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Effect of ketorolac tromethamine combined with sufentanil on pain and serum stress indicators in patients undergoing laparoscopic cholecystectomy

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Abstract: **Objective** To investigate the effects of ketorolac tromethamine combined with sufentanil on the Visual Analog Scale (VAS)scores and serum stress indicators [norepinephrine, cortisol (Cor), adrenocorticotropic hormone (ACTH)]in patients undergoing laparoscopic cholecystectomy (LC). **Methods** A retrospective analysis was conducted on the clinical data of 202 patients who underwent LC at Zhumadian Central Hospital from December 2022 to December 2024. According to the anesthesia regimen, the patients were divided into two groups: control group (n=101, received sufentanil analgesia) and experimental group (n=101, received ketorolac tromethamine combined with sufentanil analgesia. The VAS scores for resting and activity were compared between the two groups at 4 h, 8 h, 12 h, and 24 h after surgery. The levels of norepinephrine, Cor, and ACTH were compared preoperatively and at 1 d, 3 d, and 6 d after surgery. Postoperative indicators such as awakening time, time to restore spontaneous breathing, sufentanil dosage, and effective analgesia pump presses were also compared between the two groups. **Results** The VAS scores for activity at 4 h, 8 h, 12 h, and 24 h after surgery were lower in the experimental group than those in the control group (P<0.05). The levels of Cor, norepinephrine, and ACTH at 1 d, 3 d, and 6 d after surgery were also lower in the experimental group (P<0.05). Compared to the control group, the experimental group used less sufentanil [(72. 63± 3. 88)μg *vs* (95. 84±5. 19)μg, t=35. 997, P<0. 01]and had fewer effective analgesia pump presses [(3. 22±1. 10)times *vs* (6. 85 ± 1. 39)times, t=20. 581, P<0. 01], with statistically significant differences. **Conclusion** Ketorolac tromethamine combined with sufentanil can reduce postoperative pain, alleviate the stress response, and decrease sufentanil usage and analgesia pump presses in LC patients.

Keywords: Laparoscopic cholecystectomy; Ketorolac tromethamine; Sufentanil; Visual Analog Scale; Norepinephrine; Cortisol; Adrenocorticotropic hormone; Patient-controlled intravenous analgesia

Laparoscopic cholecystectomy (LC), as a common minimally invasive surgical approach, has been widely applied in the clinical treatment of gallbladder diseases due to its advantages of minimal trauma and rapid recovery [1]. Although LC is less invasive than traditional open surgery, traumatic intraoperative procedures such as skin incision, intubation, and pneumoperitoneum establishment can cause varying degrees of pain stimulation in patients, which in turn triggers a systemic stress response [2]. Postoperative pain not only affects patient comfort, but also may delay the rehabilitation process and increase the risk of postoperative complications. Therefore, an effective postoperative analgesic regimen is particularly crucial for improving the prognosis of LC patients [3].

At present, multimodal analgesia strategies are widely adopted in clinical practice, which combine analgesic drugs with different mechanisms of action to achieve better analgesic effects and reduce the adverse reactions caused by single-drug administration [4-5]. Sufentanil is a potent opioid analgesic that acts on opioid receptors in the central nervous system (CNS), effectively inhibiting pain signal transmission and exerting strong analgesic effects [6]. However, the use of a single analgesic often results in incomplete pain relief, thus necessitating combination with other drugs to achieve a synergistic effect [7].

Ketorolac tromethamine, a non-steroidal anti-inflammatory drug (NSAID), possesses favorable peripheral anti-inflammatory and analgesic properties. It can alleviate pain stress at the surgical incision and surrounding tissues by inhibiting cyclooxygenase (COX) activity and reducing the synthesis of inflammatory mediators such as prostaglandins [8]. Currently, there are relatively few reports on the application of ketorolac tromethamine combined with sufentanil in LC patients. Based on this, the present study aimed to investigate the effects of ketorolac tromethamine combined with sufentanil analgesia on the Visual Analogue Scale (VAS) scores and serum stress indicators in 202 LC patients treated at Zhumadian Central Hospital.

1 Materials and Methods

1.1 General Information

A retrospective analysis was conducted on the clinical data of 202 patients who underwent LC at Zhumadian Central Hospital from December 2022 to December 2024. The patients were divided into a control group (n=101) and an experimental group (n=101) according to different anesthesia regimens. Inclusion criteria: Underwent LC; American Society of Anesthesiologists (ASA) physical

status classification I–II [9]; No history of long-term oral opioid use before surgery; Complete clinical data; Signed informed consent for surgery and anesthesia. Exclusion criteria: Contraindications to anesthesia; Severe organic diseases of the heart, liver, or kidney; Active gastric ulcer or coagulation dysfunction; History of abdominal surgery; History of analgesic or anesthetic abuse; History of chronic pain; Complicated with respiratory, immune, or hematological system diseases; Complicated with malignant tumors; Mental disorders, cognitive impairment, or consciousness disturbance. There were no statistically significant differences in general data including gender, age, body mass index (BMI), disease type, and ASA classification between the two groups (P>0.05), as shown in **Table 1**. This study was approved by the Medical Ethics Committee of Zhumadian Central Hospital (Approval No.: 2025-03-KY002).

Tab.1 Comparison of general data between two groups (n=101）

Group	Gender (M/F, case)	Age (years, $\bar{x}\pm s$)	BMI (kg/m², $\bar{x}\pm s$)	Disease Type			ASA Grade	
				Calculous Cholecystitis	Gallbladder Polyp	Gallbladder Adenomyosis	I	II
Experimental Group	58/43	48.24±3.28	22.41±0.12	41(40.60)	37(36.63)	23(22.77)	35(34.65)	66(65.35)
Control Group	52/49	47.73±3.11	22.38±0.18	39(38.62)	36(35.64)	26(25.74)	39(38.61)	62(61.39)
t/χ^2 **value**	0.719	1.134	1.394		0.247		0.341	
P **value**	0.397	0.258	0.165		0.884		0.559	

1.2 Methods

All patients fasted for 8 hours and abstained from drinking for 2 hours before surgery. Upon admission to the operating room, routine monitoring of vital signs including heart rate, blood pressure, pulse, and anesthesia depth was performed. Peripheral venous access was established, and intravenous infusion of compound sodium chloride injection was administered.

1.2.1 Anesthesia Regimen

Both groups received anesthesia induction with intravenous injection of midazolam 0.04 mg/kg (Manufacturer: Ruitaifuren Pharmaceutical, Batch No.: AB40602811) + sufentanil 0.4 μg/kg (Manufacturer: Jiangsu Nhwa Pharmaceutical Co., Ltd., Batch No.: NSF24E03) + propofol 2 mg/kg (Manufacturer: Chenxin Pharmaceutical Co., Ltd., Batch No.:D24122573) + cisatracurium 0.2 mg/kg (Manufacturer: Jiangsu Hengrui Medicine Co., Ltd., Batch No.:250111XA). Tracheal intubation was performed after the disappearance of the patient's eyelash reflex, followed by connection to a ventilator for mechanical ventilation. The ventilation parameters were set as follows: tidal volume 6–10 mL/kg, inspiratory-expiratory ratio 1:2, oxygen concentration 100%, and respiratory rate 12–14 breaths/min. Anesthesia was maintained with continuous intravenous pump infusion of propofol 80 μg/(kg·min) + remifentanil 0. 1–0. 2 μg/(kg·min) (Manufacturer: Jiangsu Nhwa Pharmaceutical Co., Ltd., Batch No.: TRF25A04), combined with inhalation of 2%–3% sevoflurane (Manufacturer: Shanghai Hengrui Medicine Co., Ltd., Batch No.: 24121531) at an oxygen flow rate of 2 L/min. During the operation, intermittent additional doses of cisatracurium were administered to maintain muscle relaxation according to changes in vital signs.

1.2.2 Control Group

A loading dose of sufentanil 5–10 μg was administered 30 minutes before the end of surgery. After the patient regained consciousness and tracheal extubation was performed postoperatively, a disposable patient-controlled analgesia (PCA) pump was connected for patient-controlled intravenous analgesia (PCIA). The PCIA solution was prepared by dissolving sufentanil 2 μg/kg and tropisetron 5 mg (Manufacturer: Zhejiang Zhenyuan Pharmaceutical Co., Ltd., Batch No.: 250301) in 0. 9% normal saline to a total volume of 100 mL. The pump was programmed with a background infusion rate of 2 mL/h, a bolus dose of 2 mL per demand, and a lockout interval of 20 minutes.

1.2.3 Experimental Group

A loading dose of ketorolac tromethamine 30 mg (Manufacturer: Yunnan Longhai Natural Plant Pharmaceutical Co., Ltd., Batch No.: 1LB250207) was administered 30 minutes before the end of surgery. After the patient regained consciousness and tracheal extubation was performed postoperatively, a disposable PCA pump was connected for PCIA. The PCIA solution was prepared by dissolving ketorolac tromethamine 150 mg, sufentanil 1. 5 μg/kg, and tropisetron 5 mg in normal saline to a total volume of 100 mL. The pump was programmed with a background infusion rate of 2 mL/h, a bolus dose of 2 mL per demand, and a lockout interval of 20 minutes.

1.3 Observation Indicators

VAS scores at rest and during movement at 4 h, 8 h, 12 h, and 24 h after surgery [10]. Serum stress indicators: Peripheral venous blood samples (3 mL each) were collected from both groups before surgery, and at 1 d, 3 d, and 6 d after surgery. The samples were centrifuged at 4,000 r/min for 10 min with a centrifugal radius of 8 cm. The supernatant was extracted for subsequent assays. The serum norepinephrine (NE) level was determined by a modified fluorometric method; the serum cortisol (Cor) level was measured by radioimmunoassay; and the serum adrenocorticotropic hormone (ACTH) level was detected by enzyme-linked immunosorbent assay (ELISA). Postoperative related

indicators: The recovery time of spontaneous breathing, awakening time, total sufentanil dosage, and the number of effective PCA pump presses were recorded and compared between the two groups.

1.4 Statistical Methods

Data analysis was performed using SPSS 25. 0 statistical software. Measurement data conforming to a normal distribution were expressed as $\bar{x}\pm s$, and comparisons between two groups were conducted using the independent-samples t-test. Comparisons of data at multiple time points were performed using repeated measures analysis of variance (ANOVA), with pairwise comparisons using the least significant difference *t*-test (LSD-*t* test). Count data were expressed as cases (percentage) [case (%)], and comparisons between groups were conducted using the chi-square χ^2 test. A P value < 0.05 was considered statistically significant.

2 Results

2.1 Comparison of VAS Scores at Rest and During Movement Between the Two Groups

For VAS scores at rest, there was a statistically significant time effect (P<0.05), but no significant intergroup effect or interaction effect (P>0.05) between the two groups. For VAS scores during movement, there were statistically significant time effects, intergroup effects, and interaction effects (P<0.05) between the two groups. The VAS scores at rest and during movement in both groups showed a gradual decreasing trend over time (P<0.05). At 4 h, 8 h, 12 h, and 24 h after surgery, there were no statistically significant differences in VAS scores at rest between the experimental group and the control group (P>0.05), while the VAS scores during movement in the experimental group were significantly lower than those in the control group (P<0.05). See **Table 2**.

2.2 Comparison of Serum Stress Indicators Between the Two Groups

There were statistically significant time effects, intergroup effects, and interaction effects (<0. 01) on the serum levels of Cor, NE, and ACTH between the two groups. The serum levels of Cor, NE, and ACTH in both groups showed a trend of first increasing and then decreasing before surgery and at 1 d, 3 d, and 6 d after surgery (P<0.05). At 1 d, 3 d, and 6 d after surgery, the serum levels of Cor, NE, and ACTH in the experimental group were significantly lower than those in the control group (P<0.05). See **Table 3.**

2.3 Comparison of Postoperative Related Indicators Between the Two Groups

There were no statistically significant differences in awakening time and recovery time of spontaneous breathing between the two groups (P>0.05). The total sufentanil dosage and the number of effective PCA pump presses in the experimental group were significantly lower than those in the control group (P<0. 01). See **Table 4**.

Tab.2 Comparison of VAS scores during rest and activity between two groups (n=101, point, $\bar{x}\pm s$)

Group	VAS at rest				VAS during movement			
	4 h after surgery	8 h after surgery	12 h after surgery	24 h after surgery	4 h after surgery	8 h after surgery	12 h after surgery	12 h after surgery
Experimental Group	2.15±0.10	1.65±0.20	1.02±0.14	0.41±0.10	3.12±0.14[a]	2.44±0.18[a]	1.48±0.23[a]	1.11±0.25[a]
Control Group	2.17±0.13	1.67±0.17	1.05±0.17	0.39±0.12	3.27±0.11	2.81±0.20	2.02±0.33	1.53±0.29
F value	4.843/0.265/0.625				8.246/2.865/6.208			
P value	0.026/0.786/0.384				＜0.001/0.008/＜0.001			

Note: Compared with the control group at the same time point, [a]P<0.05.

Tab.3 Comparison of serum stress indicators between two groups (n=101, $\bar{x}\pm s$)

Time Point	Cor (nmol/mL)		Norepinephrine (pg/mL)		ACTH (pg/mL)	
	Experimental Group	Control Group	Experimental Group	Control Group	Experimental Group	Control Group
Before surgery	168.28±11.22	167.88±10.31	143.85±10.58	144.24±11.22	24.77±5.31	25.13±5.51
1 d after surgery	187.96±11.21[ab]	208.14±11.58[a]	204.48±10.69[ab]	268.18±9.08[a]	39.86±6.34[ab]	48.23±7.11[a]
3 d after surgery	198.24±10.29[ab]	234.18±12.42[a]	271.48±11.15[ab]	295.48±12.85[a]	55.45±6.47[ab]	63.89±7.34[a]
6 d after surgery	185.48±9.63[ab]	192.54±10.68[a]	262.48±9.04[ab]	281.48±10.56[a]	48.20±5.41[ab]	55.53±6.48[a]
$F_{group}/F_{time}/F_{interaction}$ value	855.062/264.498/325.648		1 468.284/102.849/354.146		658.239/256.490/428.545	
$P_{group}/P_{time}/P_{interaction}$ value	＜0.001/＜0.001/＜0.001		＜0.001/＜0.001/＜0.001		＜0.001/＜0.001/＜0.001	

Note: Compared with pre-op in the same group, [a]P<0.05; Compared with the control group at the same time point, [b]P<0.05.

Tab.4 Comparison of postoperative indicators between two groups (n=101, $\bar{x}\pm s$)

Group	Sufentanil Dosage (μg)	Number of Effective PCA Presses	Awakening Time (min)	Spontaneous Breathing Recovery Time (min)
Experimental Group	72.63±3.88	3.22±1.10	10.75±2.08	5.88±1.15
Control Group	95.84±5.19	6.85±1.39	11.20±2.18	6.12±1.22
t value	35.997	20.581	1.501	1.439
P value	＜0.001	＜0.001	0.135	0.152

3 Discussion

Postoperative pain not only affects patient comfort and induces complications such as respiratory depression and deep vein thrombosis, but also imposes psychological burden on patients, leading to depression and anxiety, which in turn hinders the rehabilitation process [11-12]. PCIA allows patients to flexibly adjust the dosage of analgesic drugs according to their own pain perception, achieving individualized analgesia. It can effectively relieve postoperative pain, improve comfort, and facilitate postoperative recovery [13-15]. However, different postoperative analgesic modes yield varying analgesic effects; among them, the combined analgesic mode can enhance the analgesic effect through the synergistic action of different drugs and reduce the adverse reactions caused by excessive administration of a single drug [16-17].

Sufentanil can bind to μ-opioid receptors in the CNS with high affinity. By inhibiting pain signal transmission, reducing the release of excitatory neurotransmitters, and activating the endogenous analgesic system, it exerts potent analgesic effects. It is also involved in regulating the neuroplastic changes of the CNS, playing a role in long-term pain modulation and the impact on pain memory. In multimodal analgesia regimens, it can assist other drugs in significantly enhancing the analgesic effect [3,18-19]. In this study, the VAS scores during movement in the experimental group at 4 h, 8 h, 12 h, and 24 h after surgery were lower than those in the control group. The underlying reason may be that ketorolac tromethamine can inhibit COX activity, reduce the synthesis of inflammatory mediators such as prostaglandins, alleviate inflammatory pain induced by movement, thereby reducing the subjective pain perception of patients and lowering the VAS score [20]. The stress response is a natural reaction of the body to surgical trauma. Moderate stress can help the body resist external injuries, while excessive stress can stimulate pain receptors, resulting in delayed postoperative recovery and increased risk of complications [21-22]. Lin Hongjiao *et al.* [23] found that ketorolac tromethamine has a more significant postoperative analgesic effect compared with butorphanol, which can reduce the levels of stress indicators such as Cor and NE in patients after surgery by improving the inflammatory response. This retrospective analysis of the changes in Cor, NE, and ACTH levels at 1 d, 3 d, and 6 d after surgery in the two groups revealed that the levels of the above stress indicators in the experimental group were lower than those in the control group. The possible mechanism is that ketorolac tromethamine exerts anti-inflammatory and analgesic effects to alleviate inflammatory pain at the surgical site, while inhibiting the pain stimulation signals of the body's stress regulation system, reducing the activation degree of the hypothalamic-pituitary-adrenal axis and the sympathetic-adrenal medullary system, thereby decreasing the excessive secretion of stress hormones such as Cor, NE, and ACTH [24]. The analgesic mechanism of ketorolac tromethamine combined with the effect of sufentanil in regulating pain signal transmission in the CNS can synergistically exert analgesic effects at both peripheral and central levels. Compared with the single use of sufentanil, this combination can more comprehensively and effectively alleviate postoperative pain stress [25].

This study found that the total sufentanil dosage and the number of effective PCA pump presses in the experimental group were lower than those in the control group, indicating that ketorolac tromethamine can reduce the dosage of analgesic drugs and the frequency of postoperative analgesia. When sufentanil is used alone for analgesia, its blood concentration fluctuates with metabolism in the body, which may lead to unstable analgesic effects. During the trough period of blood concentration, the patient's pain perception intensifies, prompting them to frequently press the PCA pump to increase the drug dosage for maintaining analgesic effects [26]. In contrast, when ketorolac tromethamine is combined with sufentanil, their synergistic effect blocks pain transmission and inhibits pain production through multiple pathways, providing more stable and sustained analgesic effects, and suppressing pain stimulation caused by fluctuations in analgesic efficacy. Therefore, this combination can reduce the frequency of PCA pump presses and the dependence on a single analgesic drug [25].

In conclusion, ketorolac tromethamine combined with sufentanil can reduce the degree of postoperative pain, alleviate the stress response, and decrease the dosage of sufentanil and the number of PCA pump presses in LC patients.

Conflict of interest None

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·论　著·

酮咯酸氨丁三醇联合舒芬太尼对腹腔镜胆囊切除术患者疼痛及血清应激指标的影响

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摘要：目的　探讨酮咯酸氨丁三醇联合舒芬太尼对腹腔镜胆囊切除术（LC）患者视觉模拟评分（VAS）及血清应激指标［去甲肾上腺素、皮质醇（Cor）、促肾上腺皮质激素（ACTH）］的影响。**方法**　回顾性分析2022年12月至2024年12月于驻马店市中心医院202例行LC患者的临床资料，根据麻醉方案分为两组，采用舒芬太尼镇痛的为对照组（n=101），采用酮咯酸氨丁三醇联合舒芬太尼镇痛的为试验组（n=101）。对比两组术后4 h、8 h、12 h、24 h的静息及活动时VAS评分，对比两组术前和术后1 d、3 d、6 d时的去甲肾上腺素、Cor、ACTH水平，对比两组术后相关指标（苏醒时间、自主呼吸恢复时间、舒芬太尼用量、有效按压镇痛泵次数）。**结果**　试验组术后4 h、8 h、12 h、24 h的活动时VAS评分均低于对照组（P<0.05）。试验组术后1 d、3 d、6 d的Cor、去甲肾上腺素、ACTH水平均低于对照组（P<0.05）。与对照组相比，试验组舒芬太尼用量［（72.63±3.88）μg *vs* （95.84±5.19）μg，t=35.997，P<0.01］和有效按压镇痛泵次数［（3.22±1.10）次 *vs* （6.85±1.39）次，t=20.581，P<0.01］较少，差异有统计学意义。**结论**　酮咯酸氨丁三醇联合舒芬太尼可降低LC患者术后疼痛程度，减轻应激反应，减少舒芬太尼用量和镇痛泵使用次数。

关键词：腹腔镜胆囊切除术；酮咯酸氨丁三醇；舒芬太尼；视觉模拟评分；去甲肾上腺素；皮质醇；促肾上腺皮质激素；患者自控静脉镇痛

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Effect of ketorolac tromethamine combined with sufentanil on pain and serum stress indicators in patients undergoing laparoscopic cholecystectomy

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Abstract: Objective　To investigate the effects of ketorolac tromethamine combined with sufentanil on the Visual Analog Scale (VAS) scores and serum stress indicators [norepinephrine, cortisol (Cor), adrenocorticotropic hormone (ACTH)] in patients undergoing laparoscopic cholecystectomy (LC). **Methods**　A retrospective analysis was conducted on the clinical data of 202 patients who underwent LC at Zhumadian Central Hospital from December 2022 to December 2024. According to the anesthesia regimen, the patients were divided into two groups: control group (n=101, received sufentanil analgesia) and experimental group (n=101, received ketorolac tromethamine combined with sufentanil analgesia). The VAS scores for resting and activity were compared between the two groups at 4 h, 8 h, 12 h, and 24 h after surgery. The levels of norepinephrine, Cor, and ACTH were compared preoperatively and at 1 d, 3 d, and 6 d after surgery. Postoperative indicators such as awakening time, time to restore spontaneous breathing, sufentanil dosage, and effective analgesia pump presses were also compared between the two groups. **Results**　The VAS scores for activity at 4 h, 8 h, 12 h, and 24 h after surgery were lower in the experimental group than those in the control group (P<0.05). The levels of Cor, norepinephrine, and ACTH at 1 d, 3 d, and 6 d after surgery were also lower in

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experimental group (P<0.05). Compared to control group, the experimental group used less sufentanil [(72.63±3.88) μg *vs* (95.84±5.19) μg, t=35.997, P<0.01] and had fewer effective analgesia pump presses [(3.22±1.10) times *vs* (6.85±1.39) times, t=20.581, P<0.01], with statistically significant differences. **Conclusion** Ketorolac tromethamine combined with sufentanil can reduce postoperative pain, alleviate the stress response, and decrease sufentanil usage and analgesia pump presses in LC patients.

Keywords: Laparoscopic cholecystectomy; Ketorolac tromethamine; Sufentanil; Visual Analog Scale; Norepinephrine; Cortisol; Adrenocorticotropic hormone; Patient-controlled intravenous analgesia

腹腔镜胆囊切除术(laparoscopic cholecystectomy, LC)作为常见的微创手术方式,凭借其创伤小、恢复快等优势,已在临床上广泛应用于胆囊疾病的治疗[1]。尽管LC手术创伤比传统开腹手术小,但术中切皮、插管、建立气腹等创伤性操作会造成不同程度的疼痛刺激,进而引发机体应激反应[2]。术后疼痛不仅会影响患者舒适度,还可能延缓患者康复进程,增加术后并发症发生风险,故有效的术后镇痛方案对改善LC患者预后尤为重要[3]。目前,临床上多采用多模式镇痛策略,联合应用不同作用机制的镇痛药物,以达到更好的镇痛效果并减少单一药物使用带来的不良反应[4-5]。舒芬太尼是一种强效阿片类镇痛药,作用于中枢神经系统的阿片受体,能有效抑制疼痛信号传导,发挥强效的镇痛功效[6]。然而单一采用镇痛药物易出现镇痛效果不完全,故需联合其他药物以发挥增效作用[7]。酮咯酸氨丁三醇作为一种非甾体抗炎药,具有良好的外周抗炎、镇痛作用,可通过抑制环氧合酶(cyclooxygenase, COX)活性,减少前列腺素等炎性介质合成,从而缓解手术切口及周围组织的疼痛应激[8]。目前关于酮咯酸氨丁三醇联合舒芬太尼用于LC患者的报道尚不多见,基于此,本研究以驻马店市中心医院行LC的202例患者为对象,旨在探讨经酮咯酸氨丁三醇联合舒芬太尼镇痛对患者视觉模拟评分(Visual Analogue Scale, VAS)及血清应激指标的影响。

1　资料与方法

1.1　一般资料　收集2022年12月至2024年12月期间驻马店市中心医院202例行LC患者的临床资料并进行回顾性分析。按不同麻醉方案分为对照组(n=101)和试验组(n=101)。纳入标准:均行LC手术;符合美国麻醉医师协会(American Society of Anesthesiologists, ASA)分级[9]Ⅰ~Ⅱ级;术前无长期口服阿片类药物记录;临床资料完整;患者签署手术及麻醉同意书。排除标准:麻醉禁忌证;有严重心、肝、肾等脏器疾病者;存在活动性胃溃疡及凝血功能障碍;有腹部手术史;镇痛药、麻醉药滥用史;慢性疼痛病史;合并呼吸、免疫、血液等系统疾病者;合并恶性肿瘤;存在精神异常、认知功能、意识障碍等。

两组性别、年龄、身体质量指数、疾病类型、ASA分级等一般资料差异无统计学意义(P>0.05),见表1。本研究经驻马店市中心医院医学伦理委员会审批通过(审批号:2025-03-KY002)。

1.2　方法　所有患者术前8 h禁食,2 h禁饮,入室后常规监测心率、血压、脉搏、麻醉深度等生命体征,建立外周静脉通路并给予静脉输注复方氯化钠注射液。

1.2.1　麻醉方案　两组均给予0.04 mg/kg咪达唑仑(生产厂家:瑞太人福医药,批号:AB40602811)+0.4 μg/kg舒芬太尼(生产厂家:江苏恩华药业,批号:NSF24E03)+2 mg/kg丙泊酚(生产厂家:辰欣药业,批号:D24122573)+0.2 mg/kg顺阿曲库铵(生产厂家:江苏恒瑞医药,批号:250111XA)行麻醉诱导,待患者睫毛反射消失后行气管插管,连接麻醉机通气,设定潮气量6~10 mL/kg,吸呼比1∶2,氧浓度100%,呼吸频率12~14次/min。麻醉维持采用微量泵泵注80 μg/(kg·min)丙泊酚+0.1~0.2 μg/(kg·min)瑞芬太尼(生产厂家:江苏恩华药业,批号:TRF25A04),同时吸入2%~3%七氟烷(生产厂家:上海恒瑞医药,批号:24121531),氧流量2 L/min,术中根据生命体征变化间断追加顺阿曲库铵以维持肌松。

1.2.2　对照组　于手术结束前30 min给予舒芬太尼5~10 μg负荷量,待患者术毕清醒拔除气管后连接一次性自控镇痛泵,行患者自控静脉镇痛(patient-controlled intravenous analgesia, PCIA):2 μg/kg舒芬太尼、5 mg托烷司琼(生产厂家:浙江震元制药,批号:250301)均溶于0.9%生理盐水至100 mL,设定背景剂量2 mL/h,自控剂量2 mL/次,锁定时间20 min。

1.2.3　试验组　于手术结束前30 min给予酮咯酸氨丁三醇(生产厂家:云南龙海天然植物药业有限公司,批号:1LB250207)30 mg负荷量,待患者术毕清醒拔除气管后连接一次性自控镇痛泵,行PCIA:150 mg酮咯酸氨丁三醇、1.5 μg/kg舒芬太尼、5 mg托烷司琼均溶于生理盐水至100 mL,设定背景剂量2 mL/h,PCIA剂量2 mL/次,锁定时间20 min。

1.3　观察指标　(1)术后4 h、8 h、12 h、24 h静息及

活动时的VAS评分[10]。(2) 血清应激指标：于术前、术后1 d、术后3 d、术后6 d抽取两组外周静脉血3 mL，离心分离10 min(离心速度为4 000 r/min，离心半径为8 cm)，提取上清液后采用改良荧光法测定去甲肾上腺素水平，采用放射免疫法测定皮质醇(cortisol，Cor)水平，采用酶联免疫法检测促肾上腺皮质激素(adrenocorticotropic hormone，ACTH)水平。(3) 记录对比两组苏醒时间、自主呼吸恢复时间、舒芬太尼用量、有效按压镇痛泵次数。

1.4　统计学方法　经SPSS 25.0软件处理数据。符合正态分布的计量资料以$\bar{x}\pm s$表示，比较采用t检验；多时点比较采用重复测量资料方差分析，两两比较采用LSD-t检验。计数资料以例(%)表示，采用χ^2检验。P<0.05为差异有统计学意义。

2　结　果

2.1　两组静息及活动时VAS评分比较　两组静息时VAS评分存在时间效应(P<0.05)，而不存在组间效应和交互效应(P>0.05)；两组活动时VAS评分时间效应、组间效应和交互效应均有统计学意义(P<0.05)。两组静息、活动时VAS评分随时间均呈逐渐下降趋势(P<0.05)，术后4 h、8 h、12 h、24 h试验组静息时VAS评分与对照组比较差异无统计学意义(P>0.05)，试验组活动时VAS评分均低于对照组(P<0.05)。见表2。

2.2　两组血清应激指标比较　两组血清Cor、去甲肾上腺素、ACTH水平的时间、组间、交互效应均有统计学意义(P<0.01)。术前和术后1 d、3 d、6 d两组血清Cor、去甲肾上腺素、ACTH水平均呈先升高后下降趋势(P<0.05)，术后1 d、3 d、6 d时试验组血清Cor、去甲肾上腺素、ACTH水平均低于对照组(P<0.05)。见表3。

2.3　两组术后相关指标比较　两组苏醒时间和自主呼吸恢复时间比较差异无统计学意义(P>0.05)；试验组舒芬太尼用量和有效按压镇痛泵次数均少于对照组(P<0.01)。见表4。

表1　两组一般资料对比　(n=101)

Tab.1　Comparison of general data between two groups　(n=101)

组别	性别(男/女，例)	年龄($\bar{x}\pm s$，岁)	身体质量指数($\bar{x}\pm s$，kg/m^2)	疾病类型[例(%)]			ASA[例(%)]	
				结石性胆囊炎	胆囊息肉	胆囊腺肌症	Ⅰ级	Ⅱ级
试验组	58/43	48.24±3.28	22.41±0.12	41(40.60)	37(36.63)	23(22.77)	35(34.65)	66(65.35)
对照组	52/49	47.73±3.11	22.38±0.18	39(38.62)	36(35.64)	26(25.74)	39(38.61)	62(61.39)
t/χ^2值	0.719	1.134	1.394	0.247			0.341	
P值	0.397	0.258	0.165	0.884			0.559	

表2　两组静息及活动时VAS评分比较　(n=101，分，$\bar{x}\pm s$)

Tab.2　Comparison of VAS scores during rest and activity between two groups　(n=101，point，$\bar{x}\pm s$)

组别	静息时VAS				活动时VAS			
	术后4 h	术后8 h	术后12 h	术后24 h	术后4 h	术后8 h	术后12 h	术后24 h
试验组	2.15±0.10	1.65±0.20	1.02±0.14	0.41±0.10	3.12±0.14[a]	2.44±0.18[a]	1.48±0.23[a]	1.11±0.25[a]
对照组	2.17±0.13	1.67±0.17	1.05±0.17	0.39±0.12	3.27±0.11	2.81±0.20	2.02±0.33	1.53±0.29
$F_{时间}/F_{组间}/F_{交互}$值	4.843/0.265/0.625				8.246/2.865/6.208			
$P_{时间}/P_{组间}/P_{交互}$值	0.026/0.786/0.384				<0.001/0.008/<0.001			

注：与同一时间点的对照组相比，[a]P<0.05。

表3　两组血清应激指标比较　(n=101，$\bar{x}\pm s$)

Tab.3　Comparison of serum stress indicators between two groups　(n=101，$\bar{x}\pm s$)

时点	Cor(nmol/mL)		去甲肾上腺素(pg/mL)		ACTH(pg/mL)	
	试验组	对照组	试验组	对照组	试验组	对照组
术前	168.28±11.22	167.88±10.31	143.85±10.58	144.24±11.22	24.77±5.31	25.13±5.51
术后1 d	187.96±11.21[ab]	208.14±11.58[a]	204.48±10.69[ab]	268.18±9.08[a]	39.86±6.34[ab]	48.23±7.11[a]
术后3 d	198.24±10.29[ab]	234.18±12.42[a]	271.48±11.15[ab]	295.48±12.85[a]	55.45±6.47[ab]	63.89±7.34[a]
术后6 d	185.48±9.63[ab]	192.54±10.68[a]	262.48±9.04[ab]	281.48±10.56[a]	48.20±5.41[ab]	55.53±6.48[a]
$F_{时间}/F_{组间}/F_{交互}$值	855.062/264.498/325.648		1 468.284/102.849/354.146		658.239/256.490/428.545	
$P_{时间}/P_{组间}/P_{交互}$值	<0.001/<0.001/<0.001		<0.001/<0.001/<0.001		<0.001/<0.001/<0.001	

注：与本组术前相比，[a]P<0.05；与同一时间点对照组相比，[b]P<0.05。

表4 两组术后相关指标比较 （n=101，$\bar{x}\pm s$）

Tab.4 Comparison of postoperative indicators between two groups （n=101，$\bar{x}\pm s$）

组别	舒芬太尼用量(μg)	有效按压镇痛泵次数(次)	苏醒时间(min)	自主呼吸恢复时间(min)
试验组	72.63±3.88	3.22±1.10	10.75±2.08	5.88±1.15
对照组	95.84±5.19	6.85±1.39	11.20±2.18	6.12±1.22
t值	35.997	20.581	1.501	1.439
P值	<0.001	<0.001	0.135	0.152

3 讨 论

术后疼痛不仅会影响患者舒适度、引发呼吸抑制、深静脉血栓等并发症，还会给患者带来心理负担，导致情绪低落、焦虑，进而影响康复进程[11-12]。PCIA能让患者依据自身疼痛感受灵活调控镇痛药物剂量，实现个体化镇痛，可有效缓解术后疼痛，提升舒适度，利于患者术后恢复[13-15]。然而不同的术后镇痛模式会产生不同的镇痛效果，其中联合镇痛模式可通过不同药物协同作用，强化镇痛效果，减少单一药物过量产生的不良反应[16-17]。

舒芬太尼与中枢神经系统的μ阿片受体结合亲和力高，能通过抑制痛觉传导，减少兴奋性神经递质释放，激活内源性镇痛系统，从而发挥强效镇痛作用，其还参与调节中枢神经系统的神经可塑性变化，可在长期疼痛调节以及对疼痛记忆影响等方面发挥作用，在多模式镇痛方案中，可协助其他药物明显增强镇痛效果[3,18-19]。本研究中试验组术后4 h、8 h、12 h、24 h的活动时VAS评分均低于对照组，分析原因是酮咯酸氨丁三醇能抑制COX活性，减少前列腺素等炎性介质合成，缓解活动引发的炎性疼痛，进而减轻患者主观痛感，降低VAS评分[20]。应激反应是机体对手术创伤的自然反应，适度的应激可促使机体抵御外来伤害，但过度的应激则可刺激痛觉感受器，导致术后恢复延迟，增加并发症风险[21-22]。林洪娇等[23]发现，酮咯酸氨丁三醇相较于布托啡诺用于术后镇痛的效果更明显，其可通过改善炎性反应，减少患者术后Cor、去甲肾上腺素等应激指标含量。本研究回顾性分析了两组术后1 d、3 d、6 d的Cor、去甲肾上腺素、ACTH水平变化，发现试验组上述应激指标水平均低于对照组。分析原因是酮咯酸氨丁三醇通过发挥抗炎、镇痛作用，缓解手术部位炎性疼痛，同时抑制机体应激调节系统的疼痛刺激信号，降低对下丘脑—垂体—肾上腺轴和交感—肾上腺髓质系统的激活程度，从而减少Cor、去甲肾上腺素、ACTH等应激激素的过度分泌[24]。酮咯酸氨丁三醇镇痛机制与舒芬太尼调节中枢神经系统的痛觉传导的作用联合，能从外周和中枢两个不同层面协同发挥镇痛作用，相比单一使用舒芬太尼，可更全面、有效地缓解术后疼痛应激[25]。

本研究发现，试验组舒芬太尼用量、有效按压镇痛泵次数均少于对照组，说明酮咯酸氨丁三醇可减少镇痛药物的使用，降低术后镇痛程度。单一使用舒芬太尼进行镇痛时，随着药物在体内代谢，其血药浓度会出现波动，可能导致镇痛效果不稳定，在血药浓度低谷时患者疼痛感受增强，从而促使患者频繁按压镇痛泵增加药物剂量来维持镇痛效果[26]。而酮咯酸氨丁三醇与舒芬太尼联合应用时，由于两者协同作用通过多途径、全方位地阻断疼痛传导和抑制疼痛产生，能提供更稳定、持续的镇痛效果，抑制因镇痛效果波动带来的疼痛刺激，故可减少频繁按压镇痛泵的次数及对单一镇痛药物的依赖[25]。

综上，酮咯酸氨丁三醇联合舒芬太尼可降低LC患者术后疼痛程度，减轻应激反应，减少舒芬太尼药物用量和镇痛泵使用次数。

利益冲突 无

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