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Original Article

Changes of recovery quality and early cognitive function after treatment of sevoflurane combined with propofol in the elderly undergoing cholecystectomy

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Abstract: Objective: To explore the application value of sevoflurane + propofol in elderly patients undergoing cholecystectomy. Methods: A total of 121 elderly patients undergoing cholecystectomy in our hospital from February 2017 to March 2020 were enrolled. Among them, 58 patients were assigned to Group A given, anesthesia with sevoflurane during operation, and 63 patients to Group B who were given anesthesia with sevoflurane + propofol during the operation. The Mini-Mental State Examination (MMSE) was adopted to evaluate the cognitive function of the two groups at 1 hour (T1), 3 hours (T2) and 12 hours (T3) after operation, and enzyme-linked immuno-sorbent assay (ELISA) was used to determine inflammatory factors. The incidence of postoperative adverse reactions was compared between the two groups. Results: The heart rate (HR) of patients at T2 was significantly lower than that at T1 and T3, and their HR at T3 was lower than that at T1 ($P<0.05$). There were differences in systolic blood pressure (SBP) and diastolic blood pressure (DBP) at different time points in each group (both $P<0.001$). The mean artistic pressure (MAP) of patients at T2 was significantly lower than that at T1 and T3, and their MAP at T3 was lower than that at T1 ($P<0.05$). Additionally, oxygen saturation (SpO_2) of patients at T2 was also significantly lower than that at T1 and T3, and their SpO_2 at T3 was lower than that at T1 ($P<0.05$). Moreover, Group B showed significantly lower levels of serum inflammatory factors than Group A at T2 and T3 ($P<0.05$), and also got greatly lower Observer Assessment of Sedation (OAA/S) scores than Group A ($P<0.05$). Conclusion: Sevoflurane + propofol can effectively improve the recovery quality and cognitive function and reduce inflammation after cholecystectomy in the elderly, so it is worthy of clinical promotion.

Keywords: Elderly patients, cholecystectomy, sevoflurane, propofol, recovery quality, early cognitive function

Introduction

Cholecystectomy is the most common abdominal operation in western countries, which can be applied for various indications [1, 2]. Despite the decreases in morbidity and mortality after cholecystectomy by minimally invasive methods, there are still increasingly rare and unique complications of cholecystectomy [3, 4]. After cholecystectomy, patients usually suffer persistent or recurrent pain. For elderly patients, the anesthetic effect is crucial for the success rate of cholecystectomy. Anesthesia concentration during operation must be enough to ensure the completion of the corresponding operation, and the stability of hemodynamics to be unaffected [5, 6]. Therefore, it is particularly important to choose and maintain a stable, safe, controllable and effective clinical anesthesia program.

Sevoflurane and propofol are often applied in surgery for various cardiovascular diseases as they are favorable clinical anesthetic drugs, and they also plays a crucial role in gastroscopy [7, 8]. Propofol is an intravenous sedative and hypnotic drug that does not cause much of an allergic reaction [9]. Compared with other intravenous drugs and more traditional anesthesia schemes, propofol dominates in daytime operation anesthesia [10]. Sevoflurane is a safe inhalation anesthetic widely used to induce and maintain anesthesia in inpatient and outpatient surgery [11]. Among all anesthetics applied at present, sevoflurane has the most ideal physical, pharmacodynamic and pharmacokinetic characteristics, as it causes the least adverse effects on the cardiovascular and respiratory system [12]. At present, the efficacy of sevoflurane and propofol in cholecystectomy anesthesia needs to be improved. This experiment aimed to explore the role of propofol combined with sevoflurane on elderly patients undergoing cholecystectomy by testing and analyzing its clinical efficacy and related factors, so as to provide reference for clinical implementation of elderly patients undergoing cholecystectomy.

Materials and methods

Patient data

Altogether 121 elderly patients undergoing cholecystectomy from February 2017 to March 2020 were enrolled as research participants. Among them, 58 patients were assigned to Group A and given anesthesia with sevoflurane during operation, and 63 patients were assigned to Group B who were given anesthesia with sevoflurane + propofol during operation. These patients were aged 31-77 years, with an average age of (65.29±4.14). The inclusion criteria: Patients with complete cases and indications of percutaneous microwave ablation, patients who had not received relevant medical treatment in other hospitals, patients whose preoperative mini mental state examination (MMSE) [13] score was more than 23 points. The exclusion criteria: Patients with allergic reactions to the drugs applied in this research, patients with acute gastrointestinal bleeding or other tumors, patients who had taken opioids for a long time, patients with kidney and coagulation defects or insufficient baseline data, patients who dropped out halfway, and patients with communication disorders or cognitive disorders. The informed consent forms were obtained from the subjects and their families.

Methods

Both groups of patients received thorough examination before anesthesia, and the anesthetic dose was adjusted according to the patient's weight and age strictly in accordance with the clinical standard. The two groups of patients were fasted drom solids and liquids. Before operation, the indexes and BIS index of patients were closely observed. The two groups of patients were given the same anesthesia induction method.

Group A was given 7% sevoflurane (Guangdong Jiabo Pharmaceutical Co., Ltd., State Food and Drug Administration (SFDA) approval number: H20143369) inhalation, which was added into the pipe of the oxygen inhalation machine. The oxygen flow rate was set at 8 L·min-1. Remifentanil (4 μg/kg-1) was injected intravenously. Sevoflurane (Lunan Beite Pharmaceutical Co., Ltd., SFDA approval number: H20080681) and remifentanil (Jiangsu Nhwa Pharmaceutical Co., Ltd., SFDA approval number: H20143315) [0.1-1 μg/(kg·min)] were given to maintain anesthesia. Both groups were given Vecuronium Bromide intravenously (0.1 mg·kg-1) to maintain muscle relaxation.

Group B received intravenous induction with propofol (2 mg/kg) on the basis of Group A. Remifentanil hydrochloride (4 μg/kg-1) was applied for injection, and tracheal intubation and ventilator connection were performed. Propofol [4-9 μg/(kg·H)] and remifentanil [0.1-1 μg/(kg·min)] were given to maintain anesthesia.

Outcome measures

The changes of heart rate (HR), hemodynamic indexes (systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and oxygen saturation (SpO_2)) were measured at 1 hour (T1), 3 hours (T2), and 12 hours (T3) after operation. The awake time, hospitalization time, MMSE score of Observer Assessment of Sedation (OAA/S) [14], and the incidence of perioperative adverse reactions were tested.

Statistical analyses

SPSS 19.1 was applied for statistical analysis, and GraphPad Prism 8 software was adopted to illustrate the figures. Counting data were represented as percentage [n (%)], and compared using Chi-square test. Measurement data were represented as mean ± SD, and compared by t test. The variance analysis of repeated measurements was adopted for comparison of multiple time points within the group. $P<0.05$ indicated a statistically remarkable difference.

Table 1. Basic data [n (%)]

	Group A (58)	Group B (63)	X^2	P
Gender			0.000	0.998
Man	35 (60.34)	38 (60.32)		
Woman	23 (39.66)	25 (39.68)		
Age (years)			0.1873	0.665
≤65	19 (32.76)	23 (36.51)		
>65	39 (67.24)	40 (63.49)		
Weight (kg)			1.041	0.307
≤60	25 (43.10)	33 (52.38)		
>60	33 (56.90)	30 (47.62)		
History of abdominal surgery			0.226	0.635
Yes	10 (17.24)	13 (20.63)		
No	48 (82.76)	50 (79.37)		
History of diabetes/hypertension			0.326	0.568
Yes	21 (36.21)	26 (41.27)		
No	37 (63.79)	37 (58.73)		
Disease type			0.368	0.832
Acute calculous cholecystitis	28 (48.28)	32 (50.80)		
Gallbladder polyps	6 (10.34)	8 (12.70)		
Chronic calculous cholecystitis	24 (41.38)	23 (36.51)		
Abnormal liver function			0.532	0.466
Yes	9 (15.52)	13 (20.63)		
No	49 (84.48)	50 (79.37)		

Results

Patient data

There was no remarkable difference in gender, age, weight, alcoholism, tumor number, liver cirrhosis and TNM stage between the two groups (all P>0.05) (**Table 1**).

Hemodynamic changes

SBP and DBP: There was no remarkable difference in SBP and DBP at T1 (P>0.05). SBP and DBP in both groups declined markedly at T2 (both P<0.001), but elevated markedly at T3, and there were remarkable differences in SBP and DBP at different time points in both groups (both P<0.001) (**Figure 1**).

MAP and HR: HR at T1, T2 and T3 in Group A were (83.52±8.39) times/min, (72.45±8.12) times/min, and (79.36±7.37) times/min, respectively, while those in Group B were (84.12±7.85) times/min, (81.68±8.64) times/min, and (82.95±7.91) times/min, respectively. Therefore, there was no remarkable difference in HR at T1 between the two groups (P>0.05), and HR of Group A at T2 and T3 was markedly lower than that of Group B (P<0.001). In addition, there was remarkable difference in HR among patients in Group A (P<0.001). HR at T2 declined markedly compared with that at T1 and T3, and HR at T3 declined compared with that at T1 (all P<0.05). There was no obvious change in HR of patients in Group B (P>0.05) (**Figure 2A**). Moreover, there was no remarkable difference in MAP at T1 and T3 (P>0.05). MAP at T2 in Group A was markedly lower than that in Group B (P<0.001), and the difference of MAP in Group A was statistically remarkable (P<0.001). MAP at T2 declined markedly compared with that at T1 and T3, and MAP at T3 declined compared with that at T1 (P<0.05). MAP in Group B showed no obvious fluctuation and no remarkable difference (P>0.05) (**Figure 2B**).

SpO_2: There was no remarkable difference in SpO_2 in the two groups at T1 (P>0.05). SpO_2 at T2 and T3 in Group A declined markedly compared with that in Group B (P<0.001). There was remarkable difference in SpO_2 among patients in Group A (P<0.001). SpO_2 at T2 declined markedly compared with that at T1 and T3, and SpO_2 at T3 declined compared with that at T1 (P<0.05). There was no remarkable fluctuation of SpO_2 in Group B (P>0.05) (**Figure 3**).

Changes of inflammatory factors

There was no remarkable difference in TNF-α, IL-1β and IL-10 between the two groups at T1 (all P>0.05). TNF-α, IL-1β and IL-10 in both groups elevated markedly at T2 and T3 (all P<0.05), and the levels of TNF-α, IL-1β and IL-10 in Group B were markedly lower than

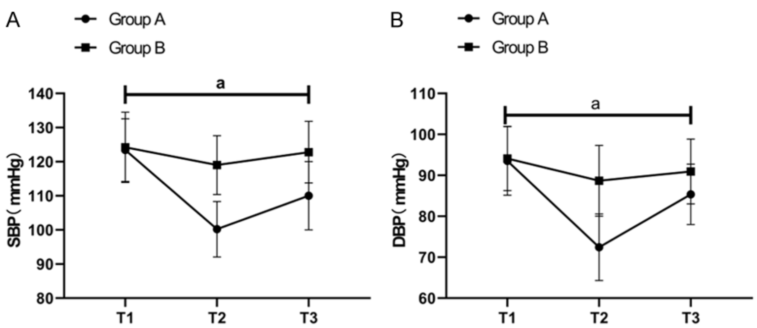

Figure 1. SBP and DBP. SBP and DBP in both groups declined markedly at T2 (P<0.001), and elevated markedly at T3, and there were remarkable differences in SBP and DBP at different time points in each group (P<0.001). Note: a means P<0.05.

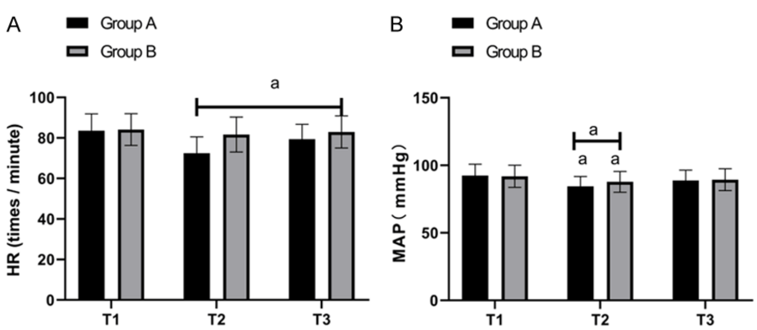

Figure 2. HR andMAP. A. HR of Group A at T2 and T3 was markedly lower than that of Group B (P<0.001). There was remarkable difference in HR among patients in Group A (P<0.001). HR at T2 declined markedly compared with that at T1 and T3, and HR index at T3 declined compared with that at T1 (P<0.05). B. MAP at T2 declined markedly compared with that at T1 and T3, and MAP at T3 declined compared with that at T1 (P<0.05). Note: a means P<0.05.

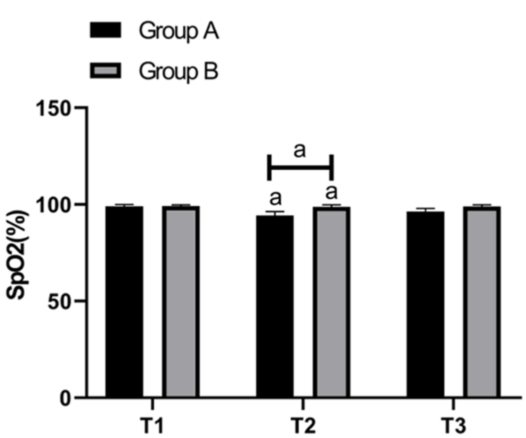

Figure 3. SpO_2. SpO_2 at T2 declined markedly compared with that at T1 and T3, and SpO_2 at T3 declined compared with that at T1 (P<0.05). Note: a means P<0.05.

those in Group A at T2 and T3 (all P<0.05) (**Figure 4**).

Comparison of awake time, hospitalization time, extubation time and OAA/S score

In this study, we compared the MMSE scores, awake time, hospitalization time and extubation time of the two groups after treatment, and found no significant difference between the two groups in these items (P>0.05). In addition, we found through comparison that the OAA/S scores of patients in Group B were significantly lower than those in Group A (P<0.05) (**Table 2**).

Comparison of perioperative complications

At the end of the study, we compared the incidence of adverse reactions between the two groups, and found that no notable difference between the two groups in the number of patients with nausea, vomiting, dizziness, arrhythmia and blood pressure drop (P>0.05) (**Table 3**).

Discussion

Cholecystectomy is the first choice for symptomatic cholelithiasis. Many surgeons adopt intraperitoneal anesthetics during or perform it after surgery to relieve postoperative pain [15, 16]. In terms of nociceptive stimulation, inhibiting central nerve sensitization by intraperitoneal local anesthesia before it triggers activation of pain pathways can alleviate postoperative pain [17, 18]. There is little evidence about which type of local anesthesia is most effective, and the available data is limited. General anesthesia obviously affects the brain function after operation, and it is often reported to impair attention, memory, reaction time and consciousness [19]. Delays in functional recovery due to cognitive dysfunction will prolong hospital stay. This is crucial in the case of short discharge time after anesthesia, such as lapa-

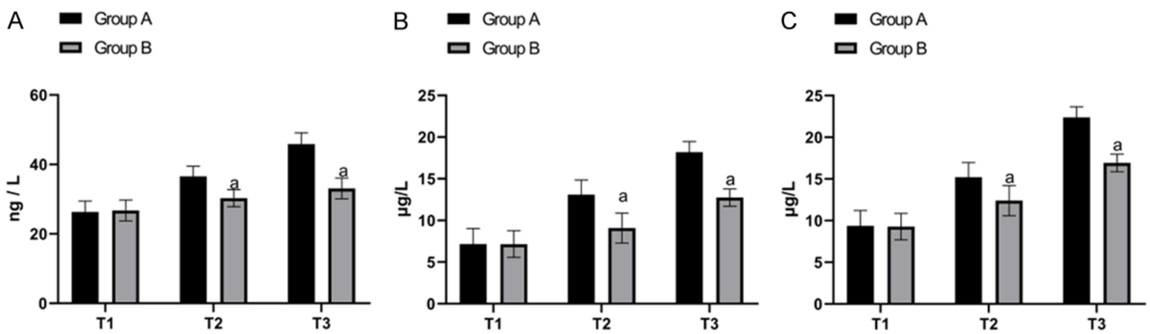

Figure 4. Inflammatory factors. The levels of TNF-α, IL-1β and IL-10 in Group B were markedly lower than those in Group A at T2 and T3 (P<0.05). Note: a means P<0.05.

Table 2. Comparison of awake time, hospitalization time, OAA/S and postoperative MMSE score

	Group A (58)	Group B (63)	t	P
Awake time (min)	10.53±3.37	9.34±3.52	1.896	0.060
Extubation time (min)	11.65±4.20	10.30±4.10	1.788	0.76
Hospital stay (d)	14.00±5.15	13.74±5.00	0.282	0.779
OAA/S score	2.87±0.45	2.67±0.31	2.866	0.005
MMSE score	16.28±4.20	15.20±4.00	1.449	0.150

Table 3. Comparison of adverse reactions [n (%)]

	Group A (58)	Group B (63)	X^2	P
Nausea	2 (3.45)	2 (3.17)	-	-
Vomiting	2 (3.45)	2 (3.17)	-	-
dizziness	2 (3.45)	2 (3.17)	-	-
arrhythmia	1 (1.72)	0 (0.00)	-	-
Blood pressure decline	1 (1.72)	1 (1.59)	-	-
total	8 (13.79)	8 (12.70)	0.032	0.859

roscopic cholecystectomy. There are many factors affecting the recovery of cognition and memory for a long time after anesthesia and operation. Various studies have shown that propofol and sevoflurane can cause cognitive dysfunction [20].

First of all, we analyzed the relevant vital signs of patients during perioperative period, and found that the HR of patients treated with sevoflurane anesthesia alone was markedly lower than that of patients treated with sevoflurane combined with propofol anesthesia, and in the sevoflurane combined with propofol group, the heart rate and other hemodynamic indexes fluctuated little at different time points. Propofol and sevoflurane have good anesthetic effect [21]. In a clinical experiment of gastroscopy anesthesia for elderly patients, it was shown that propofol combined with sevoflurane is safer and has better anesthetic effect. In addition, the combination of the two drugs can improve the hemodynamic stability, reduce side effects and provide rapid recovery to complete active state [22]. Compared with sevoflurane or propofol alone, sevoflurane combined with propofol has better effect and can better maintain hemodynamic stability [23], which are similar to the results of this experiment. To sum up, the combined use of sevoflurane and propofol has a good effect on the hemodynamic stability of patients. With combination of them, the perioperative complications of nausea, vomiting, dizziness, arrhythmia and blood pressure decline were less, and the awake, hospitalization and extubation time of patients in the two groups were shorter.

Then, by observing the changes of inflammatory factors in patients, it was found that the postoperative IL-10 of patients treated with combined anesthesia was higher than that of patients treated with single anesthesia. Studies have shown that cholecystectomy is an invasive treatment method in stomach surgery. Anesthesia and surgical trauma will lead to immune and inflammatory reactions by affecting airway epithelial cells [24]. In this case, sevoflurane and propofol can regulate the inflammatory response in the local airway environment [25]. Sevoflurane can increase IL-6 and IL-8 [26]. In clinical practice, related concentrations of propofol can down-regulate IL-6 and IL-8. Previous studies have shown that compared with isoflurane inhalation anesthesia for abdominal surgery, patients receiving propofol anesthesia have a stronger anti-inflammatory reaction and higher IL-10 levels [27]. Propofol may play an anti-inflammatory role in the respiratory tract by inducing the production of IL-10 and inhibiting the production of IL-6 and IL-8, thus reducing postoperative complications [28]. Therefore, compared with sevoflurane anesthesia, sevoflurane combined with propofol can inhibit inflammation disturbance caused by surgical stress more effectively in cholecystectomy, so it has attracted more attention in the clinic.

In this study, the anesthetic doses of the two groups were adjusted according to the weight and age of the patients, and then the hemodynamic changes of the patients during operation were observed. We found that due to the limited medical resources in our hospital, there are some disputes in the results, and it is not excluded that patients with different genders or ages have different reactions after anesthesia. Therefore, we will conduct a longer follow-up investigation on this subject, and constantly improve our experiment in the future to achieve more accurate experimental results.

To sum up, sevoflurane combined with propofol can achieve satisfactory anesthetic effects in percutaneous microwave ablation of liver cancer, and combination of the two can effectively stabilize the vital signs of patients with little side effects and little influence on patients' cognitive function, so it is worthy of popularization and application in clinical practice.

Disclosure of conflict of interest

None.

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