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Effects of different doses of esketamine at anesthesia induction and maintenance during abdominal surgery

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Abstract: Objective To explore the effects of different doses of esketamine (ESK) combined during anesthesia induction and maintenance in patients undergoing abdominal surgery, so as to provide a reference for clinical selection of the appropriate dose of ESK. **Methods** A total of 80 patients scheduled for abdominal surgery under general anesthesia in Zhongshan Hospital Xiamen University from May to November 2023 were selected as the research objects. They were randomly divided into three groups using a random number table: control group (CON group, *n*=20), low- dose ESK group (L-ESK group, *n*=30), and medium-dose ESK group (M-ESK group, *n*=30). Anesthesia induction: all three groups were intravenously injected with midazolam 1-3 mg, sufentanil 0.3-0.6 μg/kg, propofol 2-3 mg/ kg, and cisatracurium 0.2 mg/kg, followed by tracheal intubation. Immediately after intubation, patients in the L-ESK group and M-ESK group were intravenously injected with ESK 0.25 mg/kg and 0.5 mg/kg, respectively, while patients in the CON group were given the same volume of normal saline. Anesthesia maintenance: the CON group was continuously infused with propofol 4-6 mg/(kg·h) and cisatracurium 0.05 mg/(kg·h) by pump. The L-ESK group and M-ESK group were additionally given continuous pump infusion of ESK 0.125 mg/(kg·h) and 0.25 mg/(kg·h), respectively, on the basis of the CON group. Postoperatively, all patient received sufentanil by patient-controlled intravenous analgesia. Hemodynamic parameters (blood pressure and heart rate), anesthesia recovery indicators, pain degree[Visual Analogue Scale (VAS)]at different time points, and the incidence of postoperative adverse reactions were compared among the three groups. **Results** Compared with the pre-anesthesia values in the same group, the heart rate, diastolic blood pressure (DBP), and systolic blood pressure (SBP)in the three groups were significantly decreased before intubation (P<0.05), and significantly increased after intubation (P<0.05). There was no statistically significant difference in heart rate, DBP, and SBP between post-extubation and pre-anesthesia (P>0.05). Compared with the CON group, the anesthesia recovery time, extubation time, consciousness recovery time, and spontaneous breathing recovery time in the L-ESK group and M-ESK group were significantly shorter (P<0.05), the VAS scores on the postoperative day 1 and 2 were significantly lower (P<0.05). Compared with the L-ESK group, the anesthesia recovery time, extubation time, consciousness recovery time, and spontaneous breathing recovery time in the M-ESK group were further shorter (P<0.05), the VAS scores on the postoperative day 1 and 2 were significantly lower (P<0.05). The overall incidence of adverse reactions was 65.00% (13/20)in the CON group, 23.33% (7/30) in the L-ESK group, and 26.67% (8/30) in the M-ESK group. There was a statistically significant difference among three groups (χ^2=10.623, P=0.005), with the CON group being higher than both the L-ESK group and M-ESK group (P< 0.017). However, there was no statistically significant difference between the L-ESK group and the M-ESK group (P> 0.017). **Conclusion** The combined application of ESK during the anesthesia induction and maintenance stages in patients undergoing abdominal surgery can effectively shorten the postoperative recovery time and alleviate the degree of postoperative pain. Compared with the dose of 0.125 mg/(kg·h), dose of 0.25 mg/(kg·h) ESK can further shorten the recovery time and relieve pain without increasing the incidence of adverse reactions.

Keywords: Esketamine;Propofol;Anesthesia induction;Anesthesia maintenance;Abdominal surgery;Tracheal intubation

Abdominal surgery is a common clinical treatment method. Anesthesia helps to avoid stress responses in patients caused by surgical pain during the perioperative period and improve surgical safety and success rates [1-2]. To reduce opioid consumption in patients undergoing abdominal surgery, non-opioid drugs and analgesic interventions can improve and alleviate opioid-related side effects. Ketamine is a non-selective N-methyl-D-aspartate (NMDA) receptor inhibitor with partial non-opioid analgesic properties [3]. Studies have shown that low-dose intravenous infusion of ketamine can be used as an adjuvant drug for the treatment of acute and chronic postoperative pain [4]. Postoperative intravenous administration of opioids may cause hyperalgesia and opioid tolerance, both of which are partially related to NMDA receptor activation. Prevention and postoperative analgesia with NMDA receptor antagonists can prevent acute opioid tolerance and reduce the occurrence of neuropathic pain [5]. Esketamine (ESK) is the *S* (+) isomer of ketamine, and its analgesic effect is twice that of racemic ketamine. ESK has advantages such as fewer side effects, faster recovery, reducing the minimum alveolar concentration (MAC) of sevoflurane, and protecting hypoxic pulmonary vasoconstriction

during one-lung ventilation [6]. Studies have shown that combined application of low/medium doses of ESK has a significant effect in perioperative pain management of video-assisted thoracoscopic pulmonary resection [7]. However, the application dose and analgesic effect of ESK in abdominal surgery are currently unknown. This study explores the comparison of effects of combined application of different doses of ESK during anesthesia induction and maintenance phases in patients undergoing abdominal surgery.

1 Materials and Methods

1.1 Clinical Data

This study was approved by the Ethics Committee of Zhongshan Hospital Xiamen University [Approval No.: xmzsyykyl (2024-533)] and obtained informed consent from all patients. A total of 80 patients scheduled for laparoscopic surgery under general anesthesia admitted to the hospital from May to November 2023 were enrolled. They were divided into three groups via the random number table method: control group (CON group, *n*=20), low-dose ESK group (L-ESK group, *n*=30), and medium-dose ESK group (M-ESK group, *n*=30). There were no statistically significant differences were observed in gender, age, body mass index (BMI), or surgical type among the three groups (P>0.05), indicating comparability. See **Table 1**.

Tab. 1 Comparison of general information among three groups

Items	CON group (*n*=20)	L-ESK group (*n*=30)	M-ESK group (*n*=30)	χ^2 / *F* value	*P* value
Male/female (case)	10/10	16/14	15/15	0.083	0.959
Age (years, $\bar{x}$ ±s)	43.12±9.23	44.96±10.45	42.87±9.05	0.400	0.671
BMI(kg/m², $\bar{x}$ ±s)	23.48±3.19	23.92±3.07	23.82±3.43	0.111	0.895
Type of surgery [case(%)]					
Gastrointestinal surgery	8(40.00)	13(43.33)	12(40.00)		
Urinary system surgery	7(35.00)	11(36.67)	13(43.33)	0.736	0.947
Hepatobiliary surgery	5(25.00)	6(20.00)	5(16.67)		

Inclusion criteria: (1) age ranged 20–70 years; (2) American Society of Anesthesiologists (ASA) physical status classification Ⅰ; (3) consent to receive patient-controlled intravenous analgesia (PCIA); (4) meeting indications for abdominal surgery.

Exclusion Criteria: (1) history of allergy to anesthetics, ropivacaine, or ketamine; allergy or contraindications to non-steroidal anti-inflammatory drugs (NSAIDs); (2) comorbid mental illness or chronic pain that may interfere with analgesic effect assessment; (3) inability to read/write Chinese or communicate effectively; (4) emergency surgery or trauma patients; (5) history of intraoperative consciousness disturbance; (5) need for postoperative transfer to the ICU.

1.2 Methods

Routine monitoring included blood pressure, electrocardiogram (ECG), pulse oximetry (SpO_2), end-tidal CO_2 concentration ($EtCO_2$), etc. General Anesthesia Induction: intravenous midazolam (1–3 mg), sufentanil (0.3–0.6 μg/kg), propofol (2–3 mg/kg), and cisatracurium (0.2 mg/kg) were administered as needed, followed by tracheal intubation. Both patients in the L-ESK and M-ESK groups received intravenous ESK at 0.25 mg/kg and 0.50 mg/kg immediately after intubation. The CON group received the same volume of normal saline post-induction. Anesthesia Maintenance: the CON group received continuous infusion of propofol [4–6 mg/(kg·h)] and cisatracurium [0.05 mg/(kg·h)]. The L-ESK and M-ESK groups added ESK at 0.125 mg/(kg·h) and 0.25 mg/(kg·h) to the CON group regimen for combined maintenance. Anesthetic doses were dynamically adjusted based on blood pressure and heart rate (HR) changes. Total intraoperative sufentanil dose was 0.4–1.0 μg/kg, with intermittent 0.1–0.2 μg/kg boluses as needed. Systolic blood pressure (SBP) and HR were maintained within 30% of baseline. Vasoactive drugs were used if necessary to preserve perfusion. Postoperatively, patients received PCIA (100 mL): sufentanil at 0.03 μg/(kg·h), continuous infusion at 1.5 mL/h for 48 h, with a 1.5 mL patient-controlled bolus and 10-minute lockout time. Pain intensity was assessed via the Visual Analogue Scale (VAS): PCIA was suspended if VAS <1 point; 40 mg parecoxib sodium was intravenously administered for rescue analgesia if VAS >4 points. Antibiotics and antiemetics were also given postoperatively.

1.3 Observation Indicators

(1) HR, diastolic blood pressure (DBP), and systolic blood pressure (SBP) at different time points (before anesthesia, before intubation, after intubation, after extubation) were recorded using an electrocardiogram monitor. (2) Postoperative anesthesia recovery time, extubation time, consciousness recovery time, and spontaneous breathing recovery time were monitored and recorded. (3) The VAS scores of patients at 1 day and 2 days after surgery were evaluated and recorded. The total score ranges from 0 to 10, with higher scores indicating more severe pain. (4) The dosages of sufentanil and propofol during the perioperative period were recorded. (5) The incidence of postoperative adverse reactions (nausea and vomiting, respiratory depression, agitation, pruritus) was recorded.

1.4 Statistical Methods

Data were analyzed using SPSS 22.0 software. Quantitative data conforming to normal distribution were described as $\bar{x}$ ±s. Comparisons among multiple groups were performed using one-way analysis of variance (ANOVA) or repeated measures ANOVA, and pairwise comparisons were conducted using the SNK-*q* test. Qualitative data were described as n (%), and comparisons were made using the chi-square test, with pairwise comparisons performed using the Bonferroni method. A *P* value < 0.05 was considered statistically significant.

2 Results

2.1 Comparison of Sufentanil and Propofol Dosages Among Three Groups

The dosages of sufentanil and propofol in the M-ESK group were less than those in the CON group and L-ESK group, with statistically significant differences (*P*<0.05). See **Table 2**.

2.2 Comparison of Blood Pressure and HR Among Three Groups

Compared with the pre-anesthesia period in the same group, the HR, DBP, and SBP of the CON group, L-ESK group, and M-ESK group significantly decreased before intubation (*P*<0.05), and significantly increased after intubation (*P*<0.05). There was no statistically significant difference between post-extubation and pre-anesthesia (*P*>0.05). No statistically significant differences were observed in HR, DBP, and SBP among the three groups at the same time points (*P*>0.05). See **Table 3**.

2.3 Comparison of Postoperative Recovery Time Among Three Groups

The anesthesia recovery time, extubation time, consciousness recovery time, and spontaneous breathing recovery time of the L-ESK group and M-ESK group were shorter than those of the CON group (*P*<0.05). Compared with the L-ESK group, the above recovery times of the M-ESK group were even shorter (*P*<0.05). See **Table 4**.

2.4 Comparison of VAS Scores Among Three Groups

Compared with the CON group, the VAS scores of the L-ESK group and M-ESK group at 1 and 2 days after surgery were lower (*P*<0.05). Compared with the L-ESK group, the VAS scores of the M-ESK group at 1 and 2 days after surgery were lower (*P*<0.05). See **Table 5**.

2.5 Postoperative Adverse Reactions Among Three Groups

The total incidence of postoperative adverse reactions in the L-ESK group and M-ESK group was lower than that in the CON group (*P*<0.017). There was no statistically significant difference in the total incidence of postoperative adverse reactions between the L-ESK group and M-ESK group (P>0.017). See **Table 6**.

Tab.2 Comparison of sufentanil and propofol dosage among three groups ($\bar{x}$ ±s)

Group	Cases	Sufentanil dosage (μg)	Propofol dosage (mg)
CON group	20	160.22±31.45	1 138.91±97.34
L-ESK group	30	157.59±27.36	1 102.37±61.28
M-ESK group	30	126.25±15.38[ab]	827.94±65.97[ab]
***F* value**		16.065	146.763
***P* value**		<0.001	<0.001

Note: [a]*P*<0.05 indicates a statistically significant difference compared with the CON group; [b]*P*<0.05 indicates a statistically significant difference compared with the L-ESK group.

Tab.3 Comparison of hemodynamic parameters among three groups ($\bar{x}$ ±*s*)

Group	HR (beats/min)				F/P_{group} value	F/P_{time} value	$F/P_{interaction}$ value
	Pre-anesthesia	Before intubation	After intubation	After extubation			
CON group	76.13±11.27	67.55±9.28[a]	88.56±10.37[a]	77.91±11.32			
L-ESK group	77.21±8.15	69.83±7.58[a]	85.65±8.11[a]	79.32±7.02	18 327.591/<0.001	51.942/<0.001	7.419/0.029
M-ESK group	77.36±10.54	68.92±8.49[a]	86.44±10.25[a]	78.19±10.05			

Group	SBP (mmHg)				F/P_{group} value	F/P_{time} value	$F/P_{interaction}$ value
	Pre-anesthesia	Before intubation	After intubation	After extubation			
CON group	130.18±15.20	105.96±12.52[a]	145.08±16.33[a]	128.30±12.98			
L-ESK group	132.40±15.73	110.55±14.32[a]	140.28±13.02[a]	134.08±11.60	26 947.378/<0.001	61.423/<0.001	11.494/0.018
M-ESK group	128.17±12.84	115.82±13.36[a]	142.25±16.28[a]	130.69±18.29			

Group	DBP (mmHg)				F/P_{group} value	F/P_{time} value	$F/P_{interaction}$ value
	Pre-anesthesia	Before intubation	After intubation	After extubation			
CON group	73.38±10.28	66.17±11.08[a]	85.32±11.07[a]	72.54±10.85			
L-ESK group	75.44±11.52	67.93±10.60[a]	84.19±11.65[a]	77.17±10.92	13 878.252/<0.001	31.796/<0.001	4.642/0.037
M-ESK group	73.23±10.53	66.35±10.10[a]	80.32±9.05[a]	75.71±10.32			

Note: [a]*P*<0.05 indicates a statistically significant difference compared with the pre-anesthesia.

Tab.4 Comparison of postoperative recovery time among three groups (min, $\bar{x}$ ±s)

Group	Cases	Anesthesia recovery time	Extubation time	Consciousness recovery time	Spontaneous breathing recovery time
CON group	20	38.52±4.61	9.24±1.36	13.94±2.86	7.52±1.96
L-ESK group	30	32.19±3.22[a]	8.42±1.12[a]	9.95±1.89[a]	5.58±1.25[a]
M-ESK group	30	28.46±2.95[ab]	6.85±1.27[ab]	7.28±1.65[ab]	4.87±1.10[ab]
***F* value**		48.870	24.342	60.916	21.692
***P* value**		<0.001	<0.001	<0.001	<0.001

Note: [a]*P*<0.05 indicates a statistically significant difference compared with the CON group; [b]*P*<0.05 indicates a statistically significant difference compared with the L-ESK group.

Tab.5 Comparison of VAS scores among three groups ($\bar{x}$ ±*s*)

Group	Cases	1 day after surgery	2 days after surgery
CON group	20	2.08±0.52	3.72±0.74
L-ESK group	30	1.64±0.41[a]	3.26±0.52[a]
M-ESK group	30	1.39±0.37[ab]	2.88±0.64[ab]
***F* value**		16.094	10.943
***P* value**		<0.001	<0.001

Note: [a]*P*<0.05 indicates a statistically significant difference compared with the CON group; [b]*P*<0.05 indicates a statistically significant difference compared with the L-ESK group.

Tab.6 Postoperative adverse reactions occurred in three groups [case(%)]

Group	Cases	Nausea and vomiting	Respiratory depression	Agitation	Pruritus	Total adverse reactions
CON group	20	8(40.00)	1(5.00)	2(10.00)	2(10.00)	13(65.00)
L-ESK group	30	5(16.67)	0(0.00)	1(3.33)	1(3.33)	7(23.33)[a]
M-ESK group	30	6(20.00)	0(0.00)	2(6.67)	0(0.00)	8(26.67)[a]
χ^2 value						10.623
***P* value**						0.005

Note: [a]*P*<0.017 indicates a statistically significant difference compared with the CON group.

3 Discussion

Abdominal surgery typically induces postoperative pain, which requires prompt and effective relief to accelerate healing, promote recovery, and prevent complications. However, 80% of patients report inadequate relief of their postoperative pain [8]. In specific patient populations and surgical settings, opioid-free anesthesia offers superior pain control [9]. ESK, the *S* (+) isomer of ketamine, exhibits potent analgesic effects [10]. Previous research has demonstrated that in patients with chronic opioid dependence, perioperative intravenous administration of ESK [0.5 mg/kg for anesthetic induction followed by 0.25 mg/(kg·h) for maintenance] can alleviate pain [11]. A study by Qi Yu *et al.* [7] found that during thoracoscopic lung resection, combining ESK [0.5 or 1.0 mg/kg for induction and 0.25 or 0.5 mg/(kg·h) for maintenance] provides favorable analgesia, with the 0.5 mg/kg dose effectively reducing adverse reaction rates.

The results of this study show no statistically significant differences in hemodynamic parameters (HR, DBP, SBP) among the CON group, L-ESK group, and M-ESK group. This suggests that both conventional propofol-based maintenance (CON group) and ESK-combined maintenance (L-ESK and M-ESK groups) yield similar hemodynamic stability, possibly because the ESK dose was insufficient to fully block sympathetic activation pathways. Additionally, compared with the CON group, ESK combination significantly improved post-anesthesia recovery, with the medium-dose ESK (M-ESK group) showing better recovery outcomes. This may be attributed to ESK's role as an NMDA receptor antagonist: it delivers effective analgesia, enhances postoperative metabolic function, and shortens recovery time [12-14]. Comparative analysis of VAS scores further confirmed ESK's positive effect on pain reduction, with the medium dose achieving more ideal pain relief. This dual mechanism of ESK likely contributes to these outcomes: it inhibits NMDA receptor-mediated central sensitization (reducing postoperative hyperalgesia) and promotes synaptic plasticity of glutamatergic neurons (accelerating neural function reorganization).

Opioids have long been the mainstay for postoperative pain control in abdominal surgery. However, clinical use of opioids is associated with excessive consumption, potential dependence, respiratory depression, nausea and vomiting, delayed gastric emptying, and postoperative ileus, the latter two of which being key drivers of prolonged hospital stays after abdominal surgery [15-16]. Studies have shown that a single 0.5 mg/kg dose of ESK is safe and well-tolerated in patients undergoing painless gastroscopy [17]. This study found that ESK combination significantly reduced adverse reactions compared with the CON group, while no statistically significant difference in total adverse reaction rates was observed between the L-ESK and M-ESK groups. Limitations of this study include its single-center design and small sample size, which prevented evaluation of ESK's impact on long-term chronic pain. Future research should include multicenter studies combined with quantitative electroencephalography monitoring to explore ESK's optimal plasma concentration range. Additionally, only low/medium doses of ESK were tested here; the effects of high-dose ESK require further investigation.

In conclusion, combining 0.5 mg/kg ESK for induction and 0.25 mg/(kg·h) for maintenance in abdominal surgery patients effectively shortens recovery

time, reduces pain intensity, improves postoperative comfort, and minimizes opioid-related adverse reactions.

Conflict of Interest None

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·论 著·

不同剂量艾司氯胺酮在腹部手术麻醉诱导和维持阶段的应用效果

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摘要：目的 探讨腹部手术患者麻醉诱导及麻醉维持阶段复合应用不同剂量艾司氯胺酮(ESK)的效果，为临床选择合适剂量的ESK提供参考。**方法** 选取厦门大学附属中山医院2023年5月至11月收治的80例拟行全身麻醉腹部手术的患者为研究对象，采用随机数字表法分为对照组(CON组，n=20)、低剂量ESK组(L-ESK组，n=30)和中剂量ESK组(M-ESK组，n=30)。麻醉诱导时三组均静脉注射咪达唑仑1~3 mg、舒芬太尼0.3~0.6 μg/kg、丙泊酚2~3 mg/kg及顺阿曲库铵0.2 mg/kg，后行气管插管，L-ESK组及M-ESK组患者插管后即刻分别静脉注射0.25、0.5 mg/kg ESK，CON组患者给予相同容量生理盐水注射。麻醉维持中CON组采用丙泊酚4~6 mg/(kg·h)和顺阿曲库铵0.05 mg/(kg·h)持续泵注；L-ESK组及M-ESK组在CON组基础上分别给予ESK 0.125、0.25 mg/(kg·h)进行复合麻醉维持。术后给予舒芬太尼患者自控静脉镇痛持续泵注。比较三组不同时间点血流动力学参数(血压、心率)、术后麻醉恢复情况、疼痛程度[视觉模拟评分法(VAS)]及术后不良反应情况。**结果** 与同组麻醉前相比，CON组、L-ESK组、M-ESK组插管前的心率、舒张压、收缩压均显著降低(P<0.05)，插管后的心率、舒张压、收缩压均显著升高(P<0.05)，拔管后与麻醉前相比差异无统计学意义(P>0.05)。与CON组相比，L-ESK组和M-ESK组麻醉恢复时间、拔管时间、意识恢复时间及自主呼吸恢复时间更短(P<0.05)，术后1、2 d的VAS评分均更低(P<0.05)。与L-ESK组相比，M-ESK组麻醉恢复时间、拔管时间、意识恢复时间及自主呼吸恢复时间较短(P<0.05)，术后1、2 d的VAS评分均较低(P<0.05)。总不良反应发生率方面，CON组为65.00%(13/20)，L-ESK组为23.33%(7/30)，M-ESK组为26.67%(8/30)，三组间差异有统计学意义(χ^2=10.623，P=0.005)，CON组分别高于L-ESK组和M-ESK组(P<0.017)，但L-ESK组和M-ESK组比较差异无统计学意义(P>0.017)。**结论** 腹部手术患者麻醉诱导及麻醉维持阶段复合应用ESK可有效缩短患者术后恢复时间，减轻疼痛程度。相对于0.125 mg/(kg·h)的剂量，0.25 mg/(kg·h)的ESK可进一步缩短恢复时间，减轻疼痛，且不增加不良反应发生率。

关键词： 艾司氯胺酮；丙泊酚；麻醉诱导；麻醉维持；腹部手术；气管插管
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Effects of different doses of esketamine at anesthesia induction and maintenance during abdominal surgery

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Abstract: Objective To explore the effects of different doses of esketamine (ESK) during anesthesia induction and maintenance in patients undergoing abdominal surgery, so as to provide a reference for clinical selection of the appropriate dose of ESK. **Methods** A total of 80 patients scheduled for abdominal surgery under general anesthesia in Zhongshan Hospital Xiamen University from May to November 2023 were selected as the research objects. They were randomly divided into three groups using a random number table: control group (CON group, n=20), low-dose ESK group (L-ESK group, n=30), and medium-dose ESK group (M-ESK group, n=30). Anesthesia induction: all three

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groups were intravenously injected with midazolam 1-3 mg, sufentanil 0.3-0.6 μg/kg, propofol 2-3 mg/kg, and cisatracurium 0.2 mg/kg, followed by tracheal intubation. Immediately after intubation, patients in the L-ESK group and M-ESK group were intravenously injected with ESK 0.25 mg/kg and 0.5 mg/kg, respectively, while patients in the CON group were given the same volume of normal saline. Anesthesia maintenance: the CON group was continuously infused with propofol 4-6 mg/(kg·h) and cisatracurium 0.05 mg/(kg·h) by pump. The L-ESK group and M-ESK group were additionally given continuous pump infusion of ESK 0.125 mg/(kg·h) and 0.25 mg/(kg·h), respectively, on the basis of the CON group. Postoperatively, all patient received sufentanil by patient controlled intravenous analgesia. Hemodynamic parameters (blood pressure and heart rate), anesthesia recovery indicators, pain degree [Visual Analogue Scale (VAS)] at different time points, and the incidence of postoperative adverse reactions were compared among the three groups. **Results** Compared with the pre-anesthesia values in the same group, the heart rate, diastolic blood pressure (DBP), and systolic blood pressure (SBP) in the three groups were significantly decreased before intubation (P<0.05), and significantly increased after intubation (P<0.05). There was no statistically significant difference in heart rate, DBP, and SBP between post-extubation and pre-anesthesia (P>0.05). Compared with the CON group, the anesthesia recovery time, extubation time, consciousness recovery time, and spontaneous breathing recovery time in the L-ESK group and M-ESK group were significantly shorter (P<0.05), while the VAS scores on the postoperative day 1 and 2 were significantly lower (P<0.05). Compared with the L-ESK group, the anesthesia recovery time, extubation time, consciousness recovery time, and spontaneous breathing recovery time in the M-ESK group were further shorter (P<0.05), while the VAS scores on the postoperative day 1 and 2 were significantly lower (P<0.05). The overall incidence of adverse reactions was 65.00% (13/20) in the CON group, 23.33% (7/30) in the L-ESK group, and 26.67% (8/30) in the M-ESK group while the difference among three groups was significant (χ^2=10.623, P=0.005), with the CON group being higher than both the L-ESK group and M-ESK group (P<0.017). However, there was no statistically significant difference between the L-ESK group and the M-ESK group (P>0.017). **Conclusion** The combined application of ESK during the anesthesia induction and maintenance stages in patients undergoing abdominal surgery can effectively shorten the postoperative recovery time and alleviate the degree of postoperative pain. Compared with the dose of 0.125 mg/(kg·h), dose of 0.25 mg/(kg·h) ESK can further shorten the recovery time and relieve pain without increasing the incidence of adverse reactions.

Keywords: Esketamine; Propofol; Anesthesia induction; Anesthesia maintenance; Abdominal surgery; Tracheal intubation

腹部手术是临床上常见的治疗手段，麻醉有助于避免手术疼痛引起的患者应激反应，提高手术安全性及成功率[1-2]。为了减少腹部手术患者阿片类药物的消耗，非阿片类药物和镇痛干预措施可改善并减轻阿片类药物引起的相关副作用。氯胺酮是一种非选择性N-甲基-D-天冬氨酸(N-methyl-D-aspartate，NMDA)受体抑制剂，具有部分非阿片类镇痛特性[3]。研究表明，低剂量静脉输注氯胺酮可作为急性和慢性术后疼痛治疗的辅助药物[4]。术后静脉给予阿片类药物可能引起痛觉过敏和阿片类药物耐受，这两者都与NMDA受体激活部分相关。NMDA受体拮抗剂预防和术后镇痛可以预防阿片类药物的急性耐受性，减少神经性疼痛的发生[5]。艾司氯胺酮(esketamine，ESK)是氯胺酮的右旋异构体，其镇痛作用是外消旋氯胺酮的两倍。ESK具有副作用少、恢复快、降低七氟醚最低肺泡有效浓度(minimum alveolar concentration，MAC)、保护单肺通气时缺氧肺血管收缩等优点[6]。研究表明，复合应用低/中剂量ESK在胸腔镜肺切除术围手术期疼痛治疗中具有显著效果[7]。但目前对ESK腹部手术中的应用剂量及镇痛效果尚不明确。本研究探讨腹部手术患者麻醉诱导、维持阶段复合应用不同剂量ESK的效果对比。

1 资料与方法

1.1 临床资料 本研究经厦门大学附属中山医院伦理委员会批准[批号：xmzsyyky伦审第(2024-533)号]，并获得所有患者知情同意。选取厦门大学附属中山医院2023年5月至11月收治的拟行全身麻醉腹腔镜手术的80例患者作为研究对象，采用随机数字表法分为3组：对照组(CON组，n=20)、低剂量ESK组(L-ESK组，n=30)、中剂量ESK组(M-ESK组，n=30)。三组患者性别、年龄、身体质量指数(body mass index，BMI)、手术类型比较差异无统计学意义(P>0.05)，具有可比性。见表1。

纳入标准：(1) 年龄20~70岁；(2) 美国麻醉医师

协会(American Society of Anesthesiologists, ASA)分级Ⅰ级;(3)同意使用患者自控静脉镇痛(patient controlled intravenous analgesia, PCIA);(4)符合腹部手术指征。排除标准:(1)对麻醉剂、罗哌卡因或氯胺酮有过敏史;对非甾体抗炎药过敏或有任何禁忌证;(2)合并可能混淆镇痛效果的精神疾病或慢性疼痛;(3)不能读写中文,沟通困难;(4)急诊手术或创伤患者;(5)有术中意识障碍史;(6)术后转入重症监护室。

1.2 方法 常规监测血压、心电图、外周血氧饱和度、呼气末CO_2浓度等。全身麻醉诱导:根据需要静脉注射咪达唑仑1~3 mg、舒芬太尼0.3~0.6 μg/kg、丙泊酚2~3 mg/kg以及顺阿曲库铵0.2 mg/kg,后行气管插管,L-ESK组及M-ESK组患者插管后即刻分别静脉注射0.25、0.50 mg/kg ESK,CON组患者在麻醉诱导后接受相同容量生理盐水注射。麻醉维持:CON组采用丙泊酚4~6 mg/(kg·h),顺阿曲库铵0.05 mg/(kg·h)持续泵注;L-ESK组及M-ESK组在CON组基础上分别给予ESK 0.125 mg/(kg·h)和0.25 mg/(kg·h)复合麻醉维持。根据血压和心率的变化来动态调节麻醉药物用量,术中舒芬太尼总剂量为0.4~1.0 μg/kg,根据需要间歇性添加0.1~0.2 μg/kg。在手术过程中,收缩压和心率将保持在基线的30%以内,必要时给予血管活性药物维持灌注。术后给予患者总容积为100 mL的PCIA:舒芬太尼0.03 μg/(kg·h),以1.5 mL/h的速率连续输注48 h,自控容量为1.5 mL,锁定时间为10 min。并通过视觉模拟评分法(Visual Analogue Scales, VAS)评估患者疼痛程度,若VAS<1分则暂停PCIA,若VAS>4分则静脉注射帕瑞昔布钠40 mg补救镇痛。术后给予患者抗生素及抗恶心呕吐药物。

1.3 观察指标 (1)通过心电监护仪记录不同时间点(麻醉前、插管前、插管后、拔管后)的心率、舒张压、收缩压;(2)监测记录术后麻醉恢复时间、拔管时间、意识恢复时间、自主呼吸恢复时间;(3)评估并记录患者术后1 d及术后2 d的VAS评分,总分0~10分,分值越大代表疼痛程度越高;(4)记录围手术期舒芬太尼及丙泊酚用量;(5)记录术后不良反应(恶心呕吐、呼吸抑制、躁动、瘙痒)发生情况。

1.4 统计学方法 采用SPSS 22.0软件分析数据。符合正态分布的计量资料以$\bar{x}\pm s$描述,多组间比较采用单因素方差分析或重复测量资料的方差分析,两两比较采用SNK-q检验;计数资料以例(%)描述,比较采用χ^2检验,并采用Bonferroni法进行两两比较。P<0.05为差异有统计学意义。

2 结 果

2.1 三组患者舒芬太尼及丙泊酚用量比较 M-ESK组舒芬太尼及丙泊酚用量少于CON组及L-ESK组,差异有统计学意义(P<0.05)。见表2。

2.2 三组患者血压和心率比较 与同组麻醉前相比,CON组、L-ESK组、M-ESK组插管前心率、舒张压、收缩压均显著降低(P<0.05),插管后的心率、舒张压、收缩压均显著升高(P<0.05),拔管后与麻醉前相比差异无统计学意义(P>0.05);三组同时间点心率、舒张压、收缩压相比差异无统计学意义(P>0.05)。见表3。

2.3 三组患者术后恢复时间比较 L-ESK组和M-ESK组麻醉恢复时间、拔管时间、意识恢复时间及自主呼吸恢复时间均短于CON组(P<0.05);与L-ESK组相比,M-ESK组麻醉恢复时间、拔管时间、意识恢复时间及自主呼吸恢复时间更短(P<0.05)。见表4。

2.4 三组患者VAS评分比较 与CON组相比,L-ESK组和M-ESK组术后1、2 d的VAS评分更低(P<0.05),与L-ESK组相比,M-ESK组术后1、2 d的VAS评分更低(P<0.05)。见表5。

2.5 三组患者术后不良反应发生情况 L-ESK组和M-ESK组的总不良反应发生率低于CON组(P<0.017);L-ESK组和M-ESK组的总不良反应发生率比较差异无统计学意义(P>0.017)。见表6。

表1 三组一般资料比较

Tab.1 Comparison of general data among three groups

项目	CON组(n=20)	L-ESK组(n=30)	M-ESK组(n=30)	χ^2/F值	P值
男/女(例)	10/10	16/14	15/15	0.083	0.959
年龄(岁,$\bar{x}\pm s$)	43.12±9.23	44.96±10.45	42.87±9.05	0.400	0.671
BMI(kg/m^2,$\bar{x}\pm s$)	23.48±3.19	23.92±3.07	23.82±3.43	0.111	0.895
手术类型[例(%)]					
胃肠道手术	8(40.00)	13(43.33)	12(40.00)		
泌尿系统手术	7(35.00)	11(36.67)	13(43.33)	0.736	0.947
肝胆手术	5(25.00)	6(20.00)	5(16.67)		

表2 三组舒芬太尼及丙泊酚用量比较 ($\bar{x}\pm s$)

Tab.2 Comparison of sufentanil and propofol dosage among three groups ($\bar{x}\pm s$)

组别	例数	舒芬太尼用量(μg)	丙泊酚用量(mg)
CON组	20	160.22±31.45	1 138.91±97.34
L-ESK组	30	157.59±27.36	1 102.37±61.28
M-ESK组	30	126.25±15.38^{ab}	827.94±65.97^{ab}
F值		16.065	146.763
P值		<0.001	<0.001

注:与CON组相比,^aP<0.05;与L-ESK组相比,^bP<0.05。

表3　三组血流动力学参数比较　（$\bar{x}\pm s$）

Tab.3　Comparison of hemodynamic parameters among three groups　（$\bar{x}\pm s$）

组别	例数	心率(次/分)				$F/P_{组间}$值	$F/P_{时间}$值	$F/P_{交互}$值
		麻醉前	插管前	插管后	拔管后			
CON组	20	76.13±11.27	67.55±9.28[a]	88.56±10.37[a]	77.91±11.32			
L-ESK组	30	77.21±8.15	69.83±7.58[a]	85.65±8.11[a]	79.32±7.02	0.054/0.948	51.942/<0.001	0.419/0.866
M-ESK组	30	77.36±10.54	68.92±8.49[a]	86.44±10.25[a]	78.19±10.05			
组别	例数	收缩压(mmHg)				$F/P_{组间}$值	$F/P_{时间}$值	$F/P_{交互}$值
		麻醉前	插管前	插管后	拔管后			
CON组	20	130.18±15.20	105.96±12.52[a]	145.08±16.33[a]	128.30±12.98			
L-ESK组	30	132.40±15.73	110.55±14.32[a]	140.28±13.02[a]	134.08±11.60	0.575/0.565	61.423/<0.001	1.494/0.181
M-ESK组	30	128.17±12.84	115.82±13.36[a]	142.25±16.28[a]	130.69±18.29			
组别	例数	舒张压(mmHg)				$F/P_{组间}$值	$F/P_{时间}$值	$F/P_{交互}$值
		麻醉前	插管前	插管后	拔管后			
CON组	20	73.38±10.28	66.17±11.08[a]	85.32±11.07[a]	72.54±10.85			
L-ESK组	30	75.44±11.52	67.93±10.60[a]	84.19±11.65[a]	77.17±10.92	1.336/0.261	31.796/<0.001	0.642/0.697
M-ESK组	30	73.23±10.53	66.35±10.10[a]	80.32±9.05[a]	75.71±10.32			

注：与同组麻醉前相比，[a]P<0.05。

表4　三组术后恢复时间比较　（min，$\bar{x}\pm s$）

Tab.4　Comparison of postoperative recovery time among three groups　（min，$\bar{x}\pm s$）

组别	例数	麻醉恢复时间	拔管时间	意识恢复时间	自主呼吸时间
CON组	20	38.52±4.61	9.24±1.36	13.94±2.86	7.52±1.96
L-ESK组	30	32.19±3.22[a]	8.42±1.12[a]	9.95±1.89[a]	5.58±1.25[a]
M-ESK组	30	28.46±2.95[ab]	6.85±1.27[ab]	7.28±1.65[ab]	4.87±1.10[ab]
F值		48.870	24.342	60.916	21.692
P值		<0.001	<0.001	<0.001	<0.001

注：与CON组相比，[a]P<0.05；与L-ESK组相比，[b]P<0.05。

表5　三组VAS评分比较　（分，$\bar{x}\pm s$）

Tab.5　Comparison of VAS scores among three groups　（point，$\bar{x}\pm s$）

组别	例数	术后1 d	术后2 d
CON组	20	2.08±0.52	3.72±0.74
L-ESK组	30	1.64±0.41[a]	3.26±0.52[a]
M-ESK组	30	1.39±0.37[ab]	2.88±0.64[ab]
F值		16.094	10.943
P值		<0.001	<0.001

注：与CON组相比，[a]P<0.05；与L-ESK组相比，[b]P<0.05。

表6　三组术后不良反应发生情况　［例(%)］

Tab.6　Postoperative adverse reactions occurred in three groups　［case(%)］

组别	例数	恶心呕吐	呼吸抑制	躁动	瘙痒	总不良反应
CON组	20	8(40.00)	1(5.00)	2(10.00)	2(10.00)	13(65.00)
L-ESK组	30	5(16.67)	0(0.00)	1(3.33)	1(3.33)	7(23.33)[a]
M-ESK组	30	6(20.00)	0	2(6.67)	0	8(26.67)[a]
χ^2值						10.623
P值						0.005

注：与CON组相比，[a]P<0.017。

3　讨　论

腹部手术通常会引起术后疼痛，应尽快有效地减轻疼痛，促进愈合过程和康复，并预防并发症，然而，80%的患者报告其术后疼痛没有得到充分缓解[8]。在特定的患者和手术中，使用无阿片类药物麻醉对疼痛的控制更有效果[9]。ESK作为氯胺酮的右旋异构体，具有很强的镇痛作用[10]。先前的研究表明，在慢性阿片类药物依赖人群中，围手术期静脉注射ESK 0.5 mg/kg麻醉诱导，随后注射0.25 mg/(kg·h)麻醉维持，可减轻疼痛[11]。戚钰等[7]的研究表明在行胸腔镜肺切除术时，麻醉诱导复合使用0.5或1.0 mg/kg的ESK，麻醉维持阶段复合使用0.25或0.5 mg/(kg·h) ESK对患者具有较好的镇痛效果，且0.5 mg/kg ESK的使用有效地降低了不良反应率。

本研究结果显示，CON组、L-ESK组、M-ESK组三组的血流动力学参数（心率、舒张压、收缩压）比较差异无统计学意义。这表明无论是单纯采用常规丙泊酚等药物维持麻醉的CON组，还是复合不同剂量ESK的L-ESK组和M-ESK组，在整体血流动力学的维持上呈现出相似的变化趋势，可能是因为ESK剂量限制未能完全阻断交感神经激活通路。同时，本研究发现，与CON组相比，复合使用ESK显著改善了患者麻醉后的恢复，且中剂量ESK的恢复效果更好。可能原因是ESK作为NMDA受体拮抗剂，可以产生有效的镇痛作用，改善患者术后机体代谢，缩短患者术后恢复时间[12-14]。本研究中对VAS评分的对比分析进一步证实了复合应用ESK对减轻患者疼痛的积极作用，且中等剂量ESK改善疼痛的效果更为理想。这可能源于ESK的双重作用机制：一方面通过抑制NMDA受体介导的中枢敏化，降低术后痛觉过敏发生率；另一方面其促进谷氨酸能神经元突触可塑性的特性，加速了神经功能重整。

使用阿片类药物一直是腹部手术后疼痛控制的主要手段。研究表明，临床上使用阿片类药物进行麻醉镇痛易导致阿片类药物消耗过多、潜在的麻醉依赖性、呼吸抑制、恶心和呕吐、胃排空延迟和术后回肠梗阻，后两者是腹部手术后住院时间延长的主要原因[15-16]。研究表明，在接受无痛胃镜检查的患者中，给予单次剂量0.5 mg/kg ESK通常是安全且患者可耐受的[17]。本研究表明，与CON组相比，复合使用ESK显著减少了患者不良反应的发生，而L-ESK组和M-ESK组的总不良反应发生率相比差异无统计学意义。本研究受限于单中心设计和样本量，且未能评估ESK对远期疼痛慢性化的影响，且未来需开展多中心研究，结合定量脑电图监测，探索ESK最佳血药浓度区间；且本研究只采用了低/中剂量ESK，对于高剂量ESK的作用效果需进一步研究。

综上所述，腹部手术患者麻醉诱导复合应用0.5 mg/kg ESK，麻醉维持复合使用0.25 mg/(kg·h) ESK，能有效缩短恢复时间，减轻疼痛程度，提高患者术后舒适度，且可有效减少阿片类药物使用导致的不良反应。

利益冲突　无

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