# RESEARCH

**BMC** Anesthesiology



# Comparison of the effects of remimazolam and dexmedetomidine on the quality of recovery in functional endoscopic sinus surgery: a randomized clinical trial



Yaqiong Li<sup>1</sup>, Hui Zhou<sup>1</sup>, Fanfan Gao<sup>1</sup>, Qianqian Guan<sup>1</sup>, Shengbin Wang<sup>1</sup>, Yvqing Tan<sup>1\*</sup> and Shenghong Hu<sup>1\*</sup>

# Abstract

**Background** Postoperative pain usually occur in patients who have undergone functional endoscopic sinus surgery (FESS). Remimazolam and dexmedetomidine could enhance the quality of recovery (QoR) after surgery. The aim of this study was to compare the effects of remimazolam and dexmedetomidine with respect to the QoR-40 score of patients who have undergone FESS.

**Methods** A total of 120 patients (18–65 years) scheduled for FESS were randomly allocated to Group R, Group D or Group C. Group R received 0.075 mg/kg remimazolam loading and 0.1 mg/kg/h infusion. Group D received dexmedetomidine (1.0 µg/kg loading, 0.5 µg/kg/h infusion). Group C received a placebo equal to dexmedetomidine. Anaesthesia was induced with propofol, sufentanil and cisatracurium. Anaesthesia maintenance was performed via target-controlled infusions (TCIs) of propofol and remifentanil. The primary outcome was the QoR-40 score on the day before surgery and postoperative Day 1 (POD1). The secondary outcomes were the time to return to consciousness, length of stay in the PACU, sedation score upon PACU arrival, pain, postoperative nausea and vomiting (PONV) and cumulative consumption of propofol and remifentanil. Adverse effects were recorded.

**Results** The total QoR-40 scores (median, IQR) on POD1 decreased less (154.5, 152.0 -159.0) in Groups R and D (155.0, 154.8 -159.3) than in Group C (139.0, 136.8 -142.0) (P < 0.001). The time to return of consciousness and the length of stay in the PACU were significantly shorter in Groups R and C than in Group D (P < 0.001). The level of sedation upon PACU arrival (median, IQR) in Groups R (-2.0, -2.0—-1.0) and D (-2.0, -3.0—-2.0) was greater than that in Group C (1.0, 0.0 -1.0) (P < 0.001). The cumulative consumption rates of propofol and remifentanil in Groups R and D were lower than that in Group C (P < 0.001). Compared with that in Group C, the pain intensity was lower in Groups R and D (P < 0.001). The number of patients occurring PONV was less in Groups R (3/40) and D (4/40) than in Group C (11/40) (P = 0.024). Fifteen patients had bradycardia in Group D, whereas no bradycardia was noted in Groups R or C (P < 0.001).

**Conclusion** Administration of remimazolam could provide a similar QoR to that of dexmedetomidine. In addition, remimazolam may be a promising option for improving the QoR of patients who have undergone FESS.

\*Correspondence: Yvqing Tan tyqaq\_2007@163.com Shenghong Hu hushenghong-1@163.com Full list of author information is available at the end of the article



© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

**Trial registration** ChiCTR2300076209. (Prospectively registered). The initial registration date was 27/9/2023. **Keywords** Remimazolam, Dexmedetomidine, Quality of recovery, Chronic rhinosinusitis, Functional endoscopic sinus surgery

## Background

Chronic rhinosinusitis (CRS) is a common disease affecting patients' quality of life. Failure of medication is an indication for functional endoscopic sinus surgery (FESS), which can provide short- and long-term improvement in disease symptoms and quality of life [1]. However, 65% of patients who underwent functional endoscopic sinus surgery (FESS) experienced mild to moderate pain on postoperative Day 1 (POD1) [2]. Currently, the quality of recovery (QoR) score is an objective measure of patient-centred general health status after surgery and anaesthesia. The QoR-40 questionnaire is characterized by time efficiency and a high rate of response and completion, and it has been validated in patients undergoing various surgical procedures [3].

Dexmedetomidine, a highly selective  $\alpha$ -2 adrenergic agonist, was administered to improve the QoR because of its sedative, analgesic and sympathetic properties [4]. A previous studies had showed that intravenous dexmedetomidine could enhance QoR after elective surgery in adult patients [5]. Remimazolam, despite being a new ultrashort-acting benzodiazepine agent with haemodynamic stability and no considerable side effects, is being rapidly established in clinical practice as a sedativeanaesthetic agent. However, remimazolam has potential anti- inflammatory, immunomodulatory and analgesic properties [6-8]. Notably, a previous study reported that remimazolam could reduce propofol-induced injection pain by enhancing the synaptic inhibitory effects of GABAergic neurotransmission and reducing the release of proinflammatory cytokines [9]. In addition, Choi et al. [10] reported that the QoR by remimazolam-based total intravenous anaesthesia was not inferior to that by propofol-based total intravenous anaesthesia and that remimazolam lowered pain intensity and analgesic consumption more than did propofol, the reason might be linked to the sedative and analgesic potency of remimazolam. However, the effects of remimazolam and dexmedetomidine on the QoR of patients who have undergone FESS have not been compared.

Therefore, the aim of this study was to compare the effects of intravenous administration of remimazolam and dexmedetomidine on the QoR of patients who had undergone FESS. We hypothesized that intravenous administration of remimazolam is a promising option for improving the QoR.

# Methods

# Participants

This single-blind, randomized controlled clinical trial was prospectively registered at the Chinese Clinical Trial Registry (ChiCTR2300076209, registration date: 27/9/2023) and was conducted at Anqing Medical Center of Anhui Medical University (Anqing Municipal Hospital) from October 1, 2023, to February 29, 2024. The study protocol was approved by the Ethics Committee of Anqing Medical Center of Anhui Medical University. Written informed consent was obtained from each selected patient before surgery. Our study followed the Consolidated Standards and Regulations.

Following ethics approval and informed consent, CRS subjects were prospectively enrolled following the following criteria: synchronous sinonasal symptoms present for more than 12 weeks, sinusitis evidenced by a sinus computerized tomography (CT) scan, age between 18 and 65 years, American Society of Anaesthesiologists (ASA) physical status I or II, and scheduled for elective FESS. The exclusion criteria included patients with systemic diseases (including neuropsychiatric diseases, respiratory diseases, circulatory disease,etc.), hypovolemia, bradycardia (HR < 50 beats per minute or lower), second- or third-degree atrioventricular blockage, BMI > 30 kg/m<sup>2</sup>, a recent history of acute upper respiratory tract infection or pulmonary infection, the use of any sedative before surgery, a history of food and drug allergy, opioid medication misuse, and a refusal to participate in the study.

A total of 120 patients eligible for this study were randomized to Group R, Group D or Group C with a 1:1:1 allocation. Block randomization was performed via a computer-generated random table. Given the complete difference in infusion protocols among the three groups, the clinical trial was a single-blinded study. The medical care personnel and researcher staff who performed the infusion protocols could not remain blinded to the study group allocation. However, all eligible participants, data collectors and assessors of the study outcomes were independent. Details of the QoR-40 scale, visual analogue scale (VAS) score and postoperative nausea or vomiting (PONV) intensity were explained to each patient 1 day before surgery. The patients were not given any preoperative medication.

## Study protocol

Standard monitoring, including electrocardiography (ECG), heart rate (HR), mean arterial pressure (MAP), and the peripheral pulse oximeter value  $(SPO_2)$ , was monitored throughout the procedure (Philips MX500, Boeblingen, Germany). In Group D, a loading dose of 1.0 µg/kg dexmedetomidine was infused over 10 min before anaesthesia induction, followed by maintenance infusion at 0.5  $\mu$ g/kg per hour until the end of surgery. In Group R, a loading dose of 0.075 mg/kg for remimazolam was infused over 1 min before anaesthesia induction, followed by a maintenance infusion at 0.1 mg/ kg per hour until the end of surgery, and the infusion was stopped when hypotension (MAP less than 60 mm Hg) occurred. Patients in Group C were given the same amount of placebo equal to dexmedetomidine. Anaesthesia was induced with propofol (2.0 mg/kg), sufentanil (0.5  $\mu$ g/kg), and cisatracurium (1.5 mg/kg). After endotracheal intubation (ID:7.5 mm or 7.0 mm), anaesthesia was maintained with propofol and remifentanil at the effect site, followed by target-controlled infusion (TCIs) of propofol and remifentanil via a TCI pump. The initial TCI levels of plasma propofol and remifentanil were set as 3.0  $\mu$  g/ml and 5.0  $\mu$  g/ml, respectively. Mechanical ventilation was applied in volume-control mode with a tidal volume (VT) of 8-10 ml/kg at a respiratory rate (RR) of 10-12 beats per minute (bpm) to provide an end-tidal carbon dioxide concentration of 35-45 mm Hg. The inspired oxygen fraction (FiO<sub>2</sub>) was 0.5 (balanced with air) throughout the anaesthesia period. The depth of anaesthesia was maintained at a BIS range between 45 and 60, as were the mean arterial pressure and heart rate within 20% of the baseline values, by adjusting the TCI concentration of plasma propofol and remifentanil during surgery. Atropine (0.5 mg) was intravenously injected to treat bradycardia. Cisatracurium 2.0 to 4.0 mg was intermittently used for muscle relaxation, and all surgeries were performed by the same team. The operating table was placed in the 15-degree reverse Trendelenburg position during surgery. To prevent PONV, ondansetron (4 mg) was administered intravenously 10 min prior to the end of surgery. After surgery, all patients were transferred to the postanaesthesia care unit (PACU), with the endotracheal tube retained. The endotracheal tube was removed after full return of consciousness and spontaneous ventilation, and the train-of-four ratio was  $\geq 0.9$ . The discharge criteria from the PACU included stable vital signs, a pain score of 2 or less, the absence of PONV, and a calm and alert patient. If the visual analogue scale (VAS) score exceeded 3, intravenous tramadol 50 mg served as rescue analgesia.

## Data collection

The main goal of this study was to assess the global QoR-40 score 3on the day before surgery and postoperative Day 1 (POD1), which includes five dimensions: emotional state (9 items), physical comfort (12 items), physical independence (5 items), psychological support (7 items), and pain (7 items), and each item is rated on a 5-point numerical scale, the score of the QoR-40 ranges from 40 to 200, and the recovery state is proportional to the score (40 = extremely poorest recovery quality, 200 = best recovery quality) [3]. Demographic variables such as sex, age, height, weight and ASA score were recorded. Haemodynamic parameters, including MAP and HR, were measured and recorded before anaesthesia induction (T0), before intubation (T1), immediately after intubation (T2), at the end of surgery (T3), immediately after extubation (T4), and upon PACU arrival (T5). The durations of anaesthesia and surgery were recorded. The cumulative consumption of propofol and remifentanil during surgery was recorded. The time to return of consciousness, which was calculated from the time of stopping narcotic agent infusion until sustained eye opening (for > 5 s), and the length of stay at the PACU were documented. The time to first rescue analgesia was recorded. The maximal VAS pain scores in the PACU and ward were measured with the VAS scale; this 10-point scale ranges from 0 (no pain) to 10 (the most pain imaginable) [11]. The level of sedation upon PACU arrival was documented via a 10-point Richmond Agitation Sedation Scale (+4=combative, -5=unarousable) [12]. PONV( assessed by a verbal descriptive scale as 0: no nausea, 1: mild nausea, 2: moderate nausea, 3: severe nausea and vomiting) [13], the need for vasopressors, and prolonged respiratory support were recorded.

## Statistical analysis

As described by Hu et al. [14], the calculation of sample size was based on the quality of recovery on the day before surgery and postoperative Day 1. The allowable error was 0.05, and each group needed 36 patients (assuming a power of 80%). Forty patients were included per group, resulting in a 10% dropout rate. Data analysis was performed via SPSS version 23.0 (SPSS Inc., Chicago, IL). The Shapiro–Wilk test was used to evaluate the normal distribution of the data. Continuous variables are presented as the mean (standard deviation, SD). Normally distributed variables were compared via Student's t test. Nonnormally distributed variables are presented as the median and interquartile range [M (IQR)] and were compared via the Kruskal–Wallis H test. Qualitative data

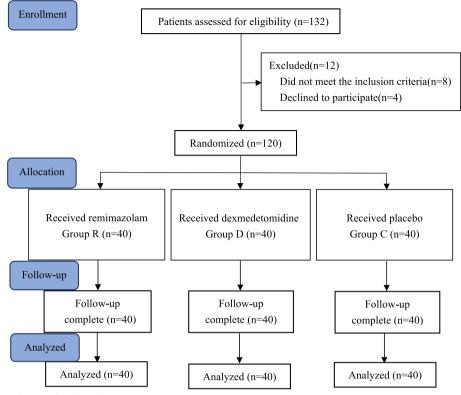


Fig. 1 CONSORT flow diagram for the study

are presented as numbers or percentages and were compared via the chi-square test. P values of less than 0.05 were considered statistically significant.

## Results

The study assessed 132 patients for eligibility. Eight patients did not meet the inclusion criteria, and 4 patients refused to participate in the present study. Therefore, 120 subjects were enrolled for follow-up. The details are shown in Fig. 1. The baseline general characteristics of the patients, including age, height, weight, ASA physical status, duration of surgery and anaesthesia, were not significantly different (Table 1). Compared with those in Group *C*, the cumulative consumption rates of propofol and remifentanil were significantly lower in Groups R and D (P<0.001) (Table 1). As shown in Table 1, the time to return of consciousness and the length of stay at the PACU were significantly lower in Groups R and C than in Group D (P=0.001 and P<0.001, respectively).

The QoR-40 scores are shown in Table 2. At POD1, the total score of the QoR-40 (median, IQR) was lower in Groups R (154.5,152.0–159.0) and D (155.0,154.8–159.3) than in Group C (139.0,136.8 -142.0) (P<0.001). There was no significant difference in the total QoR-40 score between Groups R and D. The scores of the emotional

state, physical comfort and pain dimensions were lower in Groups R and D than in Group C on POD1 (P < 0.005).

As shown in Table 3, the time to first rescue analgesia (median, IQR) was longer in Groups R (9.3,8.9–10.5) and D (10.1,8.5-11.0) than in Group C (5.5,5.1-6.4) (P < 0.001). The number of patients requiring rescue analgesia was less in Groups R (7/40, 17.5%) and D (6/40, 15.0%) than in Group C (18/40, 45.0%) (P=0.003). As detailed in Table 3, fifteen patients (15/40, 37.5%) in Group D experienced bradycardia during surgery. After intravenous administration of 0.5 mg of atropine, the heart rate of these patients gradually recovered to between 60 and 70 beats/minute, but no patients in Groups R and C experienced bradycardia (P=0.000). The number of patients occurring PONV was less in Groups R (3/40) and D (4/40) than in Group C (11/40) (P=0.024). Hypotension, the need for vasopressors or prolonged respiratory support were not observed.

As detailed in Table 4, the maximal VAS pain score was lower in the PACU and ward in Groups R and D than in Group C (P < 0.001). The RASS score was lower upon PACU arrival in Groups R and D than in Group C (P < 0.001).

As detailed in Fig. 2, compared with the baseline values, the fluctuations in the MAP values in Groups R

## Table 1 Baseline demographic and clinical characteristics

| Variables                                   | Group R ( <i>n</i> =40) | Group D ( <i>n</i> =40) | Group C ( <i>n</i> = 40) | P-value |
|---|-------------------------|-------------------------|--------------------------|---------|
| Age (years)                                 | 40.7±14.6               | 42.4±13.2               | 41.3±12.4                | 0.834   |
| Height(cm)                                  | 171.1±8.1               | 168.8±8.2               | 167.7±10.1               | 0.448   |
| Weight (kg)                                 | $66.5 \pm 11.4$         | $64.9 \pm 10.1$         | 65.9±13.2                | 0.905   |
| Gender (male/female)                        | 11/29                   | 14/26                   | 12/28                    | 0.762   |
| ASA physical status (I/II)                  | 25/15                   | 28/12                   | 24/16                    | 0.627   |
| Duration of surgery(min)                    | 100.2±8.7               | $100.3 \pm 10.7$        | 123.4±16.6               | < 0.001 |
| Duration of anesthesia (min)                | 119.6±12.5 <sup>*</sup> | 119.4±13.9 <sup>*</sup> | 136.4±17.5               | 0.001   |
| Time to return of consciousness (min)       | $20.6 \pm 5.4^{+}$      | 25.9±2.3                | $22.2 \pm 4.1^{+}$       | < 0.001 |
| Length of PACU stay (min)                   | $48.8 \pm 7.9^{+}$      | $53.2 \pm 5.8$          | $37.2 \pm 7.8^{\dagger}$ | < 0.001 |
| Cumulative consumption of propofol (mg)     | $469.5 \pm 96.3^{*}$    | 514.4±48.9 <sup>*</sup> | 605.3±133.9              | < 0.001 |
| Cumulative consumption of remifentanil (µg) | 1188.9±207.9*           | 1093.0±172.5*           | 1379.5±244.5             | < 0.001 |

Values are presented as the mean  $\pm$  SD (standard deviation) or number

Group R iv. remimazolam, Group D iv. dexmedetomidine, Group C iv. placebo, Time to return of consciousness the time of stopping narcotic agent infusion until sustained eye opening (for > 5 s), ASA American Society of Anesthesiologists, PACU postanesthesia care unit

\* *p* < 0.05 vs. group C

<sup>†</sup> *p* < 0.05 vs. group D

# Table 2 Preoperative and POD1 global QoR-40 Score

|                       | Group R ( <i>n</i> =40)       | Group D ( <i>n</i> = 40) | Group C ( <i>n</i> = 40) | P-value |
|-----------------------|-------------------------------|--------------------------|--------------------------|---------|
| Preoperative          |                               |                          |                          |         |
| Total QoR-40 Score    | 161.0 (158.0 -164.0)          | 162.0 (159.0 -163.0)     | 162.0 (158.3 -163.8)     | 0.928   |
| POD1                  |                               |                          |                          |         |
| Emotional state       | 35.0 (33.8 -36.3)*            | 34.5 (33.8—36.0)*        | 29.5 (28.8—31.0)         | < 0.001 |
| Physical comfort      | 42.5 (42.0—44.3)*             | 42.0 (40.0—43.3)*        | 40.0 (38.0-41.3)         | 0.004   |
| Physical independence | 22.0 (21.0—22.0)              | 22.0 (20.8—22.0)         | 20.5 (20.0—22.0)         | 0.219   |
| Psychological support | 28.0 (26.8—29.0)              | 28.0 (26.0—29.0)         | 27.0 (26.0—28.0)         | 0.475   |
| Pain                  | 29.0 (28.0—30.3) <sup>*</sup> | 30.0 (28.0—30.3)*        | 25.5 (24.8—27.0)         | < 0.001 |
| Total QoR-40 Score    | 154.5 (152.0 -159.0)*         | 155.0 (154.8 -159.3)*    | 139.0 (136.8 -142.0)     | < 0.001 |

Variables are presented as the median and interquartile range

Group R iv. remimazolam, Group D iv. dexmedetomidine, Group C iv. placebo, POD1 postoperative day 1, QoR-40 quality of recovery 40

\* *p* < 0.05 vs. group C

# Table 3 Recovery profiles after surgery

| Variables                                       | Group R ( <i>n</i> = 40) | Group D ( <i>n</i> = 40) | Group C ( <i>n</i> = 40) | P-value |
|---|--------------------------|--------------------------|--------------------------|---------|
| Time to first require rescue analgesia (h)      | 9.3 (8.9–10.5)*          | 10.1 (8.5–11.0)*         | 5.5(5.1–6.4)             | < 0.001 |
| Number of patients requiring analgesia(n,%)     | 7 (17.5%)*               | 6 (15.0%) <sup>*</sup>   | 18(45.0%)                | 0.003   |
| Bradycardia(n,%)                                | 0 (0.0) <sup>†</sup>     | 15(37.5)                 | 0 (0.0) <sup>†</sup>     | < 0.001 |
| Number of patients occurring PONV (n) (0/1/2/3) | 37/2/1/0*                | 36/2/2/0*                | 29/8/2/1                 | 0.024   |

Variables are presented as the median and interquartile range or number (proportion)

Group R iv. remimazolam, Group D iv. dexmedetomidine, Group C iv. placebo, PONV postoperative nausea or vomiting was assessed by a verbal descriptive scale as 0: no nausea, 1: mild nausea, 2: moderate nausea, 3: severe nausea and vomiting

\* *p* < 0.05 vs. group C

<sup>†</sup> p < 0.05 vs. group D

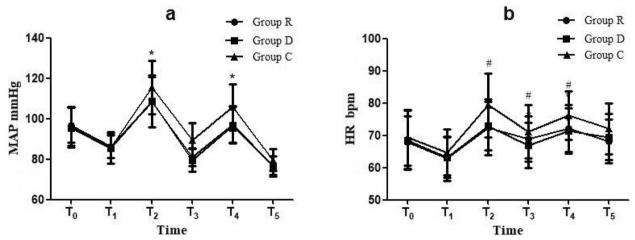
| Variables                     | Group R ( <i>n</i> = 40) | Group D ( <i>n</i> = 40) | Group C( <i>n</i> = 40) | P-value |
|-------------------------------|--------------------------|--------------------------|-------------------------|---------|
| Maximal VAS score (PACU)      | 3.0 (2.0—3.0)*           | 3.0 (2.0—3.0)*           | 3.0 (3.0—4.0)           | < 0.001 |
| Maximal VAS score (ward)      | 4.0 (3.8—4.3)*           | 4.0 (3.0—4.0)*           | 4.5 (4.0—5.0)           | < 0.001 |
| RASS score(upon PACU arrival) | -2.0 (-2.0—-1.0)*        | -2.0 (-3.0—-2.0)*        | 1.0 (0.0—1.0)           | < 0.001 |

 Table 4
 Maximal VAS score in the PACU or ward and RASS score upon PACU arrival

Variables are presented as the median and interquartile range

Group R iv. remimazolam, Group D iv. dexmedetomidine, Group C iv. placebo, VAS visual analogue scale, PACU postanesthesia care unit, RASS Richmond Agitation Sedation Scale

<sup>\*</sup> *p* < 0.05 vs. group C



**Fig. 2** Perioperative hemodynamic variables including (**a**) MAP and (**b**) HR.Variables are presented as mean  $\pm$  SD (standard deviation).T0:before anesthesia induction;T1:before intubation;T2: immediately after intubation; T3:at the end of surgery;T4:immediately after extubation; T5: upon PACU arrival.Group R: iv. remimazolam; Group D: iv. dexmedetomidine; Group C: iv. placebo. MAP: mean arterial pressure; HR:heart rate.\*p < 0.05 vs. group C; #p < 0.05 vs. group D

and D were lower at T2 and T4. However, the fluctuations in the HR values in Groups R and C were lower than those in Group D at T2, T3 and T4 (P<0.05).

## Discussion

The results of the present study demonstrated that the total QoR-40 scores decreased less on POD1 in patients following FESS who received remimazolam or dexmedetomidine than in those who received a placebo. Treatment with remimazolam or dexmedetomidine also reduced the cumulative consumption rates of propofol and remifentanil, and lowered the pain intensity and the number of patients occurring PONV. Additionally, compared with those in Group D,the time to return of consciousness and length of stay in the PACU were shorter in Groups R and C. At the dose selected in the study, bradycardia was noted in 15 patients in Group D, but no bradycardia was recorded in Groups R and C.

The effectiveness and reliability of the QoR-40 have validated in general surgery patients. Furthermore, a study revealed that total intravenous anaesthesia was more beneficial for physical comfort and physical independence out of five dimensions of the QoR-40 questionnaire than inhalation anaesthesia [12, 15]. Another study reported that remimazolam-based anaesthesia was more effective than sevoflurane-based anaesthesia in preventing PONV and improving the quality of recovery in cervical spine surgery [16]. Additionally, Matsumoto et al. [17] compared the effects of remimazolam and propofol on PONV, and the results revealed that there was no significant difference in the incidence of PONV15. Similar to these results, the number of patients occurring PONV in Groups R and D was lower than in Group C. Although otolaryngological procedures without prophylactic antiemetics are considered risk factors for PONV, only 3 and 4 patients in Groups R and D, respectively, experienced PONV. Moreover, intraoperative opioid use has a positive relationship with PONV. In the present study, the cumulative consumption of remifentanil was lower in Groups R and D than in Group C. Hence, the main reason for the inhibition of PONV in this study

may be the opioid-sparing effect of remimazolam and dexmedetomidine.

In addition, Erskine et al. [18] reported that mood disturbances are highly prevalent in patients with CRS and negatively impact patients' quality of life. Recent studies reported that emotion was regulated by remimazolam and dexmedetomidine [19, 20]. Our findings revealed that the scores of the emotional state were greater in Groups R and D than in Group C. These results suggested that remimazolam and dexmedetomidine improved patients' emotional state. Given the potential antidepressant properties of remimazolam or dexmedetomidine, the total score of the QoR-40 decreased less in Groups R and D than in Group C. Nevertheless, the current findings contradict the results of a recent study. In their study, the scores of physical comfort and emotional state were lower in the remimazolam group than in the propofol group, an undesirable desensitization-like effect at the top end of the response curve and a rebound phenomenon upon the termination of the agent contributed to the reason [19], whereas a low-dose infusion of remimazolam was used as a narcotic adjunct in the study, and no significant difference was observed between Groups R and D.

Various factors, such as sex, age, concurrent turbinectomy, and the number of sinuses addressed, might be associated with increased POD1 pain scores [8, 10]. However, the aforementioned risk factors, which were not assessed to predict higher POD1 scores, were not significantly different in the present study. FESS is commonly used in clinical practice and is associated with a better tolerated procedure, greater symptom improvement, and fewer complications than the traditional open approach [1]. However, patients who have undergone FESS experienced mild to moderate postoperative pain on POD1 [2]. Many nociceptive, inflammatory, and neuropathic pathways contribute to perioperative pain20. Antkowiak et al. [21] reported that GABAA receptors assemble from five protein subunits, harbouring  $\alpha_1$  and  $\beta_2$  subunits, to mediate sedative actions and  $\alpha_2$  subunits to mediate antihyperalgesic actions, and that remimazolam also alleviates neuropathic pain potentially through the modulation of translocator proteins as a subtype formerly known as the peripheral benzodiazepine receptor in the spinal cord. Additionally, a previous study has found that remimazolam may attenuate mechanically evoked pain and clinically relevant pain outcomes, potentially due to its effects on GABA receptors or its residual sedative properties [22]. Several studies have shown that remimazolam can alleviate or stabilize inflammatory responses [7, 23], but inflammatory response indexes such as IL-6, SAA, CRP, and PCT were not detected in our study. So the anti-inflammatory effect of remimazolam may not offer additional benefits in postoperative analgesia. Furthermore, a clinical study has shown that intravenous infusion of dexmedetomidine during surgery can significantly reduce postoperative pain intensity, opioid use, and the incidence of opioid-related adverse events [4]. Moreover, the administration of dexmedetomidine relieved neuropathic pain and inflammatory responses through different signalling pathways [24]. Therefore, these findings indicate that the analgesic effect of dexmedetomidine or remimazolam may be the main reason for the reduction in postoperative pain intensity.

Moreover, the half-life of dexmedetomidine is 2–3 h [25], whereas that of remimazolam is 1–2 h, and remimazolam has its own antagonist, flumazenil [26]. Thus, the time to return of consciousness and the length of stay in the PACU in Group R were significantly shorten than those in Group D. Intravenous infusion of high doses of both agents might lead to adverse effects such as delayed recovery and respiratory or cardiovascular depression [27, 28]. However, no patients required postoperative respiratory support, and no serious cardiovascular or other adverse reactions occurred in Groups R and D, suggesting that the infusion dose selected for dexmedetomidine or remimazolam in this study was safe.

There were several limitations in this study. First, inflammatory response indices were not tested in our study, so the anti-inflammatory effect of remimazolam may not offer additional benefits in postoperative analgesia.Second, the relationship between the severity of chronic sinusitis and the quality of recovery was not analysed. Third, the number of patients enrolled was small, the study was a single-centre clinical study, and the conclusions were further supported by large-sample and multicentre studies. Therefore, the results of this study are limited in their ability to be generalized.

## Conclusions

The administration of remimazolam and dexmedetomidine could increase the quality of recovery and alleviate the intensity of pain after FESS. Compared with those of dexmedetomidine, the efficacy and safety of remimazolam are not inferior.

# Abbreviation

| ADDIEVIa | lions                                 |
|----------|---------------------------------------|
| CRS      | Chronic Rhinosinusitis                |
| CT       | Computerised Tomography               |
| QoR      | Quality of Recovery                   |
| FESS     | Functional Endoscopic Sinus Surgery   |
| ASA      | American Society of Anesthesiologists |
| POD      | Postoperative Day                     |
| PACU     | Postanesthesia Care Unit              |
| PONV     | Postoperative Nausea or Vomiting      |
| MAP      | Mean Arterial Pressure                |
|          |                                       |

HR Heart Rate

| ECG              | Electrocardiogram            |
|------------------|------------------------------|
| SPO <sub>2</sub> | Peripheral Pulse Oximeter    |
| VT               | Tidal Volume                 |
| RR               | Respiratory Rate             |
| FiO <sub>2</sub> | Inspired Oxygen Fraction     |
| Ce               | Effect -Site Concentration   |
| BIS              | Bispectral Index             |
| VAS              | Visual Analogue Scale        |
| SD               | Standard Deviation           |
| ANOVA            | One-way analysis of variance |
| IQR              | Inter- quartile Range        |

# **Supplementary Information**

The online version contains supplementary material available at https://doi. org/10.1186/s12871-024-02860-8.

Supplementary Material 1.

#### Acknowledgements

Not applicable.

## Authors' contributions

SHH, QYT and YQL conceived the study design and drafted the study protocol. SHH, QYT, YQL, FFG,HZ,QQG and SBW all participated in the study design and coordination. YQL,HZ,FFG and QQG contributed to data collection. SHH, and QYT were the principal investigator and has overall responsibility for this study. SHH and YQL performed the statistical analysis for the study protocol. SHH,YQL,HZ and QYT drafted and revised the manuscript. SHH, YQL,HZ and QYT critically revised the manuscript. All authors have read and approved the final manuscript.

#### Funding

This research received no external funding.

#### Data availability

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

## Declarations

## Ethics approval and consent to participate

This study was approved by the Institutional Medical Ethics Committee of Anging Medical Center of Anhui Medical University. Written informed consent was obtained from all subjects before surgery. This study was prospective registered in the Chinese Clinical Trial Registry (ChiCTR2300076209). Initial registration date was 27/9/2023.

### **Consent for publication**

Not applicable.

### **Competing interests**

The authors declare no competing interests.

### Author details

<sup>1</sup>Department of Anesthesiology, Anqing Medical Center of Anhui Medical University, the Fifth Clinical Medical School of Anhui Medical University, No.87 Tianzhushan East Road, Anqing 246003, Anhui, China.

## Received: 20 April 2024 Accepted: 11 December 2024 Published online: 23 December 2024

#### References

 Alanin MC, Hopkins C. Effect of Functional Endoscopic Sinus Surgery on Outcomes in Chronic Rhinosinusitis. Curr Allergy Asthma Rep. 2020;20(7):27. https://doi.org/10.1007/s11882-020-00932-6.

- Finkensieper M, Poller K, Wittekindt C, Meissner W, Guntinas-Lichius O. Postoperative pain assessment after functional endoscopic sinus surgery (FESS) for chronic pansinusitis. Eur Arch Otorhinolaryngol. 2013;270(1):157–66. https://doi.org/10.1007/s00405-012-2015-6.
- Chen Y, Liu S, Li B, Lin R, Lai W, Liu D, et al. Application of the quality of recovery-40 questionnaire to evaluate the effectiveness of enhanced recovery after surgery protocols in gastric cancer. Updates Surg. 2024;76(4):1365–75. https://doi.org/10.1007/s13304-023-01719-w.
- Kim SY, Kim JM, Lee JH, Song BM, Koo BN. Efficacy of intraoperative dexmedetomidine infusion on emergence agitation and quality of recovery after nasal surgery. Br J Anaesth. 2013;111(2):222–8. https://doi.org/10. 1093/bja/aet056.
- Miao M, Xu Y, Li B, Chang E, Zhang L, Zhang J. Intravenous administration of dexmedetomidine and quality of recovery after elective surgery in adult patients: A meta-analysis of randomized controlled trials. J Clin Anesth. 2020;65: 109849. https://doi.org/10.1016/j.jclinane.2020.109849.
- Tsukimoto S, Kitaura A, Kuroda H, Imaizumi U, Yoshino F, Yoshida A. Anti-inflammatory potential of remimazolam: A laboratory and clinical investigation. ImmunInflamm Dis. 2024;12(3): e1218. https://doi.org/10. 1002/iid3.1218.
- Xing Q, Zhou X, Zhou Y, Shi C, Jin W. Comparison of the effects of remimazolam tosylate and propofol on immune function and hemodynamics in patients undergoing laparoscopic partial hepatectomy: a randomized controlled trial. BMC Anesthesiol. 2024;24(1):205. https://doi.org/10.1186/ s12871-024-02589-4.
- Peng Y, Zhang Y, Wang W, Liu B, Zhang Z, Gong Z, et al. Potential role of remimazolam in alleviating bone cancer pain in mice via modulation of translocator protein in spinal astrocytes. Eur J Pharmacol. 2024;979: 176861. https://doi.org/10.1016/j.ejphar.2024.176861.
- Yuan R, Wen J, Xing Q, Chao L, Hu C, Ren J, et al. Efficacy of pretreatment with remimazolam on prevention of propofol-induced injection pain in patients undergoing gastroscopy. Sci Rep. 2023;13(1):19683. https://doi. org/10.1038/s41598-023-47151-3.
- Choi JY, Lee HS, Kim JY, Han DW, Yang JY, Kim MJ, et al. Comparison of remimazolam-based and propofol-based total intravenous anesthesia on postoperative quality of recovery: A randomized non-inferiority trial. J Clin Anesth. 2022;82: 110955. https://doi.org/10.1016/j.jclinane.2022. 110955.
- Nahman-Averbuch H, Hughes C, Hoeppli ME, White K, Peugh J, Leon E, et al. Communication of pain intensity and unpleasantness through magnitude ratings: Influence of scale type, but not gender of the participant. Eur J Pain. 2023;27(10):1161–76. https://doi.org/10.1002/ejp.2147.
- Deljou A, Soleimani J, Martin DP, Schroeder DR, Sprung J, Weingarten TN. Anesthetic Management and Deep Sedation After Emergence From General Anesthesia: A Retrospective Cohort Study. Anesth Analg. 2023;136(6):1154–63. https://doi.org/10.1213/ANE.000000000006470.
- Lee SC, Jung JW, Choi SR, Chung CJ, Lee TY, Park SY. Comparison of Postoperative Nausea and Vomiting Incidence between Remimazolam and Sevoflurane in Tympanoplasty with Mastoidectomy: A Single-Center, Double-Blind, Randomized Controlled Trial. Medicina (Kaunas). 2023;59(7):1197. https://doi.org/10.3390/medicina59071197.
- Hu S, Shu T, Xu S, Ju X, Wang S, Ma L. Ultrasound-guided bilateral superficial cervical plexus block enhances the quality of recovery of uremia patients with secondary hyperparathyroidism following parathyroidectomy: a randomized controlled trial. BMC Anesthesiol. 2021;21(1):228. https://doi.org/10.1186/s12871-021-01448-w.
- Lee WK, Kim MS, Kang SW, Kim S, Lee JR. Type of anaesthesia and patient quality of recovery: a randomized trial comparing propofol-remifentanil total i.v. anaesthesia with desflurane anaesthesia. Br J Anaesth. 2015;114(4):663–668. https://doi.org/10.1093/bja/aeu405.
- Lee J, Han DW, Kim NY, Kim KS, Yang Y, Yang J, et al. Comparison of Remimazolam versus Sevoflurane on the Postoperative Quality of Recovery in Cervical Spine Surgery: A Prospective Randomized Controlled Double-Blind Trial. Drug Des Devel Ther. 2024;18:121–32. https://doi.org/10.2147/ DDDT.S441622.
- Matsumoto A, Satomi S, Kakuta N, Narasaki S, Toyota Y, Miyoshi H, et al. Remimazolam's Effects on Postoperative Nausea and Vomiting Are Similar to Those of Propofol after Laparoscopic Gynecological Surgery: A Randomized Controlled Trial. J Clin Med. 2023;12(16):5402. https://doi.org/10. 3390/jcm12165402.

- Erskine SE, Hopkins C, Clark A, Anari S, Robertson A, Sunkaraneni S, et al. Chronic rhinosinusitis and mood disturbance. Rhinology. 2017;55(2):113– 9. https://doi.org/10.4193/Rhin16.111.
- Li X, Tian M, Deng Y, She T, Li K. Advantages of Sedation With Remimazolam Compared to Midazolam for the Removal of Impacted Tooth in Patients With Dental Anxiety. J Oral Maxillofac Surg. 2023;81(5):536–45. https://doi.org/10.1016/j.joms.2023.02.001.
- Al-Alawi M, Brietzke E, Carvalhal A, Soares CN. The potential anti-depressant properties of dexmedetomidine infusion: a review of mechanistic, preclinical, and clinical evidence. Rev Neurosci. 2020;31(6):649–58. https://doi.org/10.1515/revneuro-2020-0001.
- Antkowiak B, Rudolph U. New insights in the systemic and molecular underpinnings of general anesthetic actions mediated by γ-aminobutyric acid A receptors. Curr Opin Anaesthesiol. 2016;29(4):447–53. https://doi. org/10.1097/ACO.00000000000358.
- Lee C, Lim J, Hong H, Yu H, Lee H. Effect of Remimazolam on Pain Perception and Opioid-Induced Hyperalgesia in Patients Undergoing Laparoscopic Urologic Surgery-A Prospective, Randomized, Controlled Study. Medicina (Kaunas). 2024;60(1):123. https://doi.org/10.3390/medic ina60010123.
- Deng W, Zeng Z, Liu Q, Deng J, Wang L, Li H, et al. Effects of Propofol, Low and High Doses of Remimazolam on Hemodynamic and Inflammatory Response in Laparoscopic Surgery. Drug Des Devel Ther. 2024;18:3329– 36. https://doi.org/10.2147/DDDT.S459885.
- 24. Wang X, Liu Q. Dexmedetomidine relieved neuropathic pain and inflammation response induced by CCI through HMGB1/TLR4/NF-κB signal pathway. Biol Pharm Bull,2021,20. https://doi.org/10.1248/bpb. b21-00329.
- Yu P, Zhang J, Zou Y, Wang J. Effect of Preventive Analgesia with Nalbuphine and Dexmedetomidine in Endoscopic Sinus Surgery.Pain research & management, 2022, 2344733. https://doi.org/10.1155/2022/ 2344733.
- Kilpatrick GJ. Remimazolam:Non-Clinical and Clinical Profile of a New Sedative/ Anesthetic Agent. Front Pharmacol. 2021;12: 690875. https:// doi.org/10.3389/fphar.2021.690875.
- Ye E, Wu K, Ye H, Zhang W, Chu L, Zhang K, et al. Comparison of 95% effective dose of remimazolam besylate and propofol for gastroscopy sedation on older patients: A single- centre randomized controlled trial. Br J Clin Pharmacol. 2023;89(11):3401–10. https://doi.org/10.1111/bcp. 15839.
- Ingebrigtson M, Miller JT. Adverse Hemodynamic Effects of Dexmedetomidine in Critically III Elderly Adults. J Pharm Pract. 2023;36(6):1319–23. https://doi.org/10.1177/08971900221110159.

# **Publisher's Note**

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.