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Effect of Dexmedetomidine on Perioperative Stress Response and Immune Function in Patients With Tumors

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Abstract

Objective: This study aims to investigate the effect of dexmedetomidine on perioperative stress response and immune function in patients with tumors. **Methods:** Sixty patients who underwent selective radical gastrectomy for cancer were randomly divided into 3 groups: remifentanil group (group R), dexmedetomidine group (group D), and sufentanil group (group S). Remifentanil, dexmedetomidine, and sufentanil were used as general anesthetics. Endotracheal intubation and mechanical ventilation were performed after the spontaneous respiration disappeared. Then, the data were recorded, and blood samples were collected at all time points. **Results:** The heart rate significantly increased ($P < 0.05$) at T1 in group S, and both heart rate and mean arterial pressure significantly increased ($P < 0.05$) in group R when compared to group D. The heart rate significantly increased ($P < 0.05$) at T2 in group S and group R. Furthermore, the heart rate significantly increased ($P < 0.05$) at T3 and T4 in group S and group R. Intra-group comparison: The heart rate at T1–T4 and mean arterial pressure at T1–T4 significantly increased ($P < 0.05$) in group S, and the heart rate at T1 and T4, and mean arterial pressure at T2–T4 significantly increased ($P < 0.05$) in group R when compared to T0. The serum IL-6, IFN-γ, and β-EP significantly increased ($P < 0.05$) at T0' in group S and group R when compared to group D. Blood glucose, and serum IL-10, IFN-γ, and β-EP significantly increased ($P < 0.05$), while IL-18 significantly decreased ($P < 0.05$) at T1' in group S and group R. **Conclusion:** Continuous infusion of dexmedetomidine in combination with the inhalation of sevoflurane is superior to sevoflurane + remifentanil or sufentanil in patients undergoing tumor surgery.

Keywords

dexmedetomidine, opioids, cytokines, immune function, hemodynamic stability

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Introduction

Surgical resection has become the major method used for most tumor treatments. However, the surgery and anesthesia itself also have a certain inhibitory effect on immune functions.[1] Immunosuppression and autoimmune surveillance may decrease prior to the operation in patients with malignant tumors. The postoperative immune function is closely associated with postoperative infection and the growth and metastasis of residual tumor cells.[1] The anxiety and tension before the operation may affect sleep and diet. It may also aggravate the stress reaction of patients with tumors, thereby inhibit their immune function. Hence, these may have a negative effect on the postoperative recovery and prognosis of tumors.[2] Both the emotional response before the operation and operational stimulation after starting the operation may cause a patient's

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sympathetic nervous system to become excited, thus increasing their blood pressure and heart rate. Perioperative hemodynamic fluctuations have adverse effects on cardiovascular and cerebrovascular diseases and increase the immunosuppressive state of the body. Cytokines are immunomodulatory bioactive factors secreted by immune cells. Therefore, cytokines can reflect the immune status of patients.[3] The anesthesia and operation may influence immune function.[4] For example, opioids may have a certain inhibitory effect on immune function by suppressing the activity of NK cells and the production of antibodies.[5] In addition, patients often suffer from severe pain after an operation. The pain-induced stress response has adverse effects on postoperative recovery and immune function.[5]

Therefore, it is of great significance for the prognosis of patients with tumors to correctly evaluate their physical condition before the operation and select appropriate anesthesia methods and drugs. This will reduce the inhibition of perioperative immune function in patients with tumors and regulate the perioperative immune function. Dexmedetomidine is a highly selective α-2-adrenoceptor agonist. It can inhibit the excitation of the sympathetic nervous system, reduce the release of norepinephrine, decrease the concentration of catecholamine in blood, and maintain the stability of circulation by activating the peripheral α-2-receptor.

Previous studies have shown that the combination of general anesthesia and epidural anesthesia can effectively reduce patients' immunosuppression. However, for patients who are not suitable for epidural anesthesia, the inhibitory effect of anesthesia on immune functions can be reduced by optimizing the anesthetic scheme and selecting appropriate anesthetics. In the present study, 3 general anesthesia methods were used for patients undergoing radical gastrectomy for cancer. These were to evaluate the effect of different anesthetic maintenance methods on immune functions during anesthesia, assess the advantages of dexmedetomidine, and provide guidelines for patients with tumors to choose suitable general anesthesia methods.

Methods

General Information of Patients

The Medical Ethics Committee approved the present study, and all patients and their family members provided signed informed consent. A total of 60 patients received radical gastrectomy for cancer. These patients were aged between 30–70 years, with an American Society of Anesthesiologists (ASA) grade I or II rating. Patients who suffered from hypertension, hypotension, diabetes mellitus, severe heart disease, sinus bradycardia and cardiac conduction block, severe liver function impairment, immune system diseases, or infectious diseases were excluded before the operation. Patients who recently received immunosuppressive agents, radiotherapy, or chemotherapy were also excluded. No blood transfusion was carried out during the perioperative period. These patients were randomly divided into 3 groups ($n = 20$, each group) using a random table method: remifentanil group (group R), dexmedetomidine group (group D), and sufentanil group (group S). Two patients in group D and group R and one patient in group S withdrew from the study. Therefore, 18 patients in group D, 18 patients in group R, and 19 patients in group S were included in the final statistical analysis.

Reagent

The dexmedetomidine hydrochloride injection was purchased from Jiangsu Hengrui Pharmaceutical Co. Ltd. (2091834). The penehyclidine hydrochloride (PHCD) injection was purchased from Chengdu List Pharmaceutical Co., Ltd. (11208). The midazolam injection was purchased from Jiangsu Nhwa Pharmaceutical Co., Ltd. (20120628). The sufentanil citrate injection was purchased from IDT Biologika GmbH, Germany (130315). The etomidate fat emulsion injection was purchased from Jiangsu Nhwa Pharmaceutical Co., Ltd. (20120905). The rocuronium bromide injection (Xianju) was purchased from Zhejiang Xianju Pharmaceutical Co., Ltd. (131102). The remifentanil hydrochloride for injection was purchased from Yichang Humanwell Pharmaceutical Co., Ltd. (6120610). The flurbiprofen ester injection was purchased from Beijing Tide Pharmaceutical Co., Ltd. (5013A). The dezocine injection was purchased from Yangtze River Pharmaceutical Group Co., Ltd. (13020221). The human IL-6, IL-10, IL-18, β-endorphin, and γ-INF ELISA kits were purchased from Bio-Swamp (Shanghai, China).

Anesthesia Method

After entering the operating room, the peripheral vein access of patients in the 3 groups was opened. Their vital signs were monitored and recorded, including blood pressure, electrocardiogram (ECG), pulse oxygen saturation, and bispectral index (BIS). Then, dorsal foot artery puncture with an indwelling catheter was performed under local anesthesia for invasive arterial blood pressure monitoring. In group D, 0.6–1.0 μg/kg of dexmedetomidine was continuously pumped in as the loading dose before the induction, and this was changed to 0.2–0.7 μg/(kg·h) for continuous pumping. According to the procedures, the dose was gradually reduced and stopped 30 minutes before the operation ended. In group R and group S, the same amount of 0.9% NS was pumped in 10 minutes before the induction. Then, 0.5–1.0 μg/(kg·min) of remifentanil was continuously pumped in until the end of the operation for patients in group R. In group S, sufentanil *iv* bolus was given according to the intensity of the surgical stimulation, which was at 5 μg each time. Anesthesia induction: Penehyclidine hydrochloride of 0.01 mg/kg, midazolam of 0.05 mg/kg, sufentanil of 0.25 μg/kg, etomidate of 0.03 mg/kg, and rocuronium of 0.6 mg/kg were successively intravenously injected. The patient's spontaneous breathing completely disappeared after 2 minutes, and treatment with endotracheal intubation and mechanical ventilation (TV = 8–10 ml/kg, RR = 13/min) was performed. The inhaled oxygen flow rate was adjusted to 0.8–1.0 L/min, and PETCO2 was controlled at 35–45 mmHg.

All patients in these 3 groups were given maintenance anesthesia by inhaling sevoflurane during the operation. The concentration was adjusted to 2%–4%, and the minimal alveolar concentration (MAC) of sevoflurane was maintained at 1.2–1.6. The dosage was adjusted according to the degree of stimulation. The inhalation was stopped at the end of the operation, and intermittent intravenous injections of rocuronium were given to maintain suitable muscle relaxation.

At 5 minutes before the skin incision, all patients in these 3 groups were given 10 μg of sufentanil to eliminate the pain stimulation of the skin incision. During the operation, 5 μg of sufentanil was given for adjuvant analgesia, according to the changes in vital signs. The mean arterial pressure (MAP) was maintained within 70–105 mmHg, and BIS was within 40–55 during the operation. Then, a crystalloid solution was given during the operation, according to the patient's specific condition. The plasma substitute was at a ratio of 2:1. If the blood pressure was too low (MAP < 70 mmHg), 5 mg of ephedrine was intravenously administered. If the heart rate (HR) was <50/min, 0.3–0.5 mg of atropine was intravenously administered. This was repeated when necessary. If HR was >100/min, 0.5 mg/kg of intravenous esmolol was given. If the MAP increased by more than 30% of the basic value, 20 mg of intravenous urapidil was given. At the end of the operation, these patients were extubated after awakening, sent to the recovery room after anesthesia, and observed for 1 hour. All patients in these 3 groups were treated using an AI Peng automatic injection pump for patient-controlled epidural analgesia (PCEA). The analgesic drugs included 250 mg of flurbiprofen axetil injection plus 25 mg of dezocine injection, diluted to 300 ml with normal saline. The PCEA was set with a background dose of 5 ml/h, a self-controlled dose of 3 ml/time, and a locking time of 15 minutes. These patients were followed up for 24 and 48 hours after the operation. The use of PCEA and the related adverse reactions were determined, and the PCEA dose adjusted accordingly.

Observation Index

The HR and MAP? values of patients in the 3 groups were immediately recorded at 10 minutes after going into the room and lying still (T0), immediately after tracheal intubation (T1), a minute after the skin incision (T2), a minute after intraperitoneal exploration (T3), and immediately after the extubation of the trachea catheter (T4). The blood glucose levels were recorded before the anesthesia induction (T0'), during the operation (immediate *in vitro* specimen) (T1'), immediately after extubation of the trachea catheter at the end of the operation (T2'), and at 1 hour after the operation (T3'). The levels of serum IL-6, IL-10, IL-18, INF-γ, and β-endorphin were measured by enzyme-linked immunosorbent assay (ELISA). The operation method of ELISA was carried out in strict accordance with the kit instructions. Postoperative follow-up and evaluation of pain (Numerical Rating Scale, NRS), as well as the drug dose in the PCEA, were performed.

The Numerical Rating Scale (NRS). The NRS was used to change the Visual Analog Scale (VAS), which was presented through numbers. The degree of pain was presented by 11 numbers of 0 to 10, in which 0 indicates no pain and 10 indicates the most painful. Furthermore, the patient is instructed to choose 1 of the 11 numbers to represent the degree of pain.

Performance
Anodynia
Mild pain, but tolerable.
The patient feels pain that affects sleep, but is tolerable
The patient has growing pain, which is intolerable, and affects appetite and sleep

The Richmond Agitation-Sedation Scale (RASS). Statistical

Performance	
Offensive	Violent
Very restless	Tries to remove the breathing tube, gastric tube, or needles
Agitated and anxious	Violent body movement, patient and ventilator dyssynchrony
Restless	Anxious or apprehensive, but the movements were not aggressive or vigorous
Awake and calm	Awake and in a natural state
Drowsy	Not fully awake, but has sustained awakening for more than 10 seconds
Minimal sedation	Briefly awakens for less than 10 seconds
Moderate sedation	Responds to voice
Severe sedation	Responds to physical stimulus
Coma	No response to voice or physical stimulus

Process

The data were analyzed using the SPSS 17.0 statistical software, and the measurement data were presented as mean ± standard deviation ($\bar{x} \pm s$). The variance analysis of repeated measurement data was used for comparisons within groups. The simple effect analysis was used to compare the differences between groups at each time point. The enumeration data were compared by Fisher's exact test or Chi-square tests. $P < 0.05$ was considered statistically significant.

Results

Comparison of General Data and Intraoperative Conditions Among the 3 Groups

As shown in Table 1, the difference in tumor stage, gender, age, height, weight, intraoperative blood loss, intraoperative fluid replacement, and urine volume among the 3 groups was not statistically significant ($P > 0.05$).

Comparison of Perioperative HR and Blood Pressure Among the 3 Groups

As shown in Figure 1, the results of the comparison among groups revealed that the difference in HR and MAP at T0 was

Table 1. Comparison of General Data and Intraoperative Conditions Among the 3 Groups.

Index	Group D (N = 18)	Group R (N = 18)	Group S (N = 19)	P
Gender				
Male	11	12	12	0.9404
Female	7	6	7	
Age (year)	57.28 ± 8.98	53.45 ± 8.85	54.37 ± 7.96	0.3829
Height (cm)	167.06 ± 8.99	168.06 ± 7.91	167.47 ± 8.04	0.9366
Weight (kg)	63.89 ± 13.77	65.61 ± 10.99	60.47 ± 10.19	0.4033
Tumor stage				
I	7	8	12	0.273
II	6	8	5	
III	5	1	2	
IV	0	1	0	
Anesthesia time (min)	219.72 ± 45.19	203.06 ± 28.91	201.05 ± 27.77	0.1439
Operative time (min)	177.78 ± 37.62	168.33 ± 27.65	165.26 ± 28.16	0.4596
Intraoperative fluid replacement (mL)	1947.22 ± 359.11	2072.22 ± 256.23	1836.84 ± 256.49	0.0603
Intraoperative blood loss (mL)	258.89 ± 80.21	282.78 ± 80.35	261.58 ± 81.36	0.6237
Urine volume (mL)	256.67 ± 139.66	300 ± 151.23	322.11 ± 117.60	0.343

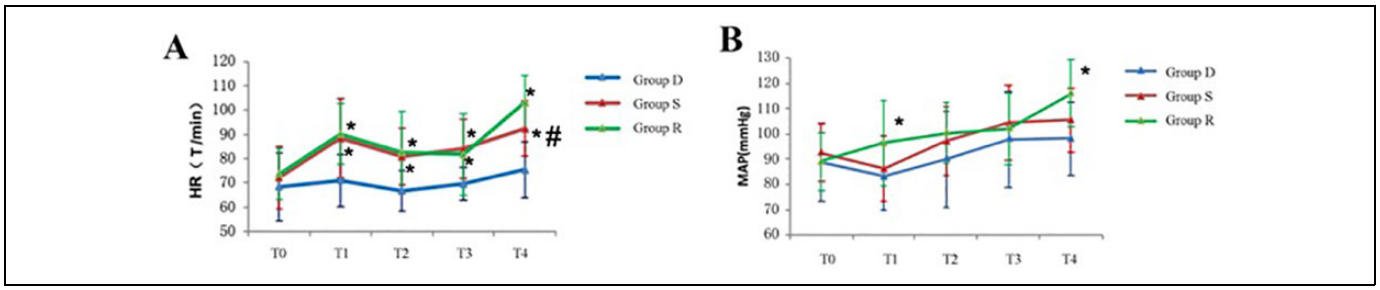

Figure 1. The change trend of HR and MAP during anesthesia among the 3 groups; (A) HR; (B) MAP. * Means there was a significant difference compared with group D (P < 0.05); Δ means there was a significant difference compared with group S (P < 0.05).

not statistically significant between group S and group R when compared to group D. The HR increased significantly ($P < 0.05$) at T1 in group S, and both HR and MAP increased significantly ($P < 0.05$) in group R. The HR increased significantly ($P < 0.05$) at T2 in group R and group S. The HR at T3 and T4 was significantly higher in group S and group R when compared to group D. The difference was statistically significant ($P < 0.05$).

The intra-group comparison results revealed that the difference in HR and MAP at each time point in group D was not statistically significant ($P > 0.05$). In group S, the MAP of HR at T1–T4 and MAP at T2–T4 increased significantly ($P < 0.05$) when compared to T0. In group R, the MAP of HR at T1–T4 and MAP at T2–T4 increased significantly ($P < 0.05$) when compared to T0.

Comparison of Perioperative Blood Glucose and Cytokines Among the 3 Groups

The perioperative blood glucose and cytokines in the 3 groups are presented in Figure 2.

The difference in blood glucose at T0' was not statistically significant among the 3 groups. The blood glucose at T1' and T3' in group S and at T1'–T3' in group R increased significantly ($P < 0.05$) when compared to group D. Blood glucose increased significantly ($P < 0.05$) at T2' in group R when compared to group S. Blood glucose increased at T1'–T3' among the 3 groups when compared to T0'. However, the blood glucose at each time point increased significantly in group S and group R, and the difference was statistically significant ($P < 0.05$).

The level of IL-6 gradually increased from T0'–T2' and decreased at T3' among the 3 groups. The changes in group S and group R were more significant (IL-6 increased at T2' and T3' in group S, and at T2' in group R) ($P < 0.05$) when compared to group D.

The difference in IL-10 at T0' was not statistically significant among the 3 groups. From T0' to T3', IL-10 gradually decreased in group D, while the other 2 groups exhibited an upward trend. The level of IL-10 at T1'–T3' increased ($P < 0.05$) in group S and group R when compared to group D. The level of IL-10 at T2' and T3' increased significantly ($P < 0.05$) in group R when compared to group S. In group D, IL-10 gradually decreased at T1'–T3' when compared to T0'. In group S and group R, IL-10 increased significantly ($P < 0.05$) at T1'–T3', when compared to T0'.

The difference in IL-18 at T0' was not statistically significant among the 3 groups. From T0' to T3', IL-10 exhibited a

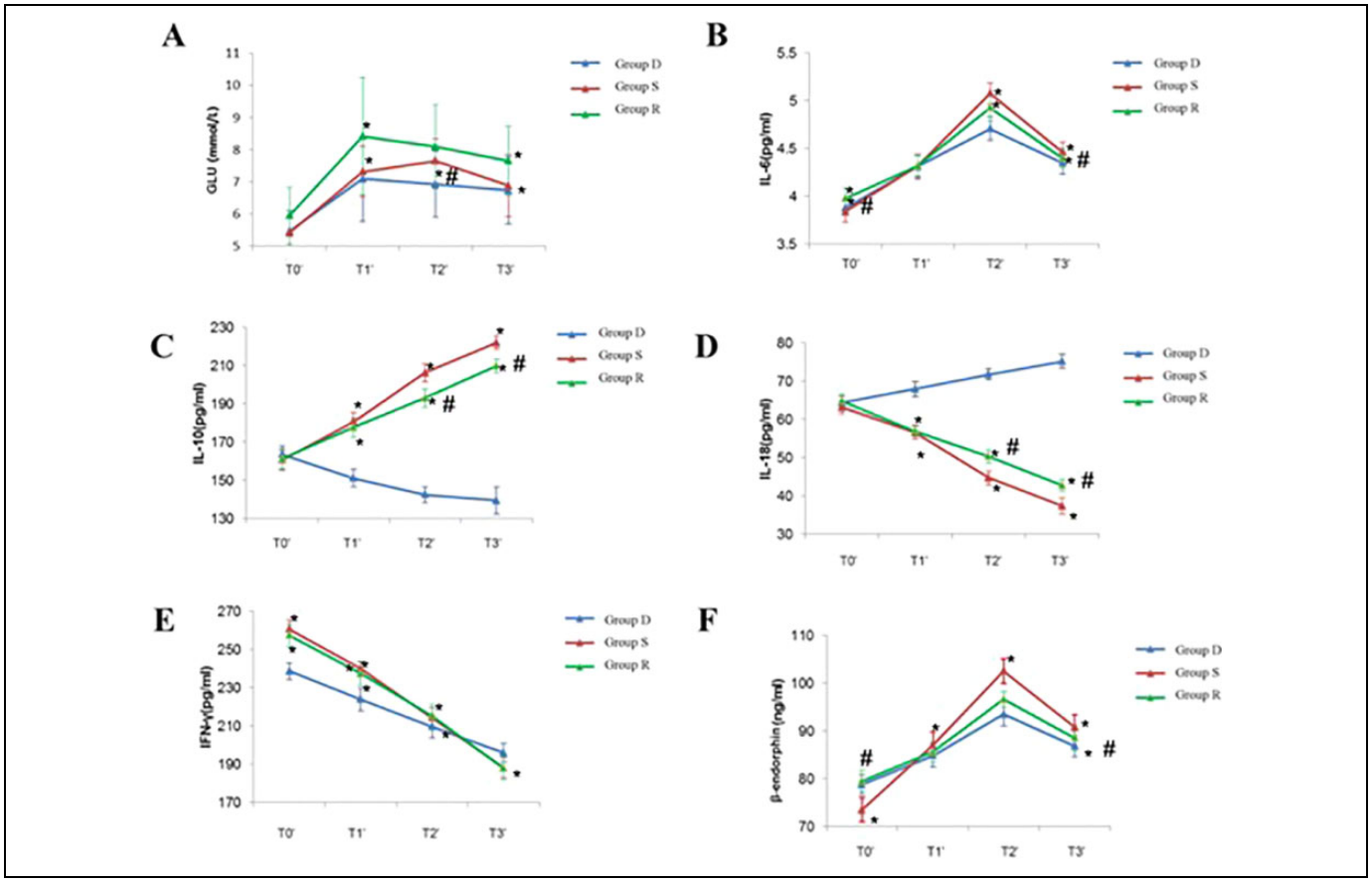

Figure 2. The change trend of blood glucose and cytokines during anesthesia among the 3 groups; (A) Blood glucose, (B) IL-6, (C) IL-10, (D) IL-18, (E) IFN-γ, (F) β-EP. * Means there was a significant difference compared with group D ($P < 0.05$); Δ means there was a significant difference compared with group S ($P < 0.05$).

gradual upward trend in group D, while the other 2 groups exhibited a decreasing trend. In group D, IL-10 increased significantly ($P < 0.05$) at T1'–T3', when compared to T0'. In group S and group R, IL-10 decreased significantly ($P < 0.05$) at T1'–T3', when compared to T0'.

IL-18 decreased at T1–T3 among the 3 groups when compared to T0, but this significantly decreased ($P < 0.05$) in group S and group R.

The β-enkephalin increased at T1'–T3' among the 3 groups when compared to T0', and β-enkephalin significantly increased ($P < 0.05$) at T1'–T3', when compared to group D.

Comparison of the Doses of Sufentanil in Group D and Group S

The dose of sufentanil was significantly lower in group D ($P < 0.001$) than in group S (39.58 $\pm$ 5.30 μg).

Comparison of Pain Scores and Agitation Scores Among the 3 Groups

As shown in Figure 3, the pain scores were significantly higher in group R ($P < 0.0001$) than in group D and group S. The agitation scores were significantly higher in group S and group R ($P < 0.0001$) than in group D.

Comparison of Postoperative Follow-Up Indexes Among the 3 Groups

As shown in Figure 3, the pain scores at 24 and 48 hours were significantly higher when compared to those in group D. The number of effective and total presses on the PCEA was significantly higher in group S and group R ($P < 0.05$) when compared to group D, within 24–48 hours after the operation. The PCEA dose was higher in group S and group R when compared to group D, and the dose was greater in group R when compared to group D, within 24–48 hours, but the difference was not statistically significant ($P > 0.05$).

Comparison of Adverse Reactions Within 48 Hours After the Operation Among the 3 Groups

Five patients in group D experienced nausea and vomiting. Six patients in group S and 6 in group R experienced nausea and vomiting within 48 hours of the operation. However, the

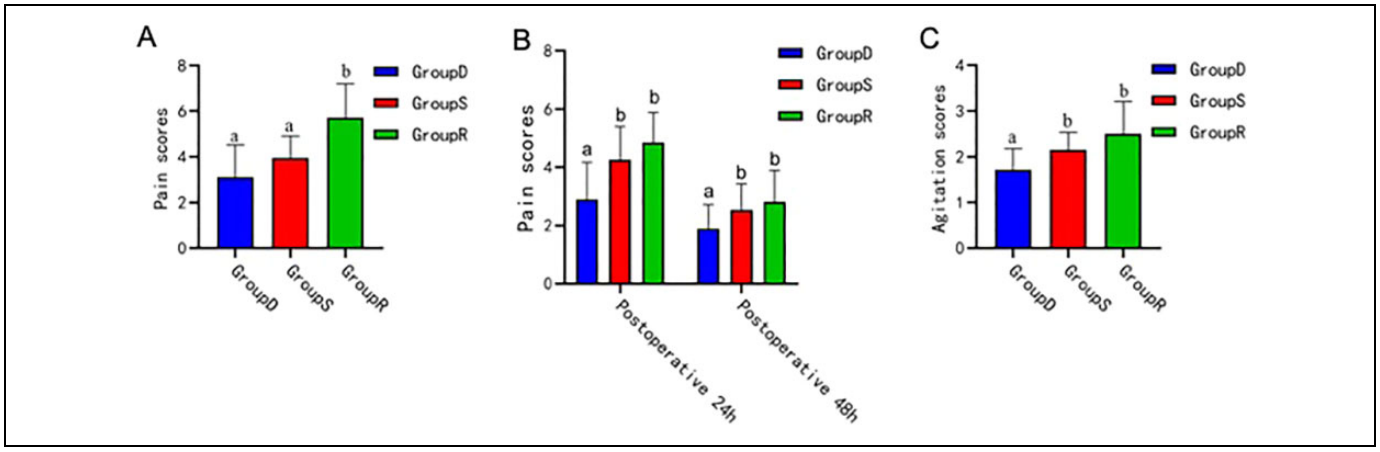

Figure 3. A and B, Comparison of pain scores and agitated scores between the 3 groups at the end of the surgery ($n_{D,\ R} = 18$, $n_S = 19$). B, Comparison of the pain scores between groups postoperatively ($n_{D,\ R} = 18$, $n_S = 19$). There were no significant differences between the groups with the same letter ($P > 0.05$). C, Comparison of the agitation scores between groups postoperatively ($n_{D,\ R} = 18$, $n_S = 19$).

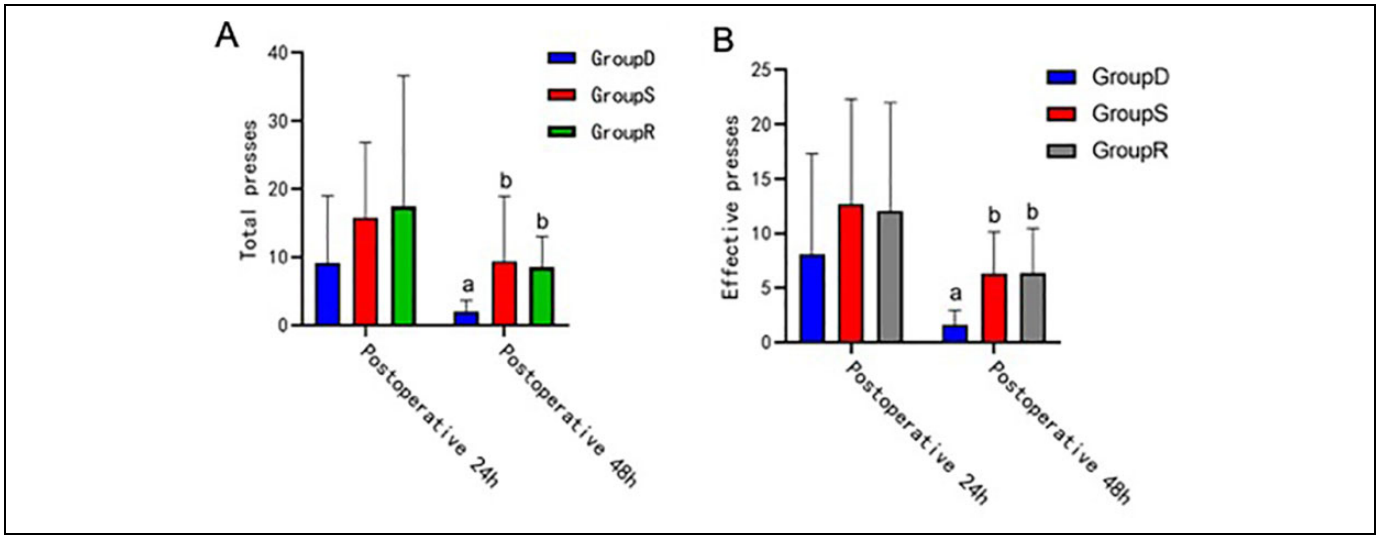

Figure 4. A, Comparison of the total presses between groups postoperatively ($n_{D,\ R} = 18$, $n_S = 19$). B, Comparison of the total presses between groups postoperatively ($n_{D,\ R} = 18$, $n_S = 19$). There were no significant differences between the groups with the same letter ($P > 0.05$).

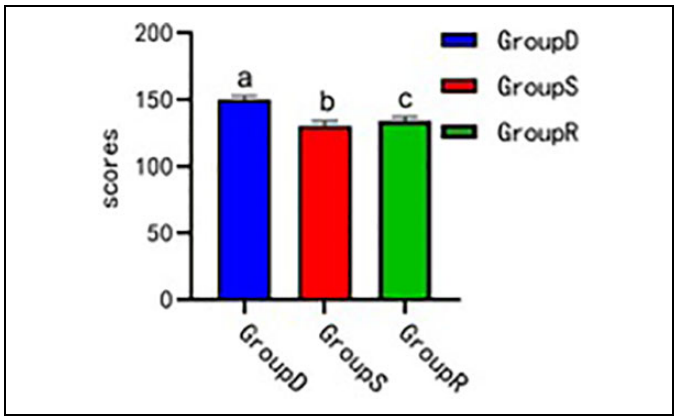

Figure 5. Comparison of the postoperative quality of recovery score (QoR-40) ($n_{D,\ R} = 18$, $n_S = 19$). There were no significant differences between the groups with the same letter ($P > 0.05$).

difference was not statistically significant ($P > 0.05$) among the 3 groups (Figure 4 and 5).

Recovery Rate

The QoR-40 scores at 72 h post-surgery are significantly different among the 3 groups ($^*P < 0.001$) and are also significantly different when comparing each group against another ($^*P < 0.001$).

Discussion

The study results show that blood pressure and HR fluctuated significantly during the operation in group S and group R, while the hemodynamics were stable in group D. This suggests that the continuous infusion of dexmedetomidine during the perioperative period can effectively inhibit sympathetic

nervous system excitation and maintain hemodynamic stability, thereby reducing the immunosuppression caused by circulatory fluctuations. The reason may be due to patients' emotional reactions before and after the operation and the skin incision and exploration of operational stimuli after the procedure started. These can cause sympathetic nervous system excitement, and an increase in catecholamine concentration in the blood, resulting in an increase in blood pressure and HR. Perioperative hemodynamic fluctuations not only have adverse effects on cardiovascular and cerebrovascular diseases but also increase the immunosuppressive state of the body. Dexmedetomidine is a highly selective α-2-adrenoceptor agonist. It can inhibit the excitation of the sympathetic nervous system, reduce the release of norepinephrine, decrease the concentration of catecholamine in blood, and maintain the stability of circulation by activating the peripheral α-2-receptor.

In the present study, the blood glucose level increased during the perioperative period among the 3 groups. However, the blood glucose level in group S and group R increased significantly during the operation. The blood glucose level in group D also increased, but less significantly. This may be due to the anti-sympathetic effect of dexmedetomidine, which weakens the stress response of the surgical stimulation and induces the perioperative blood glucose level to change slightly.

The reason for this is because patients with tumors are often in a highly stressed state. Before the operation, these patients' anxiety and tension affect their sleep and diet, aggravating their stress reaction. An excessive stress response can inhibit the immune function of patients and induce adverse effects on the postoperative recovery and prognosis of patients with tumors.[6-8] The function of the adrenal cortex in the body is enhanced under a stress state, and strong stress reactions can increase the concentration of cortisol in the blood. This can cause blood sugar to increase and induce abnormal body metabolism. Studies have confirmed that elevated blood glucose can be deemed an important feature of the surgical stress response.[9] The β-endorphin is the endogenous opioid peptide in the body, which is associated with stress reactions, and this has an important immunomodulating effect. The concentration of β-endorphin in the blood increases through the activation of the hypothalamic-pituitary-adrenal axis under a stress state. The experimental results show that the concentration of β-endorphin initially increased and subsequently decreased among the 3 groups. The concentration of β-endorphin was higher in group S and group R when compared to group D. The action of the sympathetic-adrenal cortex system may be affected due to the inhibition of sympathetic activity by dexmedetomidine, thereby effectively reducing the stress response.

Cytokines are biologically active factors secreted by immune cells, which have an immunoregulation effect. The *in vivo* cytokine level reflects the state of the cellular immune function of the body. Therefore, the cytokine changes were also investigated. The study results reveal that serum IL-6 gradually increased during the operation and subsequently decreased after the operation among the 3 groups. The level of IL-6 changed significantly in group S and group R when compared to group D. However, the concentration of IL-10 at each time point gradually decreased in this group and increased in the other 2 groups. Furthermore, the concentration of IL-10 at the same time point was higher in group S and group R when compared to group D. This suggests that dexmedetomidine hydrochloride may effectively inhibit perioperative overstress and reduce the inhibition of immune function by activating the postsynaptic α-2-receptor, thereby reducing the sympathetic activity and affecting the action of the hypothalamic-pituitary-adrenal axis. IL-6 is a major cytokine in the acute phase reaction. This has a variety of biological activities. It has an important regulatory effect on cellular immunity and closely correlates to tumor occurrence and development.[10] When the body is under stress, IL-6 can increase the secretion of corticotropin-releasing hormones and activate the hypothalamic-pituitary-adrenal axis mediated by the adrenoceptor. IL-10 is an immunosuppressive factor, which inhibits cellular immune function through various mechanisms, and this increases after stress reactions, such as surgical trauma.[11] In addition, the serum concentration of IFN-γ exhibited a downward trend among the 3 groups, but this decreased more significantly in group S and group R. Since IFN-γ is a key medium to initiate phagocytosis and bactericidal effects,[12] this also has strong anti-tumor and immunomodulatory effects. These results show that the perioperative application of dexmedetomidine weakens the cellular immunosuppression of patients with tumors and has a protective effect in maintaining the stability of cytokine levels in patients with gastric cancer. In comparing patients in group R with group S, patients in group R presented with little effects on immunosuppression. It was also found that the concentration of IL-18 gradually decreased in group S and group R, while this exhibited an upward trend in group D. This indicates that dexmedetomidine may also reduce the inhibitory effect of anesthesia on IL-18 expression and enhance an inhibitory function mechanism on tumor growth for patients with tumors. However, the specific mechanism needs to be investigated further. IL-18 plays an important role in regulating both innate and acquired immune responses, and this is closely associated with the occurrence and development of tumors.[13] The anti-tumor immunity of the body is mainly cellular immunity, and this occurs primarily through the inhibitory effect of NK cells on tumor cells. IL-18 can induce the maturation of NK cells and mediate the anti-tumor immunity of NK cells *in vivo*. Furthermore, patients with tumors have low immune functions, and the anesthesia and operation would further affect their immune function.[14] It has been confirmed that opioids have a certain inhibitory effect on the immune function by suppressing the activity of NK cells and the production of antibodies.[15] In the present study, the dose of sufentanil in group D and group S was compared, and the results reveal that the dose of opioids in group D decreased significantly. This suggests that the analgesic effect of dexmedetomidine can effectively reduce the dose of opioids. This may help relieve the inhibitory effect on perioperative immune functions and protect the immune function to a certain extent.

Patients often suffer from severe pain after an operation. This pain-induced stress response has adverse effects on postoperative recovery and immune functions.[16] The use of PCEA after an operation can effectively relieve postoperative pain. In the present study, these patients were followed up for 48 hours after their operation. The results reveal that the agitation scores at the end of the operation and postoperative pain scores were significantly lower in group D when compared to group S and group R, and the number of presses on the PCEA decreased significantly. This shows that the sedative and analgesic effects of dexmedetomidine could effectively reduce the occurrence of emergence agitation, relieve postoperative pain, and prolong the action time of painkillers, thereby relieving the suppression of pain-related immune function and improving the postoperative recovery of patients. The number of patients with nausea and vomiting, which occurred within 48 hours after the operation, were compared among the 3 groups, and the difference was not statistically significant. Nausea and vomiting are probably correlated to the surgical stimulation, placement of the gastric tube, and recovery of gastrointestinal function because all 3 groups of patients received gastric surgery, and the gastric tube was retained after the operation.

The results showed that the comfort and postoperative recovery of the dexmedetomidine group were significantly better than those of the sufentanil group and the remifentanil group. This was related to the effect of dexmedetomidine on relieving respiratory depression and anxiety, which auxiliary confirmed the advantages of dexmedetomidine in perioperative applications.

There are still some limitations to the present study. First, patients in group S have not continuously pumped the sufentanil during the anesthesia maintenance period and were changed to intermittent *iv* bolus, which may cause human errors in the comparative investigation. However, considering the long metabolic time of sufentanil, the delayed recovery may have been caused by not stopping the drug in time. In the present study, drug metabolism was good by the end of the operation, and this did not affect the recovery time of patients. Second, the detection time range of serum factors was narrow, and no blood samples were collected at 24 and 48 hours after the operation. The reason was that the blood samples were collected only during the controllable anesthesia. This was done so the study results would not be affected since the postoperative conditions of patients with gastrointestinal tumors differ, and the postoperative management is diverse. Hence, further in-depth studies are needed to improve the study design and allow for the selection of more suitable types of diseases.

Conclusion

In conclusion, compared with the 3 intravenous inhalational anesthesia methods, the sevoflurane combined with dexmedetomidine method used in the general anesthesia exhibited a significant effect in stabilizing the hemodynamic indexes during the perioperative period. It reduced the emergence agitation, decreased the postoperative pain, and cut down the dose of opioid analgesics, thereby effectively reducing the stress reaction of patients undergoing radical gastrectomy for cancer, and improved the immunosuppression state of patients with tumors. This will be beneficial for the postoperative recovery of these patients and improve their prognosis.

Authors' Note

Lihong Zheng and Juan Zhao contributed equally to this study. All participants signed a document of informed consent. I confirm that I have read the Editorial Policy pages. This study was conducted with approval from the Ethics Committee of Harbin Medical University Cancer Hospital (approval no. KY2014-03). This study was conducted in accordance with the declaration of Helsinki. All patients provided written informed consent prior to enrollment in the study.

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