Comparison of recovery effect for sufentanil and remifentanil anesthesia with TCI in laparoscopic radical resection during colorectal cancer

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Abstract. The aim of the present study was to compare the recovery of sufentanil and remifentanil anesthesia by target-controlled infusion (TCI) in elderly patients with laparoscopic-assisted radical resection of colorectal cancer. The effect of anesthesia on patient stress response and cellular immune function was also observed. Elderly patients (n=192) who underwent laparoscopic radical resection of colorectal cancer between July 2014 and October 2015 were randomly divided into the sufentanil and remifentanil groups (n=96 per group). The two groups used sufentanil- and remifentanil-based anesthesia by TCI. The wake-up time, extubation time, orientation recovery time, vital signs, stress response, distribution of T-cell subsets and incidence of adverse reactions were recorded and compared. The wake-up and extubation times of the remifentanil group were significantly shorter than those of the sufentanil group. The difference of orientation recovery time was not statistically significant. The differences in heart rate, mean arterial pressure, and arterial oxygen saturation following anesthesia and during surgery and those prior to anesthesia of the sufentanil group were not statistically significant. However, those of the remifentanil group significantly improved following anesthesia. The concentrations of glucose, cortisol (COR), and interleukin-6 and C-reactive protein were stable in the sufentanil group, whereas the indices in the remifentanil group had a tendency of increasing during the anesthesia and surgery, and had a longer postoperative recovery time. The decreasing degree of T-cell subsets in the sufentanil group was significantly lower than that in the remifentanil group, and had a short recovery of cellular immunity following surgery. The adverse reactions rate during anesthesia of the remifentanil group was significantly higher than that of the sufentanil group. In conclusion, sufentanil- and remifentanil-based anesthesia with TCI has certain advantages, including improved recovery effect, less stress response, less inhibition of cellular immunity and fewer adverse reactions. It has the potential to become the first choice of anesthetic in the clinic for elderly patients who undergo laparoscopic radical resection for colorectal cancer.

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Introduction

Colorectal cancer is one of the most common types of digestive tract tumors affecting 1.23 million individuals per year (9.7% of overall cancers) and is the fourth most common cause of mortality from cancer worldwide (608,000 cases, 8% of overall cancer deaths) (1). Currently, laparoscopic radical resection is the most widely used clinical treatment for colorectal cancer, however, it causes great discomfort for the patient (2). To improve the quality of anesthesia in the laparoscopic radical resection of colorectal cancer is a challenge for the medical field (3,4). Target-controlled infusion (TCI) is a new approach of anesthesia. TCI has the advantages of rapid drug delivery and simple operation (5). It has greatly improved the controllability and safety of clinical anesthesia, and has attracted increasing attention.

Sufentanil and remifentanil are opioid receptor agonists with a great analgesic effect during surgery (6-11). However, there are few comparative studies available on the application of the two agonists in the laparoscopic radical resection of colorectal cancer with TCI. The aim of the present study was to sufentanil and remifentanil anesthesia with TCI in the laparoscopic radical resection of colorectal cancer, and examine their impact on patient stress response and cellular immunity to provide a theoretical reference for clinical anesthesia.

Patients and methods

General information. A total of 192 elderly patients were selected to perform laparoscopic radical resection of colorectal cancer between July 2014 and October 2015. The patients included 106 males and 86 females, aged 62-81 years, with an average age of 74.3±3.1 years, and a weight of 54-82 kg, with an average weight of 67.6±2.5 kg. The selected cases were confirmed as colorectal cancer following colonoscopy and pathological examination. Patients who had previously used opioid drugs or had an allergy to sufentanil and remifentanil,

Table I. Comparison of the quality of anesthesia recovery in the two groups (min).

Group	No.	Wake-up time	Extubation time	Orientation recovery time
Sufentanil	96	17.3±7.7	23.5±2.6	16.4±3.6
Remifentanil	96	8.7±3.4	13.1±1.8	15.5±3.2
P-value		<0.01	<0.01	>0.05

Table II. Comparison of vital signs in the two groups (n=96).

Group	Vital signs	T_0	T_1	T_2	T_3	T_4
Sufentanil	HR, min	74±4	75±6[a]	77±4[a]	74±5	73±4
Remifentanil		75±3	82±7[b]	85±4[b]	74±6	73±5
Sufentanil	MAP, mmHg	93±6	91±8[a]	92±8[a]	93±6	93±7
Remifentanil		92±5	85±7[b]	87±6[b]	92±5	92±6
Sufentanil	SpO_2 (%)	95±2	94±3[a]	95±2[a]	94±6	95±1
Remifentanil		94±1	89±2[b]	91±3[b]	94±4	94±2

Compared with T_0, [a]P>0.05, [b]P<0.05. HR, heart rate; MAP, mean arterial pressure; SpO_2, arterial oxygen saturation.

or had serious damage of the heart, lung, liver, kidney function or other malignant tumor were excluded. The patients were divided randomly into the sufentanil and remifentanil groups (n=96 per group). The differences between the two groups with regard to gender, age and weight were not statistically significant (P>0.05), which was comparable.

Method. Prior to surgery, electrocardiogram and monitoring of vital signs were implemented in the two groups of patients, and an intramuscular injection of atropine (0.5 mg) and sodium phenobarbital (0.1 g) was performed. After 3 min of breathing with oxygen mask, rapid establishment of venous access and anesthesia induction was performed.

The sufentanil group used TCI sufentanil anesthesia (Langfang branch of Sinopharm Chemical Reagent Co., Ltd.; national medicine permission no. H20123298; Shanghai, China) at a concentration of 0.4 μg/l. Propofol was produced by Xi'an Libang Pharmaceutical Co., Ltd. (national medicine permission no. H20123318; Xi'an, China) at a concentration of 4 mg/l. Mechanical ventilation was carried out when plasma concentration of patients was in a state of equilibrium. During surgery, the concentration of propofol was controlled at 4 mg/l and rocuronium bromide, produced by Zhejiang Xianju Pharmaceutical Co., Ltd. (national medicine permission no. H20123188; Hangzhou, China), was injected continuously. The injection of sufentanil was ceased at the end of surgery.

The remifentanil group used TCI remifentanil anesthesia (Yichang Humanwell Pharmaceutical Co., Ltd.; national medicine permission no. H20030197; Yichang, China), at a concentration of 4.0 μg/l. The specific surgical process was the same as that of the sufentanil group. The injection of remifentanil was ceased at the end surgery. Temperature-holding nursing was implemented for the two groups. After patients regained their respiratory function and consciousness, catheters were removed and patients were sent to the recovery room.

Observation index. Observation indices were recorded for wake-up time, extubation time, orientation recovery time and adverse reactions, as well as vital signs [heart rate (HR), mean arterial pressure (MAP), arterial oxygen saturation (SpO_2)] prior to (T_0) and after (T_1) anesthesia, at the end of surgery (T_2) and 24 h after surgery (T_3), 72 h after surgery (T_4). The distribution of the stress response index [cortisol (COR), interleukin (IL)-6 and IL-10, glucose (GLU)] and T-lymphocyte subsets (CD3, CD4, CD8 and CD4/CD8).

Statistical analysis. SPSS 21.0 software (IBM SPSS, Armonk, NY, USA) was used for data analysis. Measurement data were presented as mean ± standard deviation and differences between the two groups were determined by the t-test. Enumeration data were presented as a percentage and comparisons between groups were made using the χ^2 test. P<0.05 was considered to indicate statistically significant results.

Results

Comparison of the quality of anesthesia recovery in the two groups. The wake-up and extubation times of the remifentanil group were significantly lower than those in the sufentanil group (P<0.01), and the difference of orientation recovery time in the two groups was not statistically significant (P>0.05; Table I).

Comparison of the changes of vital signs in the two groups. The differences of vital signs (HR, MAP, SpO_2) after the anesthesia (T_1) and at the end of surgery (T_2) were not statistically significant (P>0.05). However, the remifentanil group

Table III. Stress response indices in the two groups (n=96).

Group	Stress response index	T0	T1	T2	T3	T4
Sufentanil	COR, μg/l	205.71±19.42[a]	227.55±24.72[b]	245.23±27.51[b]	212.46±20.13[b]	207.58±19.32[b]
Remifentanil		205.36±21.62	231.68±23.41	256.45±26.15	236.92±23.84	211.37±21.19
Sufentanil	IL-6, pg/ml	46.52±3.17[a]	51.54±4.67[b]	64.17±5.22[b]	48.73±4.01[b]	47.67±3.72[b]
Remifentanil		47.12±3.24	57.14±5.13	71.76±6.21	57.58±4.51	52.12±4.03
Sufentanil	CRP, mg/l	4.35±0.33[a]	5.21±0.42[b]	6.12±0.53[b]	5.37±0.44[b]	4.82±0.37[b]
Remifentanil		4.31±0.34	7.87±0.75	9.17±0.67	10.75±1.16	6.54±0.77
Sufentanil	GLU, mmol/l	4.58±0.37[a]	4.75±0.48[b]	5.04±0.46[b]	4.51±0.42[b]	4.47±0.36[b]
Remifentanil		4.57±0.39	6.15±0.51	8.41±0.76	6.57±0.53	5.36±0.48

Comparison was made in the same period, [a]P>0.05, [b]P<0.05. COR, cortisol; IL, interleukin; CRP, C-reactive protein; GLU, glucose.

Table IV. Distribution of T lymphocyte subsets in the two groups (n=96).

Group	Immunoglobulin	T0	T1	T2	T3	T4
Sufentanil	CD3 (%)	60.74±5.28[a]	50.42±4.21[b]	47.16±3.73[b]	57.38±4.14[b]	60.37±5.13[b]
Remifentanil		60.28±5.14	47.76±4.73	44.22±3.28	50.42±4.76	55.62±5.58
Sufentanil	CD4 (%)	40.35±3.09[a]	37.42±2.84[b]	31.87±2.11[b]	33.59±2.83[b]	39.86±3.08[b]
Remifentanil		41.46±3.17	31.33±2.36	27.14±1.74	29.22±2.18	33.04±2.26
Sufentanil	CD8 (%)	26.15±1.74[a]	23.19±1.23[b]	22.27±1.09[b]	21.96±1.35[b]	24.67±1.55[b]
Remifentanil		25.92±1.66	21.62±1.08	19.24±1.73	20.62±1.74	21.74±1.34
Sufentanil	CD4 /CD8	1.57±0.07[a]	1.46±0.05[b]	1.37±0.04[b]	1.44±0.05[b]	1.47±0.06[b]
Remifentanil		1.55±0.06	1.27±0.03	1.13±0.02	1.27±0.04	1.31±0.05

Comparison was made in the same period, [a]P>0.05, [b]P<0.05.

Table V. Comparison of adverse reactions in the two groups.

Group	No.	Coughing	Dysphoria	Nausea and vomiting	Shivering	Adverse reactions rate, %
Sufentanil	96	5	3	6	9	25.0
Refentanil	96	12	10	10	15	49.0
P-value						<0.05

had obvious changes after anesthesia (T_1) and at the end of surgery (T_2) in that HR improved, whereas MAP and SpO_2 significantly decreased (P<0.05; Table II).

Comparison of stress response indices in the two groups. The concentration of GLU, COR, IL-6 and C-reactive protein (CRP) of patients in the sufentanil group maintained stability, while the indices in the remifentanil group exhibited an increasing trend during the process of anesthesia and surgery, with a longer recovery following surgery. The differences of indices of GLU, COR, IL-6 and CRP between the two groups in T_0 were not statistically significant (P>0.05). However, statistical significance was observed for (P<0.05) in T_1, T_2, T_3, T_4 (Table III).

Distribution of T-cell subsets in the two groups. The degree of reduction of T-lymphocyte subsets in the sufentanil group was lower than that in the remifentanil group, with the sufentanil group having a shorter recovery of cell immune function. The differences of indices of CD3, CD4, CD8, and CD4/CD8 between the two groups in T_0 were not statistically significant (P>0.05), whereas, there was statistical significance (P<0.05) for T_1, T_2, T_3, T_4 (Table IV).

Comparison of adverse reactions in the two groups. Adverse reactions rate in the sufentanil group during the wake-up process was significantly lower than that in the remifentanil group (P<0.05; Table V).

Discussion

Sufentanil is a type of narcotic drug and opioid receptor agonist, and contains citrate as the main pharmacological

component (2-4). Sufentanil is easily transferred through the blood-brain barrier with its high lipid solubility, and can bind with plasma protein for a good analgesic effect, with a longer interval for anesthesia (12,13). Refentanil as an opioid agonist is easily hydrolyzed in human tissues and blood, which has characteristics of rapid onset, short duration of anesthesia and no accumulation inside the human body (14).

The findings of the present study have shown that the wake-up and extubation times of the remifentanil group were significantly longer than those in the sufentanil group ($P<0.01$). The difference in orientation recovery time between two groups had no statistical significance ($P>0.05$). Sufentanil injection can be ceased at the end of surgery for its brief duration in the body and short biological half-life, which is controllable in the clinic.

Change of vital signs is an important indicator of surgical anesthesia. The present findings showed that the differences of HR, MAP, SpO_2 in T_1 and T_2 were not statistically significant in the sufentanil group compared with those prior to surgery ($P>0.05$). However, in the remifentanil group those parameters have obviously altered following surgery. HR increased significantly while MAP and SpO_2 decreased significantly in T_1 and T_2 compared with those prior to surgery ($P<0.05$). Therefore, sufentanil-based anesthesia with TCI maintains perioperative vital signs in a stable condition and hardly affected patient respiratory function and hemodynamics indices.

Radical resection for colorectal cancer leads to stress response in patients (15,16). Stress response is a non-specific defense reaction that occurs in the human body when externally stimulated. Previous findings (2,17,18) have shown that, stress responses initiated from anesthesia and surgery occur during the perioperative period, with a certain impact on recovery of patients following surgery. Serum COR and blood GLU can reflect t the intensity of stress response in the human body and IL-6 and IL-10 are important cytokines that are involved in the inflammatory response and injury repair and reflect the degree of human stress (19).

In the present study, the concentration of GLU, COR, IL-6 and CRP of patients in the sufentanil group maintained stability, whereas this concentration was increased during anesthesia and surgery in the remifentanil group, and the latter group had a longer recovery period following surgery. The differences of indices of GLU, COR, IL-6, and CRP for the two groups in T_0 were not statistically significant ($P>0.05$), but there was significance for T_1, T_2, T_3 and T_4 ($P<0.05$). This result suggested that sufentanil is able to maintain the blood GLU and COR in a stable condition and has much less stress response than remifentanil.

T lymphocytes and their subsets are the main immune active cells in the body's anti-tumor immunity, of which CD3 can effectively recognize the role of antigen, and is expressed on the surface of mature T lymphocytes. CD4 assists human B-cells to further differentiate and produce antibodies, while CD8 inhibits T-cell proliferation. CD4 and CD8 are expressed on the surface of suppressor cells and cytotoxic T lymphocytes (20-22). The degree of immune function disorder is defined by the ratio CD4/CD8. In the present study, the degree of reduction of T-lymphocyte subsets in the sufentanil group was significantly lower than that in the remifentanil group, with a rapid recovery of cellular immune function. The differences of indices of CD3, CD4, CD8, and the CD4/CD8 ratio in T_0 exhibited no statistical significance ($P>0.05$), whereas statistical significance was identified for T_1, T_2, T_3, T_4 ($P<0.05$). Thus, TCI of sufentanil anesthesia for laparoscopic radical resection for colorectal cancer effectively inhibits the cellular immune function, which recovers in a short time after surgery.

The present study analyzed adverse reactions in the process of wake-up and recovery. The results have shown that the incidence of adverse reactions, which include coughing and dysphoria, in the sufentanil group was significantly lower than that in the remifentanil group ($P<0.05$). Therefore, the TCI of sufentanil anesthesia is safe and reliable with few side effects. Thus, TCI of sufentanil anesthesia maintains stable hemodynamic and respiratory function and causes less stress response, less inhibition of cellular immunity and fewer side effects in its application. It thus has the potential to become the first choice of anesthesic to be used in the clinic for elderly patients who undergo laparoscopic radical resection for colorectal cancer and therefore may be promoted in the clinic.

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