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ORIGINAL RESEARCH

Efficacy and safety of remimazolam besylate in patients with obesity undergoing painless colonoscopy: a prospective, double-blind, randomized controlled trial

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Abstract

Remimazolam besylate helps relieve mild respiratory depression and stabilizes cardiac circulation. We designed a randomized controlled trial to compare sedative potential of remimazolam besylate with propofol in obese patients undergoing painless colonoscopy. A total of 100 obese patients undergoing colonoscopy were recruited and randomly divided into group RB and group P. Anesthesia was induced by 0.15 mg/kg remimazolam besylate or 2 mg/kg propofol combined with 0.1 μg/kg sufentanil. General conditions of patients of both groups were noted. Similarly, the respiratory parameters, hemodynamic parameters, duration of colonoscopy, induction time, orientation recovery time, and post-anesthesia care unit (PACU) stay time were noted. The incidence of nausea and vomiting, dizziness, headache, lethargy, abdominal pain, and distension after the examination were recorded. The satisfaction scores of endoscopists, anesthesiologists and patients were also noted. Only 26% of patients of RB group suffered from apnea during induction which is less than 50% in group P ($p = 0.003$). Similarly, 32% of patients of RB group developed hypoxemia, while 66% of patients in group P developed hypoxemia ($p = 0.001$). The incidence of hypotension during induction in both groups was statistically different, exactly 36% in group RB and 66% in group P ($p = 0.005$). During induction, 8% of patients suffering from pain at the injection site in group RB, significantly less than the 34% in group P ($p = 0.003$). The satisfaction score of patients in group RB was significantly higher compared to group P (8.93 ± 1.08 *vs.* 7.97 ± 1.31, $p = 0.001$, $p < 0.05$). The remimazolam besylate-sufentanil is safer than propofol-sufentanil for painless colonoscopy in obese patients, and can reduce the incidence of hypoxemia, injection pain, and improve satisfaction of patients. Therefore, this anesthetic scheme is worth promoting in clinical practice.

Keywords

Remimazolam besylate; Propofol; Patients with obesity; Painless colonoscopy

1. Introduction

Painless colonoscopy is a widely used technique for the diagnosis and treatment of colonic diseases [1]. Propofol in combination with opioid analgesics is the most used anesthetic scheme in painless colonoscopy due to its rapid onset and recovery characteristics [2]. But, the dose-dependent use of propofol as anesthetic in obese patients often increases the risk of apnea, hypoxemia and hypotension during the anesthetic procedure [3–6]. Further, the pain of propofol injection reduces the satisfaction of patients undergoing painless colonoscopy [5, 7].

With the improvement of people's living standards and health awareness, more and more obese patients are accepting painless colonoscopy as a part of physical examination or diagnosed intestinal disease [8, 9]. Obese patients have more chances to develop hypoxemia, owing to the changes in the anatomical structure of the respiratory tract, such as the short neck, decreased functional residual volume, reduced chest wall compliance, and a narrow airway [10]. Further, propofol intake in patients with obesity undergoing painless colonoscopy carries a dose-dependent risk of hemodynamic and respiratory compromise [6, 11, 12]. Hence, hypoxemia duration is longer in patients with obesity and additional airway intervention measures are often needed [13]. Anesthetic management in obese patients accepting painless colonoscopy ensures the safety of the airway, stabilizes the cardiac circulation, increasing comfort level of patients and the satisfaction of examiners, which poses a huge challenge for anesthesiologists [14, 15]. Hence a safe and efficacious anesthesia plan for obese patients is required.

Remimazolam besylate, a new kind of benzodiazepine seda-

tive with characteristics of quick onset of effects, short maintenance and recovery times, is a kind of ultra-short acting gamma-aminobutyric-acid type A ($GABA_A$) receptor agonist [16, 17]. It does not accumulate in tissues, and its metabolism is independent of liver and kidney functions [16, 18]. Due to its unique metabolic pattern, remimazolam besylate is an ideal sedative for patients with obesity undergoing painless colonoscopy. Recent studies indicate that intake of remimazolam besylate helps relieve symptoms of respiratory depression and hemodynamic fluctuations in painless gastroscopy [19, 20]. However, there are no relevant reports for obese patients in painless colonoscopy.

In the study, we conducted a prospective, double-blind, randomized controlled trial to investigate the efficacy and safety of remimazolam besylate combined with sufentanil compared to propofol combined with sufentanil in obese patients experiencing painless colonoscopy. We suggest that the combination of remimazolam besylate and sufentanil may be an ideal anesthesia plan with less security incidents.

2. Materials and methods

2.1 Inclusion and exclusion criteria

A prospective, double-blind, randomized controlled trial was performed in the Deyang People's Hospital between 07 February 2021, and 30 November 2023. Patients admitted for selective painless colonoscopy were eligible for participation in this study if they: (I) had an American Society of Anesthesiologists (ASA) physical status II–III; (II) were 18–65 years old; (III) had a body mass index (BMI) $\geq$28 kg/m^2; (IV) volunteered to sign the informed consent form; and (V) did not experience painless colonoscopy within the past 3 months.

The exclusion criteria was consistent with one of the following: (I) refusal to participate in this study; (II) resistance to opioid drugs; (III) sleep disorders and mental illnesses; (IV) exposure to similar anesthetic drugs within 3 months; (V) severe cardiovascular or cerebrovascular diseases or severe renal insufficiency; (VI) contraindications to use of propofol, sufentanil or benzodiazepines; (VII) history of head, chest, and intracranial surgery, or stroke within 4 weeks before operation; (VIII) history of hypertension, hypotension; (IX) pregnant or lactating women; (X) respiratory infection; and (XI) other situations that were not suitable for entering the experiment.

2.2 Randomization and blinding

All eligible subjects were screened by a preoperative evaluation at the anesthesia clinic in the Deyang People's Hospital. Participates signed an informed consent form and were subsequently divided into two groups using a computer-generated randomized number table. The subject list was maintained by a nurse anesthetist who did not participate in the consequent procedures of this study. According to the grouping results, the participants were grouped to remimazolam besylate or propofol groups namely group RB and group P respectively. Group RB patients were intravenously injected with remimazolam besylate (0.15 mg/kg) plus sufentanil (0.1 μg/kg) for anesthesia induction while in group P received intravenous infusion of propofol (2 mg/kg) plus the same dose of sufentanil which group RB patients received. To sustain blinding to the investigation, the nurse anesthetist who kept the subject list helped preparing and distributing the medicines in identically opaque syringes marked with research numbers merely. Specifically, it meant that each anesthetic drug was divided into induction and addition purpose using an independent syringe. The dose of the required drug in the syringe during induction was marked as inducer 1, inducer 2. Drugs for once additional dosage were also prepared in advance, and labeled as additional drugs 1, 2, 3, 4, 5, *etc*. When additional sedative was required, it was taken according to the marked number. The anesthetic drugs were injected by the frontline anesthesiologist who performed the anesthesia work on the day (this anesthesiologist did not involve in this study), and data collection and evaluation were carried out by the research team. Blindness could only be uncovered when severe security incidents occurred.

2.3 Interventions and assessments

All participants fasted before the examination, and none of medication was used preoperatively except the necessary reagent for intestinal preparation. Intestinal preparation was performed using polyethylene glycol electrolyte powder (I) with drinking water (2000 mL). After the patient entered the anesthesia preparation room, the baseline vital signs were collected in the left lying position, including noninvasive blood pressure (NIBP), electrocardiogram (ECG), heart rate (HR), and peripheral oxygen saturation (SPO_2), respiratory rate (RR) and reliable peripheral venous access was opened immediately before painless colonoscopy slowly infusing with 500 mL physiological saline solution. After entering the endoscopy room, patients were routinely monitored for basic vital signs. Oxygen was inhaled at a rate of 4 L/min through a breathing mask. Anesthesia machines, emergency tracheal intubation tools and laryngeal masks were in standby mode.

For anesthesia induction, a bolus intravenous injection of sufentanil (0.1 μg/kg) was administered, followed by remimazolam besylate (0.15 mg/kg) in group RB or propofol (2 mg/kg) in group P. When the eyelash reflex disappeared, there was no obvious body movement, and the modified observer's assessment of alertness/sedation scale (MOAA/S) (Table 1) reached smaller than 3 points, the endoscopist began the colonoscopy. Fluctuations of blood pressure and heart rate were evaluated at various time intervals during the operation process to maintain the MOAA/S score less than or equal to 3 points. If the MOAA/S score was greater than 3 points, an additional dose of remimazolam besylate (2.5 mg) was administered in group RB, while propofol (0.5 mg/kg) was administered in group P. Once the NIBP decreased (exceeding 30% of the baseline value), metaraminol 0.4 mg was intravenously injected. When there was an increase in blood pressure (exceeding 30% of the baseline value), the score of MOAA/S was evaluated again. If the score of MOAA/S was greater more than 3 points, sedative drugs were added. If it was less than or equal to 3 points, nicardipine (0.4 mg) was intravenously injected. Atropine (0.5 mg) was administered when HR was below 45/min, which was repeated if needed, with a maximum dose of 2 mg. When there was an increase in heart rate (exceeding 20% of the baseline value),

if the MOAA/S score was greater than 3 points, an additional dose of sedative drug was administered, and if that was less than or equal to 3 points, esmolol was administered. The treatments for opening the airway, such as head-tilt, chin lift, and jaw-thrust, were performed by the anesthesiologist when the SpO_2 was below 95%. If the SpO_2 decreased below 90% and hypoxemia wasn't alleviated by the previously mentioned treatments, the operation was stopped immediately. Positive pressure ventilation by anesthesia machine was consequently applied and emergency tracheal intubation or laryngeal mask insertion was performed if necessary. Other perioperative security incidents were also noted and treated in accordance with the clinical operation standards of Deyang People's Hospital.

TABLE 1. The modified observer's assessment of alertness/sedation scale.

Sore	Meaning
5	Responds readily to name spoken in normal tone
4	Lethargic response to name spoken in normal tone
3	Responds only after name is called loudly and/or repeatedly
2	Responds only after mild prodding or shaking
1	Responds only after painful trapezius squeeze
0	No response after painful trapezius squeeze

After completion of the colonoscopy, patients were transferred into the post anesthesia recovery room with continuous monitoring. Symptoms of nausea and vomiting, dizziness and headache, drowsiness and fatigue, abdominal pain and bloating were noted. The patients with a Steward score $\geq$4 and stable vital signs were allowed to leave the anesthesia recovery room accompanied by their family members. Satisfaction scores of patients, endoscopists and anesthesiologists were evaluated in the both groups by a 10-point Likert scale (1 = highly unacceptable, 10 = outstanding) (Table 2) [21–23].

TABLE 2. The 10-point Likert scale.

Sore	Meaning
10	Outstanding
9	Excellent
8	Very good
7	Good
6	Above average
5	Average
4	Below average
3	Less than acceptable
2	Unacceptable
1	Highly unacceptable

The induction time was the seconds from the beginning of sufentanil medication to the status that MOAA/S score reached $\leq$3 points and eyelash reflex disappeared. The examination time was the time from the entry to exit of the colonoscope. The orientation recovery time was the time from exit of the colonoscope to the patient's eyes opening and being consciousness. The post anesthesia recovery room stay time was defined as the time from exit of the colonoscopy to patients leaving the recovery room. The patients could leave the anesthesia recovery room accompanied by their family members when they reached a Steward score $\geq$4 and had stable vital signs. Apnea was defined as the cessation of respiratory activity of the chest and abdomen for more than 20 seconds with stopwatch timing observed by the researcher, and hypoxemia was SpO_2 less than or equal to 90%.

The basic characteristics of the patients were collected. During the procedure, the addition of remimazolam besylate or propofol was considered as repeated medication, and the rate of repeated medication was the percentage of all additional patients in this group. Pain at the injection site during the induction period was recorded. Simultaneously, changes in basic vital signs including apnea, hypoxemia, hypotension, hypertension, heart rate slowing, heart rate increasing, body movement reaction, anaphylaxis, manual airway opening assisted breathing and mask positive pressure ventilation during the procedure were also noted.

The primary outcome was defined as the incidence of hypoxemia and sample size was calculated based on incidence of hypoxemia. Hypoxemia was the most concerning and desirable indicator for optimization in the present study. Secondary outcomes included the duration of induction, procedure, orientation recovery time, PACU stay time, sufentanil consumption, repetitive medication ratio, incidence of injection pain, incidence of security events and adverse reactions of various systems, and the satisfactions of patients, endoscopists and anesthesiologists.

2.4 Statistical analysis

According to preliminary experimental of ten cases per group (**Supplementary Table 1**), 50% of obese patients who underwent colonoscopy experienced hypoxemia. To detect a 30% difference in hypoxemia rate between both groups with a 90% power and a type I error rate of 0.05, 48 cases were needed in each group. Considering the 10% dropout, 108 patients were enrolled.

SPSS 26.0 (SPSS, Inc., Armonk, NY, USA) was used for all statistical analyses. The normality of the data distribution was assessed by the Shapiro-Wilk test. Normally distributed data are summarized as mean $\pm$ standard deviation (SD), while non-normally distributed data are expressed as median (25th and 75th percentile). Categorical data are shown as frequency and percentages. Continuous data was compared by Student's *t*-test or Wilcoxon-Mann-Whitney test based on viability of the normality assumption. Chi-square or Fisher's exact test was used to compare the categorical data. Significance was set as a two-sided p value < 0.05.

3. Results

Over a period of March 2021 to November 2023, 1256 patients were considered for eligibility, and 1094 were excluded before

grouping. Finally, 162 patients participated in random allocation (81 from each group). Of these patients, 62 patients were dropped from the analysis; twenty-seven of them had COVID-19, seventeen suffered from cold and eighteen withdrew their consent. Thus, only 100 patients were analyzed in our study, and the flow chart of the study design is shown in Fig. 1.

3.1 Basic characteristics of the patients

The flow diagram of the study design is shown in Fig. 1. These 100 patients met the inclusion and exclusion criteria and were randomly allocated into two groups. The demographic characteristics and basic values of these patients are shown in Table 3. There were no significant differences in the demographics and basic values of patients between the two groups ($p > 0.5$).

3.2 The duration of induction, colonoscopy, orientation recovery time and PACU stay time

There were no statistical differences in the duration of the induction, colonoscopy, orientation recovery and PACU stay time between both two groups ($p > 0.05$) (Table 4).

3.3 The sufentanil intake and repetitive medication ratio

No statistically significant difference was observed regarding sufentanil consumption in both groups ($p = 0.594$) (Table 5). Total repetitive medication ratio was 54% and 58% in groups RB and P, respectively. The number of patients in group RB received 1 to 4 times of additional administration was 8, 10, 6 and 3, respectively. While in group P, there were 23 patients accepted once additional propofol, 6 patients accepted twice. There were statistical differences in the repetitive medication ratio between two groups ($p = 0.001$) (Table 5).

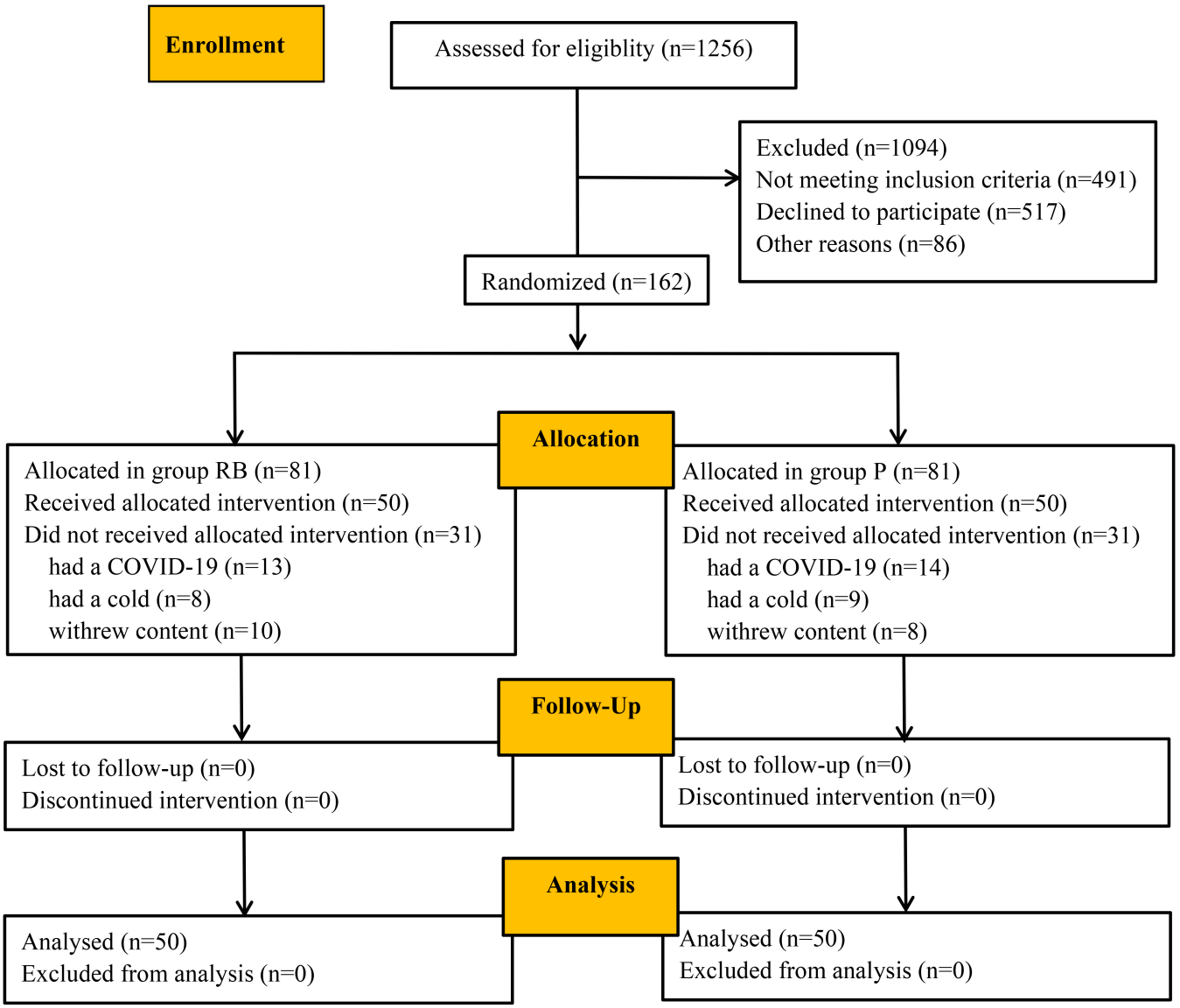

FIGURE 1. Study design flow diagram. Patient recruitment, randomization and withdrawal. Sixty-two of the 162 patients withdrew for various reasons, and 50 patients in each group were eventually included in the final analysis.

TABLE 3. Demographics and basic values of patients between the two groups.

	Group RB N = 50, no. (%)	Group P N = 50, no. (%)	Total N = 100, no. (%)	*p* value
Gender				
Male	32 (64%)	35 (70%)	67 (67%)	0.523
Female	18 (36%)	15 (30%)	33 (33%)	
Age, yr				
N	50	50	100	
Mean	45.68	46.68	46.18	
SD	10.24	10.52	10.34	0.507
Minimum	25	25	25	
Median	48.0	50.0	48.5	
Maximum	60	62	62	
BMI, kg/m^2				
N	50	50	100	
Mean	30.58	30.53	30.56	
SD	2.12	2.06	2.08	0.858
Minimum	28.00	28.01	28.00	
Median	29.81	30.11	29.99	
Maximum	36.21	37.62	37.62	
ASA score				
N	50	50	100	
II	35 (70%)	37 (74%)	72 (72%)	0.824
III	15 (30%)	13 (26%)	28 (28%)	

One hundred patients were finally analysed. The demographic characteristics and basic values of these patients were no significant differences in the demographics and basic values of patients between the two groups ($p > 0.5$).
p value, remimazolam besylate group compared to the propofol group.
Group RB: group remimazolam besylate, Group P: group propofol, BMI: body mass index, ASA: American Society of Anesthesiologists; SD: standard deviation.

3.4 Cardiovascular treatment adverse events and injection pain

During induction, 8% of patients suffered from pain at the injection site in group RB, which was significantly less than 34% in group P ($p = 0.003$). Incidence of hypotension during induction in the two groups was statistically different ($p = 0.005$). There was no significant difference in the incidence of hypertension, increased heart rate, and decreased heart rate in both groups during the examination ($p = 1.000$) (Table 6).

3.5 Respiratory treatment adverse events

Only 26% of patients faced apnea during induction in group RB, less than the 50% in group P ($p = 0.003$) (Table 6). Similarly, 32% and 66% patients developed hypoxemia in group RB and P respectively, the incidence rate of group RB was significantly lower than that of group P ($p = 0.001$) (Table 6). Significant difference was not observed between the two groups in head-tilt/chin lift/jaw-thrust ($p = 1.000$) (Table 6), while no statistically significant difference between the two groups was shown in mask positive pressure ventilation ($p = 0.002$) (Table 6). There was no emergency tracheal intubation in both groups during the whole process of anesthesia and recovery. Finally, the cases of laryngeal mask insertion were lower in group RB than group P, but significant difference was not observed between the two groups ($p = 0.487$).

3.6 Others system incidence of security events and adverse reactions of various systems

There was no significant difference in the incidence of dizziness and headache between the two groups after the patient waking up, with 6 patients in group RB and 12 cases in group P ($p = 0.192$) (Table 6). There was no significant difference in the incidence of kinetic reaction, allergic reactions, nausea and vomiting, abdominal pain and bloating, and drowsiness and fatigue between the two groups during the examination ($p > 0.05$) (Table 6).

3.7 Satisfaction of patients, endoscopists and anesthesiologists

The satisfaction score of patients in group RB was higher compared to group P (8.93 ± 1.08 *vs.* 7.97 ± 1.31, $p =$

TABLE 4. The duration of induction, procedure, orientation recovery and PACU stay time.

	Group RB N = 50	Group P N = 50	Total N = 100	*p* value
Induction time, s				
N	50	50	100	0.435
Mean	42.24	40.64	41.44	
SD	8.70	7.88	8.30	
Minimum	27.00	26.00	26.00	
Median	41.00	39.00	40.00	
Maximum	65.00	59.00	65.00	
Duration of colonoscopy, min				
N	50	50	100	0.874
Mean	9.26	9.22	9.24	
SD	4.04	3.57	3.79	
Minimum	2.17	2.03	2.03	
Median	9.03	8.73	8.95	
Maximum	21.03	20.89	21.03	
Orientation recovery time, min				
N	50	50	100	0.662
Mean	8.11	8.16	8.14	
SD	2.38	2.55	2.45	
Minimum	3.65	4.21	3.65	
Median	8.64	7.64	8.10	
Maximum	12.55	17.06	17.06	
PACU stay time, min				
N	50	50	100	0.544
Mean	20.40	21.36	20.88	
SD	10.60	9.29	9.93	
Minimum	4.23	5.49	4.23	
Median	19.07	20.06	19.40	
Maximum	40.25	40.02	40.25	

The average duration of induction, procedure, orientation recovery and PACU stay time were no statistical differences between the two groups ($p > 0.05$).
p value, remimazolam besylate group compared to the propofol group.
PACU: post-anesthesia care unit; SD: standard deviation.

0.001), while there was no difference in satisfaction scores of endoscopists (8.94 ± 0.83 *vs.* 8.83 ± 1.25, $p = 0.748$) and anesthesiologists (8.47 ± 1.67 *vs.* 8.56 ± 0.83, $p = 0.696$), respectively (Fig. 2).

4. Discussion

We conducted the study comparing remimazolam besylate to propofol in outpatients undergoing colonoscopy. The study design aimed to evaluate the incidence of hypoxemia during anesthesia with remimazolam besylate plus sufentanil *vs.* propofol plus sufentanil. Because propofol plus sufentanil is commonly used in clinical practice as an anesthesia protocol for colonoscopy, we chose propofol combined with sufentanil as the control anesthesia protocol to evaluate the safety and effectiveness of the combination of remimazolam besylate and sufentanil as a better anesthesia protocol for obese patients undergoing colonoscopy. Results suggested that remimazolam besylate plus sufentanil maintained stability of hemodynamics, decreased the incidence of respiratory depression, dizziness and headache after the patients waking up, increasing satisfaction in obese patients experiencing painless colonoscopy. Hence, the combination of remimazolam besylate and sufentanil may be a more ideal anesthesia plan for obese patients in painless colonoscopy. As far as we know, this is the first report focused on the efficacy and safety of remimazolam besylate in obese patients experiencing painless colonoscopy.

Hypoxemia and respiratory depression are the most frequent adverse events in obese patients undergoing painless

TABLE 5. The sufentanil consumption and repetitive medication ratio.

	Group RB N = 50, no. (%)	Group P N = 50, no. (%)	Total N = 100, no. (%)	*p* value
Dosage of sufentanil, μg				
N	50	50	100	0.594
Mean	8.63	8.49	8.56	
SD	0.64	0.57	0.61	
Minimum	6.90	7.30	6.90	
Median	8.60	8.45	8.60	
Maximum	10.20	9.70	10.20	
Repeated medication, n				
N	27 (54%)	29 (58%)	56 (56%)	0.001
I	8 (16%)	23 (46%)	31 (31%)	
II	10 (20%)	6 (12%)	16 (16%)	
III	6 (12%)	0 (0%)	6 (6%)	
IV	3 (6%)	0 (0%)	3 (3%)	

There was no statistical difference in the sufentanil consumption between the two groups (p = 0.594). Total repetitive medication ratio was 54% and 58% in groups RB and P, respectively. There were statistical differences in the repetitive medication ratio between two groups (p = 0.001).
p value, remimazolam besylate group compared to the propofol group.
SD: standard deviation.

TABLE 6. The Systems incidence of security events and adverse reactions of various systems.

System organ class	Group RB N = 50, no. (%)	Group P N = 50, no. (%)	*p* value
Cardiovascular treatment-emergent adverse events			
Injection pain of induction	4 (8%)	17 (34%)	0.003
Hypotension during induction	18 (36%)	33 (66%)	0.005
Hypertension during examination	1 (2%)	2 (4%)	1.000
Decreased heart rate	4 (8%)	6 (12%)	0.741
Increased heart rate	8 (16%)	5 (10%)	1.000
Respiratory treatment-emergent adverse events			
Apnea	13 (26%)	25 (50%)	0.003
Hypoxemia	16 (32%)	33 (66%)	0.001
Head-tilt/chin lift/jaw-thrust	5 (10%)	4 (8%)	1.000
Mask positive pressure ventilation	8 (16%)	23 (46%)	0.002
Tracheal intubation	0	0	
Laryngeal mask insertion	3 (6%)	6 (12%)	0.487
Kinetic reaction			
Kinetic reaction	4 (8%)	3 (6%)	1.000
Allergic reactions			
Allergic reactions	1 (2%)	2 (4%)	1.000
Gastrointestinal complications			
Nausea and vomiting	10 (20%)	9 (18%)	1.000
Abdominal pain and bloating	3 (6%)	3 (6%)	1.000
Neurological complications			
Dizziness and headache	6 (12%)	12 (24%)	0.192
Drowsiness and fatigue	5 (10%)	4 (8%)	1.000

The percentage of security events in various systems.
p value, remimazolam besylate group compared to the propofol group.

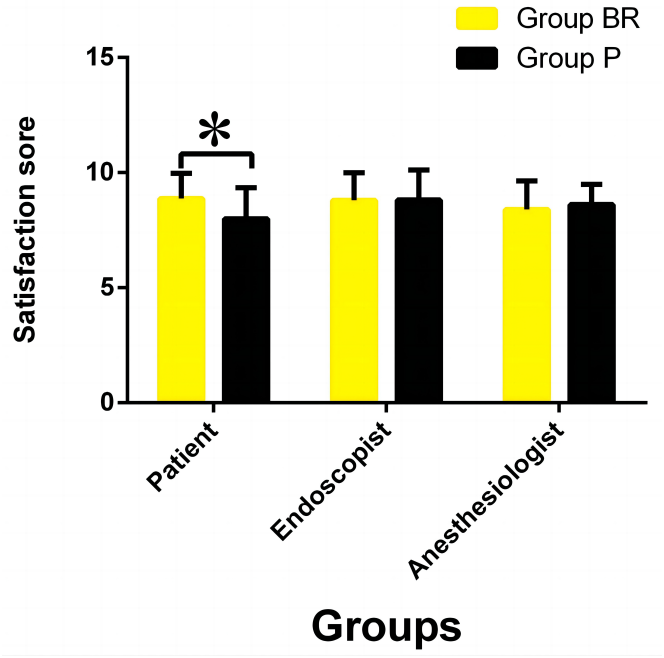

FIGURE 2. The Satisfactions of Patients, Endoscopists and Anesthesiologists. The satisfaction score of patients in group RB was significantly higher compared to group P (p = 0.001, $p < 0.05$), while there was no significant difference in satisfaction scores of endoscopists (p = 0.748, $p > 0.05$) and anesthesiologists (p = 0.696, $p > 0.05$), respectively. *$p < 0.05$ compared to the group P. Group RB: group remimazolam besylate, Group P: group propofol.

colonoscopy under propofol anesthesia [24]. Obese patients are more vulnerable to hypoxemia due to a greater dosage requirement of propofol, fat deposition around the neck, narrow upper airway and the consequence of decreased upper airway muscle tone [24]. Severe hypoxia lasting for a long time may pose a threat to the patient's life safety [25]. Therefore, it is necessary to prevent hypoxemia during painless colonoscopy in obese patients. An increased risk of airway management in obese patients exists due to the altered airway anatomy, including limited neck extension, short neck, and fat accumulation in the pharyngeal wall [26, 27]. Propofol may render airway anatomy more prone to obstruction due to decreased upper airway muscle tone [24]. Accordingly, anesthetic management for obese patients undergoing painless colonoscopy is a huge challenge for anesthesiologists requiring an effective and safe anesthetic protocol for obese patients experiencing painless colonoscopy.

Remimazolam besylate is a kind of ultra-short acting $GABA_A$ receptor agonist [16, 17]. Remimazolam besylate doesn't accumulate in human tissues and metabolism of remimazolam besylateis is independent of kidney and liver functions [16, 18]. Intake of remimazolam besylate is beneficial for respiratory depression and hemodynamic fluctuations in painless gastroscopy [19, 20], however there is no report explaining its role in obese patients in painless colonoscopy. Based on our preliminary experimental results, which explored the optimal dose concentration gradient of remimazolam besylate (**Supplementary Table 2**), a dosage of remimazolam besylate (0.15 mg/kg) plus sufentanil (0.1 μg/kg) was chose to evaluate the anesthetic effect in obese patients experiencing painless colonoscopy. It was different from previous studies, in which 0.2 mg/kg was used as the induction dosage [28, 29]. Sedation with a dos of 0.2 mg/kg remimazolam besylate is effective and safe for adults bronchoscopy [28]. There are several reasons. Firstly, the patient's body weight base in this study is relatively large. Secondly, compared with gastroscopy, colonoscopy is less harm and irritating to patients. Thirdly, the sample size of the pre-experimental study is limited, and the number of observation cases selected is relatively small.

Remimazolam besylate is different from other intravenous hypnotics, including propofol, by its advantages [30]. In our study, 32% RB group patients experienced hypoxemia, while 66% of the P group experienced the same. The rate of hypoxemia, apnea, injection pain during induction were significantly different in both groups. Our results demonstrated the advantages of decreasing hypoxemia and mild respiratory depression when remimazolam besylate was used for painless colonoscopy anesthesia in obese patients.

There was a decrease of 26% in the incidence of injection pain during induction in group RB. Propofol is insoluble in water and is formulated as a lipid-based emulsion, so it is vascular irritant when injected intravenously, increasing the incidence of injection pain [30, 31]. Contrarily remimazolam besylate is soluble in physiological saline when injected intravenously. The satisfaction score of patients sedated with remimazolam besylate was significantly enhanced in comparison with propofol, which can be ascribed to the reduced injection pain. It is the most likely reason for increased satisfaction of RB group patients, which is same with the previous study. In Mathis's study, remimazolam tosilate also showed a less injection pain compared to propofol [32].

Patients with obesity are easy suffering from hypotension due to a higher dose use of propofol [6]. Perioperative hypotension has adverse outcomes and may lead to organ dysfunction [6, 33]. The incidence of hypotension during induction reduced from 66% to 36% in the group P, which is similar to the results of previous study [17]. Therefore, it is important to prevent perioperative hypotension during painless colonoscopy in patients with obesity. Our data did not indicate any difference in BMI and other demographics between the two groups, suggesting that the risk of hemodynamic fluctuations was equal in both groups.

In addition, adverse reactions such as nausea, vomiting, dizziness, headache, abdominal pain and bloating, drowsiness and fatigue were analyzed, but none of them showed statistically significant differences in our report. A possible reason is that the patients participated in this study were less than 65, and the anesthetic dosages were ideal. Hence, remimazolam besylate is safe and effective for obese patients aged 18 to 65 undergoing painless colonoscopy.

The satisfaction of the endoscopists and anesthesiologists during the procedure was also evaluated. The satisfaction scores of the endoscopists and anesthesiologists in both groups showed no statistically significant differences, which is due to various reasons. First, hypoxemia occurred more frequently in group P, which caused many interruptions, thus the coherence

in the operation was reduced. Second, the times of repeated medication were more frequent, which contributed more workload to anesthesiologists, and the incidence of repeated medication represent fluctuation of anesthesia depth and unstable vital signs.

This study has several limitations. First, all patients' intestinal preparation was conducted before 8 o'clock on the operation day. But some patients were examined in the morning while others were examined in the afternoon, which may cause hemodynamic fluctuations. Second, propofol is a white fat emulsion difficult to blend completely during intravenous injection when the anesthesiologist administered, even when placed in an opaque container. Finally, patients aged >65 or <18 years were excluded from this study. The sedation regimen for elder and younger patients with obesity should be explored in future.

5. Conclusions

In conclusion, remimazolam besylate-sufentanil is safer than propofol-sufentanil for painless colonoscopy in obese patients, and can decrease the incidence of hypoxemia, injection pain, and improve satisfaction of patients. Therefore, this anesthetic scheme should be promoted in clinical practice.

ABBREVIATIONS

PACU, post-anesthesia care unit; GABAA, gamma-aminobutyric-acid type A; ASA, American Society of Anesthesiologists; BMI, body mass index; NIBP, noninvasive blood pressure; ECG, electrocardiogram; HR, heart rate; SPO_2, peripheral; oxygen saturation; RR, respiratory rate; MOAA/S, modified observer's assessment of alertness/sedation scale; SD, standard deviation; COVID-19, corona virus disease 2019.

AVAILABILITY OF DATA AND MATERIALS

The patients' data included in the study can be accessed with approval from the corresponding author 6 months after publication. The study protocol, statistical analyses, and clinical study report will also be available.

AUTHOR CONTRIBUTIONS

LD and YHP—carried out the experimental design work, participated in the data analysis, design of the study and drafted the manuscript; RZ, XJZ and WCJ—carried out the statistical analyses; WHZ, XMC, CX, YKZ and LQX—conceived and coordinated the study. All authors participated in the patient recruitment. All authors gave final approval for publication.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study protocol was approved by the Medical Ethics Committee of the Deyang People's Hospital (Ethics Number: LWH-OP-006-A04-V2.0), and the study was registered in the Chinese Clinical Trial Registry (ChiCTR: 2300073543). All participants signed an informed consent form. This study was performed in accordance with the relevant guidelines.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at https://oss.signavitae.com/mre-signavitae/article/1810198033609965568/attachment/Supplementary%20material.docx.

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