroscopic surgery. **Methods** A total of 80 patients scheduled for hysteroscopic surgery undergoing intravenous general anesthesia at Wuxi 9th People's Hospital were prospectively selected and randomly divided into Group P (esketamine + propofol, n=40) and Group R (esketamine + remimazolam, n=40). The intraoperative motor response grading scores, blood pressure, heart rate, recovery time and adverse reactions of the two groups were compared. **Results** Compared with Group P, the proportion of patients with a motor response score ⩾3 in the Group R was significantly higher [47.5% (19/40) *vs* 17.5% (7/40), χ^2=8.205, P=0.004] and lowest and highest intraoperative systolic blood pressure were higher in Group R (P<0.01). The heart rate of Group R after anesthesia were faster than that of Group P (P<0.01). Compared with Group P, Group R had a shorter recovery time [(3.6±1.4) min *vs* (6.4±1.7) min, t=8.200, P<0.01], and the lower incidence rate of injection pain [2.50% (1/40) *vs* 30.00% (12/40), χ^2=11.114, P<0.01], bradycardia [0 *vs* 15.00% (6/40), χ^2=4.505, P=0.034] and hypotension [2.50% (1/40) *vs* 20.00 (8/40), χ^2= 4.507, P=0.034]. **Conclusion** The combination of esketamine and remimazolam is safe and effective for use in hysteroscopic surgery, offering stable circulation, short recovery time, and minimal adverse reactions, though it is associated with a higher incidence of motor response.

Keywords: Remimazolam; Esketamine; Hysteroscopic surgery; Motor response; Hemodynamics; Adverse reaction

Fund program: Wuxi Municipal Health Commission Major Scientific Research Project (Z202218); Wuxi Municipal Project for Promoting Appropriate Maternal and Child Health Technologies (FYTG202206)

Hysteroscopic surgery is an important modality for gynecological diagnosis and treatment. However, intraoperative procedures such as cervical dilation often induce severe pain and discomfort in patients, necessitating the use of safe and effective intravenous anesthesia regimens. Traditional intravenous anesthesia predominantly employs short-acting sedatives (e.g., propofol) in combination with opioids [1]. Nevertheless, propofol is associated with drawbacks including injection pain, respiratory depression, hypotension, and bradycardia [2]. Moreover, the combination of opioids and propofol exerts considerable impacts on respiration and circulation, potentially leading to hypotension and hypoxemia [3]. In recent years, esketamine has garnered increasing attention for its unique synergistic sedative and analgesic effects, with studies confirming the safety of esketamine-propofol combination in hysteroscopic surgery [4]. Remimazolam is a novel ultra-short-acting benzodiazepine indicated for intravenous sedation and anesthesia, characterized by rapid onset, minimal hemodynamic impact, short half-life, and quick recovery [5]. This study aims to compare the anesthetic efficacy and safety of esketamine combined with remimazolam versus esketamine combined with propofol in hysteroscopic surgery, providing evidence-based insights for optimizing anesthesia protocols.

1 Materials and Methods

1.1 General Information

This study was approved by the Ethics Committee of Wuxi 9th People's Hospital (approval number: KS2023084), and all patients signed informed consent forms. Inclusion criteria: Scheduled for hysteroscopic examination requiring intravenous anesthesia; American Society of Anesthesiologists (ASA) physical status classification I or II; Aged 20–65 years; Body mass index (BMI) 18–25 kg/m². Exclusion criteria: Complicated with cardiac or pulmonary diseases; with a history of alcoholism; Hepatic or renal dysfunction; Long-term use of sedatives, opioids, or antidepressants; Hypersensitivity or contraindications to any study-related drugs or their components; Difficult cervical dilation (cervical dilation duration>5 min); Obstructive sleep apnea-hypopnea syndrome; Participation in other clinical trials; Other conditions precluding participation in clinical research.

1.2 Grouping

Patients were randomly assigned to two groups using a random number table method: Esketamine-Propofol Group (Group P) and Esketamine-Remimazolam Group (Group R). Anesthesia nurses placed corresponding syringes into sealed, light-impermeable envelopes. Anesthesiologists opened the envelopes sequentially by code to administer anesthesia and were not involved in data collection and analysis. Both surgeons and patients were blinded to the grouping. There were no statistically significant differences in age, height, body weight, or surgical duration between the two groups (P < 0.05) (see **Table 1**).

1.3 Anesthesia Methods

All patients fasted and abstained from fluids according to routine protocols. After lying supine for 5 minutes in the operating room, electrocardiographic monitoring was initiated. Blood pressure, heart rate (HR), and saturation of peripheral oxygen (SpO_2) were measured three times at 2-minute intervals to obtain baseline values. Continuous nasal oxygen inhalation was provided at a flow rate of 4 L/min, and intravenous access was established on the wrist for infusion of warm acetate Ringer's solution. Patients were placed in the lithotomy position. After surgical disinfection and sterile draping, anesthesia was administered as follows.

Group P: Anesthesia induction was performed with an intravenous injection of esketamine (Jiangsu Hengrui Pharmaceutical Co., Ltd.; National Medical Product Administration Approval No. H20193336; Batch No. 231126BL) at a dose of 0.5 mg/kg combined with propofol at 1 mg/kg. Once the Modified Observer's Assessment of Alertness/Sedation (MOAA/S) score reached 0 (response to painful stimuli), a continuous intravenous infusion of propofol (Corden Pharma S.P.A.; National Medical Product Administration Approval No. HJ20171277; Batch No. X23025B) was initiated at a rate of 5 mg/(kg·h). Group R: Anesthesia induction was performed with an intravenous injection of esketamine at 0.5 mg/kg combined with remimazolam (Jiangsu Hengrui Pharmaceutical Co., Ltd.; National Medical Product Administration Approval No. H20190034; Batch No. 240330AU) at a dose of 0.2 mg/kg. Once the MOAA/S score reached 0, a continuous intravenous infusion of remimazolam was initiated at a rate of 1 mg/(kg·h). If the MOAA/S score exceeded 0 or the body movement response scale score was ≥ 3 during induction or surgery, Group P received an additional intravenous bolus of propofol 0.5 mg/kg; Group R received an additional intravenous bolus of remimazolam 2.5 mg. Repeat doses were permitted as needed.

If systolic blood pressure (SBP) decreased to less than 80% of the baseline value, 6 mg of ephedrine was administered intravenously. If SBP increased to more than 120% of the baseline value, 1 mg of nicardipine was administered intravenously. If intraoperative HR fell below 50 beats per minute, 0.5 mg of atropine was administered intravenously. If intraoperative SpO_2 dropped below 90%, jaw thrust maneuver and mask positive-pressure ventilation were performed. If nausea and vomiting occurred during anesthesia emergence, 4 mg of tropisetron was administered intravenously. After surgery, patients were transferred to the post-anesthesia care unit for 30 minutes of observation. They were returned to the ward only after full recovery of consciousness and no complaints of discomfort.

1.4 Observation Indicators

Primary outcome: Number of patients with body movement response scale score ≥ 3.

Secondary outcomes: (1) Blood pressure, HR, and SpO_2 at the following time points: T0(5 minutes after lying supine in the operating room); T1(When MOAA/S score reached 0); T2(Time of the lowest intraoperative SBP); T3(Time of the highest intraoperative SBP); T4(At anesthesia emergence). (2) Number of patients requiring additional doses of propofol or remimazolam during surgery. (3) Emergence time. (4) Uterine contraction pain intensity at 5, 15, and 30 minutes after emergence, assessed using the Numerical Rating Scale (NRS). (5) Peri-anesthetic adverse reactions, including propofol injection pain, jaw thrust intervention, nausea and vomiting, hypotension (SBP < 80% of baseline), hypertension (SBP > 120% of baseline), and bradycardia (HR < 50 beats/min).

Body Movement Response Scale, 0 points: No body movement; 1 point: Wrist movement only; 2 points: Arm movement only; 3 points: Leg and/or arm movement; 4 points: Trunk movement. NRS for Uterine Contraction Pain, 0 points: No pain;1–3 points: Mild pain;4–6 points: Moderate pain;7–10 points: Severe pain.

1.5 Statistical Methods

Based on preliminary pilot data indicating a 35% difference in the incidence of body movement responses between the esketamine-remimazolam and esketamine-propofol combinations, with $\alpha = 0.05$ and $\beta = 0.01$, a sample size of 33 patients per group was calculated. Considering a potential 20% loss to follow-up, a total of 80 patients were enrolled, with 40 patients per group. Statistical analysis was performed using SPSS 24.0 software. Normally distributed measurement data were expressed as mean ± standard deviation, with independent samples *t*-test for inter-group comparisons and repeated measures analysis of variance for comparisons across multiple time points. Count data were expressed as cases (%), with chi-square test and its correction methods for inter-group comparisons. Ranked data were analyzed using the rank-sum test. A P value < 0.05 was considered statistically significant.

2 Results

2.1 Comparison of Body Movement Responses

There was a statistically significant difference in body movement response scale scores between the two groups ($P < 0.05$). The proportion of patients with body movement response scale score ≥ 3 was significantly higher in Group R than in Group P (47.5% vs. 17.5%, $\chi^2 = 8.205$, $P = 0.004$) (see Table 2).

2.2 Comparison of Blood Pressure and Heart Rate

Intraoperative SBP and diastolic blood pressure (DBP) at T2 and T3 were significantly higher in Group R than in Group P ($P < 0.05$). In Group P, SBP and DBP at T2 were significantly lower than baseline values at T0 ($P < 0.05$). HR at T1–T4 after anesthesia induction was significantly faster in Group R than in Group P ($P < 0.05$) (see Table 3).

Tab.1 Comparison of general characteristics between two groups (n=40, $\bar{x}\pm s$)

Group	Age (years)	Height (cm)	Body Weight (kg)	Surgical Duration (min)
Group P	38.9±9.1	161.1±3.4	57.5±6.6	20.0±7.4
Group R	40.7±10.7	159.3±4.6	60.1±8.4	21.7±7.2
***t* value**	0.811	1.952	1.528	0.852
***P* value**	0.420	0.055	0.131	0.307

Tab.2 Comparison of body movement responses between two groups (case)

Group	*n*	0 Point	1 Point	2 Points	3–4 Points
Group P	40	20	6	7	7
Group R	40	10	5	6	19
***Z* value**			2.886		
***P* value**			0.004		

Tab.3 Comparison of blood pressure and heart rate at different time points between two groups (n=40, $\bar{x}\pm s$)

Time Point	SBP(mmHg)		DBP(mmHg)		HR(beats/min)	
	Group P	Group R	Group P	Group R	Group P	Group R
T0	120.5±13.9	122.411.2	74.4±8.9	76.2±8.4	75.4±10.8	77.4±12.9
T1	115.0±16.1	121.7±16.1	72.6±13.3	76.1±10.9	73.5±9.7	84.2±12.1[a]
T2	102.9±11.9[b]	114.7±12.1[a]	64.9±12.3[b]	74.3±15.9[a]	71.9±10.9	78.7±13.0[a]
T3	124.5±17.7	133.6±18.4[a]	77.3±11.8	83.7±10.2[a]	73.8±11.4	80.4±11.8[a]
T4	115.2±15.7	119.9±13.4	72.2±12.5	76.3±11.5	72.7±9.9	78.6±13.7[a]
$F_{group}/F_{time}/F_{interaction}$ **value**	21.090/19.350/1.340		18.330/8.675/1.256		29.850/1.134/1.395	
$P_{group}/P_{time}/P_{interaction}$ **value**	<0.001/<0.001/0.254		<0.001/<0.001/0.287		<0.001/<0.340/0.235	

2.3 Comparison of Emergence Time and Additional Medication Requirements

Postoperative emergence time was significantly shorter in Group R than in Group P ($P < 0.05$), while the number of patients requiring additional intraoperative doses was significantly higher in Group R ($P < 0.05$) (see **Table 4**).

2.4 Comparison of NRS Scores for Uterine Contraction Pain

There was no statistically significant difference in uterine contraction pain intensity at 5, 15, and 30 min after emergence between the two groups ($P > 0.05$) (see **Table 5**).

2.5 Comparison of Adverse Reactions

The incidence of intraoperative adverse reactions including injection pain, bradycardia, and hypotension was significantly lower in Group R than in Group P ($P < 0.05$) (see **Table 6**).

Tab.4 Comparison of the recovery time and additional medication of two groups (n=40)

Group	Recovery Time（min，$\bar{x}\pm s$）	Additional Medication (case)
Group P	6.4±1.7	7
Group R	3.6±1.4	19
***t*/χ^2 value**	8.200	8.205
***P* value**	<0.001	0.008

Tab.5 Comparison of NRS scores at different time points after awakening between two groups (n=40, case)

Group	5 min			15 min			30 min		
	Mild	Moderate	Severe	Mild	Moderate	Severe	Mild	Moderate	Severe
Group P	39	1	0	38	2	0	36	4	0
Group R	38	2	0	37	3	0	37	3	0
***Z* value**		0.585			0.459			0.393	
***P* value**		0.559			0.646			0.694	

Tab.6 Comparison of the incidence of adverse reactions between two groups (n=40, case)

Group	Injection Pain	Jaw Thrust	Nausea and Vomiting	Bradycardia	Hypotension	Hypertension
Group P	12	4	3	6	8	2
Group R	1	3	2	0	1	7
χ^2 value	11.114	0	0	4.505	4.517	2.003
***P* value**	0.001	1.000	1.000	0.034	0.034	0.157

3 Discussion

Intraoperative stimuli during hysteroscopic surgery can trigger stress responses in patients. During cervical dilation and traction, insufficient sedation depth may lead to nausea and body movements, which hinder smooth surgical progression, increase the risk of tissue damage at the surgical site, and cause adverse reactions such as tissue rupture and bleeding [6]. Therefore, maintaining appropriate sedation and analgesia levels and stable hemodynamics in patients undergoing hysteroscopic surgery under general anesthesia is a key focus in clinical anesthesia research.

Propofol is the most commonly used intravenous anesthetic for hysteroscopic surgery, featuring rapid onset, short duration, and favorable recovery [7]. However, it carries risks including injection pain, tongue fall, and respiratory-circulatory depression [2]. Remimazolam exerts sedative effects by activating benzodiazepine receptors on the α-subunit of gamma-aminobutyric acid (GABA) receptors, increasing the opening frequency of chloride channels and inducing postsynaptic inhibition [2, 5]. Its main advantages include rapid onset/offset, predictable duration of action, organ-independent metabolism, availability of reversal agents, and stable hemodynamic maintenance [8].

Esketamine is the dextrorotatory isomer of ketamine, combining anesthetic, analgesic, and sympathomimetic properties. Its anesthetic and analgesic effects are primarily mediated by binding to N-methyl-D-aspartate

(NMDA) receptors, GABA receptors, and dopamine receptors [9]. Esketamine blocks sodium channels in brainstem parasympathetic nerves, inhibits cardiac parasympathetic electrical activity, and increases cardiac output [10]. It also inhibits neuronal uptake of norepinephrine, elevating norepinephrine concentrations to induce sympathetic excitation and increase peripheral vascular resistance [11]. Leveraging esketamine's parasympathetic inhibitory effect can antagonize vagal excitation during hysteroscopy. Studies have shown that esketamine used in anesthesia for painless procedures offers advantages such as optimal anesthetic depth and stable intraoperative blood pressure and heart rate [12].

In this study, the esketamine-remimazolam combination effectively avoided propofol-related injection pain and circulatory depression. Thus, Group R exhibited more stable intraoperative blood pressure and lower incidences of hypotension and bradycardia. However, Group R had slightly more cases of intraoperative hypertension (though not statistically significant), which may be associated with remimazolam's milder circulatory suppression compared to propofol. Therefore, caution is advised when using this regimen in patients with a preoperative history of hypertension.

Patients in Group R had faster recovery, possibly because remimazolam is metabolized by esterases in vivo, has a shorter half-life, and supports faster recovery and early cognitive function restoration [13]. Additionally, remimazolam's sedative effects can be rapidly reversed by flumazenil (a specific benzodiazepine antagonist) [14], accelerating recovery and facilitating enhanced postoperative recovery. If recovery is delayed, flumazenil can be clinically administered to further shorten recovery time and significantly reduce adverse reaction rates.

The remimazolam dose in this study was referenced from relevant research [4], but Group R had more intraoperative body movements. Since no anesthetic depth monitoring was performed in this study, whether this is related to insufficient remimazolam dosage requires further investigation. This study also has limitations, including a small sample size; future studies should expand the sample size to validate these results.

In conclusion, compared with the esketamine-propofol combination, esketamine-remimazolam for hysteroscopic surgery provides more stable hemodynamics, shorter recovery time, and lower incidences of adverse reactions (e.g., intraoperative hypotension, bradycardia, and injection pain), but is associated with more intraoperative body movements.

Conflict of interest None

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Submission Received: 2025-09-01 / **Revised:** 2025-11-04

·论 著·

艾司氯胺酮复合瑞马唑仑用于宫腔镜手术的效果

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摘要：目的 探讨艾司氯胺酮复合瑞马唑仑用于宫腔镜手术的麻醉效果及安全性。**方法** 前瞻性选择2023年7月至2024年7月在无锡市第九人民医院择期行静脉麻醉下宫腔镜手术患者80例，随机分为P组（艾司氯胺酮+丙泊酚，n=40）和R组（艾司氯胺酮+瑞马唑仑，n=40），比较两组患者术中体动反应分级评分、血压、心率、苏醒时间及不良反应。**结果** 与P组相比，R组体动反应分级评分≥3分患者占比[47.5%（19/40）*vs* 17.5%（7/40），χ^2=8.205，P=0.004]、术中最低收缩压和最高收缩压更高（P<0.01）。R组患者麻醉后的心率均快于P组（P<0.01）。与P组相比，R组患者苏醒时间更短[（3.6±1.4）min *vs*（6.4±1.7）min，t=8.200，P<0.01]，且术中注射痛[2.5%（1/40）*vs* 30.0%（12/40），χ^2=11.114，P<0.01]、心动过缓[0 *vs* 15.0%（6/40），χ^2=4.505，P=0.034]、低血压[2.5%（1/40）*vs* 20.0%（8/40），χ^2=4.507，P=0.034]等不良反应发生率更低。**结论** 艾司氯胺酮复合瑞马唑仑可安全有效地用于宫腔镜手术，且循环稳定，苏醒时间短，不良反应少，但体动反应较多。

关键词： 瑞马唑仑；艾司氯胺酮；宫腔镜手术；体动反应；血流动力学；不良反应

中图分类号： R614.2 R713.4 **文献标识码：** A **文章编号：** 1674-8182(2025)12-1813-04

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Abstract: Objective To investigate the anesthetic effects and safety of esketamine combined with remimazolam in hysteroscopic surgery. **Methods** A total of 80 patients scheduled for hysteroscopic surgery undergoing intravenous general anesthesia from July 2023 to July 2024 at Wuxi Ninth People's Hospital were prospectively selected and randomly divided into Group P (esketamine+propofol, n=40) and Group R (esketamine+remimazolam, n=40). The intraoperative motor response grading scores, blood pressure, heart rate, recovery time and adverse reactions of the two groups were compared. **Results** Compared with Group P, the proportion of patients with a motor response score ≥3 in the Group R was significantly higher [47.5% (19/40) *vs* 17.5% (7/40), χ^2=8.205, P=0.004] and lowest and highest intraoperative systolic blood pressure in Group R were higher (P<0.01). The heart rate of Group R after anesthesia were faster than that of Group P (P<0.01). Compared with Group P, Group R had a shorter recovery time [(3.6±1.4) min *vs* (6.4±1.7) min, t=8.200, P<0.01], and the lower incidence of injection pain [2.5% (1/40) *vs* 30.0% (12/40), χ^2=11.114, P<0.01], bradycardia [0 *vs* 15.0% (6/40), χ^2=4.505, P=0.034] and hypotension [2.5% (1/40) *vs* 20.0% (8/40), χ^2=4.507, P=0.034]. **Conclusion** The combination of esketamine and remimazolam is safe and effective for use in hysteroscopic surgery, offering stable circulation, short recovery time, and minimal adverse reactions, though it is associated with a higher incidence of motor response.

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DOI: 10.13429/j.cnki.cjcr.2025.12.005

基金项目： 无锡市卫生健康委科研重大项目(Z202218)；无锡市妇幼健康适宜技术推广项目(FYTG202206)

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出版日期： 2025-12-20

QR code for English version

宫腔镜手术是妇科诊疗的重要手段，但术中宫颈扩张等操作常引发患者剧烈疼痛及不适，需依赖安全有效的静脉麻醉方案。传统静脉麻醉多采用短效镇静药物如丙泊酚联合阿片类药物[1]，但丙泊酚存在注射疼痛、呼吸抑制、低血压和心动过缓等缺点[2]，阿片类药物联合丙泊酚对呼吸和循环的影响比较大，会引起低血压和低氧血症[3]。近年来，艾司氯胺酮因其独特的镇痛与镇静协同作用逐渐受到关注，已有研究证实其复合丙泊酚可安全用于宫腔镜手术[4]。瑞马唑仑是一种新型的超短效苯二氮䓬类药物，用于静脉镇静和麻醉。它具有起效快、对血流动力学影响小、半衰期短、恢复快等优点[5]。本研究旨在比较艾司氯胺酮复合瑞马唑仑与复合丙泊酚在宫腔镜手术中的麻醉效果及安全性，为优化麻醉方案提供循证依据。

1 资料与方法

1.1 一般资料 本研究前瞻性选择 2023 年 7 月至 2024 年 7 月在无锡市第九人民医院择期行静脉麻醉下宫腔镜手术患者 80 例，获得无锡市第九人民医院伦理委员会的批准（批件号：KS2023084），且患者均已签署知情同意书。纳入标准：（1）计划行需静脉麻醉的宫腔镜检查；（2）美国麻醉医师协会（American Society of Anesthesiologists，ASA）分级为Ⅰ或Ⅱ级；（3）年龄 20~65 岁；（4）身体质量指数（body mass index，BMI）18~25 kg/m^2。排除标准：（1）存在心脏或肺脏相关疾病；（2）酗酒；（3）肝肾功能障碍；（4）长期使用镇静药、阿片类药物或抗抑郁药；（5）对本研究中药物及药物组分过敏或存在使用禁忌；（6）宫颈扩张困难，即宫颈扩张持续时间>5 min；（7）阻塞性睡眠呼吸暂停低通气综合征；（8）参与其他临床研究；（9）其他不适合临床研究的原因。

1.2 分组 采用随机数字表法将患者分两组：艾司氯胺酮复合丙泊酚组（P 组）和艾司氯胺酮复合瑞马唑仑组（R 组）。麻醉护士将相应注射器放入密闭不透光信封，麻醉医师按顺序编码打开信封为患者实施麻醉，实施麻醉的麻醉医师不参与数据收集与分析。外科医生和患者均不知道分组情况。两组患者年龄、身高、体质量、手术时间等差异均无统计学意义（P<0.05）。见表 1。

1.3 麻醉方法 所有患者常规禁食禁饮，入室平卧 5 min 后，接心电监护仪，每隔 2 min 测量 3 次血压、心率、外周血氧饱和度（saturation of peripheral oxygen，SpO_2）作为基础值。持续鼻导管给氧，氧流量 4 L/min，开通手腕部静脉通路，接温醋酸林格液。患者置于截石位，外科消毒铺单后，P 组静脉注射艾司氯胺酮（江苏恒瑞医药，国药准字 H20193336，批号：231126BL）0.5 mg/kg+丙泊酚 1 mg/kg 进行麻醉诱导，待改良警觉/镇静（Modified Observer's Assessment of Alertness/Sedation，MOAA/S）评分为 0 分（对疼痛刺激无反应）后静脉泵注丙泊酚（Corden Pharma S.P.A.，国药准字 HJ20171277，批号：X23025B）5 mg/（kg·h）；R 组静脉注射艾司氯胺酮 0.5 mg/kg+瑞马唑仑（江苏恒瑞医药，国药准字 H20190034，批号：240330AU）0.2 mg/kg 进行麻醉诱导，待 MOAA/S 评分为 0 分后静脉泵注瑞马唑仑 1 mg/（kg·h）。诱导后或手术过程中若 MOAA/S 评分>0 分或出现体动反应分级评分≥3 分，P 组静脉注射丙泊酚 0.5 mg/kg，R 组静脉注射瑞马唑仑 2.5 mg，可以重复多次给药。

术中若收缩压下降低于基础值的 80%，则静脉注射麻黄碱 6 mg；若收缩压升高超过基础值的 120%，则静脉注射尼卡地平 1 mg；若术中心率<50 次/min，则静脉注射阿托品 0.5 mg；若术中 SpO_2<90%，则托下颌并面罩加压给氧；若麻醉苏醒期出现恶心呕吐，则静脉注射托烷司琼 4 mg。手术结束后送至术后恢复室观察 30 min，待患者意识完全清醒且无不适主诉后返回病房。

1.4 观察指标 主要指标：体动反应分级评分≥3 分的患者数。次要指标：患者入室平卧 5 min 后（T0）、MOAA/S 评分为 0 分时（T1）、手术过程中收缩压最低（T2）和最高时（T3）以及患者苏醒时（T4）的血压、心率、SpO_2，术中追加丙泊酚和瑞马唑仑的例数、苏醒时间。使用数字模拟评分法（Numerical Rating Scale，NRS）判断苏醒后 5、15、30 min 宫缩疼痛程度，以及围麻醉期的不良反应［包括丙泊酚注射痛、托下颌、恶心呕吐、低血压（<基础值的 80%）、高血压（>基础值的 120%）、心动过缓（<50 次/min）等］。

体动反应分级评分标准：0 分，无体动反应；1 分，仅有手腕部动作；2 分，仅有手臂动作；3 分，有腿部和/或手臂动作；4 分，有躯干部动作。宫缩疼痛程度：NRS 评分 0 分，无痛；NRS 评分 1~3 分，轻度疼痛；NRS 评分 4~6 分，中度疼痛；NRS 评分 7~10 分，重度疼痛。

1.5 统计学方法 根据前期预试验发现艾司氯胺酮复合瑞马唑仑与艾司氯胺酮复合丙泊酚体动反应程度差异达 35%，取 α=0.05，β=0.01，每组需要 33 例，考虑可能 20% 的失访率，最终纳入患者 80 例，每组 40 例。采用 SPSS 24.0 软件对数据进行统计学分析。正态分布的计量资料以 $\bar{x}\pm s$ 表示，比较采用独立样本 t

检验，多个时间点比较采用重复测量方差分析。计数资料以例(%)表示，组间比较采用χ^2检验及其校正法。等级资料比较采用秩和检验，P<0.05为差异有统计学意义。

2　结　果

2.1　体动反应比较　两组体动反应分级评分差异有统计学意义(P<0.05)。R组体动反应分级评分≥3分患者占比显著高于P组(47.5% *vs* 17.5%，χ^2=8.205，P=0.004)。见表2。

2.2　血压及心率比较　R组患者术中T2和T3时点的收缩压和舒张压均高于P组(P<0.05)；P组T2时点的收缩压和舒张压均低于T0(P<0.05)；R组患者麻醉后T1~T4的心率均快于P组(P<0.05)。见表3。

2.3　苏醒时间和追加药物情况比较　R组患者术后苏醒时间短于P组(P<0.05)；但R组患者术中追加药物患者例数更多(P<0.05)。见表4。

2.4　NRS评分比较　两组患者苏醒后5、15、30 min宫缩疼痛程度比较差异没有统计学意义(P>0.05)。见表5。

2.5　不良反应比较　R组患者术中注射痛、心动过缓、低血压等不良反应的发生率显著低于P组(P<0.05)。见表6。

表1　两组一般情况的比较　(n=40，$\bar{x}\pm s$)

Tab.1　Comparison of general characteristics between two groups　(n=40，$\bar{x}\pm s$)

组别	年龄(岁)	身高(cm)	体质量(kg)	手术时间(min)
P组	38.9±9.1	161.1±3.4	57.5±6.6	20.0±7.4
R组	40.7±10.7	159.3±4.6	60.1±8.4	21.7±7.2
t值	0.811	1.952	1.528	0.852
P值	0.420	0.055	0.131	0.307

表2　两组体动反应分级评分的比较　(例)

Tab.2　Comparison of body movement responses between two groups　(case)

组别	例数	0分	1分	2分	3~4分
P组	40	20	6	7	7
R组	40	10	5	6	19
Z值	2.886				
P值	0.004				

表3　两组不同时间点血压和心率的比较　(n=40，$\bar{x}\pm s$)

Tab.3　Comparison of blood pressure and heart rate at different time points between two groups　(n=40，$\bar{x}\pm s$)

时间点	收缩压(mmHg)		舒张压(mmHg)		心率(次/min)	
	P组	R组	P组	R组	P组	R组
T0	120.5±13.9	122.4±11.2	74.4±8.9	76.2±8.4	75.4±10.8	77.4±12.9
T1	115.0±16.1	121.7±16.1	72.6±13.3	76.1±10.9	73.5±9.7	84.2±12.1[b]
T2	102.9±11.9[a]	114.7±12.1[b]	64.9±12.3[a]	74.3±15.9[b]	71.9±10.9	78.7±13.0[b]
T3	124.5±17.7	133.6±18.4[b]	77.3±11.8	83.7±10.2[b]	73.8±11.4	80.4±11.8[b]
T4	115.2±15.7	119.9±13.4	72.2±12.5	76.3±11.5	72.7±9.9	78.6±13.7[b]
$F_{组间}/F_{时间}/F_{交互}$值	21.090/19.350/1.340		18.330/8.675/1.256		29.850/1.134/1.395	
$P_{组间}/P_{时间}/P_{交互}$值	<0.001/<0.001/0.254		<0.001/<0.001/0.287		<0.001/<0.340/0.235	

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

表4　两组苏醒时间和追加药物情况的比较

Tab.4　Comparison of the recovery time and additional medication of two groups

组别	例数	苏醒时间(min，$\bar{x}\pm s$)	追加药物(例)
P组	40	6.4±1.7	7
R组	40	3.6±1.4	19
t/χ^2值	8.200		8.205
P值	<0.001		0.004

表5　两组苏醒后不同时间点NRS评分的比较　(n=40，例)

Tab.5　Comparison of NRS scores at different time points after awakening between two groups　(n=40，case)

组别	5 min			15 min			30 min		
	轻度	中度	重度	轻度	中度	重度	轻度	中度	重度
P组	39	1	0	38	2	0	36	4	0
R组	38	2	0	37	3	0	37	3	0
Z值	0.585			0.459			0.393		
P值	0.559			0.646			0.694		

表6　两组不良反应发生情况的比较　(n=40，例)

Tab.6　Comparison of the incidence of adverse reactions between two groups　(n=40，case)

组别	注射痛	托下颌	恶心呕吐	心动过缓	低血压	高血压
P组	12	4	3	6	8	2
R组	1	3	2	0	1	7
χ^2值	11.114	0	0	4.505	4.507	2.003
P值	0.001	1.000	1.000	0.034	0.034	0.157

3　讨　论

宫腔镜手术术中操作等刺激会引起患者的应激反应，而在宫颈扩张、牵引过程中，如果患者因镇静深度不足而产生恶心、肢体运动，则不利于手术顺利进行，更容易对手术部位组织造成损伤，引起组织破裂、出血等不良反应[6]。因此，管理好全身麻醉下宫

腔镜手术中的镇痛镇静水平，保持患者血流动力学的稳定，是临床麻醉中需要重视和研究的方向。

丙泊酚是宫腔镜手术最常用的静脉麻醉药，具有起效快、时间短、恢复效果好等优点[7]。但它存在注射痛、舌后坠和呼吸循环抑制等风险[2]。瑞马唑仑的镇静作用是通过激活γ-氨基丁酸（gamma-aminobutyric acid，GABA）受体α亚基上的苯二氮䓬受体，增加氯离子通道打开的频率，从而诱导突触后抑制[2,5]，其主要优点包括起效/失效快、作用持续时间可预测、代谢独立于器官功能、可获得逆转药物、维持稳定的血流动力学[8]。

艾司氯胺酮是氯胺酮中的右旋异构体，它结合了麻醉、镇痛和拟交感神经的特性，其麻醉镇痛作用主要通过与N-甲基-D-天冬氨酸受体、GABA 受体和多巴胺受体等相结合[9]。艾司氯胺酮可阻断脑干副交感神经的钠通道，抑制心脏副交感神经的电活动，增加心输出量[10]，它还能抑制神经元对去甲肾上腺素的摄取，增加去甲肾上腺素的浓度，产生交感神经兴奋，增加周围血管阻力[11]。利用艾司氯胺酮的副交感神经抑制作用，可拮抗宫腔镜检查时的迷走神经兴奋。有研究结果表明，艾司氯胺酮应用于无痛诊疗中的麻醉具有麻醉深度理想、术中血压和心率稳定等优点[12]。

本研究中艾司氯胺酮与瑞马唑仑的复合方案有效地规避了丙泊酚的注射痛及循环抑制问题，因此R组患者术中血压更加平稳，低血压和心动过缓发生率更低；但R组中术中高血压发生例数略多，虽然差异无统计学意义，可能与瑞马唑仑的循环抑制轻于丙泊酚相关，因此术前有高血压病史患者需谨慎使用。

本研究中，R组患者苏醒更快，分析可能是与瑞马唑仑可通过酯酶在体内代谢、半衰期更短、具有更好快速恢复和早期恢复认知功能有关[13]；而且瑞马唑仑的镇静作用可被苯二氮䓬类药物的特异性拮抗剂氟马西尼迅速逆转[14]，从而加快苏醒，有利于术后加速康复。如果患者恢复延迟，可在临床应用氟马西尼进行拮抗，进一步缩短患者恢复时间，显著降低不良反应发生率。

本研究中瑞马唑仑的剂量参照相关研究结果[4]，但该组患者术中体动反应较多，由于本研究的麻醉过程中没有实施麻醉深度监测，这是否与瑞马唑仑剂量不足有关，还需要后续进行研究。然而，本研究也存在一些局限性。本研究的样本量较小，未来需要进一步增加样本量来验证本研究的结果。

综上所述，艾司氯胺酮复合瑞马唑仑用于宫腔镜手术相较于复合丙泊酚血流动力学更稳定，苏醒时间更短，术中低血压、心动过缓、注射痛等不良反应发生率更低，但术中体动反应较多。

利益冲突　无

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收稿日期：2025-09-01　**修回日期**：2025-11-04　**编辑**：许煜晗