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Different doses of oxycodone on postoperative pain-causing substance levels, tissue perfusion and intestinal barrier in patients undergoing gastrointestinal cancer surgery

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Abstract: Objective To investigate the impact of different doses of oxycodone on postoperative levels of pain-inducing substances, tissue perfusion, and intestinal barrier in patients undergoing gastrointestinal tumor surgery. **Methods** Forty-five patients with gastrointestinal tumors who underwent surgery at Lu'an Hospital of Traditional Chinese Medicine from June 2020 to January 2023 were selected and randomly divided into three groups, with 15 in each group. All patients underwent general anesthesia. During the anesthesia process, intravenous infusion of sufentanil 0.1 ug/kg+oxycodone was administered 30 minutes before the end of the surgery. The dose of oxycodone in Group A, B and C received anesthesia with 0.08, 0.10 and 0.12 mg/kg, respectively. The blood flow perfusion index (PI) was recorded at anesthesia induction (S_1), endotracheal intubation (S_2), 30 minutes after the start of surgery (S_3), and at the end of surgery (S_4). The levels of pain-inducing substances [5-hydroxytryptamine (5-HT) and substance P (SP)] were detected 1 day before surgery and 2 days after surgery. The intestinal barrier function [diamine oxidase (DAO), D-lactic acid, and endotoxin (ET)] was assessed 1 day before surgery and 2 days and 4 days after surgery. Adverse reactions during anesthesia were recorded for the three groups. **Results** The PI levels of the three groups at S_2, S_3, and S_4 were significantly higher than those at S_1, and in Group A was higher than in Group B and Group C (P<0.05). On 2 days after surgery, the serum levels of 5-HT and SP in three groups were improved than those before surgery, and in Group A was better than in Group B and Group C (P<0.05). On 2 days and 4 days after surgery, the serum levels of DAO, D-lactic acid, and ET in three groups were significantly lower than those before surgery, and in Group A was lower than in Group B and Group C (P<0.05). There was no significant difference in overall incidence of adverse reactions during anesthesia in Group A (20.00%), Group B (26.67%), and Group C (26.67%) (P>0.05). **Conclusion** Compared to 0.08 mg/kg or 0.12 mg/kg oxycodone, anesthesia with 0.10 mg/kg oxycodone can effectively improve the levels of pain-inducing substances and PI after gastrointestinal tumor surgery, and maintain the stability of intestinal barrier function, with good safety.

Keywords: Oxycodone; Gastrointestinal cancer; Pain-causing substance; Blood perfusion index; Intestinal barrier function

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Surgery is the primary method for clinically treating gastrointestinal tumors. An effective anesthetic approach is a prerequisite for the smooth progress of gastrointestinal tumor surgery. However, prolonged anesthesia during surgery may induce stress responses in patients and also affect gastrointestinal function. Therefore, implementing effective and reasonable anesthesia is particularly important. Hydrocodone is an opioid receptor agonist with high bioavailability and a long elimination half-life. It acts on the central nervous system's μ and κ receptors, effectively suppressing somatic and visceral pain [1-3]. Substances causing pain are important neurotransmitters in the pain modulation system, indirectly raising the excitatory threshold of nociceptors, sensitizing pain perception, and promoting pain development. Tissue perfusion refers to sufficient blood flow through the blood vessels of various organs to maintain their function. Inadequate tissue perfusion can lead to organ ischemia, hypoxia, metabolic disorders, and functional impairment. Additionally, due to the metabolic characteristics of tumor cells, changes occur in the metabolism of energy, carbohydrates, fats, and proteins in the patient's body, leading to dysbiosis of the gastrointestinal microbiota, damage to the gastrointestinal barrier, and delayed postoperative intestinal motility, which further exacerbates malnutrition. This study analyzes the effects of different doses of hydrocodone on postoperative levels of pain-inducing substances, tissue perfusion, and intestinal barrier in patients undergoing gastrointestinal tumor surgery, aiming to provide clinical reference.

1 Data and Methods

1.1 General Data

A total of 45 patients with gastrointestinal tumors who received surgery at Lu'an Hospital of Traditional Chinese Medicine from June 2020 to January 2023 were selected. The patients were divided into three groups according to the random number table method, 15 cases in each group. All the patients received general anesthesia During the anesthesia process, intravenous infusion of sufentanil 0.1 ug/kg+oxycodone was administered 30 minutes before the end of the surgery. The dose of oxycodone in Group A, B and C received anesthesia with 0.08, 0.10 and 0.12 mg/kg, respectively. There was no significant difference in general data among three groups (P>0.05) **[Table 1].**

Tab.1 Comparison of general data among three groups (n=15)

Group	Male/Female (case)	Age (years, $\bar{x}\pm s$)	BMI (kg/m^2, $\bar{x}\pm s$)	TNM (I/II/III,case)	Tumor location (case) [a]	ASA (I/II/III, case)	Surgical technique (case) [b]	Intraoperative lymph node dissection (case)
Group A	8/7	61.58±11.25	22.63±1.28	3/7/5	7/4/4	4/8/3	3/4/4/4	8
Group B	9/6	61.28±11.42	22.76±1.33	4/6/5	6/5/4	5/7/3	3/3/5/4	7
Group C	7/8	61.87±11.64	22.59±1.41	4/7/4	6/4/5	4/7/4	2/4/4/5	9
χ^2/F **value**	0.536	0.010	0.066	0.425	0.413	0.445	0.740	0.536
P **value**	0.765	0.990	0.936	0.980	0.981	0.979	0.994	0.765

Note: a meant the tumor was located in the stomach/colon/rectum respectively; b meant that the surgical method was total gastrectomy/distal gastric cancer radical resection/colon cancer radical resection/rectal cancer radical resection, respectively.

1.2 Inclusion Criteria and Exclusion Criteria

Inclusion Criteria: (1) Diagnosis of gastrointestinal tumors [4-5], confirmed by surgical pathology; (2) Undergoing surgical treatment for gastrointestinal tumors; (3) Meeting surgical indications; (4) ASA classification of grade I to III; (5) No severe organ failure; (6) Normal cognitive function without history of mental illness; (7) Good compliance with treatment, capable of normal communication; (8) Expected survival period of over six months; (9) Complete clinical data; (10) Voluntarily signed informed consent form for clinical enrollment.

Exclusion Criteria:(1) Concurrent significant organ dysfunction; (2) Concurrent infectious or communicable diseases; (3) Concurrent severe endocrine disorders; (4) Predisposition to esophageal or gastrointestinal perforation; (5) Concurrent immune or hematologic system diseases; (6) Pregnant or lactating women; (7) Concurrent other malignant tumors; (8) Poor compliance with treatment, unable to cooperate with the study; (9) Dependence on opioid drugs.

This study has been approved by the Ethics Committee of Lu'an Hospital of Traditional Chinese Medicine [LASZYYLL-KY (SQ)-2023002].

1.3 Methods

All patients fasted from water for 8 hours before surgery. Upon entering the operating room, intravenous access was established, and vital signs were monitored. Anesthesia induction involved intravenous administration of dexamethasone (Jiaozuo Furuitang Pharmaceutical, H41021269, 1mL:2mg) 5 mg, midazolam (Jiangsu Nhwa Pharmaceutical, H20031071, 5 mL:5 mg) 0.05 mg/kg, propofol (Guangdong Jiabo Pharmaceutical, H20163406, 10 mL:200mg) 1-2 mg/kg, and hydrocodone (Shenyang No.1 Pharmaceutical Factory, H20203622, 1 mL:10 mg) 0.3 mg/kg, followed by intravenous rocuronium (Hainan Huanglong Pharmaceutical, H20183355, 20mg) 0.2 mg/kg one minute later, with tracheal intubation after muscle relaxation. Anesthesia maintenance consisted of intravenous infusion of propofol 1.5-2.5 μg/mL and inhalation of 1%-2% sevoflurane (Hebei Shanmushi Pharmaceutical, H20213791), and bispectral index (BIS) was maintained 45-55. Thirty minutes before the end of surgery, fentanyl (Jiangsu Nhwa Pharmaceutical, H20203653, 10 mL:50μg) 0.1 μg/kg and hydrocodone (the dose in Group A, B and C received anesthesia with 0.08, 0.10 and 0.12 mg/kg, respectively.) were intravenously administered. Postoperative analgesia included patient-controlled analgesia with a pump containing sufentanil 100 μg, palonosetron (Kunming Jida Pharmaceutical, H20150034, 5mL:0.25 mg) 0.25 mg, and saline solution (Cisen Pharmaceutical, H20056758, 50 mL:0.45 g) 100 mL at a rate of 2 mL/h.

1.4 Observation Indicators

(1) Blood flow perfusion index (PI) for three groups of patients were measured and recorded at four different times: before anesthesia induction (S_1), during tracheal intubation (S_2), 30 minutes after the start of surgery (S_3), and at the end of the surgery (S_4).

(2) Levels of pain-related substances in the three groups of patients were detected one day before surgery and two days after surgery. Three mL of fasting peripheral venous blood from the patients was collected in the morning and enzyme-linked immunosorbent assay (ELISA) was used to measure serum levels of serotonin (5-HT) and substance P (SP). The kits were purchased from Ulrich (Shanghai) Life Science Co., Ltd. and Forai Biotech (Wuhan) Co., Ltd., and the procedures were strictly followed as per the kit instructions.

(3) Intestinal barrier function of the three groups of patients were evaluated on one day before surgery, and two and four days after surgery. Three mL of fasting peripheral venous blood from the patients was collected in the morning and ELISA was used to measure serum levels of diamine oxidase (DAO), D-lactic acid, and endotoxin (ET). The kits were purchased from Wuhan Fien Biotech Co., Ltd., Shanghai Bai Li Lai Biotech Co., Ltd., and Shanghai Bai Li Lai Biotech Co., Ltd,.

(4) Adverse reactions occurred during anesthesia for the three groups of patients were recorded.

1.5 Statistic Methods

SPSS 25.0 software was used for data analysis. Measurement data were expressed as $\bar{x} \pm s$. Single factor analysis and LSD- *t*-test was used for pairwise comparison. Count data were expressed as *n*(%) and analyzed by chi-square test. $P<0.05$ was considered statistically significant.

2 Results

2.1 Comparison of PI

The PI level was higher in S_1 compared with those in S_2, S_3 and S_4 in three groups, and Group A had a higher PI than Group B and Group C ($P<0.05$). And there was no significant difference between Group B and Group C ($P>0.05$) **[Table 2].**

2.2 Comparison of pain-related substances

Two days after surgery, the levels of 5-HT, SP in three group were significantly higher than those one day before surgery, and Group A had higher 5-HT and SP level than Group B and Group C ($P<0.05$) **[Table 3].**

Tab.2 Comparison of levels of PI among three groups (n=15,$\bar{x}\pm s$)

Group	S_1	S_2	S_3	S_4
Group A	4.27±0.76	5.67±0.84	5.78±0.55	5.89±0.48
Group B	4.32±0.68	4.72±0.66	5.23±0.52	5.34±0.45
Group C	4.35±0.72	4.67±0.55	5.20±0.54	5.32±0.44
***F* value**	0.047	9.896	5.551	7.516
***P* value**	0.954	<0.001	0.007	0.002

Tab. 3 Comparison of levels of pain-causing substances among three groups (n=15,$\bar{x}\pm s$)

Group	5-HT(nmol/L)		SP(nmol/L)	
	1 day before surgery	2 days after surgery	1 day before surgery	2 days after surgery
Group A	126.56±14.62	386.64±18.52[a]	33.67±5.24	44.57±6.61[a]
Group B	128.61±13.85	286.45±17.43[a]	34.28±5.41	54.42±6.42[a]
Group C	127.94±14.29	281.67±18.49[a]	34.56±5.62	57.64±6.59[a]
F value	0.081	159.908	0.106	16.259
***P* value**	0.923	<0.001	0.900	<0.001

Note: Compared with 1 day before surgery, [a]$P<0.05$.

2.3 Comparison of intestinal barrier function

Two days and four days after surgery, the serum levels of DAO, D-lactate, and ET in three groups of patients decreased compared to one day after surgery, and Group A was lower than Group B and Group C ($P<0.05$). There was no significant difference between Group B and Group C ($P>0.05$) **[Table 4]**.

2.4 Comparison of adverse reactions

There was no statistically significant difference in the total incidence of adverse reactions among the three groups of patients during anesthesia ($P>0.05$) **[Table 5]**.

Tab. 4 Comparison of intestinal barrier function among three groups (n=15,$\bar{x}\pm s$)

Group	DAO(U/L)			D-lactic acid (mg/L)			ET(U/L)		
	1 day before surgery	2 days after surgery	4 days after surgery	1 day before surgery	2 days after surgery	4 days after surgery	1 day before surgery	2 days after surgery	4 days after surgery
Group A	12.42±2.53	7.49±1.54[a]	5.52±1.24[a]	9.54±1.62	5.78±1.35[a]	4.73±1.24[a]	10.64±1.52	5.89±1.37[a]	5.14±1.27[a]
Group B	12.22±2.67	8.67±1.33[a]	7.16±1.32[a]	9.47±1.45	7.33±1.43[a]	6.34±1.31[a]	10.72±1.43	7.48±1.46[a]	6.67±1.24[a]
Group C	12.03±2.49	8.86±1.45[a]	7.32±1.37[a]	9.53±1.51	7.54±1.46[a]	6.51±1.42[a]	10.81±1.49	7.54±1.52[a]	6.78±1.32[a]
***F* value**	$F_{interation}$=51.425,F_{group}=112.532,F_{time}=59.671			$F_{interation}$=56.372,F_{group}=128.764,F_{time}=64.169			$F_{interation}$=53.124,F_{group}=119.523,F_{time}=62.258		
***P* value**	$P_{interation}$=0.001,P_{group}<0.001,P_{time}<0.001			$P_{interation}$=0.001,P_{group}<0.001,P_{time}<0.001			$P_{interation}$=0.001,P_{group}<0.001,P_{time}<0.001		

Note: Compared with 1 day before surgery,[a]$P<0.05$.

Tab. 5 Comparison of the incidence of adverse reactions among three groups (n=15, case)

Group	Respiratory depression	Blood oxygen decreasion	Hypoten-sion	Nausea /vomiting	Total [case(%)]
Group A	0	1	1	1	3(20.00)
Group B	0	1	2	1	4(26.67)
Group C	1	1	0	2	4(26.67)
χ^2 **value**					0.241
***P* value**					0.887

3 Discussion

General anesthesia is the preferred anesthesia method for gastrointestinal tumor surgery, but the use of anesthetic drugs and surgical trauma can stimulate stress responses in patients during the perioperative period. This may lead to adverse drug reactions such as respiratory depression and abnormal blood pressure, thereby increasing the surgical risks [6-7] and affecting patient recovery. Hydromorphone, a commonly used potent analgesic in clinical practice, is a pure opioid receptor agonist that stimulates opioid receptors in the central nervous system, reducing central nervous system excitability and sensitivity, thereby exerting significant analgesic effects, especially effective in visceral pain relief. It acts rapidly and has relatively long-lasting effects [8-10]. Research also indicates that preoperative

intravenous administration of hydromorphone in laparoscopic surgery effectively alleviates postoperative pain [11]. Furthermore, studies suggest that using hydromorphone for analgesia can effectively improve patients' postoperative immune function [12-13]. This study analyzed the effects of different doses of hydromorphone on gastrointestinal tumor surgery patients to determine the clinically appropriate dosage.

In this study, PI level was higher in S_1 compared with those in S_2, S_3 and S_4 in three groups, and Group A had a higher PI than Group B and Group C. This suggested that using 0.10 mg/kg or 0.12 mg/kg of hydromorphone for anesthesia, compared to 0.08 mg/kg, could effectively maintain the PI of gastrointestinal tumor surgery patients and minimally affect vasodilation. However, higher doses may lead to dependency and increase the risk of adverse reactions. Therefore, based on the study results, 0.10 mg/kg of hydromorphone is recommended for anesthesia in gastrointestinal tumor surgery patients.

This study also found that, two days after the surgery, the levels of 5-HT, SP in three group were significantly higher than those one day before surgery, and Group A had higher 5-HT and SP level than Group B and Group C. And there was no significant difference in the overall incidence of adverse reactions among the three groups. This suggested that using 0.10 mg/kg or 0.12 mg/kg of hydromorphone for anesthesia, compared to 0.08 mg/kg, effectively alleviates postoperative pain in gastrointestinal tumor surgery patients with high safety. Analysis indicates that hydromorphone acts on μ and κ receptors, effectively producing analgesia without inhibiting gastrointestinal function or respiration [14-15], and lower concentrations of hydromorphone do not achieve satisfactory analgesic effects. Furthermore, unclearly localized visceral pain may cause restlessness postoperatively, and hydromorphone effectively reduces visceral pain, providing good sedative effects, thereby reducing the risk of postoperative restlessness and adverse drug reactions, which benefits patient recovery [16-19]. Additionally, in this study, on 2nd and 4th day after surgery, the serum levels of DAO, D-lactate, and ET in three groups of patients decreased compared to 1st day after surgery, and Group A was lower than Group B and Group C. This suggested that using 0.10 mg/kg or 0.12 mg/kg of hydromorphone for anesthesia effectively maintains the stability of the intestinal barrier function in gastrointestinal tumor surgery patients postoperatively, while lower concentrations of hydromorphone meet the needs for protecting gastrointestinal barrier function. However, this study had a small sample size and insufficient data, and its exact efficacy awaits further validation through larger, randomized controlled trials.

In summary, compared to 0.08 mg/kg or 0.12 mg/kg of hydromorphone, using 0.10 mg/kg of hydromorphone for anesthesia effectively improves postoperative pain substances, PI levels, and maintains the stability of intestinal barrier function in gastrointestinal tumor surgery patients, with higher safety.

Conflict of Interest None

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·论　著·

不同剂量羟考酮对胃肠肿瘤手术患者术后致痛物质水平和组织灌注及肠道屏障的影响

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摘要：目的　探究胃肠肿瘤手术中应用不同剂量羟考酮麻醉对术后致痛物质水平、组织灌注及肠道屏障功能的影响。**方法**　选取 2020 年 6 月至 2023 年 1 月于六安市中医院接受手术治疗的 45 例胃肠肿瘤患者，随机分为 3 组，各 15 例。麻醉诱导过程中，A 组予以 0.08 mg/kg 羟考酮，B 组予以 0.10 mg/kg 羟考酮，C 组予以 0.12 mg/kg 羟考酮。分别于麻醉诱导前（S_1）、气管插管时（S_2）、手术开始后 30 min（S_3）、术毕（S_4）记录 3 组患者的血流灌注指数（PI），于术前 1 d 及术后 2 d 检测致痛物质［5-羟色胺（5-HT）、P 物质（SP）］水平，于术前 1 d 及术后 2、4 d 评估肠道屏障功能［二胺氧化酶（DAO）、D-乳酸、内毒素（ET）］，记录 3 组患者麻醉期间发生的不良反应情况。**结果**　S_2、S_3、S_4 时 3 组患者的 PI 水平较 S_1 均升高，且 A 组高于 B 组、C 组（$P<0.05$）；术后 2 d，3 组患者的血清 5-HT、SP 水平较术前 1 d 均升高，且 A 组高于 B 组、C 组（$P<0.05$）；术后 2、4 d，3 组患者的血清 DAO、D-乳酸、ET 水平较术前 1 d 均降低，且 A 组低于 B 组、C 组（$P<0.05$）。麻醉期间，A 组、B 组、C 组患者的不良反应总发生率（20.00%、26.67%、26.67%）相比差异无统计学意义（$P>0.05$）。**结论**　相较于 0.08 mg/kg 或 0.12 mg/kg 的羟考酮，采用 0.10 mg/kg 的羟考酮进行麻醉可有效维持胃肠肿瘤手术患者术后的致痛物质、PI 及肠道屏障功能的稳定性，且安全性较好。

关键词：羟考酮；胃肠肿瘤；致痛物质；血流灌注指数；肠道屏障功能
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Different doses of oxycodone on postoperative pain-causing substance levels and tissue perfusion and intestinal barrier in patients undergoing gastrointestinal cancer surgery

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Abstract: Objective　To investigate the impact of different doses of oxycodone on postoperative levels of pain-causing substances, tissue perfusion, and intestinal barrier in patients undergoing gastrointestinal tumor surgery. **Methods**　Forty-five patients with gastrointestinal tumors who underwent surgery at Lu'an Hospital of Traditional Chinese Medicine from June 2020 to January 2023 were selected and randomly divided into three groups, with 15 in each group. During the anesthesia process, group A received 0.08 mg/kg oxycodone, group B received 0.10 mg/kg oxycodone, and group C received 0.12 mg/kg oxycodone. The blood flow perfusion index (PI) was recorded at anesthesia induction (S1), endotracheal intubation (S2), 30 minutes after the start of surgery (S3), and at the end of surgery (S4). The levels of pain-causing substances [5-hydroxytryptamine (5-HT) and substance P (SP)] were detected 1 day before surgery and 2 days after surgery. The intestinal barrier function [diamine oxidase (DAO), D-lactic acid, and endotoxin (ET)] was assessed 1 day before surgery and 2 days and 4 days after surgery. Adverse reactions during anesthesia were recorded for the three groups. **Results**　The PI levels of the three groups at S2, S3, and S4 were significantly higher than those at

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S1, and in group A was higher than in groups B and C (P<0.05). On 2 days after surgery, the serum levels of 5-HT and SP in three groups were significantly higher than those before surgery, and in group A was higher than in groups B and C (P<0.05). On 2 days and 4 days after surgery, the serum levels of DAO, D-lactic acid, and ET in three groups were significantly lower than those before surgery, and in group A was lower than in groups B and C (P<0.05). The overall incidence of adverse reactions during anesthesia in groups A, B, and C (20.00%, 26.67%, 26.67%) showed no statistically significant difference (P>0.05). **Conclusion** Compared to 0.08 mg/kg or 0.12 mg/kg oxycodone, anesthesia with 0.10 mg/kg oxycodone can effectively maintain the stability of postoperative pain-causing substances, PI, and intestinal barrier function in patients undergoing gastrointestinal tumor surgery, with good safety.

Keywords: Oxycodone; Gastrointestinal cancer; Pain-causing substance; Blood perfusion index; Intestinal barrier function

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手术是临床治疗胃肠肿瘤的主要方式。而优质的麻醉方式是胃肠肿瘤手术顺利进行的先决条件,但术中长时间的麻醉可能使患者产生应激反应,还会影响胃肠道功能。因此,实施有效、合理的麻醉方式尤其重要。羟考酮为阿片受体激动剂,其生物利用度高、消除半衰期较长,可作用于中枢神经系统的μ受体和κ受体,有效抑制躯体疼痛及内脏疼痛[1-3]。致痛物质是痛觉下行调制系统的重要神经递质,其可间接提高伤害性感受器的兴奋阈值,使痛觉敏感化,并促进疼痛发展。组织灌注是指充足的血流量经过身体各器官血管以维持器官的功能,组织灌注不足会引起身体各器官缺血缺氧、代谢紊乱而导致功能受损。另外,由于肿瘤细胞的代谢特点,患者机体的能量、碳水化合物、脂肪及蛋白质代谢会出现很大程度的改变,进而使胃肠菌群失衡,导致胃肠屏障受损,且术后肠道蠕动恢复延迟会进一步加重营养不良。本研究分析不同剂量羟考酮对胃肠肿瘤手术患者术后致痛物质水平、组织灌注及肠道屏障的影响,以期为临床提供参考。

1　资料与方法

1.1　一般资料　选取 2020 年 6 月至 2023 年 1 月于六安市中医院接受手术治疗的 45 例胃肠肿瘤患者为研究对象,采用随机数字表法分为 3 组,各 15 例。麻醉诱导过程中,A 组予以 0.08 mg/kg 羟考酮,B 组予以0.10 mg/kg 羟考酮,C 组予以 0.12 mg/kg 羟考酮。3 组患者一般资料比较差异无统计学意义(P>0.05)。见表 1。本研究已获得医院伦理委员会的批准[审查编号:LASZYYLL-KY(SQ)-2023002]。

1.2　入选标准　纳入标准:(1) 符合胃肠肿瘤的诊断标准[4-5],并经胃镜或肠镜确诊;(2) 均接受胃肠肿瘤手术治疗;(3) 符合手术指征;(4) ASA 分级为Ⅰ~Ⅲ级;(5) 无严重器官衰竭;(6) 认知功能正常,无精神疾病史;(7) 治疗依从性良好,可正常沟通交流;(8) 预计生存期超过半年;(9) 临床资料完整;(10) 患者均自愿签署临床入组知情同意书。排除标准:(1) 合并重要脏器功能不全;(2) 合并感染性或传染性疾病;(3) 合并严重内分泌疾病;(4) 合并食管、胃肠道穿孔倾向;(5) 合并免疫、血液系统疾病;(6) 妊娠期或哺乳期妇女;(7) 合并其他恶性肿瘤;(8) 治疗依从性差,不能配合研究;(9) 阿片类药物依赖者。

1.3　方法　所有患者术前均禁食水 8 h。进入手术室后,建立静脉通路,监测生命体征。麻醉诱导:静脉推注地塞米松(焦作福瑞堂制药有限公司,国药准字 H41021269,规格 1 mL∶2 mg)5 mg+咪达唑仑(江苏恩华药业股份有限公司,国药准字 H20031071,规格 5 mL∶5 mg)0.05 mg/kg+丙泊酚(广东嘉博制药有限公司,国药准字 H20163406,规格 10 mL∶200 mg)1~2 mg/kg+舒芬太尼(江苏恩华药业股份有限公司,国药准字 H20203653,规格 10 mL∶50 μg)0.4 μg/kg+羟考酮(东北制药集团沈阳第一制药有限公司,国药准字 H20203622,规格 1 mL∶10 mg,A 组予0.08 mg/kg 羟考酮,B 组予 0.10 mg/kg 羟考酮,C 组予 0.12 mg/kg

表 1　3 组患者一般资料比较　(n=15)

Tab. 1　Comparison of general data among three groups　(n=15)

组别	男/女(例)	年龄(岁, $\bar{x}\pm s$)	BMI(kg/m^2, $\bar{x}\pm s$)	TNM 分期(Ⅰ/Ⅱ/Ⅲ,例)	疾病类型[a](例)	ASA 分级(Ⅰ/Ⅱ/Ⅲ,例)	手术方式[b](例)
A 组	8/7	61.58±11.25	22.63±1.28	3/7/5	7/4/4	4/8/3	3/4/4/4
B 组	9/6	61.28±11.42	22.76±1.33	4/6/5	6/5/4	5/7/3	3/3/5/4
C 组	7/8	61.87±11.64	22.59±1.41	4/7/4	6/4/5	4/7/4	2/4/4/5
χ^2/F 值	0.536	0.010	0.066	0.425	0.413	0.445	0.740
P 值	0.765	0.990	0.936	0.980	0.981	0.979	0.994

注:[a] 疾病类型为胃癌/结肠癌/直肠癌;[b] 手术方式为全胃切除术/远端胃癌根治术/结肠癌根治术/直肠癌根治术。

羟考酮，1 min 后静脉推注顺阿曲库铵（海南皇隆制药股份有限公司，国药准字 H20183355，规格 20 mg）0.2 mg/kg，待肌松起效后行气管插管。麻醉维持：静脉输注丙泊酚 1.5～2.5 μg/mL，持续吸入 1%～2%七氟烷（河北山姆士药业有限公司，国药准字 H20213791，规格 250 mL），维持脑电双频指数（BIS）45～55。术后镇痛：均予以镇痛泵自控镇痛，舒芬太尼 100 μg+帕洛诺司琼（昆明积大制药股份有限公司，国药准字 H20150034，规格 5 mL∶0.25 mg）0.25 mg+生理盐水（辰欣药业股份有限公司，国药准字 H20056758，规格 50 mL∶0.45 g）100 mL，速率 2 mL/h。

1.4　观察指标　（1）分别于麻醉诱导前（S_1）、气管插管时（S_2）、手术开始后 30 min（S_3）、术毕（S_4）测量并记录 3 组患者的血流灌注指数（PI）。（2）分别于术前 1 d 及术后 2 d 检测 3 组患者的致痛物质水平，采集患者的清晨空腹外周静脉血 3 mL，采用酶联免疫吸附法检测血清 5-羟色胺（5-HT）、P 物质（SP）水平。试剂盒购自优利科（上海）生命科学有限公司、福来德生物科技（武汉）有限公司，严格按照试剂盒流程操作。（3）分别于术前 1 d 及术后 2 d、4 d 评估 3 组患者的肠道屏障功能，采集患者的清晨空腹外周静脉血 3 mL，采用酶联免疫吸附法检测血清二胺氧化酶（DAO）、D-乳酸、内毒素（ET）水平，试剂盒分别购自武汉菲恩生物科技有限公司、上海佰利莱生物科技有限公司及上海佰利莱生物科技有限公司。（4）记录 3 组患者麻醉期间发生的不良反应情况。

1.5　统计学方法　采用 SPSS 25.0 软件分析数据。计量资料以 $\bar{x}\pm s$ 表示，采用单因素方差分析，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　3 组患者的 PI 对比　S_2、S_3、S_4 时 3 组患者的 PI 水平较 S_1 均明显升高，且 A 组高于 B 组、C 组（$P<0.05$）；而 B 组与 C 组相比差异无统计学意义（$P>0.05$）。见表 2。

2.2　3 组患者的致痛物质水平对比　术后 2 d，3 组患者的血清 5-HT、SP 水平较术前 1 d 均升高，且 A 组高于 B 组、C 组（$P<0.05$）；而 B 组与 C 组相比差异无统计学意义（$P>0.05$）。见表 3。

2.3　3 组患者的肠道屏障功能对比　术后 2、4 d，3 组患者的血清 DAO、D-乳酸、ET 水平较术前 1 d 均降低，且 A 组低于 B 组、C 组（$P<0.05$）；而 B 组与 C 组相比差异无统计学意义（$P>0.05$）。见表 4。

2.4　3 组患者的不良反应发生情况对比　麻醉期间，3 组不良反应总发生率相比差异无统计学意义（$P>0.05$）。见表 5。

表 2　3 组患者的 PI 对比　（$n=15$，$\bar{x}\pm s$）

Tab. 2　Comparison of levels of PI among three groups　（$n=15$，$\bar{x}\pm s$）

组别	S_1	S_2	S_3	S_4
A 组	4.27±0.76	5.67±0.84[a]	5.78±0.55[a]	5.89±0.48[a]
B 组	4.32±0.68	4.72±0.66[ab]	5.23±0.52[ab]	5.34±0.45[ab]
C 组	4.35±0.72	4.67±0.55[ab]	5.20±0.54[ab]	5.32±0.44[ab]

注：与同组 S_1 比较，[a]$P<0.05$；与 A 组比较，[b]$P<0.05$。

表 3　3 组患者的致痛物质水平对比　（$n=15$，$\bar{x}\pm s$）

Tab. 3　Comparison of levels of pain-causing substances among three groups　（$n=15$，$\bar{x}\pm s$）

组别	5-HT（nmol/L）		SP（nmol/L）	
	术前 1 d	术后 2 d	术前 1 d	术后 2 d
A 组	126.56±14.62	386.64±18.52[a]	33.67±5.24	57.64±6.59[a]
B 组	128.61±13.85	286.45±17.43[ab]	34.28±5.41	45.18±6.42[ab]
C 组	127.94±14.29	281.67±18.49[ab]	34.56±5.62	44.57±6.61[ab]

注：与术前 1 d 比较，[a]$P<0.05$；与 A 组比较，[b]$P<0.05$。

表 4　3 组患者的肠道屏障功能对比　（$n=15$，$\bar{x}\pm s$）

Tab. 4　Comparison of intestinal barrier function among three groups　（$n=15$，$\bar{x}\pm s$）

组别	DAO（u/L）			D-乳酸（mg/L）			ET（u/L）		
	术前 1 d	术后 2 d	术后 4 d	术前 1 d	术后 2 d	术后 4 d	术前 1 d	术后 2 d	术后 4 d
A 组	12.42±2.53	7.49±1.54[a]	5.52±1.24[a]	9.54±1.62	5.78±1.35[a]	4.73±1.24[a]	10.64±1.52	5.89±1.37[a]	5.14±1.27[a]
B 组	12.22±2.67	8.67±1.33[ab]	7.16±1.32[ab]	9.47±1.45	7.33±1.43[ab]	6.34±1.31[ab]	10.72±1.43	7.48±1.46[ab]	6.67±1.24[ab]
C 组	12.03±2.49	8.86±1.45[ab]	7.32±1.37[ab]	9.53±1.51	7.54±1.46[ab]	6.51±1.42[ab]	10.81±1.49	7.54±1.52[ab]	6.78±1.32[ab]

注：与术前 1 d 比较，[a]$P<0.05$；与 A 组比较，[b]$P<0.05$。

表 5　3 组患者的不良反应发生率对比　（例）

Tab. 5　Comparison of the incidence of adverse reactions among three groups　（case）

组别	例数	呼吸抑制	血氧饱和度下降	低血压	恶心呕吐	总发生[例（%）]
A 组	15	0	1	1	1	3（20.00）
B 组	15	0	1	2	1	4（26.67）
C 组	15	1	1	0	2	4（26.67）
χ^2 值						0.241
P 值						0.887

3　讨　论

全身麻醉是胃肠肿瘤手术的首选麻醉方式，但麻醉药物的使用及手术创伤均会刺激患者围术期出现应激反应，还可能会出现呼吸抑制、血压异常等药物不良反应，从而增加手术风险[6-7]，影响患者的恢复。羟考酮是临床上较为常见的强效镇痛药，属于纯阿片

受体激动药，其可激动中枢神经系统内的阿片受体，并降低中枢神经的兴奋性和敏感度，进而发挥显著的镇痛作用，尤其针对内脏止痛方面，且起效迅速，作用相对持久[8-10]。另有研究也证实，在腹腔镜手术前静推羟考酮，可有效缓解患者的术后疼痛[11]。还有研究指出，采用羟考酮镇痛可有效改善患者术后的免疫功能[12-13]。现本研究通过分析不同剂量羟考酮对胃肠肿瘤手术患者的影响，进而选择临床合适的用药剂量。

本研究结果显示，相较于 0.08 mg/kg 的羟考酮，采用 0.10 mg/kg 或 0.12 mg/kg 的羟考酮进行麻醉可有效维持胃肠肿瘤手术患者的 PI，且对血管扩张影响较小，但高剂量使用可能导致机体产生依赖性，甚至增加不良反应的发生风险。因此，推荐选择 0.10 mg/kg的羟考酮在胃肠肿瘤手术患者中进行麻醉。本研究还发现，相较于 0.08 mg/kg 的羟考酮，采用0.10 mg/kg或 0.12 mg/kg 的羟考酮进行麻醉可有效减缓胃肠肿瘤手术患者的术后疼痛，且安全性较高。分析是由于羟考酮能分别与 μ 受体及 κ 受体结合而发生激动作用，从而有效发挥镇痛作用，且可有效缓解内脏疼痛，不会抑制肠胃道功能或呼吸[14-15]，而较低浓度的羟考酮不能取得令人满意的镇痛效果。另有研究指出，定位不明确的内脏疼痛可能会导致患者术后出现躁动，而羟考酮可有效减轻内脏痛，且镇静效果良好，从而降低术后发生躁动的风险，并减少药物不良反应的发生，有利于患者的康复[16-19]。此外，本研究提示，相较于 0.08 mg/kg 的羟考酮，采用 0.10 mg/kg或0.12 mg/kg 的羟考酮进行麻醉可有效维持胃肠肿瘤手术患者术后的肠道屏障功能的稳定性，而较低浓度的羟考酮可以满足保护胃肠屏障功能的需求。但本研究纳入病例样本较少，数据存在一定不足，其确切疗效有待进一步大样本、随机临床对照研究进行论证。

综上所述，相较于 0.08 mg/kg 或 0.12 mg/kg 的羟考酮，采用 0.10 mg/kg 的羟考酮麻醉可有效维持胃肠肿瘤手术患者术后的致痛物质、PI 及肠道屏障功能的稳定性，且安全性较高。

利益冲突　无

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