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Application of Dexmedetomidine in Surgical Anesthesia for Gastric Cancer and Its Effects on IL-1β, IL-6, TNF-α and CRP

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ABSTRACT

This study was performed to analyze the application of dexmedetomidine (Dex) in anesthesia for gastric cancer surgery and its effect on serum inflammatory factors in patients. In this regard, a total of 78 patients with gastric cancer who were hospitalized in our hospital from January 2020 to September 2023 and received general intravenous anesthesia were randomly divided into two groups (n=39 in each group). The conventional group was given the same volume of 0.9% sodium chloride solution 10min before induction of anesthesia, and the Dex group was given Dex1μg/kg intravenous pump 10min before induction of anesthesia. The hemodynamics, serum levels of IL-1β, IL-6, TNF-α, CRP, propofol, remifentanil, and the total incidence of adverse reactions were compared between the two groups at different periods. The results showed that the mean arterial pressure (MAP), heart rate (HR), serum IL-1β, IL-6, TNF-α and CRP in the Dex group were compared with those in the routine group (P>0.05). MAP and HR in T1, T2 and T3Dex groups were lower than those in the conventional group (P<0.05). The serum levels of IL-1β, IL-6, TNF-α and CRP in T4 and T5 of the Dex group were lower than those of the routine group (P<0.05). The dosage of propofol and remifentanil in the Dex group was lower than those in the conventional group (P<0.05). The total incidence of adverse reactions in the Dex group (5.13%) was compared with that in the conventional group (10.26%), P>0.05. It was concluded that Dex can effectively maintain the stability of hemodynamics during gastric cancer surgery, reduce the dosage of propofol and other anesthetic drugs, reduce inflammation, and has a certain safety without obvious adverse reactions.

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Introduction

Gastric cancer is clinically a common gastrointestinal malignancy characterized by high morbidity and mortality, and recently, it has had a significantly increased incidence rate in China (1). At present, gastric cancer is mainly treated by radical surgery to remove tumor lesions and prolong patients' survival. However, it is more traumatic, and is, therefore, more prone to induce biochemical and physiological changes, such as releasing a large amount of interleukins and other inflammatory factors, thus damaging relevant organs and tissues and affecting postoperative recovery (2,3). Dexmedetomidine (Dex) is an α2-adrenergic agonist with hypnotic, analgesic, sympathetic, anxiolytic, and sedative effects, and functions effectively for general anesthesia adjuncts and local sedation (4,5). To investigate the application of Dex in surgical anesthesia for gastric cancer and its effects on blood interleukin-IL-1β (IL-1β), interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α) and C-reactive protein (CRP), 78 gastric cancer patients who underwent general intravenous anesthesia after being hospitalized from January 2020 to September 2023 in our hospital were recruited in this study.

Materials and Methods

General data

Seventy-eight patients undergoing general intravenous anesthesia for gastric cancer who were hospitalized in our hospital from January 2020 to September 2023 were enrolled and grouped by randomization (n=39). The Dex group contained 20 males and 19 females aged from 42 to 76 years, with a mean age of (59.82 ± 5.04) years. The diameter of the lesions ranged from 1.3 to 3.7 cm, with a mean of (2.52 ± 0.29) cm. According to the American Society of Anesthesiologists (ASA), 15 cases were classified into Grade I, 24 cases into Grade II. The operative time ranged from 232 to 300 min, with a mean of (265.18 ± 9.46) min. In the Dex group, there were 18 cases in TNM stage I, 21 in TNM stage II. In terms of pathological type, there were 30 cases of non-Indo-Rong cell carcinoma, and 10 of Indo-Rong cell carcinoma. Their body mass index (BMI) varied from 20 to 28 kg/m^2, with a mean of (24.11 ± 0.67) kg/m^2. The conventional group had 18 males and 21 females aged between 45 and 74 years, with a mean of (59.72 ± 5.11) years. The lesion diameter ranged from 1.6 to 3.4 cm, with a mean of (2.56 ± 0.24) cm. According to ASA classification, there were 13 cases in Grade I, and 26

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in Grade II. The operative time ranged from 252 to 298 min, with a mean of (264.82 ± 10.37) min. Furthermore, 22 cases were classified into TNM stage I, and 17 in stage II. In terms of pathological type, there were 33 cases of non-Indo-Rong cell carcinoma, and 6 of Indo-Rong cell carcinoma. Their BMI varied from 21 to 27 kg/m^2, with a mean of (24.18 ± 0.62) kg/m^2. P>0.05 in comparison of general data between the two groups. The study was approved by the ethics committee of the hospital.

Inclusion criteria: A. The patients met the diagnostic criteria for "gastric cancer" in the CMA Clinical Guidelines for the Diagnosis and Treatment of Gastric Cancer (2021) (6). B. All were classified into ASA Grade I-II. C. Both men and women > 18 years old. D. All were treated with radical gastric cancer for the first time. E. All met the indications for anesthesia and surgery. F. Their clinical data were complete. Exclusion criteria: A. Those with puncture site infection. B. Those with abnormal kidney and liver functions. C. Pregnant and lactating women. D. Those with combined heart failure, cerebral infarction and other diseases. E. Participants in other studies at the same time. F. Those with a history of alcohol abuse, drug use, or long-term opioid use. G. Those with immunodeficiency. H. Those with preoperative cognitive dysfunctional disorders such as mania. I. Those with impaired coagulation mechanisms. J. Those with a history of chronic malnutrition.

Methods

All patients were fasted from food and water for 12h before surgery and monitored with an electrocardiogram (ECG) after admission to the room. Induction of anesthesia: The patients were anesthetized by administration of midazolam (0.05-0.10 mg/kg), sufentanil citrate injection (0.3 μg/L), cisatracurium (0.15-0.20 mg/kg), propofol (1.5-2.0 mg/kg) through intravenous drip for tracheal intubation and mechanical ventilation with the following parameter settings: respiratory ratio: 1:2, tidal volume (VT): 8-10 mL/kg, air flow: 2L/min, the pulse rate: 12-14 BPM, and oxygen flow: 2L/min. Anesthesia maintenance: The patients received a continuous infusion of remifentanil (7-12 μg/kg-h) and cisatracurium (0.1-0.2 mg/kg-h) to maintain SPO2 at 98%, inhaled oxygen concentration (FiO2) at 0.8-1.0, and partial pressure of carbon dioxide in end-expiratory gas (PETCO2) at 35-45 mm Hg. The rate of drug infusion was adjusted according to intraoperative hemodynamics, and remifentanil, cisatracurium, and propofol were discontinued 10 min before suturing the skin. The tracheal tube was removed when the patient opened their eyes, became conscious, and was breathing on his own with SPO2 >95%. Dex was given intravenously pumped at 1 μg/kg 10 min before induction of anesthesia in the Dex group, while an equal amount of 0.9% sodium chloride solution was pumped 10 min before induction of anesthesia in the conventional group.

Observation indexes and evaluation criteria

(I) Hemodynamics: This includes mean arterial pressure (MAP) and heart rate (HR) at T0 (10 min before induction of anesthesia), T1 (immediately after tracheal intubation), T2 (at the time of skin incision), T3 (at the end of surgery). In this study, the average data of three consecutive measurements was recorded as the final value. (II) Serum IL-1β, IL-6, TNF-α, and CRP: 5mL of fasting venous blood was drawn from patients at T0, T4 (12h postoperatively) and T5 (24h postoperatively), centrifuged for 10min at 4000r/min with a centrifugal radius of 8 cm, and then detected by ELISA. (III) Propofol and remifentanil dosage. (IV) The overall incidence of adverse reactions: The overall incidence of hypertension, nausea and vomiting, hypotension, respiratory depression, and bradycardia was counted.

Statistical methods

The data were processed with SPSS 26.0 software, of which the measurement data were subjected to *t*-test and expressed as $\bar{x}\pm s$, while the count data were subjected to χ^2 test and expressed as [n/(%)]. P<0.05 indicated a difference by comparison.

Results

Hemodynamic comparison

P>0.05 by comparison of T0MAP and HR between the Dex group and the conventional group; MAP and HR at T1, T2, and T3 in the Dex group were lower than those in the conventional group (P<0.05, Figure 1 and Table 1).

Comparison of serum IL-1β, IL-6, TNF-α and CRP

P>0.05 in comparison of IL-1β, IL-6, TNF-α, and CRP between the Dex group and the conventional group at T0. At T4 and T5, the Dex group had lower IL-1β, IL-6, TNF-α, and CRP levels than the conventional group (P<0.05, Figure 2 and Table 2).

Comparison of propofol and remifentanil dosage

The Dex group was given lower dosages of propofol and remifentanil than the conventional group (P < 0.05,

Table 1. Hemodynamic Comparison ($\bar{x}\pm s$).

Item	Group	Cases (n)	T_0	T_1	T_2	T_3
MAP (mmHg)	Dex	39	86.25±5.11	86.82±6.25	87.11±4.26	85.28±3.85
	Conv	39	86.33±5.29	96.82±8.16	99.28±8.16	90.46±4.17
	t	--	0.068	6.076	8.257	5.700
	P	--	0.946	0.000	0.000	0.000
HR (BPM)	Dex	39	66.28±3.16	69.52±4.25	70.16±5.11	67.88±5.16
	Conv	39	66.38±3.26	83.62±8.14	90.52±9.46	83.62±8.37
	t	--	0.138	9.589	11.826	9.997
	P	--	0.891	0.000	0.000	0.000

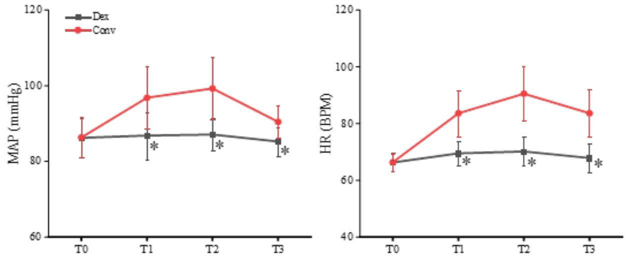

Figure 1. Hemodynamic Comparison of MAP and HR for the Dex and conventional groups. Note: $^{*}P<0.05$ *vs.* the level of the Conv group.

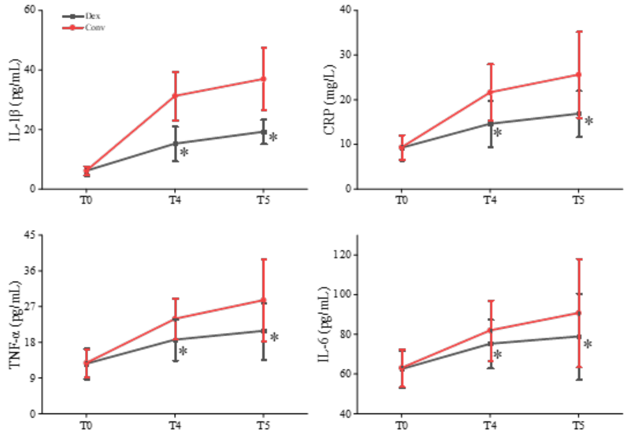

Figure 2. Comparison of serum IL-1β, IL-6, TNF-α, and CRP between the Dex and conventional groups. Note: $^{*}P<0.05$ *vs.* the level of the Conv group.

Table 3).

The overall incidence of adverse reactions

The overall incidence of adverse reactions in the Dex group was 5.13%, compared with 10.26% in the conventional group (P>0.05, Table 4).

Discussion

According to the survey, nearly 900,000 people die of gastric cancer worldwide every year, and the incidence is increasing year by year due to people's lifestyle, increased work pressure, changes in diet structure and Helicobacter pylori (HP) infection, with as many as 400,000 people developing gastric cancer each year (7). General intravenous anesthesia is mostly used in radical surgery, comprising operations such as tracheal intubation during anesthesia. That would stimulate the sympathetic nerves, and induce strong stress reactions, hemodynamic changes and frequent brain electrical activities, which have adverse effects on the cardiovascular system and the smooth progress of surgery (8,9). In addition, patients who undergo radical surgery generally experience a certain amount of pain, mechanical stress in the gastrointestinal tract and local tissue damage, which will release a large amount of inflammatory mediators, increasing the incision infection, lung infection and other complications rates (10,11). Therefore, it is especially important to strengthen anesthesia management, maintain stable vital signs and reduce the inflammatory response of the organism during radical surgery.

The present study showed that at T1, T2, and T3, MAP

Table 2. Comparison of serum IL-1β, IL-6, TNF-α, and CRP between the Dex and conventional groups ($\bar{x}$±s).

Item	Group	Cases (n)	T_0	T_4	T_5
IL-1β (pg/mL)	Dex	39	6.16±1.55	15.26±5.82	19.25±4.08
	Conv	39	6.18±1.46	31.26±8.14	36.99±10.46
	t	--	0.059	9.985	9.867
	P	--	0.953	0.000	0.000
CRP (mg/L)	Dex	39	9.26±2.82	14.62±5.17	16.88±5.16
	Conv	39	9.33±2.76	21.66±6.28	25.62±9.64
	t	--	0.111	5.405	4.992
	P	--	0.912	0.000	0.000
TNF-α (pg/mL)	Dex	39	12.62±3.82	18.66±5.18	20.88±7.14
	Conv	39	12.82±3.49	23.92±5.17	28.62±10.34
	t	--	0.241	4.488	3.847
	P	--	0.810	0.000	0.000
IL-6 (pg/mL)	Dex	39	62.52±9.34	75.26±12.25	78.99±21.62
	Conv	39	63.11±9.42	81.99±15.17	90.82±27.24
	t	--	0.278	2.155	2.124
	P	--	0.782	0.034	0.037

Table 3. Comparison of propofol and remifentanil dosage between the Dex and conventional groups ($\bar{x}$±s, mg).

Group	Cases (n)	Propofol	Rifentanil
Dex	39	958.26±152.66	3.09±0.52
Conv	39	1446.99±284.62	4.98±1.25
t	--	9.450	8.718
P	--	0.000	0.000

Table 4. Comparison of the overall incidence of adverse reactions between the Dex and conventional groups [n/(%)].

Group	Cases (n)	Nausea & vomiting	Hypotension	Hypertension	Respiratory depression	Bradycardia	Overall incidence
Dex	39	0 (0.00)	1 (2.56)	0 (0.00)	1 (2.56)	0 (0.00)	2 (5.13)
Conv	39	1 (2.56)	1 (2.56)	1 (2.56)	0 (0.00)	1 (2.56)	4 (10.26)
χ^2	--	--	--	--	--	--	0.181
P	--	--	--	--	--	--	0.671

and HR in the Dex group were lower than those in the conventional group (P<0.05). This indicates that Dex is significantly effective in maintaining hemodynamic stability in radical gastric cancer surgery. Dex works fast, with a half-life of around 6 min, and its stable plasma concentrations can agitate the α2 receptor-dense brainstem blue spot to play a hypnotic and analgesic effect. Also, Dex inhibits pain signaling and the release of injurious peptides to abirritate patients and thus avoids the occurrence of a strong stress response during intraoperative operations such as skin incision, thus maintaining and improving intraoperative hemodynamic stability (12,13). The present study also showed that the Dex group was given lower dosages of propofol and remifentanil than the conventional group (P<0.05). It indicates that the application of Dex in radical surgery can reduce the amount of anesthetic drugs while ensuring the anesthetic effect. Specifically, Dex simulates the human sleep-wake mechanism and allows patients to undergo surgery under rational sedation. This not only reduces the dosage of anesthetic drugs such as propofol but also helps patients awaken early and prevents adverse events such as agitation during the recovery period.

IL-1β is a pro-inflammatory factor that has the ability to inhibit gastric acid secretion and will increase rapidly during the development and progression of gastric cancer. Serum IL-6 levels increase when the body is irritated and infected, so they are associated with the severity of the disease and its pathological process. Serum TNF-α levels increase when patients develop tumors, autoimmune diseases, or infections. Serum CRP concentration increases gradually due to tumors, inflammation, infection, acute trauma and other factors. Numerous studies have confirmed that when patients undergoing gastric cancer surgery are subject to anesthesia, traumatic stimulation and pain during the surgery, they will have different degrees of inflammatory reactions, which eventually affect the recovery rate (14,15). Therefore, it is crucial to enhance anesthetic management and control inflammatory reactions during gastric cancer surgery. The present study further showed that at T4 and T5, serum IL-1β, IL-6, TNF-α and CRP were lower in the Dex group than in the conventional group (P<0.05). This suggested that Dex is anti-inflammatory. Dex regulates the inflammatory response by downregulating nuclear factor-κB expression to exert anti-inflammatory effects, as nuclear factor-κB regulates the release of molecules such as COX-2/PEG2 and TNF-α and reduces inflammation by activating the cholinergic anti-inflammatory pathway (16,17). Dex also exerts an anti-inflammatory effect by activating the immune system and promoting the repair of damaged tissues (18). The anti-inflammation of Dex is also related to the imidazoline structure in Dex, which has an agonistic effect on imidazoline receptors, ultimately providing an anti-inflammatory effect and reducing the risk of postoperative infection (19). According to Tang Jia et al. (20), serum TNF-α (24.35 ± 3.24) pg/mL at 5 d postoperatively in group B was lower than that in group A (36.78 ± 3.35) pg/mL (P<0.05), close to the results of this present study. It verified that Dex is anti-inflammatory and effectively reduces the postoperative inflammatory response. The present study finally showed that the overall incidence of adverse reactions was 5.13% in the Dex group, compared with 10.26% in the conventional group (P>0.05). This indicates that Dex is relatively safe and well tolerated by patients, and its adverse reactions like nausea and vomiting, hypotension, hypertension, respiratory depression, and bradycardia will disappear with drug metabolism over time. There are already many reports of factors affecting the occurrence of gastric cancer (21-27).

In summary, this study demonstrated that Dex effectively maintained the stability of intraoperative blood pressure, heart rate and other vital signs of patients undergoing radical gastric cancer surgery, inhibited the release of inflammatory mediators such as interleukins, and reduced the dosage of anesthetic drugs. Additionally, no significant adverse reactions were observed during Dex anesthesia. Therefore, this study provided a valuable reference for the promotion of Dex.

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