Effects of propofol and sevoflurane on blood glucose, hemodynamics, and inflammatory factors of patients with type 2 diabetes mellitus and gastric cancer

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Abstract. Effects of propofol and sevoflurane on blood glucose, hemodynamics, and inflammatory factors of patients with type 2 diabetes mellitus (T2DM) and gastric cancer (GC) were investigated. One hundred and ten patients with T2DM and GC, treated in The First Affiliated Hospital of Baotou Medical College (Baotou, China) from January 2017 to December 2018, were selected. Sixty patients anesthetized by propofol were included in the propofol group, whereas 50 patients anesthetized by sevoflurane were included in the sevoflurane group. The level of blood glucose, hemodynamic indicators, and inflammatory factors of the patients in the two groups were compared at T_0 (before anesthesia), T_1 (2 min after intubation), T_2 (5 min after pneumoperitoneum), and T_3 (60 min after surgery). Mini-Mental State Examination (MMSE) cognitive function scores were compared at T0 (before anesthesia), T4 (6 h after surgery), and T5 (72 h after surgery) between the two groups. The anesthetic effect and the incidence of adverse reactions were also compared between the two groups. The heart rate (HR), oxygen saturation (SpO_2) and average artery pressure decreased slightly and then increased after the surgery was started; whereas, the levels of the serum inflammatory factors first increased and then decreased, to return to their initial levels. MMSE scores of the patients in two groups at T_4 were significantly lower than those at T_0 ($P<0.05$), and the MMSE score at T_4 was significantly higher in the propofol group than that in the sevoflurane group ($P<0.05$). The time of spontaneous breathing, verbal response, eye opening, and extubation in the propofol group was significantly shorter than that in the sevoflurane group ($P<0.05$). The incidence of adverse reactions in the propofol group was lower than that in the sevoflurane group. The effect of propofol is less than that of sevoflurane, thus propofol is more suitable for the anesthesia of patients with T2DM and GC.

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Introduction

Gastric cancer (GC) is a common disease with morbidity that ranks fifth worldwide. GC is the third cause of human deaths worldwide. There are ~952,000 new cases of GC each year, and there were ~783,000 deaths in 2018 (1,2). A study has shown that diabetes is one of the independent predictive factors of gastrectomy postoperative complications of patients with GC (3). Studies have also reported that the cancer risk of patients with diabetes is increased, and the number of patients with type 2 diabetes mellitus (T2DM) and GC is increasing (4,5). These results suggest that there is relevance between T2DM and GC, probably due to their common risk factors, such as obesity, insulin resistance, and smoking. The underlying mechanism may be related to the imbalance of blood glucose levels, oxidative stress, and adverse inflammatory reactions (6). At present, the treatment methods of complications of T2DM and GC are ineffective. Surgery is still the first-line treatment method of GC; however, the anesthesia in surgery has side effects and leads to systemic dysfunction or even injury of important tissues (7,8). Therefore, the study of the effects of anesthetics on patients with T2DM and GC is important in order to improve the treatment methods and reduce the complications of T2DM and GC.

The chemical structure of propofol is 2,6-diisopropylphenol. As an intravenous injectable anesthetic, it is preferentially used for the induction and maintenance of general anesthesia during surgery, even for the anesthesia and sedation of children (9,10). A study has shown that propofol can inhibit cell apoptosis and inflammation and has a neuroprotective effect by regulating proteins associated with neuroprotection or ion homeostasis (11). Propofol's anesthetic effect is activated by γ-aminobutyric acid receptors to regulate the excitatory amino acid neurotransmitter system and protect the brain cells from oxidative stress (11). In the present study, in addition to Propofol, an intravenous injectable anesthetic, an inhaled anesthetic was

investigated. Sevoflurane is an inhaled anesthetic that is widely used in clinical practice. It takes effect in different organs or systems and does not have great side effects. Sevoflurane's anesthetic effect is safe (12). The minimum alveolar concentration (MAC) value of sevoflurane decreases with the increase of age, and the MAC value is negatively correlated with the effect of inhaled anesthetics. This indicates that the anesthetic effect of sevoflurane increases with the increase of age (13). In the study of Xu *et al* (14), it was reported that propofol and sevoflurane could protect the liver by regulating an inflammatory reaction and reducing oxidative stress and apoptosis of the liver cells. In the study of Zheng *et al* (15), patients with GC who had underwent gastrectomy were studied. It was reported that the average survival time of the patients in the propofol group was significantly longer than that of the patients in sevoflurane group. This result suggests that using propofol can significantly increase the survival rate of patients who have GC and undergo gastrectomy.

The main purpose of this study was to compare the effects of propofol and sevoflurane on blood glucose, hemodynamics, and inflammatory factors of patients in perioperative period. Mini-Mental State Examination (MMSE) cognitive function scores, the anesthetic effect, and the incidence of adverse reactions were also compared to provide clinical data on anesthesia for the completeness of the comprehensive treatment of patients with T2DM and GC.

Patients and methods

General data. One hundred and ten patients with T2DM and GC, who were treated in The First Affiliated Hospital of Baotou Medical College (Baotou, China) from January 2017 to December 2018, were selected. There were 70 males and 40 females, 30-75 years of age, with average age of 55.25±8.75 years, and weight 50-75 kg. Sixty patients were included in the propofol group and 50 patients were included in the sevoflurane group. The patients in the propofol group were anesthetized by propofol, whereas the patients in the sevoflurane group were anesthetized by sevoflurane. The study was approved by the Ethics Committee of The First Affiliated Hospital of Baotou Medical College. The patients and their family members were informed and signed written informed consents.

Inclusion and exclusion criteria. Inclusion criteria: Patients with histological and pathological examinations, and clinical symptoms conforming to T2DM and GC (16,17); patients with American Society of Anesthesiologists (ASA) grade I and II disease (18); patients with MMSE that was carried out 10 h before the operation (19); patients with score >24 points; patients with no surgical contraindications and allergies to the medicines used in this study; patients not using medicines that affect the level of blood glucose, hemodynamic indicators, and the level of inflammatory factors in the prior 15 days; patients that were informed and cooperated voluntarily for this study. Exclusion criteria: Patients with mental illness or taking a large dose of sedatives; patients with vision, hearing, or language disorder; patients complicated with other cancers; patients with severe heart, liver, lung, or kidney dysfunction. The inclusion criteria were applicable for the propofol and the sevoflurane groups.

Anesthesia methods. Before the patients in two groups were anesthetized, they fasted for 6 h, and routine examinations were performed. The fasting blood glucose level of the patients was maintained at ≤6.99 mmol/l by insulin injection. The anesthetic effect of the patients in the propofol group was induced and maintained with propofol (4-8 mg/kg/min) (B33792-100 mg; Shanghai Yuanye Bio-Technology Co., Ltd.). The anesthetic effect of the patients in the sevoflurane group was induced and maintained with 1-3% sevoflurane (XY-EP-Y0001046; Shanghai Xiyuan Biotechnology Co., Ltd.), and the patients were intubated to carry out mechanical ventilation. Propofol or sevoflurane was supplemented according to the vital signs of the patients in the two groups. After the patients were anesthetized, the mechanical ventilation was replaced by assisted breathing. When the patients regained consciousness, the tubes were pulled out and the patients were transferred to Intensive Care Unit. Venous blood (5 ml) was collected from the patients in two groups before the anesthesia was carried out, 2 min after intubation, 5 min after pneumoperitoneum, and 60 min after surgery. The change of blood glucose levels of the patients was measured by a blood glucose monitoring device in different periods (Beijing Anteng Medical Devices Co., Ltd.). The levels of serum inflammatory factors, IL-1β, IL-6, IL-10 and TNF-α, were measured by an enzyme-linked immunosorbent assay (ELISA) according to the manufacturer's instructions of human IL-1β ELISA kit, human IL-6 ELISA kit, human IL-10 ELISA kit, and human TNF-α ELISA kit (FK-R0180, FK-R0049, FK-R0066, FK-0122; Shanghai Fanke Biotechnology Co., Ltd.).

MMSE score rules. Each question was 1 point and the full score was 30 points. There were 10 questions on orientation, such as time, location, and site; 3 questions on memory; 5 questions on attention and arithmetic; 3 questions on recall; 9 questions on language ability, including name, retelling, three-step command, reading, writing and structure. The higher the MMSE score was, the better the cognitive ability was.

Observation indicators. The level of blood glucose, the hemodynamic indicators, including heart rate (HR), oxygen saturation (SpO_2), systolic blood pressure (SBP), and mean blood pressure (MBP), and the levels of the serum inflammatory factors IL-1β, IL-6, IL-10 and TNF-α, were observed and compared at T_0 (before anesthesia), T_1 (2 min after intubation), T_2 (5 min after pneumoperitoneum), and T_3 (60 min after surgery). In addition, MMSE scores were observed and compared at T_0 (before anesthesia), T_4 (6 h after surgery), and T_5 (72 h after surgery). The anesthetic effect after surgery (time of spontaneous breath, eye opening, extubation, and verbal response), and the incidence of adverse reactions (nausea, emesis, cough, bradycardia, dysphoria, breath holding, laryngospasm, and bronchospasm) were also compared between the two groups.

Statistical analysis. SPSS 19.0 (IBM Corp.) was used to carry out statistical analysis. GraphPad Prism 6 (GraphPad Software, Inc.,) was used for data visualization. The measurement data were expressed as mean ± standard deviation (mean ± SD), and the independent samples t-test was used to compare the measurement data between groups. The count data were

Table I. Comparison of the general data of patients in the two groups [n (%), mean ± SD].

Category	n	Propofol group (n=60)	Sevoflurane group (n=50)	χ^2/t-test	P-value
Sex				0.469	0.524
Male	70	40 (66.67)	30 (60.00)		
Female	40	20 (33.33)	20 (40.00)		
Age (years)				0.764	0.382
≤60	60	35 (58.33)	25 (50.00)		
>60	50	25 (41.67)	25 (50.00)		
BMI (kg/m^2)	110	22.50±4.50	22.40±4.60	0.115	0.909
Smoking history				0.177	0.860
No	45	25 (41.67)	20 (40.00)		
Yes	65	35 (58.33)	30 (60.00)		
Drinking history				2.700	0.100
No	51	23 (38.33)	28 (56.00)		
Yes	59	37 (61.67)	22 (44.00)		
Hypertension				0.046	0.831
No	43	24 (40.00)	19 (38.00)		
Yes	67	36 (60.00)	31 (62.00)		
Marital status				2.829	0.093
Unmarried	35	15 (25.00)	20 (40.00)		
Married	75	45 (75.00)	30 (60.00)		
TNM stage				0.031	0.860
I/II	65	35 (58.33)	30 (60.00)		
III/IV	45	25 (41.67)	20 (40.00)		
Pathological differentiation degree				1.604	0.205
Middle/high differentiation	70	35 (58.33)	35 (70.00)		
Low differentiation	40	25 (41.67)	15 (30.00)		
ASA grade				1.243	0.265
Grade I	53	26 (43.33)	27 (54.00)		
Grade II	57	34 (56.67)	23 (46.00)		

BMI, body mass index; ASA, American Society of Anesthesiologists.

expressed as the number of cases and percentage [n (%)], and χ^2 test was used to compare the count data between groups. ANOVA with Dunnett's post hoc test was used for comparison between multiple groups. P<0.05 was considered to indicate a statistically significant difference.

Results

General data. The general data of the patients in two groups were compared, including sex, age, body mass index (BMI), smoking history, drinking history, hypertension, marital status, TNM stage, pathological differentiation degree and ASA grade. No significant difference was found in these data (P>0.05) (Table I).

Comparison of blood glucose levels. In order to investigate the effects of propofol and sevoflurane on the blood glucose levels, a glucometer was used to measure the blood glucose levels of the patients in the propofol and sevoflurane group at T_0, T_1, T_2, and T_3. The results revealed that there was no significant difference between the blood glucose levels of the patients in the propofol group and those of the patients in the sevoflurane

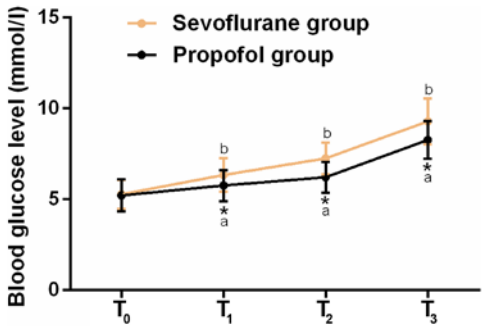

Figure 1. Comparison of the blood glucose levels of the patients in the two groups. *P<0.05, compared with the sevoflurane group at the same time-point; aP<0.05, compared with the propofol group at 0 min; bP<0.05, compared with the sevoflurane group at 0 min.

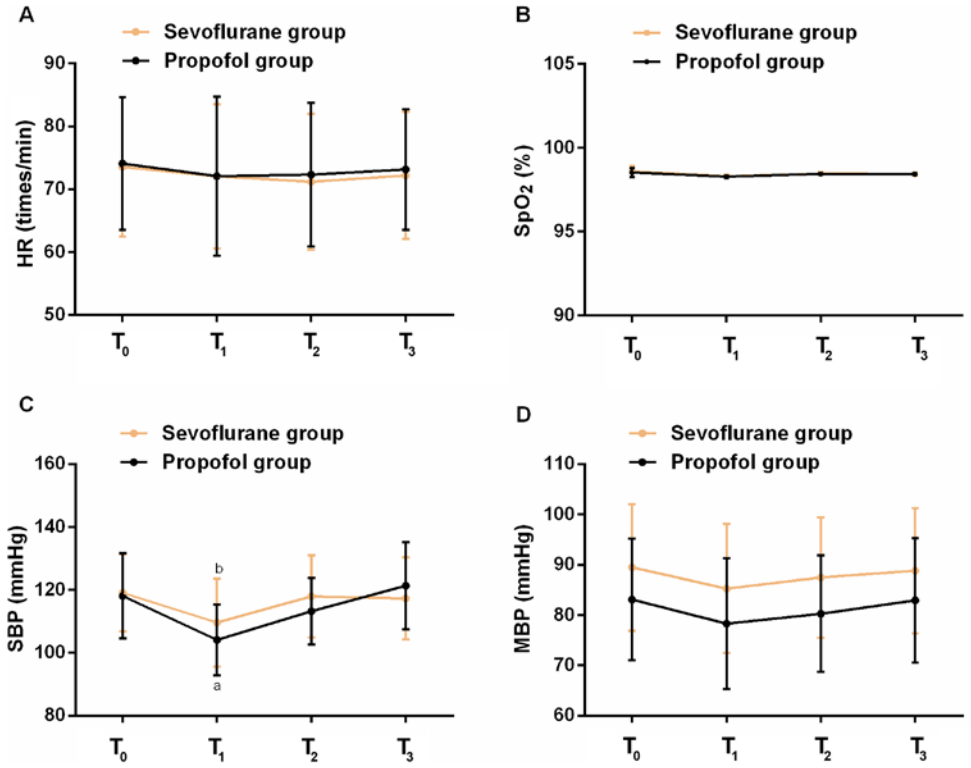

Figure 2. Comparison of the hemodynamic indicators of the patients in the two groups. Comparison of (A) HR, (B) SpO_2, (C) SBP and (D) MBP in the propofol and sevoflurane group. [a]P<0.05, compared with the propofol group at 0 min; [b]P<0.05, compared with the sevoflurane group at 0 min. HR, heart rate; SpO_2, oxygen saturation; SBP, systolic blood pressure; MBP, mean blood pressure.

group at T_0 (P>0.05). As the operation time went on, blood glucose levels of the patients at T_1, T_2, and T_3 increased and were significantly higher than those at T_0 (P<0.05). The blood glucose levels of the patients in the propofol group were significantly lower than those of the patients in the sevoflurane group at T_1, T_2 and T_3 (P<0.05) (Fig. 1).

Comparison of hemodynamic indicators. In order to investigate the effects of propofol and sevoflurane on the hemodynamic indicators, the hemodynamic indicators HR, SpO_2, SBP and MBP were observed and compared in the propofol and the sevoflurane group at T_0, T_1, T_2, and T_3. The results showed that there was no significant difference in HR, SpO_2, SBP and MBP of the patients in two groups at T_0, T_1, T_2 and T_3 (P>0.05). Compared with the hemodynamic indicators at T_0, the hemodynamic indicators of the patients in the propofol and sevoflurane group decreased at approximately T_1, whereas they increased at T_2. There was no significant difference between the hemodynamic indicators of the patients in the propofol and sevoflurane group at T_3 or T_0 (P>0.05) (Fig. 2).

Comparison of the levels of inflammatory factors. In order to investigate the effects of propofol and sevoflurane on inflammatory factors, the levels of serum inflammatory factors IL-1β, IL-6, IL-10 and TNF-α were measured in the propofol and sevoflurane group at T_0, T_1, T_2 and T_3 using ELISA. The results revealed that the levels of IL-1β, IL-6, IL-10 and TNF-α in the propofol and sevoflurane group were first increased, and then decreased to the level at T_0. There was no significant difference between the levels of IL-1β, IL-6, IL-10 and TNF-α in the propofol group and those in the sevoflurane group at T_0 (P>0.05). The levels of IL-1β, IL-6 and IL-10 in the propofol group were lower than those in the sevoflurane group at T_3, and the level of IL-6 in the propofol group was significantly lower than that in the sevoflurane group at T_1, T_2 and T_3 (P<0.05) (Fig. 3).

Comparison of MMSE cognitive function scores. In order to investigate the effects of propofol and sevoflurane on the cognitive function, MMSE cognitive function scores in the propofol group and sevoflurane group were counted at T_0, T_4, and T_5. The results showed that there was no significant difference between the MMSE cognitive function scores in the propofol and the sevoflurane group at T_0 (P>0.05). MMSE cognitive function scores in the propofol group were significantly higher than those in the sevoflurane group at T_4 (P<0.05), and MMSE cognitive function scores in the propofol group and the sevoflurane group at T_4 were significantly lower than those at T_0 (P<0.05). There was no significant difference between MMSE cognitive function scores in the propofol and the sevoflurane group at T_5 and those at T_0 (P>0.05) (Fig. 4).

Comparison of the anesthetic effect. In order to compare the anesthetic effects of propofol and sevoflurane, the time of spontaneous breath, eye opening, extubation and verbal response were observed and recorded for both groups. The results showed that the time of spontaneous breath, eye opening, extubation and verbal response in the propofol group

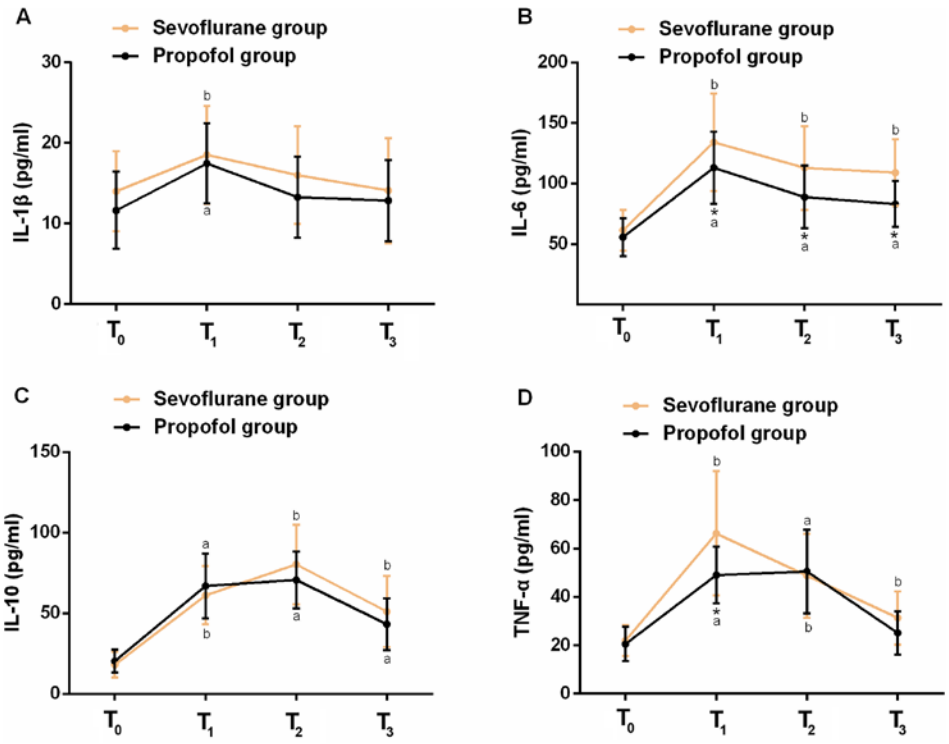

Figure 3. Comparison of the levels of serum inflammatory factors of the patients in two groups. (A) The level of IL-1β in the propofol group was lower than that in the sevoflurane group. (B) The level of IL-6 in the propofol group was significantly lower than that in the sevoflurane group (P<0.05). (C) The level of IL-10 in the propofol group was lower than that in the sevoflurane group. (D) The level of TNF-α in the propofol group was lower than that in the sevoflurane group. *P<0.05, compared with the sevoflurane group at the same time-point; aP<0.05, compared with the propofol group at 0 min; bP<0.05, compared with the sevoflurane group at 0 min.

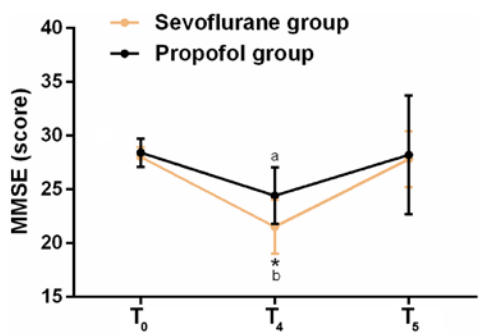

Figure 4. Comparison of MMSE cognitive function scores of the patients in the two groups. *P<0.05, compared with the propofol group at the same time-point; aP<0.05, compared with the propofol group at 0 min; bP<0.05, compared with the sevoflurane group at 0 min. MMSE, Mini-Mental State Examination.

were significantly shorter than those in the sevoflurane group (P<0.05) (Fig. 5).

Comparison of adverse reactions. In order to investigate the incidence of adverse reactions of propofol and sevoflurane, the number of patients who had nausea, vomiting, cough, bradycardia, restlessness, breath holding, laryngospasm, and bronchospasm in the propofol and the sevoflurane group was recorded. The results showed that there was no patient with breath holding, laryngospasm, or bronchospasm in the propofol or the sevoflurane group. There was 1 patient with nausea and vomiting, 1 patient with cough, and 1 patient with restlessness in the propofol group. The incidence of adverse reactions was 5% in the propofol group (3/60). There were 6 patients with nausea and vomiting, 2 patients with cough, 1 patient with bradycardia, 2 patients with restlessness in the sevoflurane group. The incidence of adverse reactions was 22% in the sevoflurane group (11/50). The results revealed that the incidence of adverse reactions in the propofol group was lower than that in the sevoflurane group (Table II).

Discussion

The results on blood glucose levels showed that there was no significant difference between blood glucose levels of the patients in the propofol group and those in the sevoflurane group before they were anesthetized (T_0). After surgery, the blood glucose levels of the patients gradually increased and were significantly higher than those before the patients were anesthetized. In addition, the blood glucose levels of the patients in the propofol group were significantly lower than those in the sevoflurane group. This result indicates that the effect of propofol was less than that of sevoflurane on glucose metabolism and the stress response of propofol was less than that of sevoflurane to surgical stimulation. A report on anesthetic management by Kitamura *et al* (20) demonstrated that the blood glucose levels of the patients in the propofol group were significantly higher than those in the sevoflurane group within 4 h after the patients were anesthetized, similarly to the results of the present study. Our results on hemodynamic indicators showed that there was no significant difference in HR, SpO_2, SBP and MBP of the patients in the two groups.

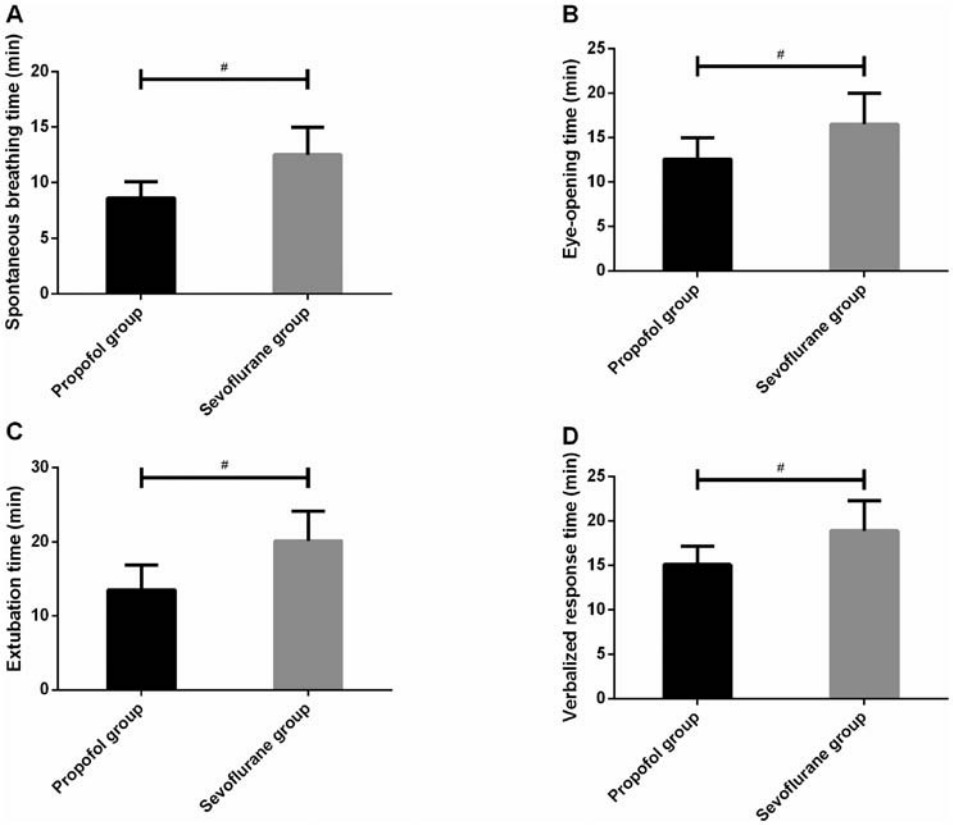

Figure 5. Comparison of the anesthetic effect of the patients in the two groups. (A) The time of spontaneous breath in the propofol group was shorter than that in the sevoflurane group (P<0.05). (B) The time of eye opening in the propofol group was shorter than that in the sevoflurane group (P<0.05). (C) The time of extubation in the propofol group was shorter than that in the sevoflurane group (P<0.05). (D) The time of verbal response in the propofol group was shorter than that in the sevoflurane group (P<0.05). #P<0.05, compared with the propofol group.

Table II. Comparison of adverse reactions of the patients in two groups [n (%)].

Category	Propofol group (n=60)	Sevoflurane group (n=50)	χ^2 test	P-value
Nausea and vomiting			4.887	<0.05
Yes	1 (1.67)	6 (12.00)		
No	59 (98.33)	44 (88.00)		
Cough			0.560	>0.05
Yes	1 (1.67)	2 (4.00)		
No	59 (98.33)	48 (96.00)		
Bradycardia			1.211	>0.05
Yes	0 (0.00)	1 (2.00)		
No	60 (100.00)	49 (98.00)		
Restlessness			0.560	>0.05
Yes	1 (1.67)	2 (4.00)		
No	59 (98.33)	48 (96.00)		
Breath holding			-	-
Yes	0 (0.00)	0 (0.00)		
No	60 (100.00)	50 (100.00)		
Laryngospasm			-	-
Yes	0 (0.00)	0 (0.00)		
No	60 (100.00)	50 (100.00)		
Bronchospasm			-	-
Yes	0 (0.00)	0 (0.00)		
No	60 (100.00)	50 (100.00)		

Compared with the hemodynamic indicators before the patients were anesthetized (T_0), the hemodynamic indicators decreased slightly and then increased after the surgery was started. There was no significant difference between the hemodynamic indicators of the patients in two groups after surgery was finished and those before surgery. This result indicates that the hemodynamic indicators of the patients in two groups were stable. Khare *et al* (21) studied the anesthesia of laparoscopic cholecystectomy, and found that SBP, DBP and MBP of the patients in the propofol group decreased in different periods compared with those in the sevoflurane group; however, there was no significant difference between the two groups. The hemodynamic indicators of the patients in two groups were stable. This result was similar to the results of our study. In this study, the results on inflammatory factors showed that there was no significant difference between baseline inflammatory factor indicators in the propofol group and those in the sevoflurane group. The levels of serum inflammatory factors IL-1β, IL-6, IL-10 and TNF-α were first increased, then decreased, and gradually returned to the preoperative level after the surgery was finished. The levels of IL-1β, IL-6 and IL-10 in the propofol group were lower than those in the sevoflurane group after pneumoperitoneum was carried out for 5 min. This result indicates that the effect of propofol is better than that of sevoflurane on reducing serum inflammatory factors. A study on propofol or sevoflurane combined with remifentanil was carried out by Shen *et al* (22) showing that the levels of serum IL-1β, IL-6 and TNF-α in the propofol and the sevoflurane group after surgery were significantly higher than those before surgery, and the levels of serum IL-1β, IL-6 and TNF-α in the propofol group were significantly lower than those in the sevoflurane group. These results suggested that remifentanil combined with propofol could reduce the concentration of serum inflammatory factors effectively in accordance to the results of the present study. The MMSE cognitive function scores showed that there was no significant difference between MMSE cognitive function scores in the propofol group and those in the sevoflurane group before the patients were anesthetized. MMSE cognitive function scores in the propofol and the sevoflurane group at 6 h after the beginning of surgery were significantly lower than those before the anesthetization of patients. MMSE cognitive function scores in the propofol group were significantly higher than those in the sevoflurane group at 6 h after the surgery was started. There was no significant difference between MMSE cognitive function scores in the propofol and the sevoflurane group at T_5 and those before the anesthetization of patients. This result indicates that the effect of propofol is less than that of sevoflurane on the cognitive function of patients with T2DM and GC. A study on effects of propofol and sevoflurane on the cognitive function of elderly patients (23), showed that propofol and sevoflurane had similar effects; however, the effect of propofol was less than that of sevoflurane on the cognitive function. This result is similar to the results of the present study. The results on the anesthetic effect showed that the time of spontaneous breath, eye opening, extubation, and verbal response in the propofol group were significantly shorter than those in the sevoflurane group, indicating that the anesthetic effect and analepsia quality of propofol are better than those of sevoflurane for patients with T2DM and GC. A study has shown that compared with general anesthesia, propofol or sevoflurane combined with epidural block is conducive in improving the analepsia quality of elderly patients with GC after undergoing anesthesia of radical surgeries, increases the stability of the patients' hemodynamics and shortens their awakening time (24). In the present study, the results on adverse reactions showed that the patients had adverse reactions, such as nausea, vomiting, cough and restlessness in the propofol and the sevoflurane group. The number of patients with nausea and vomiting in the propofol group was significantly less than that in the sevoflurane group, and the incidence of adverse reactions in the propofol group was significantly lower than that in the sevoflurane group. This result suggests that side effects of propofol might be less than those of sevoflurane, and adverse impacts of propofol are less than those of sevoflurane. A study on anesthetic postoperative pain was carried out by Peng *et al* (25), showing that the patients who were anesthetized with propofol needed less postoperative rescue analgesics than that of patients anesthetized with sevoflurane, and the execution time of postoperative analgesia was later. This result forcefully proved that the incidence of adverse reactions of propofol is lower than that of sevoflurane.

This study confirmed that the effect of propofol is less than that of sevoflurane on blood glucose, hemodynamics, and inflammatory factors of patients with T2DM and GC and that patients with high MMSE cognitive function scores have a good anesthetic effect and a low incidence of adverse reactions.

In conclusion, propofol is worthy of promotion in clinical practice for patients with T2DM and GC, and sevoflurane can be used as a second option.

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Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

JL and LY conceived and designed the study, collected, analyzed and interpreted the experiment data, drafted the manuscript, and revised it critically for important intellectual content. Both authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of The First Affiliated Hospital of Baotou Medical College (Baotou, China). Signed written informed consents were obtained from the patients and/or guardians.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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