

Study on Stress Response of Propofol Combined with Sevoflurane Combined Intravenous Inhalation General Anesthesia in Laparoscopic Cholecystectomy

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Abstract: *Objective:* To investigate the effect of propofol combined with sevoflurane combined intravenous inhalation general anesthesia on stress response in laparoscopic cholecystectomy. *Methods:* A total of 60 patients scheduled for elective laparoscopic cholecystectomy in the hospital from January 2023 to June 2025 were enrolled and randomly divided into two groups using a random number table method: the control group (30 cases) received total intravenous anesthesia with propofol for maintenance; the observation group (30 cases) received combined intravenous inhalation anesthesia with propofol and sevoflurane for maintenance. The anesthetic effects were compared between the two groups. *Results:* The observation group showed superior values compared to the control group in terms of mean arterial pressure (MAP) and heart rate (HR) during surgery and at the end of surgery, serum cortisol (Cor), norepinephrine (NE), and blood glucose (Glu) levels at 24 h postoperatively, as well as eyeopening time, spontaneous respiration recovery time, extubation time, and orientation recovery time (all $P < 0.05$). There was no statistically significant difference in the total incidence of adverse reactions between the two groups ($P > 0.05$). *Conclusion:* The application of propofol combined with sevoflurane combined intravenous inhalation general anesthesia in laparoscopic cholecystectomy can effectively maintain perioperative hemodynamic stability, inhibit stress responses induced by surgical trauma, and provide better recovery quality with good safety, thus warranting clinical promotion.

Keywords: Laparoscopic cholecystectomy; Propofol; Sevoflurane; Combined intravenous inhalation general anesthesia; Stress response

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1. Introduction

In laparoscopic cholecystectomy, the establishment of CO₂ pneumoperitoneum, tracheal intubation, and surgical trauma can activate the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic-adrenal

medullary system, leading to elevated levels of cortisol, catecholamines, and other hormones, which in turn cause hemodynamic fluctuations, hyperglycemia, and immune dysfunction, thereby affecting patient prognosis. Therefore, selecting an appropriate anesthesia method to reduce perioperative stress response is an urgent clinical issue to be addressed^[1]. Propofol is a commonly used shortacting intravenous anesthetic with advantages including rapid onset, quick recovery, and good controllability of anesthetic depth, making it a core agent for total intravenous anesthesia. However, highdose administration may cause adverse effects such as circulatory depression and injection pain. Sevoflurane is a widely used inhalational anesthetic with a low bloodgas partition coefficient, providing smooth induction and emergence, minimal impact on circulatory function, and enhanced effects of neuromuscular blockers. Combined intravenousinhalation anesthesia can integrate the advantages of both intravenous and inhalational anesthetics, exerting synergistic drug effects, maintaining adequate anesthetic depth while reducing the dosage of every single agent and lowering the risk of associated adverse reactions. This approach has attracted considerable attention in recent years and has achieved favorable outcomes. Therefore, this study focuses on analyzing the effect of propofol combined with sevoflurane combined intravenousinhalation general anesthesia on stress response in laparoscopic cholecystectomy, as detailed below.

2. General data and methods

2.1. General data

A total of 60 patients scheduled for elective laparoscopic cholecystectomy in the hospital from January 2023 to June 2025 were enrolled and randomly divided into two groups using a random number table method, with 30 cases in each group. In the observation group, there were 17 males and 13 females; age ranged from 32 to 64 years, with a mean of (47.25 ± 8.63) years; body mass index (BMI) ranged from 21.3 to 27.8 kg/m², with a mean of (24.16 ± 2.35) kg/m². In the control group, there were 16 males and 14 females; age ranged from 30 to 65 years, with a mean of (46.83 ± 9.12) years; BMI ranged from 20.8 to 28.1 kg/m², with a mean of (24.39 ± 2.51) kg/m². There were no significant differences in baseline data between the two groups ($P > 0.05$). This study complied with the requirements of the Declaration of Helsinki.

2.1.1. Inclusion criteria

- (1) Diagnosed with benign lesions such as cholelithiasis or gallbladder polyps by abdominal ultrasound or CT, meeting the indications for laparoscopic cholecystectomy;
- (2) Aged 18–65 years;
- (3) No significant abnormalities in preoperative liver and kidney function, coagulation function, or electrocardiogram;
- (4) Written informed consent obtained from patients and their families.

2.1.2. Exclusion criteria

- (1) Severe cardiac or pulmonary insufficiency, endocrine system diseases, or psychiatric/neurological disorders;
- (2) Longterm use of opioids, glucocorticoids, or antidepressants;
- (3) Allergy to propofol, sevoflurane, or other anesthetic agents;
- (4) Previous upper abdominal surgery;

- (5) Conversion to open surgery during the procedure or operation time exceeding 2 hours.

2.2. Methods

All patients underwent routine preoperative fasting for 8 h and fluid restriction for 4 h. After entering the operating room, an upper extremity venous line was established, and normal saline was infused. Routine monitoring included electrocardiogram (ECG), noninvasive blood pressure (NIBP), pulse oximetry (SpO₂), and bispectral index (BIS).

Anesthesia induction: Both groups received intravenous midazolam 0.05 mg/kg, sufentanil 0.4 µg/kg, propofol 2.0 mg/kg, and cisatracurium 0.15 mg/kg. After loss of consciousness and adequate muscle relaxation, tracheal intubation and mechanical ventilation were performed. Tidal volume was set at 8–10 ml/kg, respiratory rate at 12–14 breaths/min, and endtidal carbon dioxide partial pressure (PETCO₂) was maintained at 35–45 mmHg.

Anesthesia maintenance: In the control group, propofol was continuously infused at 4–8 mg/(kg·h) via a pump, with intermittent boluses of sufentanil and cisatracurium, and BIS was maintained at 40–60. In the observation group, sevoflurane was inhaled at 1.0%–2.0%, and the propofol infusion rate was adjusted according to BIS values and hemodynamic changes to maintain BIS at 40–60. During surgery, vasoactive agents were used as needed based on blood pressure and heart rate, and pneumoperitoneum pressure was maintained at 12–14 mmHg. At the end of surgery, all anesthetics were discontinued. After spontaneous respiration resumed, consciousness returned, and the swallowing reflex recovered, the tracheal tube was removed, and the patient was transferred to the postanesthesia care unit for monitoring.

2.3. Observation indicators

- (1) Mean arterial pressure (MAP) and heart rate (HR) were recorded and compared before surgery, during surgery (5 min after pneumoperitoneum establishment), and at the end of surgery.
- (2) Serum cortisol (Cor) levels were measured by chemiluminescence, norepinephrine (NE) concentrations by highperformance liquid chromatography, and blood glucose (Glu) levels by the glucose oxidase method before surgery and 24 h after surgery.
- (3) Eyeopening time, spontaneous respiration recovery time, extubation time, and orientation recovery time were recorded and compared.
- (4) The incidence of adverse reactions within 24 h postoperatively, including nausea and vomiting, dizziness, agitation, and cough, was recorded and compared.

2.4. Statistical analysis

Data were processed using SPSS version 24.0. Continuous variables were analyzed using the *t* test and presented as mean ± standard deviation (Mean ± SD); categorical variables were analyzed using the χ^2 test and presented as percentages (%). A *P* value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of MAP and HR at different time points between the two groups

At the time points during surgery and at the end of surgery, MAP and HR in the observation group were significantly lower than those in the control group (*P* < 0.05), as shown in **Table 1**.

Table 1. Comparison of MAP and HR at different time points between the two groups (*n*, Mean $\pm$ SD)

Group	n	MAP (mmHg)			HR (beats/min)		
		Preoperative	Intraoperative	End of surgery	Preoperative	Intraoperative	End of surgery
Observation group	30	86.34 $\pm$ 7.52	94.27 $\pm$ 8.13	95.16 $\pm$ 8.34	76.28 $\pm$ 6.43	84.36 $\pm$ 7.25	85.62 $\pm$ 7.58
Control group	30	87.15 $\pm$ 7.86	102.56 $\pm$ 9.45	104.72 $\pm$ 9.86	77.05 $\pm$ 6.71	93.47 $\pm$ 8.62	95.18 $\pm$ 9.03
<i>t</i>		0.408	3.642	4.055	0.454	4.430	4.441
<i>P</i>		0.685	0.001	0.000	0.652	0.000	0.000

3.2. Comparison of stress indicators between the two groups at different time points

At 24 hours postoperatively, the levels of cortisol (Cor), norepinephrine (NE), and glucose (Glu) in the observation group were lower than those in the control group ($P < 0.05$), as shown in **Table 2**.

Table 2. Comparison of stress indicators between the two groups at different time points (*n*, Mean $\pm$ SD)

Group	n	Cor (nmol/L)		NE (pg/ml)		Glu (mmol/L)	
		Before surgery	24 h after surgery	Before surgery	24 h after surgery	Before surgery	24 h after surgery
Observation group	30	287.46 $\pm$ 35.72	368.25 $\pm$ 42.39	152.37 $\pm$ 24.65	205.63 $\pm$ 28.74	5.12 $\pm$ 0.64	6.03 $\pm$ 0.76
Control group	30	291.38 $\pm$ 37.15	457.63 $\pm$ 54.28	156.82 $\pm$ 26.13	274.39 $\pm$ 36.52	5.20 $\pm$ 0.68	6.95 $\pm$ 0.92
<i>t</i>		0.417	7.108	0.679	8.104	0.469	4.223
<i>P</i>		0.679	0.000	0.500	0.000	0.640	0.000

3.3. Comparison of recovery quality indicators between the two groups

In terms of recovery quality, the observation group demonstrated more prominent advantages compared with the control group ($P < 0.05$), as shown in **Table 3**.

Table 3. Comparison of recovery quality indicators between the two groups (*n*, Mean $\pm$ SD, min)

Group	n	Eye opening time	Spontaneous breathing recovery time	Extubation time	Orientation recovery time
Observation group	30	5.24 $\pm$ 1.13	4.86 $\pm$ 1.05	7.35 $\pm$ 1.42	9.68 $\pm$ 1.76
Control group	30	7.15 $\pm$ 1.48	6.52 $\pm$ 1.37	9.84 $\pm$ 1.89	13.57 $\pm$ 2.34
<i>t</i>		5.618	5.268	5.769	7.277
<i>P</i>		0.000	0.000	0.000	0.000

3.4. Comparison of adverse reactions between the two groups

There was no statistically significant difference in the incidence of adverse reactions between the two groups ($P > 0.05$), as shown in **Table 4**.

Table 4. Comparison of adverse reactions between the two groups (*n*, %)

Group	n	Nausea and vomiting	Dizziness	Agitation	Choking cough	Total incidence
Observation group	30	2 (6.67)	1 (3.33)	0 (0.00)	0 (0.00)	3 (10.00)
Control group	30	3 (10.00)	0 (0.00)	1 (3.33)	1 (3.33)	5 (16.67)

χ^2	0.577
P	0.448

4. Discussion

Although laparoscopic cholecystectomy is a minimally invasive procedure, factors such as endotracheal intubation stimulation, increased intraabdominal pressure due to CO₂ pneumoperitoneum, and peritoneal traction can promote the secretion of stress hormones including catecholamines and cortisol, which in turn trigger a series of pathophysiological changes—such as elevated blood pressure, increased heart rate, and hyperglycemia—and increase the risk of perioperative cardiovascular events ^[2]. An ideal anesthetic approach should effectively inhibit perioperative stress responses while meeting the requirements for surgical sedation and analgesia, and maintaining hemodynamic stability ^[3].

Propofol is the most widely used intravenous general anesthetic in clinical practice. It primarily exerts its central inhibitory effects by enhancing the function of γ -aminobutyric acid type A (GABAA) receptors, and offers advantages including rapid onset, swift metabolic clearance, and negligible accumulation in the body. However, a large-dose single injection can easily induce adverse reactions such as circulatory depression and injection pain ^[4]. Sevoflurane is a novel halogenated inhalational anesthetic that provides smooth induction and emergence, causes minimal airway irritation, allows mask induction, has a mild impact on hemodynamics, and can potentiate the effects of muscle relaxants. Combined intravenous-inhalational anesthesia, by coadministering intravenous and inhalational agents to maintain anesthetic depth, can exploit drug synergies, reduce the dosage of individual drugs, and lower the risk of adverse effects associated with a single agent ^[5].

The results of this study showed that during surgery, both groups experienced fluctuations in MAP and HR; however, the MAP and HR levels at each time point were lower in the observation group than in the control group, indicating that propofol combined with sevoflurane intravenous-inhalational anesthesia can more effectively inhibit sympathetic excitation and maintain more stable hemodynamics. Mechanistically, sevoflurane can reduce blood pressure by inhibiting myocardial contractility and dilating peripheral vessels, thereby attenuating the cardiovascular responses induced by endotracheal intubation and extubation, while propofol exerts circulatory effects through direct peripheral vasodilation and mild inhibition of myocardial contractility. The combined application of the two agents thus provides clear complementary effects ^[6].

Cortisol is a core endocrine indicator reflecting the degree of systemic stress, and norepinephrine is an important marker of sympathetic nervous system activation. Both are significantly elevated under surgical stress, and the magnitude of elevation is positively correlated with the intensity of stress ^[7]. Hyperglycemia is also an important manifestation of the stress response, and its mechanism is closely related to cortisol and catecholamine-promoted glycogenolysis and inhibition of insulin secretion ^[8]. The results of this study showed that at 24 hours postoperatively, the levels of Cor, NE, and Glu increased in both groups compared with preoperative values, but the levels of these stress indicators were lower in the observation group than in the control group, suggesting that propofol combined with sevoflurane intravenous-inhalational anesthesia can more effectively attenuate the neuroendocrine stress response induced by surgical trauma ^[9]. This may be attributed to sevoflurane's action on the adrenal cortex and sympathetic ganglia, as well as its modulation of neuroendocrine activity in the hypothalamic paraventricular nucleus, thereby exerting synergistic antistress

effects with propofol ^[10].

Quality of recovery is an important indicator for evaluating anesthetic efficacy and directly affects the efficiency of postoperative patient recovery ^[11]. The results of this study showed that the observation group had shorter eyeopening time, spontaneous breathing recovery time, extubation time, and orientation recovery time than the control group, indicating that combined intravenousinhalational anesthesia can accelerate and improve the completeness of patient emergence. The underlying reasons include the low bloodgas partition coefficient of sevoflurane, which allows rapid pulmonary clearance after discontinuation with minimal residual accumulation in the body; simultaneously, combined anesthesia reduces the total propofol dosage, decreasing drug accumulation effects and thereby accelerating emergence and cognitive function recovery ^[12]. Sevoflurane can easily cause agitation during the emergence period, whereas propofol possesses good sedative and anxiolytic properties; their combination can reduce the risk of emergence agitation and improve recovery quality ^[13].

In terms of safety, the incidence of adverse reactions showed no statistically significant difference between the two groups ($P > 0.05$), and the reactions were mainly mild nausea, vomiting, and dizziness, all of which resolved after symptomatic treatment. This suggests that propofol combined with sevoflurane intravenousinhalational anesthesia does not increase the risk of adverse reactions and demonstrates good clinical safety ^[14]. Some studies have pointed out that sevoflurane can react with soda lime to produce compound A, and prolonged highconcentration inhalation carries a potential risk of nephrotoxicity; however, laparoscopic cholecystectomy is relatively short in duration, and lowconcentration inhalation generally does not cause significant organ damage ^[15].

5. Conclusion

In summary, for laparoscopic cholecystectomy, the administration of propofol combined with sevoflurane intravenousinhalational general anesthesia can effectively maintain perioperative hemodynamic stability, inhibit the stress response induced by surgical trauma, and provide better recovery quality with favorable safety, making it worthy of clinical promotion.

Disclosure statement

The authors declare no conflict of interest.

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