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Original Article

Dexmedetomidine contributes to reduced anesthesia dosages and improves anesthetic effectiveness in the radical resection of gastric cancer

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Abstract: Objective: This study was designed to analyze dexmedetomidine's effects on and contributions to reduced general anesthesia dosages in anesthesia for the radical resection of gastric cancer. Methods: 77 patients admitted to our hospital for gastric cancer treatment were retrospectively analyzed after undergoing radical resection of gastric cancer and randomly placed into one of two groups. The 38 patients who underwent general anesthesia using remifentanil and propofol were placed in the control group, and the other 39 were administered dexmedetomidine by intravenous infusion 15 minutes before the general anesthesia induction and until 40 mins before end of their operations were placed in the observation group. The two groups were compared in terms of BIS, MAP, HR, their dosages of anesthetic drugs, postoperative sedation, pain intensity, and adverse reactions. Results: (1) For BIS, in addition to T2 when the observation group demonstrated a value significantly lower than the control group, there was no significant difference between the two groups at the other time points of T1, T3, T4, and T5 ($P>0.05$), and for MAP and HR, the observation group reported lower values than the control group at T2, T3, T4, and T5 ($P<0.05$); (2) The dosages of propofol and remifentanil were (1012.34±216.55) mg and (3.31±1.04) mg in the observation group and (1456.92±358.49) mg and (5.13±1.28) mg in the control group ($P<0.05$); (3) Compared with the control group, the observation group achieved higher Ramsay scores for sedation and lower VAS scores for pain intensity at 1 h and 4 h after the operations ($P<0.05$); (4) The incidences of nausea and vomiting, respiratory depression, hypotension, hypertension, tachycardia, bradycardia, dysphoria and shivering were significantly lower in the observation group compared with the control group ($P<0.05$). Conclusion: The application of dexmedetomidine in general anesthesia for the radical resection of gastric cancer can sharply reduce the dosage of anesthetic drugs and improve the anesthetic effect to obtain better sedation and analgesic effects, demonstrating good application values. However, the study included a small cohort and few points of comparison, so its results may not be representative. Future studies will be more extensive and in-depth based on large sample sizes to obtain study results which are more representative and to provide a wealth of scientific guidance for anesthesia in the radical resection of gastric cancer.

Keywords: Radical resection of gastric cancer, anesthesia, dexmedetomidine, drug dose, sedation, effects

Introduction

Gastric cancer ranks first among all malignant tumors in China in terms of incidence and accounts for 1/4 [1] of the deaths due to malignant tumors and causing the deaths of almost 170,000 patients each year according to an epidemiological investigation. In recent years, increasing pressure in life and career has resulted in disordered schedules for resting and working, and changes in lifestyle and diet. As a result, gastric cancer has risen gradually in incidence based on an annual record of more than 20,000 new cases according to statistical data and has become a disease that severely affects the health of the whole human race [2].

For patients in the early stages of gastric cancer, surgery, including radical resection, is applied more extensively to thoroughly resect the primary tumors, metastatic lymph nodes, and infiltrated tissues to make sure the patients can live disease-free for a longer period of time and with a higher quality of life [3, 4]. However, radical resection of gastric cancer is

invasive and extremely painful and without any obvious surgical stress in the preoperative period, such that some aged patients may be unable to tolerate it, and it may influence their postoperative recovery. Therefore, the selection of the proper anesthesia methods and drugs is very important [5]. General anesthesia via endotracheal tube (ETT) has a wide application in the radical resection of gastric cancer at present, but it requires a large dose of anesthetic drugs. In this process, patients are vulnerable to elevated blood pressure and need more time to regain consciousness, during which, adverse reactions such as nausea, vomiting, and dysphoria are expected [6]. Houck et al. [7] found that the addition of other anesthesia drugs on the basis of general anesthesia can relieve patients' stress and improve the anesthesia's effectiveness and safety.

This study specifically analyzed the contribution of dexmedetomidine to reducing the dosages of anesthetic drugs and improving the anesthetic effect in addition to general anesthesia in the radical resection of gastric cancer in order to provide a reference for the administration of anesthetic drugs in the clinical implementation of the radical resection of gastric cancer.

Materials and methods

Materials

77 patients diagnosed with gastric cancer in our hospital were retrospectively analyzed after undergoing radical resection of gastric cancer. They were randomly divided into two groups. The control group included 38 patients with ASA anesthesia grades from I to II and ranged in age from 23 to 58, while the 39 patients in the observation group were in ASA anesthesia grades I to II and ranged in age from 25 to 61. (1) Inclusion criteria: Patients diagnosed with gastric cancer [8] over age 18, diagnosed with the disease after an imaging examination, and expecting a radical resection of gastric cancer were included, and they provided informed consent themselves or their guardians provided it on their behalf. The study was approved by the Ethics Committee of our hospital. (2) Exclusion criteria: Some patients were excluded as they had anesthesia complications, excessive obesity, nervous system diseases, mental disorders, sinus bradycardia, or severe dysfunctions of the heart, liver, kidneys, and lungs. This study was approved by the Ethics Committee of the First Affiliated Hospital of Xiamen University. All the study participants provided a written informed consent before participating in the study.

Methods

All the patients were brought to the operation room without taking any medicines, and a venous channel was established immediately afterward by puncturing the right internal vein and the left radial artery. During the operation, the heart rate (HR), the bispectral index (BIS), the oxygen saturation (SPO_2), the mean arterial pressure (MAP), and the end-tidal carbon dioxide ($P_{ET}CO_2$) were continuously monitored. Before the anesthesia, the patients were infused with Ringer's lactate solution at 6 ml/kg. For the observation group, 2 mg dexmedetomidine stoste was diluted using normal saline to 50 ml. The mixture was infused into the patients' bodies through their veins for 15 min at a dose of 0.6 μg/kg, and maintained at 0.4 μg/(kg·h) until 40 min before the end of the operation. Before the anesthesia, the patients in the control group were given normal saline at the same dose.

A target controlled infusion (TCI) of 4 μg/kg fentanyl and 3.0~3.5 μg/ml propofol was relied on to reduce the patients' BIS to 60 before the infusion of rocuronium at 0.6 mg/kg and trachea intubation 2 min later. Then, the anesthesia machine was connected for mechanical air supply at a frequency of 10-12 times/min with the tidal volume between 8 and 10 ml/kg and a $P_{ET}CO_2$ level between 4.67 and 5.99 KPa. To maintain the anesthesia status, cisatracurium and remifentanil were given at a dose of 0.1 μg/(kg·min) and remifentanil at 0.2~0.3 μg/(kg·min) while the TCI concentration of propofol was controlled in the range of 2.0 and 2.5 μg/ml. During the operation, the patients' blood pressure was allowed to fluctuate at 1/5 of the basic level, and the BIS was between 45 and 55. With the mixture of Ringer's lactate solution and 6% hetastarch (8-10 ml/(kg·h)) as the solution for the intraoperative use, the doses of remifentanil and propofol were adjusted according to the hemodynamics and BIS changes. If and when necessary, ephedrine and nicardipine

Table 1. A comparison of the general data in the observation and control groups ($\bar{x} \pm s$)/[n (%)]

Materials		Observation Group (n=39)	Control Group (n=38)	t/X^2	P
Gender	Male	21	20	0.011	0915
	Female	18	18		
Age (y)		42.68±7.59	43.35±6.82	0.407	0.685
Height (cm)		168.59±12.37	172.51±13.69	1.319	0.191
Weight (kg)		68.56±4.95	70.34±5.08	1.557	0.124
ASA grading for anesthesia	Grade I	20	21	0.123	0.726
	Grade II	19	17		
Type of cancer	Adenocarcinoma	22	23	0.134	0.714
	Signet-ring cell carcinoma	17	15		
Operation time (min)		190.06±38.49	194.37±40.17	0.481	0.632
Intraoperative blood loss (min)		200.63±41.15	205.38±42.62	0.498	0.630

Table 2. Comparison of the observation and control groups in their changes in bis, map, and HR before and after anesthesia ($\bar{x} \pm s$)

Index	Group	T1	T2	T3	T4	T5
BIS	Observation Group	96.92±1.68	73.89±6.65	49.83±5.37	49.05±3.52	96.23±2.58
	Control Group	97.46±0.93	96.53±1.89	52.39±3.86	49.36±2.78	97.15±0.86
MAP (kPa)	Observation Group	12.40±1.15	11.52±1.03	11.05±1.17	11.12±1.03	13.05±1.08
	Control Group	12.16±1.38	12.78±1.12	12.02±0.98	11.89±0.86	13.78±1.12
HR (times/min)	Observation Group	77.69±9.36	63.58±7.48	71.45±8.59	69.36±7.57	75.02±9.38
	Control Group	78.26±8.69	80.02±9.67	84.79±8.89	80.43±9.64	88.34±7.27

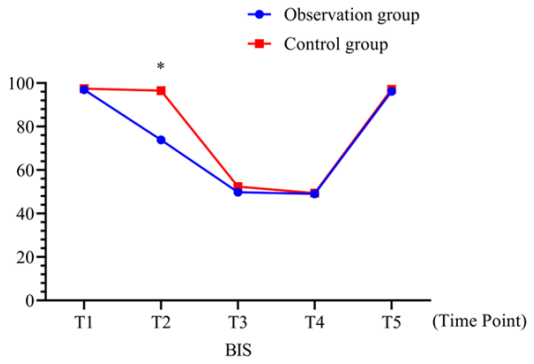

Figure 1. Comparison of the observation and control groups in terms of BIS. For the intergroup comparison at T2, the observation group yielded a lower value (P<0.05), but at T1, T3, T4, and T5, no differences were observed (P>0.05); for the intragroup comparison in the observation group, the BIS was lower at T2, T3, and T4 compared with the same at T1 (P<0.05), but in the control group, lower BIS levels were observed at T3 and T4 compared with T1 and T2 (P<0.05). * represents when the two groups compared at the T2 time point, P<0.05.

were given to control the fluctuations in the patients' blood pressure in a range of 1/5 in the case of sharp changes; for patients whose HR exceeded 100 times per minute or was lower than 50 times per minute, atropine was given. As the operation ended, the patients were administered cisatracurium during the closure of the abdominal cavity, and the administration of remifentanil and propofol was discontinued after that.

All the patients were sedated with morphine at a dose of 0.06 mg/kg before their skin incisions and at half an hour before the operation ended. Intravenous patient controlled analgesia (IV-PCA) was adopted with 100 ml solution of 2.5 μg/kg sufentanil at a rate of 2 ml/h, during which the load was 2 ml. The tubes were removed when the patients regained consciousness. They were transferred to the recovery room for 4 h of observation before being moved back to the wards in a totally conscious state.

Observation indexes

Vital signs: The two groups were measured for BIS, MAP, and HR before their drug injection (T1), anesthesia induction (T2), at 1 min after

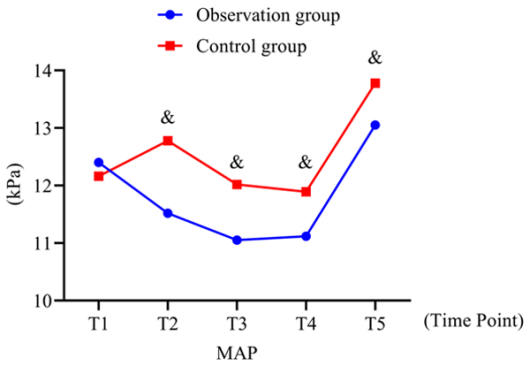

Figure 2. Comparison of the observation and the control groups in terms of MAP. The observation group reported a far lower MAP compared with the control group at T2, T3, T4 and T5 generally (P<0.05), and at T3, T4, and T5 (P<0.05) respectively. For the intragroup comparison in the control and observation groups, a higher MAP level was observed at T5 compared with T1 (P<0.05). & indicates when the two groups were compared at the same time point, P<0.05.

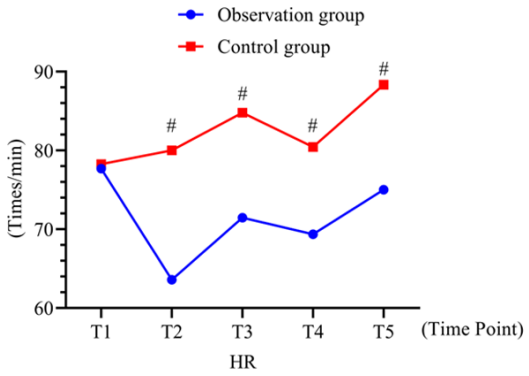

Figure 3. Comparison of the observation and control groups in terms of HR. For the intragroup comparisons, the observation group achieved a reduction from T1 to T2, T3, and T4 (P<0.05). For the intergroup comparisons, the observation group reported lower HR at T3 and T5 compared with the control group at T1 (P<0.05). For the comparisons at T2, T3, T4, and T5, the observation group achieved a significantly lower HR than the control group (P<0.05). # indicates when the two groups were compared at the same time point, P<0.05.

the tracheal intubation (T4), upon the skin incision (T5), and immediately after the extubation (T7).

Dosage of anesthetic drugs: The 2 groups were compared in terms of their doses of remifentanil and propofol.

Sedation degree: The sedation degree was evaluated using Ramsay method [9] At 1 h and 4 h after the operation according to the standards of 1 point for dysphoria, 2 points for coordination between consciousness and quietness, 3 points for drowsiness and the response to the instructions, 4 points for REM sleep, 5 points for sleeping with delayed responses after being called, and 6 points for deep sleep without response to any calls.

Pain intensity: The Visual Analogue Scale (VAS) [10] was used to evaluate the pain intensity at 1 and 4 h after the operation. A 10 cm line was drawn on a piece of paper, with 0 at one end to indicate no pain, and 10 at the other end to represent the worst possible pain. A high number corresponds to more severe pain.

Adverse reactions: The two groups were recorded and compared in terms of their incidences of various adverse reactions, including bradycardia, respiratory depression, hypotension, hypertension, tachycardia, and nausea and vomiting after extubation, dysphoria, and shivering. Bradycardia was defined as a heart rate lower than 50 times/min, tachycardia as a heart rate that increased by 20% from its preoperative basic level, respiratory depression as oxygen saturation of the blood less than 90%, or a breathing rate less than 80 times/minute, hypotension as a drop and hypertension as a rise in the BSP over 1/5 based on the basic level before the operation.

Statistical analysis

SPSS22.0 was used for the statistical analysis. The measurement data were expressed as the mean ± standard deviation, and independent-samples T tests were used for the intergroup result comparisons. The enumeration data were expressed as [n (%)], and X^2 tests were used for the inter-group result comparisons. ANVOA was used for the analysis of the intra-group multi-point comparisons and the inter-group comparisons. *P*<0.05 indicated that the difference was statistically significant.

Results

A comparison of the general data in the observation and control groups

No statistical differences were observed in the observation and control groups in terms of the proportions of male and female patients, ages, heights, weights, the proportions of

Table 3. Comparison of the observation and control groups in their doses of propofol and remifentanil ($\bar{x}$ ± s, mg)

Group	n	Propofol	Remifentanil
Observation Group	39	1012.34±216.55	3.31±1.04
Control Group	38	1456.92±358.49	5.13±1.28
t		6.606	6.856
P		0.000	0.000

patients in ASA grades I and II for anesthesia, proportion of adenocarcinoma, the proportion of patients with signet-ring cell carcinoma, the operation times, and the intraoperative blood loss (P>0.05, **Table 1**).

Comparison of the observation and control groups in their vital signs

For BIS, in addition to T2 when the observation group demonstrated a value significantly lower than the control group, there was no significant difference between the 2 groups at the other time points of T1, T3, T4, or T5 (P>0.05); for the intragroup comparisons, the BIS dropped from T1 to T2, T3, T4, and T5 in the observation group, and from T1 and T2 to T3, T4, and T5 in the control group (P<0.05). For MAP and HR, the observation group reported lower values than the control group at T2, T3, T4, and T5 (P<0.05). For the intragroup comparisons in the control group, the MAP level rose significantly from T1 to T5 (P<0.05) and the HR from T1 to T3 and T5 in the control group (P<0.05); for the intragroup comparisons in the observation group, the MAP at T4 was significantly lower than the MAP at T1 (P<0.05), and HR at T2, T3, and T4 were lower than they were at T1 (P<0.05) (**Table 2**; **Figures 1**-**3**).

Comparison of the observation and control groups in terms of the dosages of the anesthetic drugs

The observation group consumed (1012.34± 216.55) mg propofol and (3.31±1.04) mg remifentanil during the general anesthesia, amounts significantly less than the control group, in which the dosages were (1456.92± 358.49) mg and (5.13±1.28) mg respectively (P<0.05, **Table 3**; **Figure 4**).

Comparison of the observation and control groups in sedation and pain intensity

The observation group reported higher Ramsay scores for sedation and lower VAS scores for pain intensity at 1 h and 4 h after the operations (P<0.05) (**Table 4**; **Figure 5**) compared with the control group.

Comparison of the observation and the control groups in the incidence of adverse reactions

There were 7 cases of nausea and vomiting, respiratory depression, hypotension, hypertension, tachycardia, bradycardia, dysphoria, and shivering in the observation group, for a total incidence of adverse reactions of 18.42%. In the control group there were 15 cases, for a total incidence of adverse reactions of 40.54%. The incidence of adverse reactions in the observation group was significantly lower than it was in the control group. (P<0.05, **Table 5**).

Discussion

Dexmedetomidine is an imidazole derivative and a new agonist that works on the α2 adrenergic receptors in the brain and spinal marrow based on its more powerful affinity. It is more selective to the agonism of central α2-adrenergic receptors [11, 12]. According to Chang et al. [13], dexmedetomidine contributes to the reduced dosage of anesthetic drugs and plays a sedative role more effectively. It can also effectively inhibit the formation of autonomic nerves and can reduce the incidence of postoperative nausea, vomiting, and shivering.

In this study, the patients in the observation group were given dexmedetomidine before the induction of anesthesia, which resulted in lower BIS at T2, lower MAP and HR at T2, T3, T4, and T5 compared with the control group (P<0.05), and better sedation and pain scores at 1 h and 4 h after the operation (P<0.05), indicating that the application of dexmedetomidine in general anesthesia can stabilize patients' vital signs in the period around anesthesia, and fully play a part in sedation and analgesia. Before the induction of anesthesia, the patients in the observation group were injected with dexmedetomidine at a concentration of 0.6 μg/kg, which was sufficient enough to excite the central and peripheral α2 receptors and effectively suppress the release of noradrenalin. In addition, it can reduce the content of catecholamine in the plasma to achieve autonomic inhibition and sedation, control of the vital sign levels and the

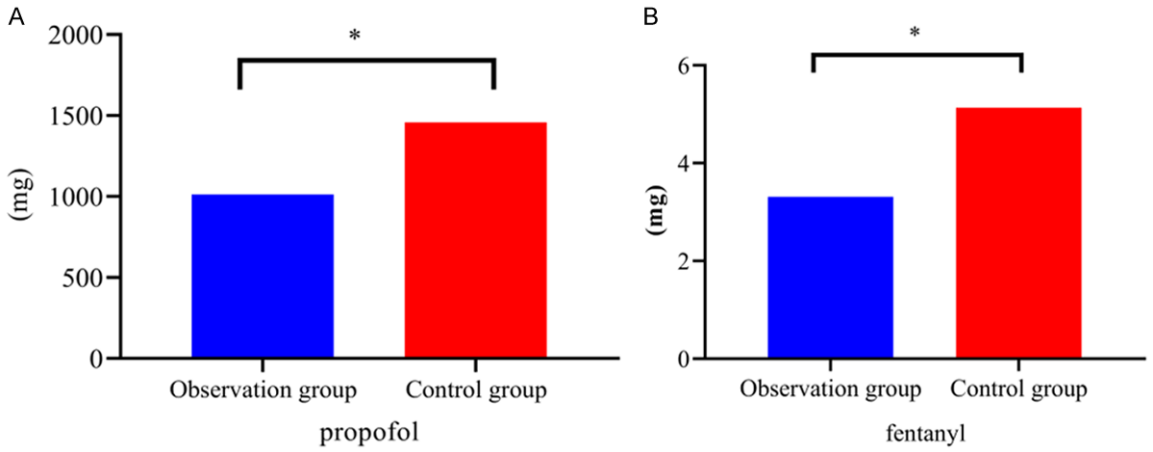

Figure 4. Comparison of the observation and the control groups in terms of their doses of propofol and remifentanil. The observation group consumed less propofol and remifentanil compared with the control group (P<0.05). * indicates when the doses between the two groups were compared, P<0.05.

Table 4. Comparisons of the observation group and control groups in terms of their sedation and pain intensity at 1 h and 4 h after the operation ($\bar{x}$ ± s, score)

Group	n	Ramsay score for sedation		VAS score for pain	
		1 h after operation	4 h after operation	1 h after operation	4 h after operation
Observation Group	39	3.23±0.78	2.31±0.79	1.53±0.64	1.33±0.38
Control Group	38	1.78±0.62	1.82±0.53	2.12±0.78	2.01±0.43
t		9.015	3.188	3.633	7.358
P		0.000	0.002	0.001	0.000

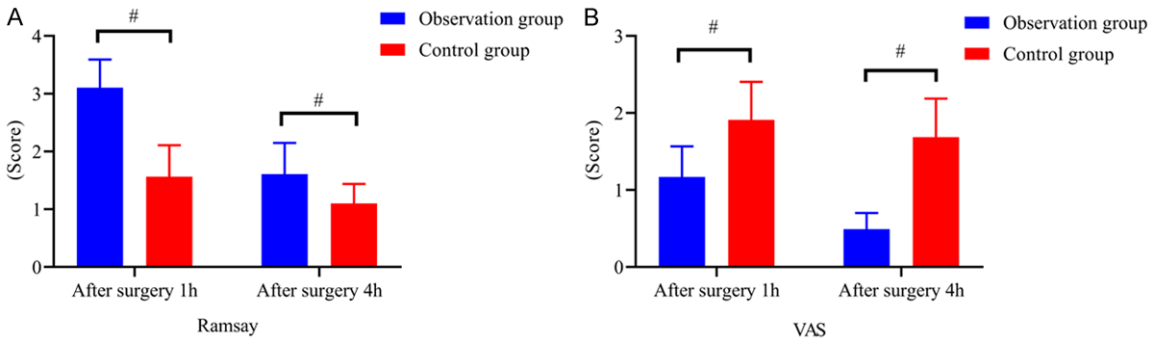

Figure 5. Comparison of the observation and control groups in their sedation and pain scores. Compared with the control group in the sedation and pain scores at 1 h and 4 h after the operations, the observation group reported significantly higher values in the first index and lower values in the second index (P<0.05). # indicates when the indicators were compared at the same time point in the two groups, P<0.05.

reduction of stress reactions [14, 15]. Furthermore, the application of anesthetic drugs after induction and before intubation can excite the vagus nerve and constrict the blood vessels, offsetting the angiectasis effect arising from for the general anesthesia drugs, so as to improve the hemodynamic stability and reduce hypotension [16].

In this study, the dosages of remifentanil and propofol were significantly lower in the observation group as compared with the control group, indicating that the combination with dexmedetomidine can effectively reduce general anesthesia dosages and play a part in easing patients' medical burdens. Propofol is a drug that inhibits NMDA and its channel activi-

Table 5. Comparisons of the observation and control groups in their incidence of adverse reactions [n (%)]

Group	Nausea and vomiting	Respiratory depression	Hypotension	Hypertension	Tachycardia	Bradycardia	Dysphoria	Shivering	Total incidence
Observation Group (n=38)	1 (2.63)	0 (0.00)	1 (2.63)	0 (0.00)	1 (2.63)	0 (0.00)	2 (5.26)	2 (5.26)	7 (18.42)
Control Group (n=37)	3 (8.11)	1 (2.70)	2 (5.41)	1 (2.70)	3 (8.11)	1 (2.70)	2 (5.41)	2 (5.41)	15 (40.54)
X^2									4.425
P									0.035

ty, and it attenuates the excitatory postsynaptic potential (EPSP) to achieve the effects of forgetting, anesthesia, and spasmolysis [17]. Propofol can also significantly inhibit patients' circulation functions, including peripheral vascular dilatation, to reduce their blood pressure levels by suppressing myocardial contraction [18]. In addition, Lee et al. [19] found that propofol is capable of respiratory depression by slowing down the breathing rate and reducing the tidal volume. In serious cases, it may result in apnea. Choi et al. [20] demonstrated that a single administration of propofol failed to achieve satisfactory analgesia, and the increase in doses raised the medical burden on the patients. Such a shortage can be complemented by other drugs including composite magnesium sulfate and lidocaine to improve the hemodynamic stability [21].

Dexmedetomidine works to relieve anxiety, hypnotization, and sedation by exciting the α2 receptors on the postsynaptic membrane in the nucleus ceruleus next to the ventriculus quartus cerebri to cause neurons to discharge and reduce the release of catecholamine [22]. Guldenmund et al. [23] observed that the combination of dexmedetomidine and propofol can turn off the synergistic reaction to achieve a better efficacy at a lower dose.

Patients who received general anesthesia reported a higher incidence of dysphoria, which can be attributed to the obvious sense of pain and discomfort due to the catheter indwelling. Dexmedetomidine leverages its attributes of hypnotization and sedation to improve patients' tolerance to tracheal catheters and pain so that the dysphoria is alleviated [24]. In the present study, the observation group showed an incidence of 5.26% for dysphoria, which was lower than the same (24.32%) in the control group. El-Boghdadly et al. [25] revealed that after the administration of dexmedetomidine, the incidence of bradycardia fell to between 30% and 40%, but in this study, it was only 2.63% in the observation group, which can be explained by the accurate control of drug doses and delivery speeds for anesthesia induction and maintenance improved drug administration safety.

In conclusion, the application of dexmedetomidine in general anesthesia for the radical resection of gastric cancer has the advantage of significantly reducing the dosages of anesthetic drugs and raising the anesthetic effect for better sedation and analgesic effects. However, the present study included a small cohort and points of comparison that were less representative. In the future studies, more attention shall be paid to in-depth studies with a larger coverage based on larger sample sizes to generate more representative study results and to provide a wealth of scientific guidance for the anesthesia of radical resection of gastric cancer.

Disclosure of conflict of interest

None.

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