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Effect of prophylactic analgesia with esketamine on postoperative status in patients with thoracolumbar fracture

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Abstract: Objective To explore the effects of prophylactic analgesia with esketamine on pain, hemodynamics, and stress response in patients with single-segment thoracolumbar fracture after percutaneous pedicle screw fixation (PPSF). **Methods** From April 2021 to April 2023, 85 patients with single-segment thoracolumbar fracture undergoing PPSF at The Sixth People's Hospital of Nantong were enrolled as the research objects. All patients underwent PPSF under tracheal intubation and general anesthesia, routine anesthesia induction, maintenance and patient controlled intravenous analgesia. Among all the patients, 42 cases in observation group were given intravenous injection of esketamine (10 mg) at 20 min before the end of the surgery, 43 cases in control group did not receive any other treatment. The postoperative pain [visual analogue scale (VAS)], hemodynamics [heart rate (HR), mean arterial pressure (MAP), oxygen saturation (SPO_2), respiratory rate], stress response [eosinophils (EOS), platelet count (PLT)] and adverse reactions were compared between the two groups. **Results** Compared with control group, observation group had higher HR and lower MAP immediately after surgery(T1), lower VAS scores at 2 h (T2) and 6 h (T3) after surgery, and lower frequency of analgesic pump compression at 48h after surgery ($P<0.05$). There was no significant difference in SPO_2, respiratory rate between two groups ($P>0.05$). At T1 and T3, EOS level was higher, while PLT level was lower in observation group than control group ($P<0.05$). There is no statistically significant difference in the incidence of adverse reactions between the observation group and the control group (9.52% vs 4.65%, $\chi^2=0.206$, $P=0.433$). **Conclusion** Prophylactic analgesia with esketamine is beneficial to relieve short-term pain, stress response and stabilize hemodynamics in patients with single-segment thoracolumbar fracture after PPSF, which has few effects on postoperative cognitive function and good safety.

Keywords: Thoracolumbar fracture; Esketamine; Prophylactic; pain; Hemodynamics; Stress response

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Thoracolumbar fractures are spinal injuries caused by trauma (such as falls from a height or traffic accidents) [1]. Changes in vertebral body height can lead to spinal instability, which restricts lumbar movement, causes lumbar pain, and affects the quality of life [2]. With the advancement of minimally invasive spinal surgical techniques, percutaneous pedicle screw fixation (PPSF) can reconstruct and maintain spinal stability in patients with thoracolumbar fractures, reduce muscle tissue damage, shorten postoperative recovery time, and decrease the risk of long-term bed rest complications [3]. However, the surgical procedure can still induce pain, enhance physiological stress responses, and cause hemodynamic abnormalities, increasing the risk of perioperative arrhythmias and postoperative infections [4]. Therefore, reducing surgical pain stimulation, physiological stress responses, and stabilizing perioperative hemodynamics is currently a focus in spinal injury surgical treatment. Preventive analgesia involves using multimodal analgesic methods to block harmful stimulation signals during the perioperative period, enhancing postoperative analgesic efficacy and alleviating postoperative pain [5]. Esketamine, a newly discovered N-methyl-D-aspartate (NMDA) receptor antagonist, has stronger sedative and analgesic effects than ketamine [6]. Research suggested that administering low-dose esketamine for induction of anesthesia based on etomidate, sufentanil, and rocuronium helps stabilize hemodynamics in patients undergoing knee arthroplasty. This study aims to investigate the effects of preventive analgesia with esketamine on postoperative pain, hemodynamics, and stress responses in patients undergoing single-segment thoracolumbar fracture PPSF.

1 Materials and methods

1.1 General information

The study selected 85 patients with single-segment thoracolumbar fractures treated at The Sixth People's Hospital of Nantong from April 2021 to April 2023.

(1) **Inclusion criteria:** ① Single-segment thoracolumbar fractures confirmed by X-ray or CT, with intact pedicles and facet joints, and compression < 50% of the anterior vertebral body height; ②Underwent PPSF treatment with fracture to admission time < 2 weeks; ③ American Society of Anesthesiologists (ASA) classification of I or II.

(2) Exclusion criteria: ① Severe heart, liver, or kidney dysfunction, intracranial aneurysm, hyperthyroidism, strabismus, scoliosis; ② Malignant tumors; ③ Spinal cord injury, osteoporosis, vertebral tuberculosis, pathological fractures, posterior column fractures, or dislocations; ④ Coagulation disorders; ⑤ Hypertension with poorly controlled blood pressure or no blood pressure control; ⑥ Diabetes with poorly controlled blood glucose; ⑦ Cognitive impairment preoperatively; ⑧ Allergic constitution; ⑨ Use of medications affecting stress response and hemodynamic indicators preoperatively.

Among the 85 patients, 42 cases received intravenous esketamine 10 mg (observation group) 20 minutes before the end of surgery, while 43 cases received no additional treatment (control group). The study was approved by the ethics committee. There was no statistically significant difference in general data such as sex and age between the two groups (P>0.05). **See Table 1.**

Tab. 1 Comparison of general data between two groups [case (%)]

Indicator	Control group (n=43)	Observation group (n=42)	χ^2/t value	P value
Gender			0.126	0.723
Male	18（41.86）	16（38.10）		
Female	25（58.14）	26（61.90）		
Age（year）	44.12±10.27	43.26±11.84	0.358	0.721
Hypertension	5（11.63）	4（9.52）	0.001	0.970
Diabetes	4（9.30）	3（7.14）	0.001	0.974
Degree of education			0.422	0.810
Elementary school and below	3（6.98）	3（7.14）		
Junior high school	26（60.47）	28（66.67）		
College degree or above	14（32.56）	11（26.19）		
ASA degree			0.100	0.754
I	25（58.14）	23（54.76）		
II	18（41.86）	19（45.24）		
Fracture segment			0.294	0.961
T_{11}	1（2.33）	1（2.38）		
T_{12}	14（32.56）	16（38.10）		
L_1	17（39.53）	15（35.71）		
L_2	11（25.58）	10（23.81）		

1.2 Anesthesia methods

All patients received endotracheal intubation with general anesthesia. The anesthesia induction regimen included midazolam (Yichang Renfu Pharmaceutical Co., Ltd., National Drug Approval No. H20067041) 0.05 mg/kg, propofol (Guangdong Jiahe Pharmaceutical Co., Ltd., National Drug Approval No. H20051842) 2.0 mg/kg, cisatracurium (Shangyu Dongying Jiangsu Pharmaceutical Co., Ltd., National Drug Approval No. H20133373) 0.2 mg/kg, and sufentanil (China National Pharmaceutical Group Industrial Co., Ltd. Langfang Branch, National Drug Approval No. H20203712) 0.4 μg/kg. Fifteen minutes before surgery, dexmedetomidine (Yangtze River Pharmaceutical Group Co., Ltd., National Drug Approval No. H20183219) 1.0 μg/kg was infused with a maintenance time of no less than 10 minutes. The maintenance anesthesia regimen included sevoflurane (Shanghai Henrui Pharmaceutical Co., Ltd., National Drug Approval No. H20173007) and cisatracurium 0.1 mg/(kg•h).

In the observation group, 10 mg of esketamine was administered intravenously 20 minutes before the end of the surgery, while no treatment was given to the control group. Postoperatively, all patients used patient-controlled intravenous analgesia [sufentanil 150 μg + dezocine (Yangtze River Pharmaceutical Group Co., Ltd., National Drug Approval No. H20080329) 10 mg + azasetron (Nanjing Zhongda Tianqing Pharmaceutical Co., Ltd., National Drug Approval No. H20113055) 10 mg + 0.9% NaCl 100 mL], with a pump rate of 2.0 mL/h, a single dose of 2.0 mL, and a lockout interval of 15 minutes.

1.3 Observation indicators

1.3.1 Pain and postoperative analgesia pump presses

Pain was assessed using the Visual Analogue Scale (VAS) [8] before anesthesia induction (T_0), 2 hours (T_2), 6 hours (T_3), and 12 hours (T_4) after surgery, with scores ranging from 0 to 10, where higher scores indicate more severe pain. The number of analgesia pump presses within 48 hours after surgery was recorded.

1.3.2 Hemodynamics

Heart rate (HR), mean arterial pressure (MAP), peripheral oxygen saturation (SPO_2), and respiratory rate were recorded at T_0, end of surgery (T_1), T_2, and T_3. SPO_2 and respiratory rate were monitored using a Philips MP50 multi-parameter monitor.

1.3.3 Stress response

3 mL of venous blood was collected from the elbow at T_0, T_1, and T_3, and analyzed using a BS-2000M automatic biochemical analyzer (Shenzhen Mindray Bio-Medical Electronics Co., Ltd.) to measure eosinophil (EOS) and platelet (PLT) levels.

1.3.4 Perioperative adverse reactions

Adverse reactions during the perioperative period, including agitation and dizziness, were recorded.

1.4 Statistical methods

Data analysis was performed using SPSS 25.0 software. For normally distributed measurement data, independent sample t-tests were used for comparisons between groups, repeated measures ANOVA for comparisons across different time points, and the Bonferroni method for multiple comparisons. Categorical data were expressed as case (%) and compared using χ^2 tests or Fisher's exact probability tests, with $\alpha = 0.05$.

2 Results

2.1 Comparison of pain and postoperative analgesia pump presses

Compared to T_0, VAS scores in both groups decreased at T_2 to T_4 ($P < 0.05$), showing an initial decrease followed by a gradual increase. At T_2 and T_3, the VAS scores in the observation group were lower than those in the control group ($P < 0.05$). **See Table 2.** The number of analgesia pump presses within 48 hours postoperatively was (4.93±0.78) times in the observation group, lower than (7.88±1.26) times in the control group ($t = 13.064$, $P < 0.001$).

Tab. 2 Comparison of VAS scores between two groups ($\bar{x} \pm s$)

Group	*n*	T_0	T_2	T_3	T_4
Control group	43	5.47±0.67	1.91±0.43[a]	2.44±0.50[ab]	2.56±0.50[ab]
Observation group	42	5.31±0.60	1.55±0.50[ac]	2.02±0.35[abc]	2.36±0.48[ab]
$F_{组间}/F_{时间}/F_{交互}$		8.940/2396.002/3.438			
$P_{组间}/P_{时间}/P_{交互}$		0.004/<0.001/0.021			

Note: Compared with T_0 in the same group, [a]$P<0.05$; compared with T1 in the same group, [b]$P<0.05$; compared with the control group, [c]$P<0.05$.

2.2 Comparison of HR and MAP

From T_0 to T_3, HR showed an initial decrease followed by an increase, while MAP showed an initial increase followed by a decrease ($P < 0.05$). Compared to T_0, HR decreased and MAP increased at T_1 ($P < 0.05$). Compared to the control group, the observation group had higher HR and lower MAP at T_1 ($P < 0.05$). **See Table 3.**

2.3 Comparison of SPO2 and respiratory rate

There were no statistically significant differences in SPO_2 and respiratory rate between the groups from T_0 to T_3 ($P > 0.05$). **See Table 4.**

2.4 Comparison of EOS levels and PLT

EOS levels decreased and PLT levels increased from T_0 to T_3 ($P < 0.05$). Compared to the control group, the observation group had higher EOS levels and lower PLT levels at T_1 and T_3 ($P < 0.05$). **See Table 4.**

2.5 Adverse reactions in both groups

The observation group had 2 cases of agitation, 1 case of dizziness, and 1 case of nausea, with an incidence rate of 9.52% (4/42). The control group had 1 case of dizziness and 1 case of nausea, with an incidence rate of 4.65% (2/43). The difference in adverse reaction rates between the two groups was not statistically significant ($\chi^2 = 0.206$, $P = 0.433$).

Tab. 3 Comparison of HR and MAP between the two groups ($\bar{x} \pm s$)

Group	HR				MAP（mmHg）			
	T_0	T_1	T_2	T_3	T_0	T_1	T_2	T_3
Control group	89.33±6.09	76.65±6.44[a]	81.67±6.05[ab]	84.23±5.46[ab]	86.16±4.11	100.44±5.11[a]	91.67±4.98[ab]	90.65±4.14[ab]
Observation group	87.52±5.95	81.36±5.98[ac]	83.64±6.74	85.36±6.02	85.50±4.46	94.86±4.99[ac]	90.14±5.29[ab]	89.69±4.84[ab]
$F_{组间}/F_{时间}/F_{交互}$ value	1.329/784.475/90.547				4.692/1531.157/84.538			
$P_{组间}/P_{时间}/P_{交互}$ value	0.252/<0.001/<0.001				0.033/<0.001/<0.001			

Note: Compared with T_0 in the same group, [a]$P<0.05$; compared with T1 in the same group, [b]$P<0.05$; compared with the control group, [c]$P<0.05$.

Tab. 4 Comparison of SPO_2 and respiratory rate between the two groups ($\bar{x} \pm s$)

Group	SPO2（%）				Respiratory rate			
	T_0	T_1	T_2	T_3	T_0	T_1	T_2	T_3
Control group	97.51±1.22	97.81±1.05	97.49±1.12	97.84±1.17	15.49±1.55	15.33±1.46	14.98±1.64	14.84±1.59
Observation group	97.67±1.05	97.52±1.06	97.69±1.16	97.57±1.38	15.93±1.39	15.81±1.52	15.52±1.71	15.38±1.67
$F_{组间}/F_{时间}/F_{交互}$ value	0.180/0.204/1.062				0.180/0.204/1.062			
$P_{组间}/P_{时间}/P_{交互}$ value	0.672/0.893/0.366				0.672/0.893/0.366			

Tab. 5 Comparison of EOS and PLT between the two groups ($\bar{x} \pm s$)

Group	EOS (%)			PLT ($\times 10^9$/L)		
	T_0	T_1	T_3	T_0	T_1	T_3
Control group	4.74±0.38	3.86±0.35[a]	3.16±0.28[ab]	199.36±13.25	241.98±16.04[a]	268.66±16.74[ab]
Observation group	4.67±0.41	4.12±0.42[ac]	3.58±0.31[abc]	200.14±14.98	219.33±15.73[ac]	243.43±15.63[abc]
$F_{组间}/F_{时间}/F_{交互}$ value	6.925/4510.834/154.096			22.375/10798.421/697.529		
$P_{组间}/P_{时间}/P_{交互}$ value	0.010/<0.001/<0.001			<0.001/<0.001/<0.001		

Note: Compared with T_0 in the same group, [a]P<0.05; compared with T1 in the same group, [b]P<0.05; compared with the control group, [c]P<0.05.

3 Discussion

Postoperative pain is a response to harmful stimuli that can negatively impact patient experience and physiological and psychological stress, affecting immune regulation and recovery [9]. Preventive analgesia can reduce or eliminate sensitization from perioperative harmful stimuli, alleviate postoperative pain, and reduce analgesic use. Some studies showed that intravenous dezocine during general anesthesia for compressive lumbar vertebral fractures provides effective preventive analgesia and good safety [10]. Wang *et al.* [11] found that low-dose esketamine applied in cesarean section patients could relieve postoperative pain, reduce the need for postoperative opioids, as well as the incidence of postpartum depression. Qiu *et al.* [12] also reported that esketamine infusion during surgery reduces postoperative pain in gynecological laparoscopic surgery. This study showed that esketamine preventive analgesia reduced postoperative VAS scores at 2 and 6 hours and analgesia pump presses within 48 hours compared to the control group, indicating its effectiveness in reducing immediate postoperative pain and analgesic use. Esketamine provides analgesic effects by activating dopamine receptors and L-type voltage-gated calcium channels, blocking sodium channels, and activating cyclic nucleotide-gated potassium channels [13]. Thus, esketamine preventive analgesia can alleviate immediate postoperative pain in single-segment thoracolumbar fractures.

Though less invasive than traditional open surgery, PPSF still causes hemodynamic changes, reflecting alterations in cardiac, vascular, and organ function. Stable perioperative hemodynamics ensure adequate blood volume and tissue perfusion while minimizing complications from inadequate or excessive volume. HR and MAP are key hemodynamic indicators. The study found that HR decreased and then increased, and MAP increased and then decreased in both groups. However, the observation group had higher HR and lower MAP compared to the control group at the end of surgery. SPO_2 and respiratory rate differences were not statistically significant, similar to findings by Jia *et al.* [14]. This suggested hemodynamic changes during surgery, but esketamine preventive analgesia stabilized these changes. Esketamine achieves anesthesia and analgesia by non-competitively antagonizing NMDA receptors, effectively suppressing stress responses and stabilizing hemodynamics [15-16].

Normally, the body is constantly exposed to various stressors. Moderate stress can enhance immune defenses, but excessive or prolonged stress, such as surgery, can lead to organ overload and increased disease risk. Research showed that esketamine reduced short-term anxiety and depression in elderly hip replacement patients, alleviated pain and stress, and shortened bed rest time [17].

The results of this study showed that the EOS levels in both groups of patients showed a decreasing trend compared to before anesthesia induction at the end of surgery and 6 hours after surgery, while the PLT levels showed an increasing trend compared to before anesthesia induction. However, the changes in EOS and PLT levels in the observation group were weaker than those in the control group. Although PPSF is a minimally invasive surgery, the surgery itself can cause stress reactions in the body, leading to changes in hemodynamics. Hemodynamic changes can activate platelets, causing platelet levels to increase. At the same time, surgical trauma can partially damage the immune barrier, leading to an increased inflammatory response and a decrease in EOS levels [18-19]; The results of this study indicate that prophylactic analgesia with esketamine can help alleviate postoperative stress responses in patients, which may be related to the reduced sensitivity of the body to surgical stimuli and pain relief, thereby contributing to the stability of the body's stress response. Studies have shown that esketamine can provide deep sedation and anesthesia effects, which can help complete upper gastrointestinal endoscopy in children. However, high-dose esketamine can increase the incidence of adverse reactions in children [20]. Foreign scholars have found through mouse experiments that ketamine can activate the prefrontal cortex and hippocampus of mice, thereby affecting brain functional activity [21]. Ketamine achieves anesthetic and analgesic effects by inhibiting central nervous system excitability, leading to possible neurological symptoms such as dizziness and irritability after medication. The higher the dosage of the drug, the more pronounced the neurological symptoms. This study showed that there was no statistically significant difference

in the incidence of postoperative adverse reactions between the two groups of patients, indicating that prophylactic analgesia with ketamine is safer in the treatment of single segment thoracolumbar vertebral fractures with PPSF.

In summary, prophylactic analgesia with esketamine has shown better short-term analgesic effects after PPSF surgery for single segment thoracolumbar fractures, helping to stabilize hemodynamic changes, with minimal impact on patients' short-term cognitive function after surgery, and good safety.

The authors report no conflict of interest

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·论　著·

艾司氯胺酮预防性镇痛对胸腰椎骨折患者术后的影响

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摘要：目的　探讨艾司氯胺酮预防性镇痛对单节段胸腰椎骨折患者经皮椎弓根螺钉内固定术（PPSF）治疗后疼痛、血流动力学和应激反应的影响。**方法**　选取 2021 年 4 月至 2023 年 4 月上海大学附属南通医院收治的行 PPSF 治疗的单节段胸腰椎骨折患者 85 例为研究对象。所有患者于气管插管全身麻醉下行 PPSF，采取常规麻醉诱导、维持和术后自控静脉镇痛，其中 42 例患者于手术结束前 20 min 静脉推注艾司氯胺酮 10 mg（观察组），43 例患者不作该处理（对照组）。比较两组术后不同时间点疼痛［视觉模拟（VAS）评分］、血流动力学［心率（HR）、平均动脉压（MAP）、血氧饱和度（SpO_2）及呼吸频率］、应激反应［嗜酸性粒细胞（EOS）、血小板计数（PLT）水平］及不良反应。**结果**　与对照组相比，T1（术毕）时观察组 HR 高，MAP 低（$P<0.05$）；术后 2 h（T2）、术后 6 h（T3）时观察组 VAS 评分低，术后 48 h 镇痛泵按压次数少（$P<0.05$），两组各时间点 SpO_2、呼吸频率比较差异无统计学意义（$P>0.05$）；T1、T3 时观察组 EOS 水平高，PLT 水平低（$P<0.05$）。观察组和对照组不良反应发生率差异无统计学意义（9.52% *vs* 4.65%，$\chi^2=0.206$，$P=0.433$）。**结论**　艾司氯胺酮预防性镇痛有利于缓解单节段胸腰椎骨折患者 PPSF 治疗术后近期疼痛，减轻应激反应和稳定血流动力学，安全性好。

关键词： 胸腰椎骨折；艾司氯胺酮；预防性镇痛；疼痛；血流动力学；应激反应

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Abstract: Objective　To explore the effects of prophylactic analgesia with esketamine on pain, hemodynamics, and stress response in patients with single-segment thoracolumbar fracture after percutaneous pedicle screw fixation (PPSF). **Methods**　From April 2021 to April 2023, 85 patients with single-segment thoracolumbar fracture undergoing PPSF at The Sixth People's Hospital of Nantong were enrolled as the research objects. All patients underwent PPSF under tracheal intubation and general anesthesia, routine anesthesia induction, maintenance and patient controlled intravenous analgesia. Among all the patients, 42 cases in obeservation group were given intravenous injection of esketamine (10 mg) at 20 min before the end of the surgery, 43 cases in control group did not receive any other treatment. The postoperative pain [visual analogue scale (VAS)], hemodynamics [heart rate (HR), mean arterial pressure (MAP), oxygen saturation (SpO_2), respiratory rate], stress response [eosinophils (EOS), platelet count (PLT)] and adverse reactions were compared between the two groups. **Results**　Compared with control group, obeservation group had higher HR and lower MAP immediately after surgery (T1), lower VAS scores at 2 h (T2) and 6 h (T3) after surgery, and lower frequency of analgesic pump compression at 48 h after surgery ($P<0.05$). There was no significant difference in SpO_2, respiratory rate between two groups ($P>0.05$). At T1 and T3, EOS was higher, while PLT was lower in

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observation group than control group ($P<0.05$). There was no statistically significant difference in the incidence of adverse reactions between the observation group and the control group (9.52% *vs* 4.65%, $\chi^2=0.206$, $P=0.433$).

Conclusion Prophylactic analgesia with esketamine is beneficial to relieve short-term pain, stress response and stabilize hemodynamics in patients with single-segment thoracolumbar fracture after PPSF, which has few effects on postoperative cognitive function and good safety.

Keywords: Thoracolumbar fracture; Esketamine; Prophylactic analgesia; Pain; Hemodynamics; Stress response

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胸腰椎骨折常由外伤(高空坠落、车祸等)所致[1],椎体高度发生变化可引起脊柱不稳定,使胸腰椎骨折患者腰部活动受限,出现腰部疼痛症状,影响生活质量[2]。随着微创脊柱手术技术完善,经皮椎弓根螺钉内固定术(percutaneous pedicle screw fixation, PPSF)能重建、维持胸腰椎骨折患者脊柱的稳定性,减少肌肉组织损伤,缩短术后恢复时间和降低长期卧床并发症风险[3],但手术操作本身仍会使机体产生刺激疼痛,使身体应激反应增强、血流动力学异常,导致围术期心率失常、术后感染等并发症风险增加[4]。预防性镇痛是指在围术期利用多模式镇痛方法阻断伤害性刺激信号传递,增强术后镇痛疗效,缓解术后疼痛刺激[5]。艾司氯胺酮是新发现的N-甲基-D-天冬氨酸受体(NMDAR)拮抗剂,比氯胺酮具有更强的镇静、镇痛作用[6]。有研究表明在依托咪酯、舒芬太尼和罗库溴铵麻醉基础上给予低剂量艾司氯胺酮麻醉诱导有助于稳定膝关节置换术患者血流动力学[7]。本此研究旨在探讨艾司氯胺酮预防性镇痛对单节段胸腰椎骨折行 PPSF 患者术后疼痛、血流动力学和应激反应等的影响。

1　资料与方法

1.1　一般资料　择取上海大学附属南通医院于 2021 年 4 月至 2023 年 4 月收治的 85 例单节段胸腰椎骨折患者。(1) 纳入标准:① 经 X 线片或 CT 检查确认单节段胸腰椎骨折,椎弓根突和小关节突完整,压缩程度<椎体前缘高度的 50%;② 行 PPSF 治疗,骨折至入院治疗时间<2 周;③ 美国麻醉医师协会(ASA)分级为Ⅰ~Ⅱ级。(2) 排除标准:① 严重心、肝、肾功能异常,颅内动脉瘤、甲状腺功能亢进、斜视、脊柱侧弯;② 恶性肿瘤;③ 脊髓损伤,合并骨质疏松症,椎体结核,病理性骨折,后柱骨折、脱位;④ 凝血功能异常;⑤ 血压控制不佳或未接受血压控制的高血压患者;⑥ 血糖控制不佳的糖尿病患者;⑦ 术前伴认知功能障碍;⑧ 过敏体质;⑨ 术前曾服用影响应激反应和血流动力学指标的药物。85 例患者中 42 例患者于手术结束前 20 min 静脉推注艾司氯胺酮 10 mg(观察组),43 例患者不作该处理(对照组)。本研究通过本院伦理委员会审核。两组患者性别、年龄等一般资料比较差异均无统计学意义($P>0.05$)。见表 1。

表 1　两组一般资料比较　[例(%)]

Tab. 1　Comparison of general data between two groups　[case (%)]

项目	对照组($n=43$)	观察组($n=42$)	χ^2/t 值	P 值
性别				
男	18(41.86)	16(38.10)	0.126	0.723
女	25(58.14)	26(61.90)		
年龄(岁, $\bar{x}\pm s$)	44.12±10.27	43.26±11.84	0.358	0.721
高血压	5(11.63)	4(9.52)	0.001	0.970
糖尿病	4(9.30)	3(7.14)	0.001	0.974
文化程度				
小学及以下	3(6.98)	3(7.14)		
初中/中专/高中	26(60.47)	28(66.67)	0.422	0.810
大专及以上	14(32.56)	11(26.19)		
ASA 分级				
Ⅰ级	25(58.14)	23(54.76)	0.100	0.754
Ⅱ级	18(41.86)	19(45.24)		
骨折责任节段				
T_{11}	1(2.33)	1(2.38)		
T_{12}	14(32.56)	16(38.10)	0.294	0.961
L_1	17(39.53)	15(35.71)		
L_2	11(25.58)	10(23.81)		

1.2　麻醉方法　患者均采取气管插管全身麻醉,麻醉诱导方案为咪达唑仑(宜昌人福药业有限责任公司,国药准字 H20067041)0.05 mg/kg+丙泊酚(广东嘉博制药有限公司,国药准字 H20051842)2.0 mg/kg+顺式阿曲库铵(上药东英江苏药业有限公司,国药准字 H20133373)0.2 mg/kg+舒芬太尼(国药集团工业有限公司,国药准字 H20203712)0.4 μg/kg;术前 15 min 泵注右美托咪定(扬子江药业集团有限公司,国药准字 H20183219)1.0 μg/kg,泵注维持时间不低于 10 min。麻醉维持方案为七氟烷(上海恒瑞医药有限公司,国药准字 H20173007)+顺式阿曲库铵 0.1 mg/(kg·h)。观察组于手术结束前 20 min 静脉推注艾司氯胺酮 10 mg,对照组不作该处理。所有患者术后采取自控静脉镇痛[舒芬太尼 150 μg+地佐

辛(扬子江药业集团有限公司,国药准字 H20080329)10 mg+阿扎司琼(南京正大天晴制药有限公司,国药准字 H20113055)10 mg+0.9% NaCl 100 mL],泵速 2.0 mL/h,单次按压剂量 2.0 mL,锁定间隔时间 15 min。

1.3　观察指标

1.3.1　疼痛和术后镇痛泵按压次数　于麻醉诱导前(T0)、术后 2 h(T2)、术后 6 h(T3)、术后 12 h(T4)时使用视觉模拟评分(VAS)[8]评估患者疼痛情况。记录患者术后 48 h 内镇痛泵按压次数。

1.3.2　血流动力学　于 T0、术毕(T1)、T2、T3 时记录患者心率(heart rate, HR)、平均动脉压(mean arterial pressure, MAP)、血氧饱和度(saturation of peripheral oxygen, SpO_2)和呼吸频率变化,SpO_2 和呼吸频率使用 philips MP50 多参数监护仪监测。

1.3.3　应激反应　于 T0、T1、T3 时采集患者肘静脉血 3 mL,使用 BS-2000M 全自动生化分析仪(深圳迈瑞生物医疗电子股份有限公司)检测患者嗜酸性粒细胞(eosinophil, EOS)、血小板计数(blood platelet, PLT)水平。

1.3.4　围术期不良反应　记录患者围术期不良反应发生情况,包括烦躁、头晕等。

1.4　统计学方法　数据分析采用 SPSS 25.0 软件。以 $\bar{x}\pm s$ 描述年龄、VAS 评分等符合正态分布且方差齐的计量资料,两组比较采用独立样本 t 检验,不同时间点数据的比较采取重复测量方差分析,多重比较应用 Bonferroni 法。以例(%)表示性别等计数资料,比较用 χ^2 检验或 Fisher 精确概率法检验。$P<0.05$ 为差异有统计学意义。

2　结　果

2.1　疼痛和术后镇痛泵按压次数比较　与同组 T0 相比,两组 T2~T4 时 VAS 评分均降低($P<0.05$),呈先降低再缓慢升高趋势($P<0.05$);T2、T3 时,观察组 VAS 评分低于对照组($P<0.05$)。见表 2。观察组术后 48 h镇痛泵按压次数为(4.93±0.78)次,显著低于对照组的(7.88±1.26)次($t=13.064$, $P<0.01$)。

2.2　HR、MAP 比较　T0~T3 时,两组 HR 呈先降低后升高趋势,MAP 呈先升高后降低趋势($P<0.05$)。与同组 T0 相比,两组 T1 时 HR 降低、MAP 升高($P<0.05$);与对照组相比,T1 时观察组 HR 高,MAP 低($P<0.05$)。见表 3。

2.3　SpO_2、呼吸频率比较　T0~T3 时,两组 SpO_2、呼吸频率组内及组间比较差异均无统计学意义($P>0.05$)。见表 4。

2.4　EOS 水平、PLT 比较　T0、T1、T3 时,两组 EOS 呈降低趋势,PLT 呈升高趋势($P<0.05$);与对照组相比,T1、T3 时观察组 EOS 水平高、PLT 水平低($P<0.05$)。见表 5。

2.5　两组不良反应　观察组出现烦躁 2 例,头晕 1 例,恶心 1 例,发生率为 9.52%(4/42);对照组出现头晕 1 例,恶心 1 例,发生率为 4.65%(2/43);两组不良反应发生率比较差异无统计学意义($\chi^2=0.206$, $P=0.433$)。

表 2　两组 VAS 评分比较　(分, $\bar{x}\pm s$)

Tab. 2　Comparison of VAS scores between the two groups　(point, $\bar{x}\pm s$)

组别	例数	T0	T2	T3	T4
对照组	43	5.47±0.67	1.91±0.43[a]	2.44±0.50[ab]	2.56±0.50[ab]
观察组	42	5.31±0.60	1.55±0.50[ac]	2.02±0.35[abc]	2.36±0.48[ab]
$F_{组间}/F_{时间}/F_{交互}$值			8.940/2 396.002/3.438		
$P_{组间}/P_{时间}/P_{交互}$值			0.004/<0.001/0.021		

注:与同组 T0 时比较,[a]$P<0.05$;与同组 T2 时比较,[b]$P<0.05$;与对照组比较,[c]$P<0.05$。

表 3　两组 HR、MAP 比较　($\bar{x}\pm s$)

Tab. 3　Comparison of HR and MAP between the two groups　($\bar{x}\pm s$)

组别	例数	HR(次/min)			
		T0	T1	T2	T3
对照组	43	89.33±6.09	76.65±6.44[a]	81.67±6.05[ab]	84.23±5.46[ab]
观察组	42	87.52±5.95	81.36±5.98[ac]	83.64±6.74	85.36±6.02
$F_{组间}/F_{时间}/F_{交互}$值			1.329/784.475/90.547		
$P_{组间}/P_{时间}/P_{交互}$值			0.252/<0.001/<0.001		
组别	例数	MAP(mmHg)			
		T0	T1	T2	T3
对照组	43	86.16±4.11	100.44±5.11[a]	91.67±4.98[ab]	90.65±4.14[ab]
观察组	42	85.50±4.46	94.86±4.99[ac]	90.14±5.29[ab]	89.69±4.84[ab]
$F_{组间}/F_{时间}/F_{交互}$值			4.692/1 531.157/84.538		
$P_{组间}/P_{时间}/P_{交互}$值			0.033/<0.001/<0.001		

注:与同组 T0 时比较,[a]$P<0.05$;与同组 T1 时比较,[b]$P<0.05$;与对照组比较,[c]$P<0.05$。

表 4　两组 SpO_2、呼吸频率比较　($\bar{x}\pm s$)

Tab. 4　Comparison of SpO_2 and respiratory rate between the two groups　($\bar{x}\pm s$)

组别	例数	SpO_2(%)			
		T0	T1	T2	T3
对照组	43	97.51±1.22	97.81±1.05	97.49±1.12	97.84±1.17
观察组	42	97.67±1.05	97.52±1.06	97.69±1.16	97.57±1.38
$F_{组间}/F_{时间}/F_{交互}$值			0.180/0.204/1.062		
$P_{组间}/P_{时间}/P_{交互}$值			0.672/0.893/0.366		
组别	例数	呼吸频率(次/min)			
		T0	T1	T2	T3
对照组	43	15.49±1.55	15.33±1.46	14.98±1.64	14.84±1.59
观察组	42	15.93±1.39	15.81±1.52	15.52±1.71	15.38±1.67
$F_{组间}/F_{时间}/F_{交互}$值			0.180/0.204/1.062		
$P_{组间}/P_{时间}/P_{交互}$值			0.672/0.893/0.366		

表 5　两组 EOS、PLT 水平比较　($\bar{x}\pm s$)

Tab. 5　Comparison of EOS and PLT between the two groups　($\bar{x}\pm s$)

组别	例数	EOS(%)			PLT($\times10^9$/L)		
		T0	T1	T3	T0	T1	T3
对照组	43	4.74±0.38	3.86±0.35[a]	3.16±0.28[ab]	199.36±13.25	241.98±16.04[a]	268.66±16.74[ab]
观察组	42	4.67±0.41	4.12±0.42[ac]	3.58±0.31[abc]	200.14±14.98	219.33±15.73[ac]	243.43±15.63[abc]
$F_{组间}/F_{时间}/F_{交互}$值		6.925/4 510.834/154.096			22.375/10 798.421/697.529		
$P_{组间}/P_{时间}/P_{交互}$值		0.010/<0.001/<0.001			<0.001/<0.001/<0.001		

注：与同组 T0 时比较，[a]P<0.05；与同组 T1 时比较，[b]P<0.05；与对照组比较，[c]P<0.05。

3　讨　论

手术后疼痛是机体遭受伤害性刺激后产生的一种反应，不仅会给患者带来不好的手术体验感，还会引起患者生理、心理应激反应，影响患者免疫调节，不利于病情恢复[9]。预防性镇痛通过减轻或消除围术期有害刺激造成的敏化，减轻手术后疼痛以及减少镇痛药物使用量。有研究表明压缩性腰椎骨折全身麻醉术中行地佐辛静脉注射表现出较好的术后预防性镇痛效果且安全性好[10]。Wang 等[11]认为低剂量艾司氯胺酮可帮助剖宫产产妇缓解术后疼痛，降低术后吗啡类镇痛药物使用剂量，还能降低产后抑郁症发生率。Qiu 等[12]研究也表明术中输注艾司氯胺酮可以降低妇科腹腔镜术后疼痛。本研究结果显示，观察组患者术后 2 h、6 h VAS 评分及术后 48 h 内镇痛泵按压次数低于对照组患者，表明艾司氯胺酮预防性镇痛可降低患者术后近期疼痛程度，减少术后镇痛药物使用。艾司氯胺酮通过激活多巴胺受体与 L 型电压门控钙通道，阻断钠离子通道、激活环核苷酸门控钾离子通道发挥镇痛作用[13]。

PPSF 虽然较传统开放手术的创伤小，但仍属于侵入性操作，会引起患者血流动力学变化。稳定围术期患者血流动力学在满足循环血容量和组织灌注的同时，还减少因循环血容量不足或容量过负荷引起的并发症的发生。本研究结果显示，两组患者围术期心率呈先降低后升高趋势，MAP 呈先升高后降低趋势，但术毕时观察组患者 HR 水平较对照组高，而 MAP 水平低，两组患者的 SpO_2、呼吸频率比较差异均无统计学意义，与 Jia 等[14]研究结果相似，表明两组患者围术期存在血流动力学变化，但给予艾司氯胺酮预防性镇痛可以更好地稳定患者血流动力学变化。艾司氯胺酮通过非竞争性拮抗 NMDAR 发挥麻醉和镇痛效果，有效抑制手术操作引起的应激反应，从而减少血压波动，稳定血流动力学[15-16]。

正常情况下机体每时每刻都在接受各种应激源刺激，适当应激源刺激能促进机体免疫防御增强，但过度、持续性刺激（如手术等）会诱使器官系统处于高负荷运转状态，使机体过度消耗，会为某些疾病的发生、进展提供有利条件。有研究表明艾司氯胺酮能够减少老年髋关节置换术患者术后短期焦虑、抑郁发生率，减轻术后疼痛和应激反应以及缩短患者术后卧床时间[17]。本研究结果显示，两组患者术毕、术后 6 h 时 EOS 水平较麻醉诱导前呈降低趋势，而 PLT 较麻醉诱导前呈升高趋势，但是观察组患者 EOS、PLT 水平变化趋势弱于对照组。PPSF 会使机体产生应激反应，使机体血流动力学发生改变，进而激活血小板，使血小板水平升高，同时手术创伤会部分损伤免疫屏障，导致炎症反应增强，使 EOS 水平降低[18-19]；本研究结果表明艾司氯胺酮预防性镇痛有助于缓解患者术后应激反应，可能与减弱了机体对手术刺激敏感程度、疼痛减轻有关。有研究表明艾司氯胺酮可提供深度镇静、麻醉效应，有助于小儿上消化道内窥镜检查完成，但是高剂量艾司氯胺酮会增加小儿不良反应发生率[20]。国外有学者通过小鼠实验发现，艾司氯胺酮可激活小鼠的前额叶皮层、海马体，从而影响大脑功能活动[21]。艾司氯胺酮通过抑制中枢神经兴奋性达到麻醉和镇痛作用，导致用药后可能出现头晕、烦躁等神经系统症状，药物使用剂量越大，神经系统症状越明显。本研究显示，两组患者术后不良反应发生率比较差异无统计学意义，说明艾司氯胺酮预防性镇痛在单节段胸腰椎骨折 PPSF 治疗中安全性较好。

综上所述，艾司氯胺酮预防性镇痛在单节段胸腰椎骨折 PPSF 术后表现出更好的近期镇痛效果，有助于稳定血流动力学变化，对患者术后短期认知功能影响小，安全性好。

利益冲突　无

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