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The effect of subanesthetic dose of esketamine on perioperative hemodynamics in patients undergoing lumbar surgery under general anesthesia

HU Dandan*, ZHANG Lidong, DING Ying, CHEN Jie
**Department of Anesthesiology, Nanjing Jinling Hospital, Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu 210000, China*
Corresponding author: ZHANG Lidong, E-mail: ldzhang1968@163.com

Abstract: Objective To analyze the effect of a subanesthetic dose of esketamine on perioperative hemodynamics in patients undergoing lumbar spine surgery under general anesthesia. **Methods** The case data were retrospectively analyzed, and 70 patients who underwent general anesthesia lumbar spine surgery and treatment from June 2021 to June 2023 at Nanjing University School of Medicine were selected for the study. According to the way of anesthesia induction, they were divided into the conventional group (conventional intravenous anesthesia induction, n=35) and the esketamine group (subanesthetic dose of esketamine+conventional intravenous anesthesia induction, n=35). Hemodynamic indices [heart rate (HR), mean arterial pressure (MAP), and blood norepinephrine (NE) levels at each time point before induction of anesthesia (T0), in the immediate preoperative period (T1), at the end of the operation (T2), and at the time of postoperative awakening (T3), and the occurrence of the dosage of vasoactive medications (atropine and phenylephrine), and the incidence of adverse events (nausea and vomiting, postoperative agitation, respiratory depression, and bradycardia) were compared between the two groups of patients. **Results** The HR levels of patients in the conventional group were significantly lower at T1 and T2 than at T0, and significantly higher at point T3 than at T1 and T2. At T2, the HR levels of patients in the esketamine group were significantly higher than those of the conventional group (P<0.05), and the difference in HR levels of patients in the esketamine group at each time point was not statistically significant (P>0.05). The MAP levels of patients in the esketamine group at T1, T2 and T3 were significantly lower than those at T0, and the MAP levels of patients in the esketamine group were significantly higher than those in the conventional group at T1 and T2, and the MAP levels of patients in the conventional group first decreased and then increased over time, and the difference between the two groups was statistically significant (P<0.05). The NE levels of patients in both groups showed a decreasing trend at all time points, in which the NE levels of patients in the esketamine group were significantly higher than those in the conventional group at T1, T2 and T3 (P<0.05). The dosage of atropine and phenylephrine remedial drugs in patients in the esketamine group was significantly lower than that in the conventional group (P<0.05). The difference in the incidence of nausea and vomiting, postoperative agitation, and respiratory depression adverse events between the two groups were not statistically significant (P>0.05). The incidence of bradycardia in patients in the esketamine group was significantly lower than that in the conventional group[2(5.71%) *vs* 8(22.86%), χ^2=4.200, P=0.040]. **Conclusion** The subanesthetic dose of esketamine can stabilize the hemodynamic changes during surgery in patients undergoing lumbar spine surgery under general anesthesia, with a good anesthetic effect, reduce the dosage of anesthetic remedial drugs, reduce the incidence of bradycardia, and with a high degree of safety.

Keywords: Esketamine, subanesthetic dose; General anesthesia lumbar spine surgery; Perioperative period; Hemodynamics

Lumbar spine disease is a common clinical orthopedic disease, including lumbar disc herniation, lumbar spine fracture, etc., mainly in middle-aged and elderly people. The onset of the disease not only leads to pain, affecting the quality of life of the patient, but also endanger the patient's life[1-2]. Surgical treatment can be chosen when the lumbar spine disease palliative treatment effect is not good. General anesthesia is usually chosen as lumbar spine surgery is a large-scale surgery with severe trauma and pain. However, the patients with lumbar spine disease are mostly middle-aged and elderly people with poorer physiological reserve function. They have a low degree of tolerance to anesthesia drugs. Therefore, the process of the surgery may be unstable, especially in hemodynamics, and prone to anesthesia-induced hypotension, which not only affects the patient's therapeutic effect but also induces a variety of anesthesia-related complications, affecting the prognosis of the patient[3]. Esketamine is an N-methyl-D-aspartate receptor (NMDAR) antagonist, which is mainly used in the treatment of major depressive disorder (MDD)[4] and sleep disorders[5]. Zhang *et al.*[6] found that a low anesthetic dose of esketamine in total knee arthroplasty could enhance anesthetic analgesia and maintain hemodynamic stability during surgery. However, there are fewer studies on the effect of subanesthetic doses of esketamine applied in total anesthesia lumbar spine surgery. In this study, 70 patients who underwent general anesthesia lumbar spine surgery at the Medicine School of Nanjing University from June 2021 to June 2023 were

selected as the study subjects, aiming to analyze the effect of subanesthetic dosage of esketamine on the hemodynamics of lumbar spine surgery patients undergoing general anesthesia during the anesthesia induction period.

1 Information and methods

1.1 General information

Retrospectively analyze the case data, and select 70 patients who underwent general anesthesia lumbar spine surgery treatment in the Medical School of Nanjing University from June 2021 to June 2023 as the study subjects.

Inclusion criteria: (1) patients who need general anesthesia for lumbar spine surgery due to lumbar disc herniation, lumbar spine fracture, etc.; (2) no adverse reaction to the anesthesia drugs in this experiment.

Exclusion criteria: (1) combined with neurological or psychiatric diseases; (2) combined with autoimmune diseases such as rheumatoid arthritis; (3) combined with malignant tumors; (4) non-general anesthesia surgery. According to the way of anesthesia induction, they were divided into the conventional group (n=35) and the esketamine group (n=35). There was no statistically significant difference in age, gender, and comorbidities between the groups (P>0.05). The experimental operations were approved and consented by the ethics committee of the hospital (Ethics Approval Number: HA82YY202401). **[Table 1]**

Tab. 1 Analysis of general information of the two groups [case (%)]

Groups	Case	Age (years, $\bar{x}\pm s$)	Gender		Hypertension	Diabetes
			Male	Female		
Conventional group	35	58.40±8.45	19 (54.29)	16 (45.71)	6 (17.14)	4 (11.43)
Esketamine group	35	58.37±8.18	17 (48.57)	18 (51.43)	8 (22.86)	3 (8.57)
χ^2 / t value		0.014	0.229		0.357	0.159
***P* value**		0.989	0.632		0.550	0.690

1.2 *Methods*

The two groups of patients were fasted for 6 hours and forbidden to drink for 2 hours preoperatively. Intravenous access was opened when they were admitted to the room, and cardiac and electrical monitoring was given to monitor the vital signs of the patients. In the conventional group, conventional intravenous anesthesia was induced by sequential intravenous injection of 0.04 mL/kg of 0.9% sodium chloride solution (Chengdu Qingshan Likang Pharmaceutical Co., Ltd., Approval No.: State Drug Permit H20050019) 0.3 mg/kg of sufentanil (Jiangsu Enhua Pharmaceutical Co. Ltd, Approval No.: H32022999) and 0.15 mg/kg of cis-atracurium (Jiangsu Hengrui Pharmaceutical Co., Ltd, Approval No.: H20183024). In the esketamine group, subanesthetic dose of esketamine + conventional intravenous anesthesia induction was given: 0.2 mg/kg intravenous esketamine, 0.5 μg/kg sufentanil, 0.3 mg/kg etomidate, and 0.15 mg/kg cisatracurium were injected in sequence, and anesthesia was maintained with an intravenous infusion of 2 mg/kg of 1% propofol (Zhejiang Jiuxu Pharmaceutical Co., Ltd., Approval No.: H20084531) and 1 μg/(kg·min) of remifentanil (Jiangsu Nhwa Pharmaceutical Co., Ltd., Approval No.: H20143314). If systolic blood pressure <100 mmHg or less than 30% below the basal value was present, phenylephrine (Shenzhen Woland Pharmaceutical Co., Ltd, Approval No.: State Drug Permit H20033866) was given 10-30 μg/dose; if heart rate (HR) <50 bpm, atropine (Chengdu Beite Pharmaceutical Co., Ltd, Approval No.:H32021536) was given 0.25-0.5 mg/dose.

1.3 Observation indexes

Changes in hemodynamic indexes: (1) Patients were given preoperative cardiac monitoring, and changes in HR and mean arterial pressure (MAP) levels were recorded and compared between the two groups of patients before the induction of anesthesia (T0) at the immediate preoperative period (T1), at the end of the operation (T2), and at the time of postoperative awakening (T3), respectively; (2) Venous blood was collected from the patients of the two groups at T0, T1, T2, and T3, respectively. (2) Collect venous blood from two groups of patients at T0, T1, T2 and T3, respectively, centrifuge it at 3,000 r/min for 10 min, collect the serum carefully, store it at -40℃ in a low-temperature environment to avoid repeated freezing and thawing, and detect the changes in the level of norepinephrine (NE) of the patients in the two groups by using fluorescence analysis.

Recording of vasoactive agents: atropine and phenylephrine remedial drug dosages were recorded and compared between the two groups.

Occurrence of adverse reactions: monitor the condition changes and surgical process of patients in the two groups closely, and record and compare the occurrence of nausea and vomiting, postoperative agitation, respiratory depression, and bradycardia in the two groups.

1.4 Statistical methods

All data were analysed using SPSS 26.0 software. Measurement data in normal distribution were expressed as $\bar{x}\pm s$, and comparisons between groups were made using independent samples t test, and comparisons within groups were made using analysis of variance for repeated measurements or paired samples t test; measurement data not conforming to normal distribution were expressed as the M (P_{25}, P_{75}), and comparisons between groups were made using the Wilcoxon rank-sum test. Count data were expressed as frequency and percentage (%), and comparisons between groups were made using the χ^2 test

or Fisher's exact test. P<0.05 was considered a statistically significant difference.

2.1 HR levels at each time point

HR levels of patients in the conventional group at time points T1 and T2 were significantly lower than those at time point T0, HR levels at time point T3 were significantly higher than those at time points T1 and T2, and at time point T2, HR levels of patients in the esketamine group were significantly higher than those in the conventional group, and the difference was statistically significant (P<0.05), and the difference in HR levels of patients at each time point in the esketamine group was not statistically significant (P>0.05). **[Table 2]**

2.2 MAP levels at each time point

The MAP levels of patients in the esketamine group at T1, T2 and T3 were significantly lower than those at T0, and the MAP levels of patients in the esketamine group were significantly higher than those of the conventional group at T1 and T2, and the MAP levels of the patients in the conventional group firstly declined and then increased over time, and the difference between the two groups was statistically significant (P < 0.05). **[Table 2]**

2.3 Hormone indexes at each time point

The NE levels of patients in the two groups showed a decreasing trend at each time point, in which the NE levels of patients in the esketamine group were significantly higher than those of the conventional group at points T1, T2 and T3, and the difference was statistically significant (P<0.05). **[Table 3]**

2.4 The dosage of vasoactive drugs

The dosage of atropine and phenylephrine remedial drugs for patients in the esketamine group was significantly lower than that of the conventional group, and the difference was statistically significant (P < 0.05). **[Table 4]**

2.5 Adverse reactions

The difference in the incidence of adverse reactions of nausea and vomiting, postoperative agitation and respiratory depression between the two groups was not statistically significant (P > 0.05). The incidence of bradycardia in patients in the esketamine group was significantly lower than that in the conventional group, and the difference was statistically significant (P < 0.05). **[Table 5]**

Tab. 2 Comparison of HR and MAP at each time point between the two groups (n=35, $\bar{x}\pm s$)

Groups	HR (bpm)				MAP (mmHg)			
	T0	T1	T2	T3	T0	T1	T2	T3
Gonventional group	73.23±8.42	63.17±4.76[a]	64.14±7.10[a]	73.03±9.47[bc]	87.16±7.42	71.05±6.59[a]	75.41±8.02[ab]	82.44±10.07[abc]
Esketamine group	73.34±8.12	67.85±13.02	70.22±5.41[d]	72.08±10.12	88.06±4.15	80.42±10.27[ad]	82.15±6.71[ad]	84.00±8.34[a]
$F/P_{(group)}$ Value	8.480/0.006				24.060/<0.001			
$F/P_{(time)}$ Value	12.286/<0.001				28.730/<0.001			
$F/P_{(interaction)}$ Value	2.866/0.040				4.516/0.005			

Note: [a]P < 0.05 compared with the same group at T0; [b]P < 0.05 compared with the same T1; [c]P < 0.05 compared with the same T2; and [d]P < 0.01 compared with the conventional group.

Tab. 3 Comparison of NE levels at various time points between the two groups of patients (n=35, pmol/L, $\bar{x}\pm s$)

Groups	T0	T1	T2	T3
Conventional group	365.12±76.49	245.61±43.12[a]	195.85±40.48[ab]	174.56±45.19[ab]
Esketamine group	357.00±75.27	312.05±46.18[ad]	268.74±50.19[abd]	198.74±34.22[abcd]
$F/P_{(group)}$ Value	31.870/<0.001			
$F/P_{(time)}$ Value	143.252/<0.001			
$F/P_{(interaction)}$ Value	9.351/<0.001			

Note: [a]P < 0.05 compared with the same group at T0; [b]P < 0.05 compared with the same T1; [c]P < 0.05 compared with the same T2; and [d]P < 0.01 compared with the conventional group.

Tab. 4 Comparison of vasoactive drug dosage at each time point between the two groups of patients ($\bar{x}\pm s$)

Groups	Case	Atropine (mg)	Phenylephrine (μg)
Conventional group	35	0.13±0.03	52.18±15.23
Esketamine group	35	0.03±0.01	12.34±3.02
t value		18.708	15.179
P value		<0.001	<0.001

Tab. 5 Comparison of the occurrence of adverse reactions between the two groups of patients [n=35, case (%)]

Groups	Nausea and vomiting	Postoperative agitation	Respiratory depression	bradycardia
Conventional group	2 (5.71)	1 (2.86)	1 (2.86)	8 (22.86)
Esketamine group	1 (2.86)	0	1 (2.86)	2 (5.71)
χ^2 value	0.000		0.515	4.200
P value	1.000	1.000[a]	0.473	0.040

Note:[a] indicates Fisher's exact test.

3 Discussion

Lumbar spine diseases are primarily seen in middle-aged and elderly people, who have a low tolerance for adverse stimuli such as surgery and anesthesia. Moreover, lumbar spine surgery, as a major orthopedic surgery, has a large incision, severe pain, and requires general anesthesia, which may lead to large hemodynamic fluctuations during the perioperative period, which may affect the smooth progress of the surgery and also increase anesthesia-related complications, which will harm the postoperative rapid recovery and prognosis[7-8]. Therefore, investigating a novel way to stabilize the perioperative hemodynamics of general lumbar spine surgery anesthesia is essential to ensure the smooth progress of the surgery and improve the therapeutic effect and the prognosis.

Esketamine is an NMDAR antagonist with anesthetic, anti-inflammatory, and antidepressant effects. Moreover, esketamine has a unique dextrose structure, intense effect, high clearance, and relatively little effect on the respiratory and circulatory systems of the human body, and is currently used in the treatment of anesthesia, analgesia, sedation, chronic pain syndromes, and antidepressant[9-10]. Han *et al.*[11] concluded that esketamine can reduce postoperative pain, improve the quality of the anesthesia awakening period, alleviate depression in the early postoperative period without increasing postoperative adverse effects, and contribute to rapid postoperative recovery in patients undergoing radical thyroid cancer surgery. Recent studies have found that esketamine has sympathomimetic activity, which can help reduce the inhibitory effect of anesthesia drugs on the circulation so as to control the range of hemodynamic fluctuations in the perioperative period[12-13]. In addition, esketamine also has a respiratory excitatory effect, which can help dilate the bronchial tubes of the organism, and reduce the effect of anesthesia drugs on the respiratory circulation[14-15]. In this experiment, the HR and MAP levels of patients in both groups decreased. Then, there was an increase at each time point, and the fluctuation ranges of HR and MAP levels of patients in the esketamine group were lower than those of the conventional group. The NE levels of patients in both groups showed a decreasing trend at all time points, in which the NE levels of patients in the esketamine group were significantly higher than those in the conventional group at T1, T2, and T3. The subanesthetic dose of esketamine can stabilize the perioperative hemodynamic changes of general anesthesia lumbar spine surgery patients, which can help to ensure the smooth progress of the surgery and reduce the complications caused by perioperative hemodynamic fluctuations. The reason is that esketamine has a slight sympathetic excitatory effect, and the low-dose esketamine can alleviate the respiratory and circulatory inhibition in the perioperative period and the effects of anesthesia on hemodynamics. Dynamics of anesthesia drugs. Similar to the results of the study by Li *et al.*[16], this study concluded that a small dose of esketamine used for the induction of anesthesia in geriatric knee arthroplasty could maintain hemodynamic stability and has no adverse effect on the quality of early postoperative recovery.

Lumbar spine surgery, as a large orthopedic surgery, has high requirements for anesthesia effect, and general anesthesia is primarily chosen in clinics[17-18]. Bradycardia is a common complication in the perioperative period, which needs to be treated causally, stop the application of suspected medications, and give medication if necessary, which is severe and not only needs to stop the surgery, but also may endanger the patients' lives[19-20], so reducing the incidence of bradycardia can help the surgery to be carried out smoothly, and help to improve the prognosis of the patients. Therefore, reducing the incidence of bradycardia is helpful for the smooth progress of surgery and improves the prognosis of patients. In this experiment, the incidence of bradycardia in the esketamine group was significantly lower than in the conventional group. The dosage of atropine and phenylephrine vasoactive drugs in the esketamine group was significantly lower than in the conventional group. It further indicates that esketamine can regulate the hemodynamic changes during the induction of anesthesia, reduce the risk of perioperative bradycardia, and reduce the dosage of vasoactive drugs such as atropine and phenylephrine due to hypotension or excessive respiration, which can reduce the adverse effects of excessive drug intake on the body while guaranteeing the smooth progress of the surgery.

In conclusion, the subanesthetic dose of esketamine can stabilize the hemodynamic changes during the induction of anesthesia in patients undergoing lumbar spine surgery under general anesthesia, with a good anesthetic effect, reduce the dosage of vasoactive drugs during anesthesia, reduce the occurrence of bradycardia, and have high safety. However, due to the short research time of this experiment, the effect of a subanesthetic dose of esketamine on the pain and stress response after the awakening of general anesthesia lumbar spine surgery patients has not yet been analyzed. In the future, we will expand the experimental subjects and increase the research time to conduct in-depth investigations again.

Conflict of interest None

References

[1] Lessing NL, Edwards CC 2nd, Dean CL, et al. Spinal anesthesia for geriatric lumbar spine surgery: a comparative case series[J]. Int J Spine Surg, 2020, 14(5): 713-721.

[2] De Cassai A, Geraldini F, Boscolo A, et al. General anesthesia compared to spinal anesthesia for patients undergoing lumbar vertebral surgery: a meta -analysis of randomized controlled trials[J]. J Clin Med, 2020, 10(1): 102.

[3] Shao YY, Mo P, Mai YH, et al. Effects of different concentrations of dexmedetomidine in patients undergoing thoracolumbar surgery under general anesthesia and its influence on postoperative cognitive dysfunction of hemodynamics[J]. Shanxi Med J, 2020, 49(4): 434-436. **[In Chinese]**

[4] McIntyre RS, Rosenblat JD, Nemeroff CB, et al. Synthesizing the evidence for ketamine and esketamine in treatment-resistant depression: an international expert opinion on the available evidence and implementation[J]. Am J Psychiatry, 2021, 178(5): 383-399.

[5] Qiu D, Wang XM, Yang JJ, et al. Effect of intraoperative esketamine

infusion on postoperative sleep disturbance after gynecological laparoscopy: a randomized clinical trial[J]. JAMA Netw Open, 2022, 5(12): e2244514.
[6] Zhang HL. Effect of low-dose esketamine on hemodynamics and postoperative stress in patients undergoing total knee arthroplasty[J]. Drug Eval, 2023, 20(2): 217-220. **[In Chinese]**
[7] Kindris F, Zegarek G, Krappel FA, et al. Spinal versus general anesthesia for lumbar decompression or sequestrectomy in patients over 75 years[J]. Clin Spine Surg, 2023, 36(7): E329-E331.
[8] De Rojas JO, Syre P, Welch WC. Regional anesthesia versus general anesthesia for surgery on the lumbar spine: a review of the modern literature[J]. Clin Neurol Neurosurg, 2014, 119: 39-43.
[9] Urick D, Sciavolino B, Wang TY, et al. Perioperative outcomes of general versus spinal anesthesia in the lumbar spine surgery population: a systematic review and meta-analysis of data from 2005 through 2021[J]. J Clin Orthop Trauma, 2022, 30: 101923.
[10] Wang XM, Lin C, Lan LF, et al. Perioperative intravenous S-ketamine for acute postoperative pain in adults: a systematic review and meta-analysis[J J Clin Anesth, 2021.] J Clin Anesth, 2021, 68: 110071.
[11] Han LY, Gao CJ. Anesthetic effect of different doses of esketamine in radical thyroidectomy and its influence on early postoperative emotional response [J]. Shandong Med J, 2023, 63(2): 71-75. **[In Chinese]**
[12] Xiao XQ, Cheng SF, Huang JJ, et al. Anesthesia effect of esketamine combined with propofol in painless gastroenteroscopy[J]. Chin J Rural Med Pharm, 2023, 30(17): 28-29. **[In Chinese]**
[13] Schatzberg AF. Mechanisms of action of ketamine and esketamine[J]. Am J Psychiatry, 2021, 178(12): 1130.
[14] Wang X, Wang Y, Sun YB, et al. Observation of the analgesic effect of esketamine after hysteromyomectomy under gynecological laparoscopy[J]. Hebei Med, 2023, 29(8): 1382-1387. **[In Chinese]**
[15] Chen YM, Su ZH, Song JY. Effect of esketamine combined with dexmedetomidine in vertebroplasty for patients with vertebral compression fracture[J]. Chin J Clin Ration Drug Use, 2023, 16(24): 107-110. **[In Chinese]**
[16] Li J, Wang ZY, Wang AQ, et al. Clinical effects of low-dose esketamine for anaesthesia induction in the elderly: a randomized controlled trial[J]. J Clin Pharm Ther, 2022, 47(6): 759-766.
[17] Lu VM, Brusko GD, Urakov TM. Defining the time benefit of awake versus general anesthesia for single-level lumbar spine surgery[J]. World Neurosurg, 2022, 158: e793-e798.
[18] Sekerak R, Mostafa E, Morris MT, et al. Comparative outcome analysis of spinal anesthesia versus general anesthesia in lumbar fusion surgery[J]. J Clin Orthop Trauma, 2020, 13: 122-126.
[19] Türk CÇ, Gediz T, Mutlucan UO, et al. Unexpected bradycardia related to surgical manipulation during thoracolumbar spinal surgery[J]. World Neurosurg, 2023, 175: e1277-e1282.
[20] Lei YL, Ma ZZ. Effect of small dose of atropine on bradycardia in laparoscopic cholecystectomy center[J]. Chin J Curr Adv Gen Surg, 2020, 23(6): 426.**[In Chinese]**

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·论　著·

亚麻醉剂量艾司氯胺酮对全麻腰椎手术患者围术期血流动力学的影响

胡丹丹[1]，丁颖[2]，陈捷[2]，张利东[1]

1. 南京大学医学院附属金陵医院麻醉科，江苏 南京 210000；2. 淮安八二医院，江苏 淮安 223000

摘要：目的　分析亚麻醉剂量艾司氯胺酮对全麻腰椎手术患者围术期血流动力学及不良反应的影响。**方法**　回顾性分析 2021 年 6 月至 2023 年 6 月在南京大学医学院附属金陵医院行全麻腰椎手术治疗患者 70 例的临床资料。根据麻醉诱导方式分为常规组（常规静脉麻醉诱导，$n=35$）、艾司氯胺酮组（亚麻醉剂量艾司氯胺酮+常规静脉麻醉诱导，$n=35$），比较两组患者在麻醉诱导前（T0）、术前即刻（T1）、手术结束时（T2）、术后苏醒时（T3）的血流动力学指标[心率（HR）、平均动脉压（MAP）]、血液中去甲肾上腺素（NE）水平，比较两组患者血管活性药物用量（阿托品、去氧肾上腺素）、不良反应（恶心呕吐、术后躁动、呼吸抑制、心动过缓）发生情况。**结果**　常规组患者 T1、T2 点时 HR 水平低于 T0 时点，T3 点时 HR 水平高于 T1、T2 时点，T2 时点，艾司氯胺酮组患者 HR 水平高于常规组（$P<0.05$），艾司氯胺酮组患者各时点 HR 水平差异无统计学意义（$P>0.05$）。艾司氯胺酮组患者 T1、T2、T3 时点 MAP 水平低于 T0 时点，T1、T2 时点，艾司氯胺酮组患者 MAP 水平高于常规组，常规组患者 MAP 水平随时间先下降后升高（$P<0.05$）。两组患者 NE 水平各时点均呈下降趋势，其中 T1、T2、T3 时点，艾司氯胺酮组患者 NE 水平高于常规组（$P<0.05$）。艾司氯胺酮组患者阿托品、去氧肾上腺素补救药物用量低于常规组（$P<0.05$）。艾司氯胺酮组患者心动过缓发生率低于常规组（5.71% *vs* 22.86%，$\chi^2=4.200$，$P=0.040$）。**结论**　亚麻醉剂量艾司氯胺酮可稳定全麻腰椎手术患者围术期血流动力学变化，麻醉效果好，减少血管活性药物用量，降低心动过缓发生情况，安全性较高。

关键词：艾司氯胺酮，亚麻醉剂量；全身麻醉；腰椎手术；围术期；血流动力学

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HU Dandan*, DING Ying, CHEN Jie, ZHANG Lidong

** Department of Anesthesiology, Nanjing Jinling Hospital, Affiliated Hospital of Nanjing University Medical School, Nanjing, Jiangsu 210000, China*

Corresponding author: ZHANG Lidong, E-mail: ldzhang1968@163.com

Abstract: Objective　To analyze the effect of subanesthetic dose of esketamine on perioperative hemodynamics and adverse events in patients undergoing lumbar spine surgery under general anesthesia. **Methods**　The clinical data of 70 patients who underwent general anesthesia lumbar spine surgery and treatment from June 2021 to June 2023 at Nanjing Jinling Hospital, Affiliated Hospital of Nanjing University Medical School, were retrospectively analyzed. According to the way of anesthesia induction, they were divided into the conventional group (conventional intravenous anesthesia induction, $n=35$) and the esketamine group (subanesthetic dose of esketamine+conventional intravenous anesthesia induction, $n=35$). Hemodynamic indices [heart rate (HR), mean arterial pressure (MAP)], and blood norepinephrine (NE) levels at each time point before induction of anesthesia (T0), in the immediate preoperative period (T1), at the end of the operation (T2), and at the time of postoperative awakening (T3), as well as the dosage

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通信作者：张利东，E-mail：ldzhang1968@163.com

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of vasoactive medications (atropine and phenylephrine), and the incidence of adverse events (nausea and vomiting, postoperative agitation, respiratory depression, and bradycardia) were compared between the two groups. **Results** The HR levels of patients in the conventional group were significantly lower at T1 and T2 than that at T0, and significantly higher at point T3 than that at T1 and T2; at T2, the HR in the esketamine group was significantly higher than that in the conventional group ($P<0.05$), and the difference in HR levels of patients in the esketamine group at each time point was not statistically significant ($P>0.05$). The MAP levels of patients in the esketamine group at T1, T2 and T3 were significantly lower than those at T0, and the MAP levels of patients in the esketamine group were significantly higher than those in the conventional group at T1 and T2, and the MAP levels of patients in the conventional group first decreased and then increased over time, and the difference between the two groups was statistically significant ($P<0.05$). The NE levels of patients in both groups showed a decreasing trend at all time points, in which the NE levels of patients in the esketamine group were significantly higher than those in the conventional group at T1, T2 and T3 ($P<0.05$). The dosage of atropine and phenylephrine remedial drugs in patients in the esketamine group was significantly lower than that in the conventional group ($P<0.05$). The incidence of bradycardia in the esketamine group was significantly lower than that in the conventional group (5.71% *vs* 22.86%, $\chi^2=4.200$, $P=0.040$). **Conclusion** The subanesthetic dose of esketamine can stabilize the hemodynamic changes during surgery in patients undergoing lumbar spine surgery under general anesthesia, with a good anesthetic effect, reduce the dosage of anesthetic remedial drugs, reduce the incidence of bradycardia, and with a high degree of safety.

Keywords: Esketamine, subanesthetic dose; General anesthesia; Lumbar spine surgery; Perioperation; Hemodynamics

腰椎疾病是目前临床常见的骨科疾病,包括腰椎间盘突出、腰椎骨折等,多见于中老年人,病发后不仅导致患者疼痛,影响生活质量,严重还可危及生命[1-2]。腰椎疾病姑息治疗效果不佳可选择手术治疗,腰椎手术作为大型手术,创伤大、疼痛剧烈,一般选择全身麻醉方式,但由于腰椎疾病患者多为中老年人,生理储备功能较差,对麻醉药物耐受程度较低,手术过程中可能出现血流动力学不稳定情况,特别容易出现麻醉诱导后低血压,不仅影响患者治疗效果,还可能诱导多种麻醉相关并发症,影响患者预后[3]。艾司氯胺酮是一种 N-甲基-D-天冬氨酸受体(N-methyl-D-aspartate receptor, NMDAR)拮抗剂,临床多用于治疗重度抑郁症(MDD)[4]及睡眠障碍[5]。张红玲[6]研究发现,低麻醉剂量艾司氯胺酮在全膝关节置换手术中应用可增强麻醉镇痛效果,并维持手术中血流动力学稳定。但目前对于亚麻醉剂量艾司氯胺酮在全麻腰椎手术中的应用效果研究较少。本研究旨在分析亚麻醉剂量艾司氯胺酮对全麻腰椎手术患者麻醉诱导期间血流动力学的影响。

1　资料与方法

1.1　一般资料　回顾性分析病例资料,选择 2021 年 6 月至 2023 年 6 月在南京大学医学院附属金陵医院行全麻腰椎手术治疗的患者 70 例为研究对象。纳入标准:(1) 因腰椎间盘突出、腰椎骨折等原因需进行全麻腰椎手术;(2) 对本试验麻醉药物无不良反应。排除标准:(1) 合并神经系统或精神疾病;(2) 合并类风湿性关节炎等自身免疫疾病;(3) 合并恶性肿瘤。根据麻醉诱导方式分为常规组($n=35$)和艾司氯胺酮组($n=35$)。两组年龄、性别、合并症等差异无统计学意义($P>0.05$)。见表 1。本研究经医院伦理会批准同意(伦理批号:HA82YY202401)。

表 1　两组一般资料比较　[$n=35$, 例(%)]

Tab. 1　Comparison of general information between the two groups　[$n=35$, case(%)]

组别	年龄	性别		高血压	糖尿病
	(岁, $\bar{x}\pm s$)	男	女		
常规组	58.40±8.45	19(54.29)	16(45.71)	6(17.14)	4(11.43)
艾司氯胺酮组	58.37±8.18	17(48.57)	18(51.43)	8(22.86)	3(8.57)
t/χ^2 值	0.014	0.229		0.357	0.159
P 值	0.989	0.632		0.550	0.690

1.2　方法　两组患者术前禁食 6 h、禁饮 2 h,入室时均开通静脉通路,给予心电监护监测患者生命体征。常规组给予常规静脉麻醉诱导:依次静脉注射 0.9%氯化钠溶液(成都青山利康药业,批准文号:国药准字 H20050019)0.04 mL/kg、舒芬太尼(江苏恩华药业,批准文号:国药准字 H20203651)0.5 μg/kg、依托咪酯(江苏恩华药业,批准文号:国药准字 H32022999)0.3 mg/kg 及顺式阿曲库铵 0.15 mg/kg(江苏恒瑞医药股份,批准文号:国药准字 H20183024)。艾司氯胺酮组给予亚麻醉剂量艾司氯胺酮+常规静脉麻醉诱导:依次静脉注射艾司氯胺酮 0.2 mg/kg、舒芬太尼 0.5 μg/kg、依托咪酯 0.3 mg/kg 及顺式阿曲库铵 0.15 mg/kg。麻醉维持采用静脉输注 1%丙泊酚(浙江九旭药业,批准文号:国

药准字 H20084531)2 mg/kg 及瑞芬太尼(江苏恩华药业,批准文号:国药准字 H20143314)1 μg/(kg·min)。若出现收缩压<100 mmHg 或低于基础值 30%以下给予去氧肾上腺素(深圳沃兰德药业,批准文号:国药准字 H20033866)10~30 μg/次;若出现心率(HR)<50 次/分给予阿托品(成都倍特药业,批准文号:国药准字 H32021536)0.25~0.5 mg/次。

1.3　观察指标　血流动力学指标变化:(1) 患者术前给予心电监护,分别于麻醉诱导前(T0)、术前即刻(T1)、手术结束时(T2)、术后苏醒时(T3)记录并比较两组患者 HR、平均动脉压(MAP)水平变化;(2) 分别于 T0、T1、T2、T3 采集两组患者静脉血,3 000 r/min 离心 10 min,采集血清,于-40 ℃环境中低温保存,避免反复冻融,采用荧光分析法检测两组患者去甲肾上腺素(NE)水平变化。

麻醉血管活性药物记录:记录并比较两组患者阿托品、去氧肾上腺素补救药物用量。

不良反应发生情况:密切监控两组患者病情变化及手术进程,记录并比较两组患者恶心呕吐、术后躁动、呼吸抑制、心动过缓发生情况。

1.4　统计学方法　采用 SPSS 26.0 软件分析数据。符合正态分布的计量资料采用 $\bar{x}\pm s$ 表示,比较采用独立样本 t 检验及重复测量资料的方差分析,两两比较采用 LSD-t 检验;计数资料采用例(%)表示,组间比较采用 χ^2 检验或 Fisher 确切概率法。P<0.05 为差异有统计学意义。

2　结　果

2.1　两组患者各时间点 HR 水平比较　常规组患者 T1、T2 时点 HR 水平低于 T0 时点,T3 时点 HR 水平高于 T1、T2 时点;T2 时点,艾司氯胺酮组患者 HR 水平高于常规组,差异有统计学意义(P<0.05),艾司氯胺酮组患者各时点 HR 水平差异无统计学意义(P>0.05)。见表 2。

2.2　两组患者各时间点 MAP 水平比较　艾司氯胺酮组患者 T1、T2、T3 点时 MAP 水平低于 T0 时点,T1、T2 点时,艾司氯胺酮组患者 MAP 水平高于常规组,常规组患者 MAP 水平随时间先下降后升高,两两比较差异有统计学意义(P<0.05)。见表 2。

2.3　两组患者各时间 NE 水平比较　两组患者 NE 水平各时点均呈下降趋势,其中 T1、T2、T3 时点,艾司氯胺酮组患者 NE 水平高于常规组,差异有统计学意义(P<0.05)。见表 3。

2.4　两组患者血管活性药物用量比较　艾司氯胺酮组患者阿托品、去氧肾上腺素补救药物用量低于常规组,差异有统计学意义(P<0.05)。见表 4。

2.5　两组患者不良反应发生情况比较　两组患者恶心呕吐、术后躁动、呼吸抑制不良反应发生率差异无统计学意义(P>0.05)。艾司氯胺酮组患者心动过缓发生率低于常规组,差异有统计学意义(P<0.05)。见表 5。

表 2　两组患者各时间点 HR 和 MAP 比较　(n=35, $\bar{x}\pm s$)

Tab. 2　Comparison of HR and MAP at each time point between the two groups　(n=35, $\bar{x}\pm s$)

组别	HR(次/分)				MAP(mmHg)			
	T0	T1	T2	T3	T0	T1	T2	T3
常规组	73.23±8.42	63.17±4.76[a]	64.14±7.10[a]	73.03±9.47[bc]	87.16±7.42	71.05±6.59[a]	75.41±8.02[ab]	82.44±10.07[abc]
艾司氯胺酮组	73.34±8.12	67.85±13.02	70.22±5.41[d]	72.08±10.12	88.06±4.15	80.42±10.27[ad]	82.15±6.71[ad]	84.00±8.34[a]
$F/P_{组间}$值	8.480/0.006				24.060/<0.001			
$F/P_{时间}$值	12.286/<0.001				27.830/<0.001			
$F/P_{交互}$值	2.866/0.040				4.516/0.005			

注:与同组 T0 时点相比,[a]P<0.05;与同组 T1 时点相比,[b]P<0.05;与同组 T2 时点相比,[c]P<0.05;与常规组相比,[d]P<0.01。

表 3　两组患者各时间点 NE 水平比较　(n=35, pmol/L, $\bar{x}\pm s$)

Tab. 3　Comparison of NE levels at various time points between the two groups　(n=35, pmol/L, $\bar{x}\pm s$)

组别	T0	T1	T2	T3
常规组	365.12±76.49	245.61±43.12[a]	195.85±40.48[ab]	174.56±45.19[ab]
艾司氯胺酮组	357.00±75.27	312.05±46.18[ad]	268.74±50.19[abd]	198.74±34.22[abcd]
$F/P_{组间}$值	31.870/<0.001			
$F/P_{时间}$值	143.252/<0.001			
$F/P_{交互}$值	9.351/<0.001			

注:与同组 T0 时点相比,[a]P<0.05;与同组 T1 时点相比,[b]P<0.05;与同组 T2 时点相比,[c]P<0.05;与常规组相比,[d]P<0.05。

表 4　两组患者血管活性药物用量比较　($\bar{x}\pm s$)

Tab. 4　Comparison of vasoactive drug dosage between the two groups　($\bar{x}\pm s$)

组别	例数	阿托品(mg)	去氧肾上腺素(μg)
常规组	35	0.13±0.03	52.18±15.23
艾司氯胺酮组	35	0.03±0.01	12.34±3.02
t 值		18.708	15.179
P 值		<0.001	<0.001

表 5　两组患者不良反应发生情况比较　[n=35, 例(%)]

Tab. 5　Comparison of the occurrence of adverse reactions between the two groups　[n=35, case(%)]

组别	恶心呕吐	术后躁动	呼吸抑制	心动过缓
常规组	2(5.71)	1(2.86)	1(2.86)	8(22.86)
艾司氯胺酮组	1(2.86)	0	1(2.86)	2(5.71)
χ^2 值	0.000		0.515	4.200
P 值	1.000	1.000[a]	0.473	0.040

注：[a] 表示采用 Fisher 确切概率法。

3　讨　论

腰椎疾病多见于中老年人群，对手术、麻醉等不良刺激耐受程度偏低，且腰椎手术作为大型骨科手术，创口大、疼痛剧烈，需给予全身麻醉，因此围术期血流动力学波动较大，可能影响手术的顺利进行，还可能增加麻醉相关并发症，对术后的快速恢复及预后等方面造成不利影响[7-8]。

艾司氯胺酮是一种 NMDAR 拮抗剂，具有麻醉、抗炎、抗抑郁等效果，且艾司氯胺酮具有独特的右旋结构，效果强、清除率高，对人体的呼吸、循环系统影响相对较小，目前应用于麻醉、镇痛、镇静以及慢性疼痛综合征和抑郁的治疗[9-10]。韩礼业等[11]研究认为，艾司氯胺酮可减轻甲状腺癌根治术患者术后疼痛、提升麻醉苏醒期质量、缓解术后早期抑郁情绪且不增加术后不良反应，有助于术后快速恢复。近年研究发现，艾司氯胺酮具有拟交感活性，可帮助减轻麻醉药物对循环的抑制作用，从而控制围术期血流动力学波动范围[12-13]，另外艾司氯胺酮还具有呼吸兴奋作用，帮助扩张机体支气管，减轻麻醉药物对呼吸循环的影响[14-15]。本试验中，两组患者各时点 HR、MAP 水平均呈先下降后升高的变化，其中艾司氯胺酮组患者 HR、MAP 水平波动范围均低于常规组。两组患者 NE 水平各时点均呈下降趋势，其中 T1、T2、T3 时间点时，艾司氯胺酮组患者 NE 水平高于常规组。说明亚麻醉剂量艾司氯胺酮可稳定全麻腰椎手术患者麻醉围术期血流动力学变化，有助于保障手术顺利进行，降低因围术期血流动力学波动较大引起的并发症，究其原因，艾司氯胺酮具有轻微的交感神经兴奋作用，低剂量的艾司氯胺酮可缓解围术期中呼吸循环抑制情况，减轻麻醉药物对血流动力学的影响。与 Li 等[16]研究结果相近，该研究认为，老年膝关节置换术中小剂量艾司氯胺酮用于麻醉诱导，可以更好地维持血流动力学的稳定，且对术后早期恢复质量无不良影响。

心动过缓是全麻腰椎手术围术期常见的并发症，需进行对因治疗，停止可疑药物的应用，必要时还需给予药物治疗，严重时不仅需要停止手术，还可能危及患者生命[17-18]，因此降低心动过缓发生率有助于手术的顺利进行，帮助改善患者预后情况。本试验中，艾司氯胺酮组患者心动过缓发生率低于常规组，阿托品、去氧肾上腺素血管活性药物用量低于常规组。进一步说明艾司氯胺酮可调控麻醉诱导期间血流动力学变化，减少围术期心动过缓发生风险，减少因低血压或呼吸过度给予阿托品、去氧肾上腺素等血管活性药物的用量，在保障手术的顺利进行的同时，减少过度摄入药物对机体造成的不良影响。

综上所述，亚麻醉剂量艾司氯胺酮可稳定全麻腰椎手术患者麻醉诱导期间血流动力学变化，麻醉效果好，减少麻醉期间血管活性药物用量，降低心动过缓发生情况，安全性较高。但由于本试验研究时间较短，尚未分析亚麻醉剂量艾司氯胺酮对全麻腰椎手术患者苏醒后疼痛及应激反应的影响，未来将扩大实验对象及增加研究时间进行深入探究。

利益冲突　无

参考文献

[1] Lessing NL, Edwards CC 2nd, Dean CL, et al. Spinal anesthesia for geriatric lumbar spine surgery: a comparative case series[J]. Int J Spine Surg, 2020, 14(5): 713-721.

[2] De Cassai A, Geraldini F, Boscolo A, et al. General anesthesia compared to spinal anesthesia for patients undergoing lumbar vertebral surgery: a meta-analysis of randomized controlled trials [J]. J Clin Med, 2020, 10(1): 102.

[3] 邵泳尧,莫平,麦耀海,等.不同浓度右美托咪定应用于胸腰椎手术全身麻醉患者的效果及对血流动力学术后认知功能障碍的影响[J].山西医药杂志,2020,49(4):434-436.
Shao YY, Mo P, Mai YH, et al. Effects of different concentrations of dexmedetomidine in patients undergoing thoracolumbar surgery under general anesthesia and its influence on postoperative cognitive dysfunction of hemodynamics[J]. Shanxi Med J, 2020, 49(4): 434-436.

[4] McIntyre RS, Rosenblat JD, Nemeroff CB, et al. Synthesizing the evidence for ketamine and esketamine in treatment-resistant depression: an international expert opinion on the available evidence and implementation[J]. Am J Psychiatry, 2021, 178(5): 383-399.

[5] Qiu D, Wang XM, Yang JJ, et al. Effect of intraoperative esketamine infusion on postoperative sleep disturbance after gynecological laparoscopy: a randomized clinical trial[J]. JAMA Netw Open, 2022, 5(12): e2244514.

[6] 张红玲.低剂量艾司氯胺酮对全膝关节置换术患者血流动力学及术后应激的影响研究[J].药品评价,2023,20(2):217-220.
Zhang HL. Effect of low-dose esketamine on hemodynamics and postoperative stress in patients undergoing total knee arthroplasty [J]. Drug Eval, 2023, 20(2): 217-220.

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Bai YB, Chen B, Zhang HL, et al. Effects of oxycodone combined with dexmedetomidine on immune function of patients undergoing radical mastectomy with general anesthesia[J]. Anti Tumor Pharm, 2020, 10(4): 461-466.

[13] Lawson R, Čechová P, Zarrouk E, et al. Metabolic interactions of benzodiazepines with oxycodone *ex vivo* and toxicity depending on usage patterns in an animal model[J]. Br J Pharmacol, 2023, 180(7): 829-842.

[14] 周雪辉,邵国利,彭丽艳,等.羟考酮不同给药方法对 TURP 术后患者致痛物质水平及膀胱痉挛痛的影响[J].河北医学,2022,28(1):164-168.
Zhou XH, Shao GL, Peng LY, et al. Effects of different administration methods of oxycodone on the level of pain-causing substances and bladder spasm pain in patients after TURP[J]. Hebei Med, 2022, 28(1): 164-168.

[15] Schmidt HD, Zhang YF, Xi J, et al. A new formulation of dezocine, Cyc-dezocine, reduces oxycodone self-administration in female and male rats[J]. Neurosci Lett, 2023, 815: 137479.

[16] 曹东航,丁进峰,孙焕焕.羟考酮联合七氟烷用于腹腔镜胃肠癌手术麻醉患者的临床研究[J].中国临床药理学杂志,2023,39(6):791-794.
Cao DH, Ding JF, Sun HH. Clinical trial of oxycodone combined with sevoflurane in anesthesia for laparoscopic gastrointestinal cancer surgery[J]. Chin J Clin Pharmacol, 2023, 39(6): 791-794.

[17] Mercadante S, Adile C, Ferrera P, et al. Rapid titration with intravenous oxycodone for severe cancer pain and oral conversion ratio[J]. J Pain Symptom Manage, 2022, 64(6): 532-536.

[18] 普隽,李永华,羊黎晔.羟考酮与舒芬太尼用于腹腔镜胃肠外科手术麻醉的效果比较[J].药学实践杂志,2020,38(3):268-272.
Pu J, Li YH, Yang LY. Oxycodone versus sufentanil in patients undergoing laparoscopic gastrointestinal surgery[J]. J Pharm Pract, 2020, 38(3): 268-272.

[19] Polati E, Nizzero M, Rama J, et al. Oxycodone-naloxone combination hinders opioid consumption in osteoarthritic chronic low back pain: a retrospective study with two years of follow-up[J]. Int J Environ Res Public Health, 2022, 19(20): 13354.

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[7] Kindris F, Zegarek G, Krappel FA, et al. Spinal versus general anesthesia for lumbar decompression or sequestrectomy in patients over 75 years[J]. Clin Spine Surg, 2023, 36(7): E329-E331.

[8] De Rojas JO, Syre P, Welch WC. Regional anesthesia versus general anesthesia for surgery on the lumbar spine: a review of the modern literature[J]. Clin Neurol Neurosurg, 2014, 119: 39-43.

[9] Urick D, Sciavolino B, Wang TY, et al. Perioperative outcomes of general versus spinal anesthesia in the lumbar spine surgery population: a systematic review and meta-analysis of data from 2005 through 2021[J]. J Clin Orthop Trauma, 2022, 30: 101923.

[10] Wang XM, Lin C, Lan LF, et al. Perioperative intravenous S-ketamine for acute postoperative pain in adults: a systematic review and meta-analysis[J]. J Clin Anesth, 2021, 68: 110071.

[11] 韩礼业,高成杰.不同剂量艾司氯胺酮在甲状腺癌根治术中的麻醉效果及对术后早期情绪反应的影响[J].山东医药,2023,63(2):71-75.
Han LY, Gao CJ. Anesthetic effect of different doses of esketamine in radical thyroidectomy and its influence on early postoperative emotional response[J]. Shandong Med J, 2023, 63(2): 71-75.

[12] 肖小青,程善飞,黄娟娟,等.艾司氯胺酮联合丙泊酚在无痛胃肠镜中的麻醉效果[J].中国乡村医药,2023,30(17):28-29.
Xiao XQ, Cheng SF, Huang JJ, et al. Anesthesia effect of esketamine combined with propofol in painless gastroenteroscopy[J]. Chin J Rural Med Pharm, 2023, 30(17): 28-29.

[13] Schatzberg AF. Mechanisms of action of ketamine and esketamine[J]. Am J Psychiatry, 2021, 178(12): 1130.

[14] 王馨,王媛,孙艳斌,等.艾司氯胺酮用于妇科腹腔镜下子宫肌瘤剔除术后镇痛的效果观察[J].河北医学,2023,29(8):1382-1387.
Wang X, Wang Y, Sun YB, et al. Observation of the analgesic effect of esketamine after hysteromyomectomy under gynecological laparoscopy[J]. Hebei Med, 2023, 29(8): 1382-1387.

[15] 陈毓铭,苏志辉,宋建阳.艾司氯胺酮联合右美托咪定在椎体压缩性骨折患者椎体成形术中的应用效果[J].临床合理用药,2023,16(24):107-110.
Chen YM, Su ZH, Song JY. Effect of esketamine combined with dexmedetomidine in vertebroplasty for patients with vertebral compression fracture[J]. Chin J Clin Ration Drug Use, 2023, 16(24): 107-110.

[16] Li J, Wang ZY, Wang AQ, et al. Clinical effects of low-dose esketamine for anaesthesia induction in the elderly: a randomized controlled trial[J]. J Clin Pharm Ther, 2022, 47(6): 759-766.

[17] Türk CÇ, Gediz T, Mutlucan UO, et al. Unexpected bradycardia related to surgical manipulation during thoracolumbar spinal surgery[J]. World Neurosurg, 2023, 175: e1277-e1282.

[18] 雷云龙,马真真.小剂量追加阿托品对腹腔镜胆囊手术中心动过缓的疗效[J].中国现代普通外科进展,2020,23(6):426.
Lei YL, Ma ZZ. Effect of small dose of atropine on bradycardia in laparoscopic cholecystectomy center[J]. Chin J Curr Adv Gen Surg, 2020, 23(6): 426.

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