Clinical Trial/Experimental Study

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Clinical observation of the combined use of propofol and etomidate in painless gastroscopy

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Abstract

Objective: This study is aims to compare the anesthetic safety of propofol combined with etomidate for painless gastroscopy.

Methods: Three hundred patients undergoing painless gastroscopy were randomly assigned to P, PE_1, and PE_2 groups. Patients were anesthetized with propofol (P group) or propofol combined with etomidate (volume ratio 1: 1, PE_1 group; volume ratio 2: 1, PE_2 group). The hemodynamics and adverse reactions were observed. The sleep quality satisfaction and nature of dreams were recorded.

Results: Compared with pre-anesthesia, the mean arterial pressure and heart rate of the 3 groups were significantly slower during the examination and at the end of the examination. PE_1 group had a higher incidence of muscle spasm, body moving, choking, and deglutition. The incidence of hypoxemia and injection pain was higher in P group. P and PE_2 group had higher sleep quality satisfaction and dream incidence after awaking. However, there was no difference in the nature of dreams among 3 groups.

Conclusion: Our data indicate that the combination of 10 ml 1.0% propofol and 5 ml 0.2% etomidate for painless gastroscopy reduces adverse reactions while not affecting the patients respiratory function. Moreover, it is safe and effective, which is worthy of clinical application and promotion.

Abbreviations: HR = heart rate, MAP = mean arterial pressure, PADS = postanesthesia discharge score, SBP = systolic pressure, SpO_2 = oxyhemoglobin saturation.

Keywords: etomidate, painless gastroscopy, propofol

1. Introduction

As the economic level keeps increasing, patients demand for comfortable medical treatment is increasing, and painless endoscopy has become a trend. Propofol is a commonly used intravenous anesthetic in clinic that has a rapid onset, a short duration, and a quick recovery. Since its coming out, propofol has been widely recognized and can be safely applied to anesthesia of painless test.[1] Clinical practice has observed that some patients complains of good quality sleep during painless anesthesia. However, propofol has a greater impact on the hemodynamics of patients, and has the disadvantages of injection pain and obvious respiratory circulation inhibition.[2] The etomidate also has a sedative and hypnotic effect, and has little effect on hemodynamics.[3] However, etomidate alone causes muscle tremor, muscle rigidity, postoperative nausea and vomiting.[4,5] While causing serious complications, it also affects the doctors operation and reduces the patients satisfaction with sleep experience during anesthesia. Therefore, this study mixed propofol and etomidate in different proportions to explore the safety of the combined use of the 2 drugs and the satisfaction of sleep experience, as well as the impact on dreams.

2. Materials and methods

2.1. Participants

We enrolled into the study 300 patients (ASA physical status I to II, 20–65 years old) from December 2016 to December 2018, who were scheduled for painless gastroscopy. There were 150 men and 150 women, weighing between 40 and 75 kg. The patients with the following symptoms were excluded:

1. The patient has a serious history of heart, lung, brain, liver, or kidney disease;
2. Patients with diabetes, hyperlipidemia or cancer;
3. Chronic alcoholics;
4. The patient has psychosis or neuromuscular disease;
5. Allergy to anesthetics;
6. Patients are predicted to have difficult airways;
7. Patients with acute upper respiratory tract infection, asthma attack or acute severe throat disease.

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

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Table 1

The general condition, inspection time and awakening time of patients.

Variable	Groups			*P* value
	P	PE_1	PE_2	
Sex (Female/Male)	41/55	44/52	43/53	.918
Age (years)	50.81 ± 12.59	45.30 ± 15.53	50.74 ± 12.96	.141
Height (cm)	164.13 ± 6.71	166.58 ± 7.73	164.09 ± 6.81	.226
Weight (kg)	62.02 ± 7.99	63.64 ± 10.47	61.96 ± 8.07	.649
Dosage of drugs (ml)	14.13 ± 1.86	17.06 ± 4.04	14.15 ± 1.87	.124
inspection time (minutes)	7.70 ± 1.85	8.17 ± 2.19	7.72 ± 1.87	.157
awakening time (second)	107.11 ± 73.14	196.97 ± 143.01	109.30 ± 76.63	.000

The patients were randomly divided into 3 groups (n = 100): P, PE_1, and PE_2 groups. Then, we compared the general preoperative conditions of the 3 groups (Table 1). All patients were informed and gave written consent. The protocols were authorized by the Ethics Committee of Anhui Provincial Hospital (Registration number: ChiCTR-IRC-16010186).

2.2. Anesthesia method

Before the anesthesia, the patients were fasted for 8 hours and banned water more than 4 hours. Monitors, anesthesia machines, rescue medicines, tracheal intubations and related items were prepared before anesthesia. The patients took 10 ml of Dyclonine hydrochloride mucilage orally 10 minutes before entering the room. After entering the room, the patients were lying on the left side, and the peripheral venous channel was opened, and the nasal catheter was inhaled with oxygen (3–5 L/minutes). The blood pressure, heart rate and oxyhemoglobin saturation (SpO_2) of patients were routinely monitored. All patients were received intravenous injection of 50 g fentanyl, and then were given intravenous injection of sedatives 2 minutes later. Patients in P group were received intravenous injection of 20 ml of 1.0% propofol. Patients in PE_1 group were given intravenous injection of 10 ml of 1.0% propofol combined with 10 ml of 0.2% etomidate. Patients in PE_2 group were received intravenous injection of 10 ml of 1.0% propofol combined with 5 ml of 0.2% etomidate. The first injection dose is 0.2 to 0.25 ml/kg. Until the patients consciousness disappeared, the eyelash reflex disappeared, and breathing was stable, and then the endoscopy operation began. During the examination, if the patient had choking and body movements, the operation was suspended, and the patient was injected with 1/4 of initial dose. When the patients showed systolic pressure (SBP) <80 mm Hg during the examination, the patients were injected with 5 to 10 mg ephedrine, and when the heart rate (HR) was <50 times/minutes, the patients were injected with 0.5 mg atropine. When the patient's blood oxygen saturation was lower than 90% during the examination, the inhaled oxygen flow was enhanced and the mandibular angle of patients was supported. If the oxygen saturation had not improved, a breathing action can be formed by squeezing the patients thorax slightly and observing whether the patients SpO_2 was elevated. If SpO_2 was still below 90%, suspend the gastroscopy and quickly pulled out the electronic gastroscope, hold up the mandibular back mask to pressurize to assist breathing, and perform gastroscopy after SpO_2 >90%. After the examination, when the patients had severe nausea and vomiting reaction, 4 mg tropisetron was given to the patients. When the patients had severe dizziness, lie down and rest until the postanesthesia discharge score (PADS) is greater than or equal to 9 points (Supplementary Table 1, http://links.lww.com/MD/F137).

2.3. Observation indexs

The mean arterial pressure (MAP) and HR of patients were observed and recorded before anesthesia (T0), 1 minutes (T1) after being put into gastroscopy, and at the end of the examination (T2). At the same time, the dosage of anesthetics, the examination time, the anesthesia recovery time, hyoxemia, muscle spasm, injection pain, body moving, choking, deglutition, postoperative nausea, vomiting, dizziness, intraoperative awareness, etc were recorded. Hypotension: MAP < 25% before surgery. Hyoxemia: SpO_2 < 90% duration >10 second. The patient was evaluated for sleep quality 5 minutes after waking up, and whether or not dreaming and the characteristics of dreams were recorded during anesthesia.

2.4. Statistical analysis

All values were exhibited as mean ± standard deviation and analyzed by SPSS 22.0 statistical software (SPSS, USA). One-way ANOVA was used to compare the differences between groups. For comparison of unordered categorical data s, a Chi-Squared test was used. Comparison of multigroup ranked data was made using Kruskal–Wallis test. $P < .05$ was considered statistically significant.

3. Results

3.1. General condition

There was no significant difference in the general conditions of the 3 groups of patients such as age, height, weight, sex, dosage of drugs, and inspection time ($P > .05$). However, the PE_1 group had significantly longer awakening time ($P < .05$) (Table 1).

3.2. Sleep quality

There was no significant difference in sleep quality among the 3 groups before and after the operation ($P > .05$). However, there were differences in the sleep quality satisfaction among the 3 groups after waking up. The sleep quality satisfaction of the PE_1 group after waking up was significantly lower than that of the P and PE_2 group ($P < .05$) (Table 2).

3.3. Comparison of MAP and HR of patients

Compared with T0, the MAP and HR of the 3 groups at T1 was significantly decreased ($P < .05$), and the HR of the 3 groups at T2 was notably decreased ($P < .05$). Compared with PE_1 group,

Table 2

The sleep quality of patients.

Variable	Groups			*P* value
	P	PE_1	PE_2	
Usual sleep quality (very well/fine/ ordinary/poor)	28/39/18/11	26/42/15/13	27/43/16/10	.882
The nature of dreams (good/ordinary/bad)	15/10/9	5/5/3	10/9/7	.331
Sleep quality after waking up (very good/okay/fair/poor)	61/23/12/0	30/33/27/6	52/30/14/0	.001

the MAP of P group was obviously decreased at T1 ($P < .05$), whereas HR had no significant change (Table 3).

3.4. Comparison of adverse reactions of patients

The incidence of hypoxemia and injection pain in P group was significantly higher than that in PE_1 and PE_2 groups ($P < .05$). The incidence of muscle spasm, body moving, choking and deglutition in PE_1 group was higher with respect to P and PE_2 groups ($P < .05$). In the PE_1 group, there were 4 patients exhibited postoperative nausea and 2 patients showed postoperative vomiting. In the PE_1 group, there was 1 patient with severely slowed HR. The incidence of dreaming in the PE_1 and PE_2 groups was higher as compared with PE_1 group ($P < .05$). However, there was no statistical difference in the nature of dreams among the 3 groups ($P > .05$) (Table 4).

4. Discussion

With the wide application of digestive endoscopy, there is an increasing demand for painless gastroscopy in outpatient clinics. Painless technology brings comfort to patients while also presenting new challenges for anesthesiologists. Propofol is the most commonly used anesthetic in painless gastroscopy. It not only has the advantages of rapid onset, short duration of action, and rapid recovery, but also prevents postoperative nausea and vomiting. However, propofol has a significant inhibitory effect on respiration, and some patients will have severe hypoxemia after injection. Intravenous injection of propofol is likely to cause an obvious drop in blood pressure. Severe hypotension leads to insufficient blood perfusion in important organs such as heart and brain, increases the risk of cardiovascular and cerebrovascular accidents.[4] In addition, propofol also leads to injection pain, with a probability of up to 63%.[6] The mechanism may be related to the free propofol in the drug directly stimulates blood vessels or indirectly stimulates the production of bradykinin and prostaglandins.[7,8]

Etomidate is a sedative and hypnotics that has the same sedative effect as propofol. Compared with propofol, etomidate binds and activates adrenergic receptors, causing secondary vasoconstriction and stabilizing the cardiovascular system. Etomidate is suitable for older patients with unstable circulatory

Table 3

The MAP and HR of patients.

Index	Groups	Case number	T0	T1	T2
MAP(mm Hg)	P	96	91.84 ± 5.18	70.57 ± 8.65*,#	86.73 ± 8.79
	PE_1	96	90.40 ± 6.55	81.63 ± 7.35*	88.94 ± 8.04
	PE_2	96	91.12 ± 5.59	80.89 ± 9.03*	87.37 ± 7.65
HR(Times/minutes)	P	96	84.1 ± 7.4	72.3 ± 9.8*	75.7 ± 10.3*
	PE_1	96	85.3 ± 8.2	74.8 ± 9.1*	78.4 ± 7.6*
	PE_2	96	83.8 ± 8.9	75.7 ± 8.5*	77.4 ± 8.6*

Table 4

The adverse reactions of patients.

Yes/no	Groups			*P* value
	P	PE_1	PE_2	
Hyoxemia	17/77	6/90	7/89	.034
Muscle spasm	1/95	31/65	4/92	.019
Injection pain	33/66	10/86	17/79	.042
Body moving	3/93	16/80	6/90	.041
Bucking	3/93	17/79	5/91	.037
Deglutition	6/90	25/71	8/88	.012
Postoperative nausea	0/96	4/92	0/96	.000
Postoperative vomiting	0/96	2/94	0/96	.000
Postoperative dizzy	1/95	11/85	5/91	.260
Dream	34/62	13/83	28/68	.031

function.[9] The etomidate used in clinical practice has been improved. Among them, 20% of the medium and long chain triglycerides replace the propylene glycol in the liquid, which is close to the normal physiological osmotic concentration of the human body. Improved etomidate reduces the irritation to the vascular intima and reduces the incidence of injection pain. However, etomidate alone leads to myoclonus, postoperative nausea and vomiting, and muscle pain, and may also cause a decrease in adrenal function.[10] It seriously affects the operation of doctors and threatens the health of patients. Previous study has shown that the physical and chemical properties of the admixture of propofol and etomidate have not changed, it can be safely used in clinical anesthesia, and its compatibility is stable.[11] Many researches have confirmed that the admixture of propofol and etomidate not only maintains the stability of the respiratory system of patients, but also reduces the incidence of adverse reactions such as injection pain, nausea and vomiting,[12] hypoxemia,[13] hypotension and oxygen desaturation.[14]

Our work found that the admixture of propofol and etomidate maintained the stability of hemodynamic. This may be attributed to the combination of propofol and etomidate, which relatively reduces the dosage of propofol, thereby reducing its inhibitory effect on the respiratory and circulatory systems. However, etomidate has no significant inhibitory effect on the respiratory system. At the same time, etomidate reduces the oxygen consumption of the myocardium, dilates the coronary arteries, and reduces the circulation inhibition. In addition, it may be that the concentration of propofol is diluted by etomidate after the mixing of propofol and etomidate, resulting in a reduction in the release of bradykinin, thereby reducing the incidence of injection pain. Etomidate may also play a pre-administration role with propofol in the admixture.[15] Although the overall hypoxemia probability of the PE_1 group is lower than that of the other 2 groups, the probability of severe hypoxemia is higher. It may be that the depth of anesthesia is shallower than that of the other 2 groups, and the patient has a choking reaction that causes severe hypoxia. In our study, the incidence of muscle spasm in PE_1 group was higher than that in P and PE_2 groups.

It indicates that larger doses of etomidate combined with propofol still have a higher probability of muscle spasm. When etomidate is used in relatively small doses, the incidence of muscle spasm is significantly reduced. Previous study has shown that when etomidate is used for induction of anesthesia, the incidence of muscle spasm is as high as 50% to 80%, and it is dose-dependent.[12] Muscle spasm causes postoperative myalgia, increases blood potassium and other adverse reactions, especially increases gastrointestinal motility after muscle tremor, leading to an increased risk of vomiting and aspiration.

The awakening time of the PE_1 group was longer than that of the other 2 groups, which may be related to the half-life period the 2 drugs. The half-life period of propofol was about 0.5 to 1.5 hours, and the half-life period of etomidate was about 2 to 5 hours, which was significantly greater than that of propofol. In the PE_1 group, the proportion of etomidate in the admixture was the largest, so the awakening time of patients may be prolonged by the half-life period of etomidate.

Clinical practice has observed that some patients complain of good sleep during painless anesthesia after waking up. With the changes in modern lifestyles, more and more people are experiencing reduced sleep time, sleep deprivation and increased sleep debt. People are used to thinking of the loss of consciousness caused by general anesthesia as a "sleep" state. Like sleep, general anesthesia also shows reversible loss of consciousness, no memory, no autonomous activity, and no response to stimuli of corresponding intensity. Existing studies have shown that general anesthesia and sleep share part of the same regulatory mechanism.[16,17] Studies have confirmed that the need for sleep does not increase during anesthesia. On the contrary, sleep deprivation may be restored during anesthesia.[18,19] Prolonged anesthesia not only prevents the accumulation of sleep debt, but also promotes the dissipation of sleep debt. This may be 1 reason why patients experience good sleep during anesthesia.

After mixing 1.0% propofol and 2% etomidate in a certain proportion (volume ratio 1:1 or 2:1), it was found that the 2 had little effect on the patients respiratory and circulatory systems, and the incidence of injection pain was reduced. However, the former had a higher incidence of muscle spasm, body moving, choking, deglutition and postoperative nausea and vomiting. Therefore, on the premise of stabilizing the patient's respiratory and hemodynamics, the combination of 10 ml 1.0% propofol and 5 ml 0.2% etomidate can effectively reduce the incidence of hypoxemia, muscle spasm, injection pain, body moving, and choking, deglutition, and postoperative nausea and vomiting. There is no obvious adverse reaction after operation.

In summary, the combination of 10 ml 1.0% propofol and 5 ml 0.2% etomidate for painless gastroscopy can reduce adverse reactions while not affecting the patients respiratory function. Moreover, the patients sleep experience satisfaction during anesthesia is high, and it is safe and effective, which is worthy of clinical application and promotion. The limitation of this study is that it only discussed the anesthesia of painless gastroscopy in the general population. Our study has not been conducted on people at high risk of nausea, vomiting, dizziness and vertigo. Therefore, further research on high-risk groups is still needed in the future work.

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