BMC Anesthesiology

RESEARCH Open Access

Remimazolam for the prevention of emergence agitation in adults following nasal surgery under general anesthesia: a prospective randomized clinical controlled trial

Yanfei Lu[1†], Qiaomin Xu[2†], Hong Dai[2], Jimin Wu[2], Mengting Ai[2], Haiyan Lan[2], Xiaoli Dong[2] and Gongchen Duan[2*]

Abstract

Background Remimazolam is a novel intravenous sedative/anesthetic drug that belongs to the ultra-short-acting class of benzodiazepines. The purpose of this study was to evaluate the effectiveness of postoperative use of remimazolam in preventing emergence agitation (EA) in adults following nasal surgery.

Methods Patients who underwent nasal surgery were randomly divided into Group R and Group C. Propofol, sufentanil, and cis-atracurium were used for the induction of anesthesia, and 1.5–3.5% sevoflurane was used for the maintenance of anesthesia. At the end of the surgery, patients were randomly assigned to receive either remimazolam 0.1 mg kg^{-1} (Group R, $n=43$) or 0.9% saline (Group C, $n=43$). The primary outcome was the incidence of EA, which was defined as a Riker Sedation–Agitation Scale score > 4. The secondary outcomes included the incidence of severe EA, anesthesia, surgery characteristics, adverse events, mean arterial pressure, and heart rate (at different time points).

Results A total of 86 adult patients completed the study. The incidence of EA was lower in Group R than in Group C (21% vs. 49%, $P=0.007$). The incidence of severe EA was also lower in Group R than in Group C (2% vs. 19%, $P=0.035$). The maximal Sedation–Agitation Scale score during emergence was lower in Group R 4 [range 4 to 4] than in Group C 5 [range 4 to 6] ($P<0.001$). In addition, the incidence of hypertension and grade of cough in Group R were lower than in Group C ($P=0.024$). During emergence, the mean arterial pressure and heart rate of group R showed more stability than those in group C.

Conclusions Postoperative intravenous infusion of 0.1 mg/kg remimazolam into adult patients undergoing nasal surgery can reduce the incidence of EA and severe EA, and provide stable hemodynamics.

†Yanfei Lu and Qiaomin Xu contributed equally to this work and share first authorship.

*Correspondence:
Gongchen Duan
981225178@qq.com

Full list of author information is available at the end of the article

Trial registration The trial was registered, before patient enrollment, in the Chinese Clinical Trial Registry (www.chictr.org.cn) (clinical trial number: ChiCTR2300075300; Principal Investigator: Gongchen Duan; date of registration: 31 August 2023; https://www.chictr.org.cn/bin/project/edit?pid=203928).

Keywords Remimazolam, Nasal surgery, Emergence agitation, General anesthesia

Introduction

Emergence agitation (EA) is a common complication after general anesthesia, and its clinical manifestations are characterized by delirium, confusion, acute, agitation, and violent behavior [1]. If not handled properly, the patient may be seriously injured, possibly experiencing pain exacerbation, bleeding, self-extubation, or even falling out of bed, which will cause great harm to the patient [2]. Furthermore, it may increase the demand on human resources and cause medical staff injuries. Liang et al. showed that the incidence of EA in adults who used continuous inhalation of sevoflurane to maintain anesthesia was 53% [3]. Another study showed that the incidence of EA in adult ear, nose, and throat surgery under general anesthesia is as high as 55.4% [4]. The sense of asphyxia caused by nasal packing in nasal surgery makes patients more frequently appear restless during the recovery period [5]. Therefore, patients undergoing nasal surgery need appropriate sedation and analgesia during the recovery period to improve comfort and reduce the incidence of EA.

Remimazolam is a new type of ultrashort-acting benzodiazepine, which is characterized by rapid onset sedation, rapid recovery, and mild cardiovascular inhibition [6]. A clinical study indicated that remimazolam can prevent emergence delirium in children after tonsillectomy and adenoidectomy under sevoflurane anesthesia [7]. We propose the hypothesis that postoperative intravenous remimazolam can reduce the incidence of EA in adults undergoing nasal surgery. Therefore, we designed a prospective, double-blind, randomized study to explore the effect of postoperative intravenous remimazolam on EA in adults undergoing nasal surgery.

Methods

Study design

This paper has been uploaded to ResearchSquare as a preprint (https://www.researchsquare.com/article/rs-4270156/v1?).

This single-center, double-blind randomized clinical trial was approved by the Clinical Trials Ethics Committee of Lishui People's Hospital (approval no. 2023−137) by Chairperson Prof Zhichao Shi on 15 August 2023.This trial was performed in accordance with the Declaration of Helsinki. We followed the Consolidated Standards of Reporting Trials reporting guidelines, and all enrolled patients provided written informed consent.

Inclusion and exclusion criteria

This study involved 86 adult patients who were admitted to Lishui People's Hospital for nasal surgery from September 2023 to October 2023.

The inclusion criteria were (1) elective nasal surgery, (2) aged 18–65 years, (3) American Society of Anesthesiologists physical status of I or II, and (4) body mass index of 18.5–27.9 kg m^{-2}. The exclusion criteria were (1) preoperative mental disorders or communication difficulties, (2) severe arrhythmia, such as sick sinus syndrome, second- or third-degree atrioventricular block, or heart rate (HR) < 50 beats min^{-1}), (3) scheduled to be sent to the intensive care unit after surgery, and (4) allergy to benzodiazepines or a long-term history of benzodiazepine use.

Randomization and masking

Patients were randomly assigned to two groups (Group R and Group C) using computer-generated random numbers (43 patients in each group). We discreetly kept the randomization results in envelopes until the end of the study. Study drugs were prepared by a nurse who was not involved in the other parts of the study. Both remimazolam and saline are colorless liquids, and they were digitally encoded so that the researchers who were responsible for the postoperative follow-up and data processing were blinded to the group allocation during the whole study period. All anesthetists and patients were also blinded to the group allocation.

Interventions

Patients fasted for 8 h. No premedication was administered. Upon arrival in the operating room, all patients underwent pulse oxygen saturation, mean arterial pressure (MAP), and HR measurements using a Carestation 620 A2 monitor (GE Healthcare, Chicago, IL, USA). The depth of general anesthesia of the patients was continuously monitored using a bispectral index (BIS) sensor (Canwell Medical Co., Ltd., Jinhua, Zhejiang, China). All patients were anesthetized using standard protocols as follows. Anesthesia was induced with 2.0 to 2.5 mg kg^{-1} propofol (Beijing Fresenius Kabi Pharmaceutical Co., Ltd., Beijing, China), 0.4 to 0.5 μg kg^{-1} sufentanil (Yichang Humanwell Pharmaceutical Co., Ltd., Yichang, China) and 0.2 mg kg^{-1} cis-atracurium (Jiangsu Hengrui Pharmaceutical Co., Ltd., Jiangsu, China). After successful induction of general anesthesia, endotracheal intubation was performed. Volume-controlled mechanical ventilation was administered to maintain an end-tidal

carbon dioxide partial pressure of 35–45 mmHg. Anesthesia was maintained with inhalation of a mixture of 1.5–3.5% sevoflurane (Jiangsu Hengrui Pharmaceutical Co., Ltd.) and 50% oxygen (flow rate = 2 L min^{-1}). The sevoflurane concentration was controlled according to the hemodynamics and BIS value of each patient (maintaining both MAP and HR to within 20% of baseline, and a BIS value of 40–60). During the surgery, sufentanil and cis-atracurium were injected as needed. When the surgery was over, the anesthetic drugs were stopped immediately. Then, the intervention measures were started, as follows. (1) Group R (n = 43): 0.1 mg/kg remimazolam was injected intravenously after surgery, and the infusion time was 1 min. (2) Group C (n = 43): 0.9% saline was injected intravenously after surgery, and the volume and rate changes were the same as those in Group R. We confirmed the return of neuromuscular function, which was defined as three consecutive train-of-four ratios ≥ 0.9, using a train-of-four monitor. Neuromuscular blockade was reversed with 0.004 mg kg^{-1} glycopyrrolate and 0.02 mg kg^{-1} neostigmine. Then, we verbally stimulated the patients every 30 s, and the patients were extubated once they regained consciousness and were able to obey verbal commands. The Sedation–Agitation Scale (SAS) was administered by independent anesthesiologists who were blinded to the anesthetic methods every 10 s. Finally, all patients were transferred to the post-anesthesia care unit (PACU) for close observation. A well-trained nurse blinded to the study groups evaluated pain intensity every 5 min using a numeric rating scale (NRS) (range: 0–10, with higher scores indicating worse pain). Nonsteroidal anti-inflammatory drugs were administered when the NRS score ≥ 5. Postoperative adverse events included hypotension, hypertension, bradycardia, tachycardia, postoperative nausea and vomiting (PONV), laryngospasm, cough, and hypoxemia. All adverse events were recorded from the end of surgery to discharge from the PACU. If such events occurred, intravenous injection of drugs such as ephedrine, urapidil, atropine, esmolol, and tropisetron was an option. Patients were discharged from the PACU when their Aldrete score was ≥ 9 [8]. The following evaluation time points were defined: T0, admission (basal); T1, at the end of the surgery; T2, after investigational drug infusion; T3, tracheal extubation; T4, 2 min after tracheal extubation; and T5, 5 min after tracheal extubation.

Outcome measurements

Primary outcome

The primary outcome was the incidence of EA. Emergence was defined as the time interval from the end of surgery to 2 min after tracheal extubation. During emergence, EA was defined as an SAS score > 4 (1 = unarousable: no response to noxious stimuli; 2 = heavily sedated: aroused by physical stimuli but non-communicative; 3 = sedated: awakens to verbal commands or gentle shaking but drifts off again; 4 = calm: awakens easily, follows verbal commands; 5 = agitated: anxious or mildly agitated, calms down with verbal instructions; 6 = very agitated: requires physical restraint and frequent verbal reminders of limits; and 7 = dangerous agitation: pulling at tracheal tube, trying to remove catheters or striking staff [9].

Secondary outcomes

The secondary outcomes were as follows.

1. The incidence of severe EA (defined as an SAS score of 7) and the maximal SAS score during emergence were also recorded.
2. Recovery characteristics included extubation time, the length of the PACU stay, and the maximum NRS score in the PACU.
3. Hemodynamic parameters (including MAP and HR) were recorded at six different time points: T0, T1, T2, T3, T4, and T5.

Postoperative adverse events included hypotension (MAP ≤ 70% of baseline and/or < 65 mmHg), hypertension (MAP ≥ 120% of baseline), bradycardia (HR ≤ 45 beats/min), tachycardia (HR of ≥ 120% of baseline) [10], PONV, laryngospasm, cough (0 = no coughing; 1 = single cough; 2 = persistent cough lasting < 5 s; 3 = persistent cough lasting ≥ 5 s), and hypoxemia (oxygen saturation < 90%).

4. The incidence of postoperative delirium (POD) within 3 days after surgery was assessed using the Confusion Assessment Method [11].

Statistical analysis

The data processing and analyses were performed using SPSS 20.0 statistical software (IBM Corp., Armonk, NY, USA). All data are presented as mean ± SD number (%), or median (IQR) as appropriate. The normality of the data distribution was assessed with the Shapiro–Wilk test. Normally distributed data were compared between the groups using an independent-samples t-test, and non-normally distributed data were compared using the Mann–Whitney U test. The chi-square test or Fisher's exact test was used for comparison of numerical data between the groups. The significance level for the analysis was set at $\alpha = 0.05$.

A total of 40 patients completed the pre-experiment (20 patients in each group). The experimental protocol for the pre-experiment was consistent with that of the formal experiment. In the pre-experiment, the incidence of EA was 55% in Group C and 25% in Group R.

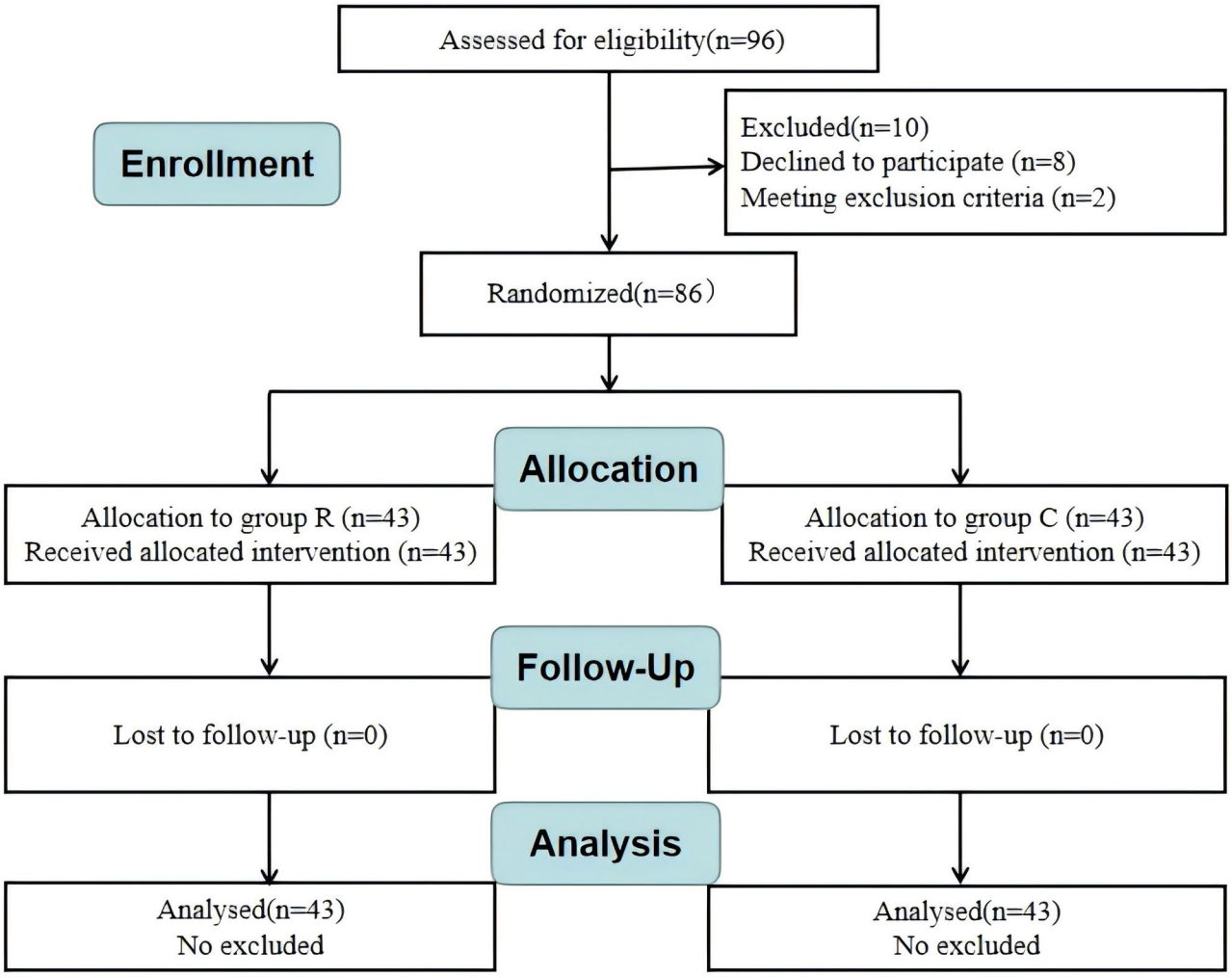

Fig. 1 Flow chart of this study

Table 1 Patient baseline characteristics

	Group R (*n* = 43)	Group C (*n* = 43)	*P* value
Age (years)	42.0 ± 11.7	42.8 ± 11.5	0.732
Height (cm)	168.9 ± 6.5	168.9 ± 6.7	0.994
Weight (kg)	72.6 ± 7.4	70.4 ± 8.1	0.194
Sex, n (%)			0.235
Male	10 (23.3)	15 (34.9)	
Female	33 (76.7)	28 (65.1)	
ASA physical status, n (%)			0.610
I	11 (25.6%)	9 (20.9%)	
II	32 (74.4%)	34 (79.1%)	
Level of education, n (%)			0.644
< Elementary school	4 (9.3%)	6 (14.0%)	
Elementary school	14 (32.6%)	16 (37.2%)	
≥Secondary school	25 (58.1%)	21 (48.8%)	

Data presented as mean ± SD were analysed using independent-samples t-test. Data presented as number (%) were analysed using chi-square test or Fisher exact test. No statistically significant differences were noted between groups

Therefore, a sample size of 76 patients was needed to provide a power of 80% at a significance level of 0.05. Assuming a 10% attrition rate, we enrolled 86 patients in this study (43 patients in each group).

Results

In total, 96 patients were initially screened for eligibility: two patients met the exclusion criteria (long-term history of benzodiazepine use) and eight patients declined to participate. Finally, data for 43 patients in Group R and 43 patients in Group C were analyzed (Fig. 1).

The patient baseline characteristics were statistically similar between the two groups (Table 1). There were no significant differences in the extubation time, length of PACU stay, NRS pain score, intraoperative sufentanil dosage, duration of surgery, amount of intraoperative fluid, and blood loss between the two groups (Table 2).

The incidence of EA in Group R was lower than in Group C (20.9% vs. 48.8%; $P=0.007$). The incidence of severe EA in Group R was also lower than in Group C

Table 2 Anaesthesia and surgery characteristics

	Group R (*n* = 43)	Group C (*n* = 43)	*P* value
Extubation time (min)	21.0 ± 4.2	20.9 ± 3.8	0.915
Length of PACU stay (min)	23.3 ± 3.2	22.5 ± 2.9	0.246
Maximum NRS score in PACU	2 (1 to 2)	2 (1 to 3)	0.450
Type of surgery, n (%)			0.892
Septoplasty	20 (46.5%)	19 (44.2%)	
Ethmoidectomy	6 (13.3%)	5 (11.6%)	
Both Septoplasty and ethmoidectomy	17 (39.5%)	19 (44.2%)	
Type of nasal packing, n (%)			0.747
Unilateral	5 (11.6%)	6 (14.0%)	
Bilateral	38 (88.4%)	37 (86.0%)	
Duration of surgery (min)	53.6 ± 15.6	53.0 ± 13.1	0.852
Sevoflurane used time (min)	59.1 ± 15.0	58.6 ± 12.7	0.856
Intraoperative sufentanil dosage (μg)	30 (28 to 30)	28 (28 to 30)	0.231
Amount of intraoperative fluid (ml)	529.1 ± 148.0	569.5 ± 86.7	0.126
Blood loss (ml)	15 (10 to 25)	10 (10 to 20)	0.477

Data presented as mean±SD were analysed using independent-samples t-test. Data presented as number (%) were analysed using chi-square test or Fisher exact test.Data presented as median (IQR) were analysed using the Mann-Whitney test.No statistically significant differences were noted between groups.PACU, post anesthesia care unit. NRS, numeric rating scale

Table 3 Emergence agitation related outcomes

	Group R (*n* = 43)	Group C (*n* = 43)	*P* value
Emergence agitation, n (%)	9(20.9%)	21(48.8%)	0.007
Severe emergence agitation, n (%)	1(2.3%)	8(18.6%)	0.035
Maximal SAS during emergence, n (%)	4 (4 to 4)	5 (4 to 6)	< 0.001

Data presented as number (%) were analysed using chi-square test or Fisher exact test.Data presented as median (IQR) were analysed using the Mann-Whitney test.SAS, Riker Sedation–Agitation Scale

(2.3% vs. 18.6%; $P=0.035$). The maximal SAS score during emergence was lower in Group R 4 [range,4–4] than in Group C 5 [range,4–6] ($P<0.001$) (Table 3).

During the emergence period, the hemodynamics of Group R showed more stable changes than group C (Figs. 2 and 3).

The incidence of hypertension was significantly lower in Group R than in Group C (4.7% vs. 20.9%, $P=0.024$), and the cough grade was significantly lower in Group R 1 (range: 0–2) than in Group C 2 (range: 1–2) ($P=0.008$). In addition, there were no significant differences in the incidence of hypotension, bradycardia, tachycardia, PONV, laryngospasm, POD, and hypoxemia between the two groups (Table 4).

Discussion

This study suggests that intravenous injection of remimazolam at a dose of 0.1 mg/kg at the end of nasal surgery in adult patients can significantly reduce the incidence of EA and severe EA, as well as the maximal SAS score during emergence. In addition, this intervention can also reduce the incidence of hypertension and cough grade, thereby providing stable hemodynamics.

The incidence of EA is related to various factors, including pain, endotracheal intubation, the inhalation of anesthetics, preoperative anxiety, male gender, age, and the type of surgical procedure. Oral surgery and ENT surgery are associated with the highest incidence rates of EA, of 60% and 55.4%, respectively [4]. Previous studies have revealed that continuous endotracheal intubation during the recovery period causes significant pain in patients, which is the most common cause of EA [12]. Therefore, this risk factor was also recorded and controlled in this study. The results also showed that there was no group difference in postoperative pain, sevoflurane use time, sex ratio, age, type of surgery, opioid dose, or type of nasal packing. This increases the validity of the conclusions of this study. Inhalation anesthesia can lead to EA in children [13]. However, there is no clear consensus as to whether inhalation anesthesia will increase the incidence of EA in adult patients. Some studies have reported that inhalation anesthesia does not increase the incidence of EA [1, 14]. However, other studies have shown that inhalation anesthesia can increase the incidence of EA [4]. In this study, sevoflurane was used to maintain general anesthesia, and the incidence of EA in the control group was 48.8%. In a retrospective study of 792 patients who underwent nasal surgery, the incidence of EA was 22.2% (702 patients on total intravenous anesthesia and 90 patients on inhalational anesthesia with sevoflurane) [15]. It is suggested that inhalational anesthesia with sevoflurane may be associated with the incidence of EA in adults undergoing nasal surgery.

Drug treatment is important to prevent EA. A study showed that intraoperative infusion of dexmedetomidine significantly reduced the incidence of EA in adult patients undergoing nasal surgery (from 52–28%) [16]. This result is similar to that of this study, in which the incidence of EA decreased from 48.8 to 20.9%. This may be because both dexmedetomidine and remimazolam are associated with more gradual awakening, while also effectively reducing the intolerable stimulation caused by tracheal intubation and nasal packing. Midazolam is a representative benzodiazepine. Specifically, in a meta-analysis published in 2010 [17], prophylactic administration of midazolam showed no preventive effect against EA in children anesthetized with sevoflurane, desflurane, or both. However, another study showed that intravenous injection of 0.03 mg/kg midazolam immediately before the end of the operation reduced EA in children undergoing strabismus surgery with sevoflurane anesthesia [18]. Benefiting from unique pharmacological properties, remimazolam not only maintains the safety advantages of midazolam but also has broader therapeutic applications.

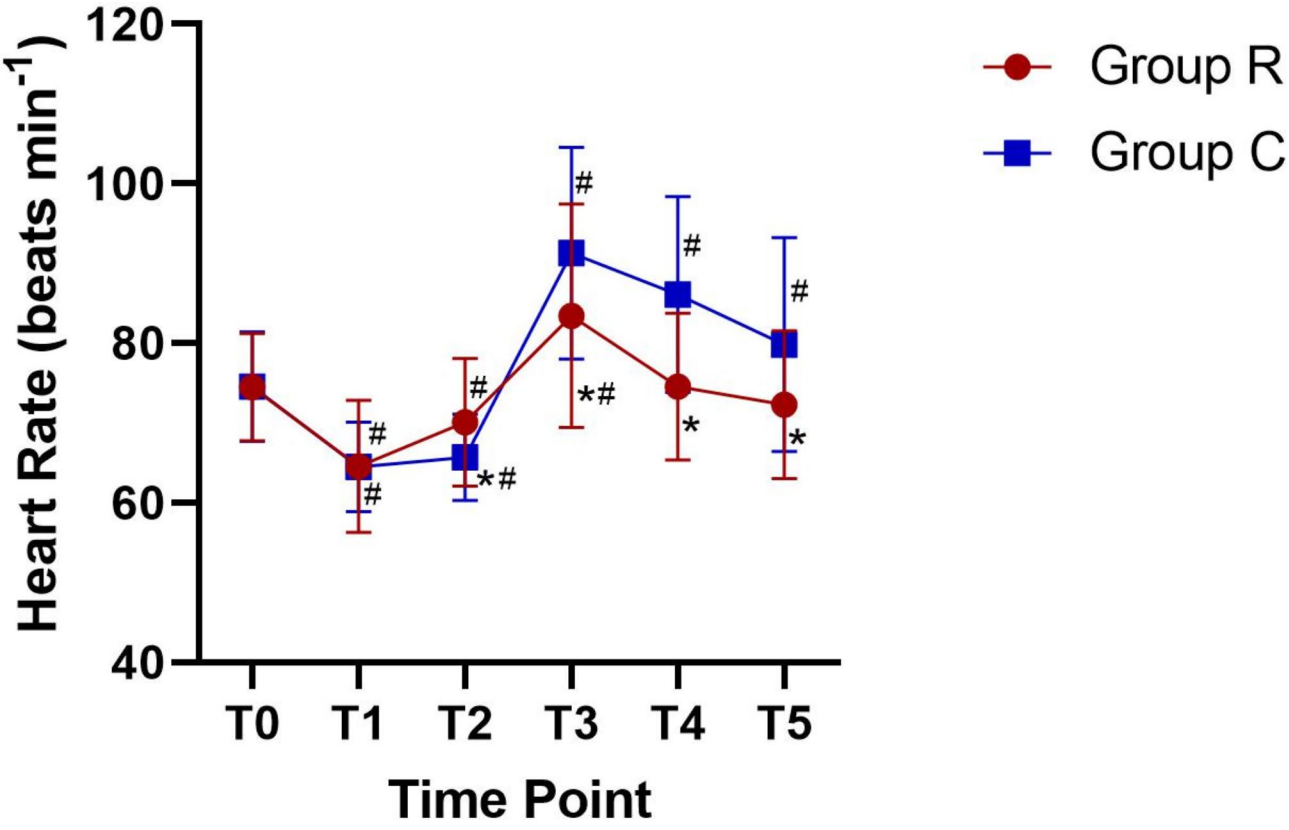

Fig. 2 HR changes during operation and emergence
T0: admission (basal); T1: at the end of the surgery; T2: after investigational drug infusion ; T3: tracheal extubation; T4: 2 min after tracheal extubation; T5: 5 min after tracheal extubation. Data were presented as mean ± SD. $^{*}P < 0.05$ compared with Group C. $^{\#}P < 0.05$ compared with T0 in each group.HR, heart rate

In a recent study by Yang et al., which enrolled children undergoing tonsillectomy and adenoidectomy under sevoflurane general anesthesia, intravenous administration of 0.2 mg/kg remimazolam at the end of surgery significantly reduced the incidence and severity of emergence delirium [7]. The results of that study are similar to our results, which show that the use of intravenous remimazolam at the end of surgery can effectively reduce the maximal SAS score, thereby reducing the incidence of EA and severe EA.

The clinical manifestations of EA include confusion, disorientation, crying, moaning, shouting, and screaming [19]. These factors may trigger severe fluctuations in hemodynamics, thereby increasing the risk of cardiovascular and cerebrovascular diseases. In this study, Group R showed more stable hemodynamics during emergence, and the incidence of hypertension and the grade of cough were significantly lower than in Group C. Remimazolam has received significant attention from many scholars since its launch. Recent studies have shown that remimazolam can not only reduce the incidence of EA during hip replacement surgery in older adults but also allow for the maintenance of more stable hemodynamic parameters [20]. In addition, compared with dexmedetomidine, remimazolam is effective in reducing the incidence of EA in older patients after orthopedic surgery [21, 22]. The results of this study also showed that postoperative intravenous remimazolam did not affect the extubation time and length of PACU stay of the two groups after general anesthesia. Furthermore, it did not cause common adverse events such as hypotension and hypoxemia. This further demonstrates that remimazolam can promote postoperative recovery in patients undergoing general anesthesia. This may be related to the pharmacological properties of remimazolam, which has been confirmed by multiple studies to have no effect on postoperative recovery time [23–25].

Although there are several limitations to this study, its results are still valuable. First, during the experimental process, we only used a single intravenous infusion dose of remimazolam, of 0.1 mg/kg. Whether this dose is the optimal effective dose remains to be confirmed in subsequent studies. Second, this study is a single-center trial, and thus multicenter studies should be conducted in the future to verify the results. Despite the above limitations, this study still has considerable value: as well as

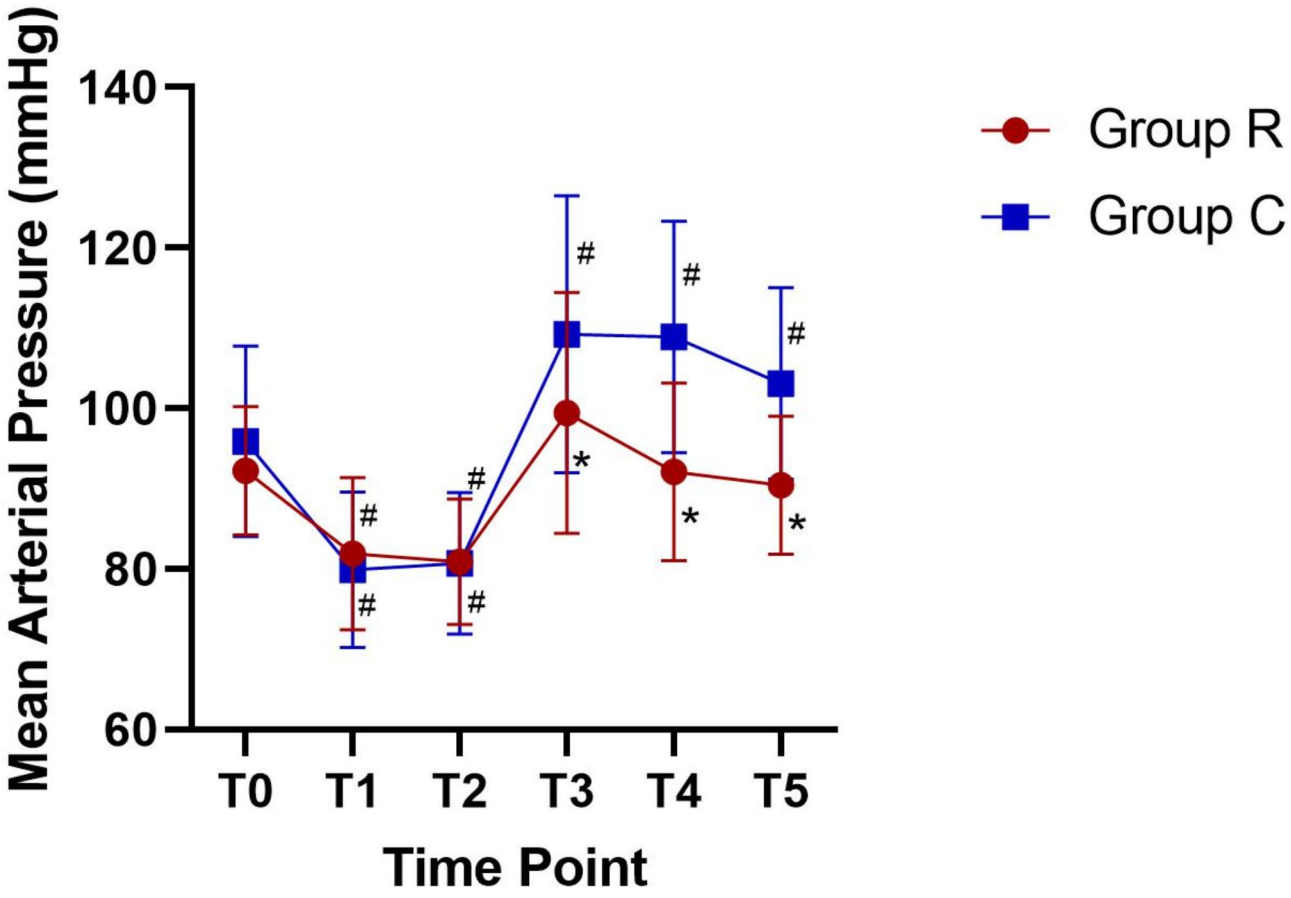

Fig. 3 MAP changes during operation and emergence
T0: admission (basal); T1: at the end of the surgery; T2: after investigational drug infusion ; T3: tracheal extubation; T4: 2 min after tracheal extubation; T5: 5 min after tracheal extubation. Data were presented as mean ± SD. $^{*}P < 0.05$ compared with Group C. $^{\#}P < 0.05$ compared with T0 in each group.MAP, mean arterial pressure

Table 4 Adverse events

	Group R ($n=43$)	Group C ($n=43$)	*P* value
Hypotension, n (%)	0 (0%)	0 (0%)	NT
Hypertension, n (%)	2 (4.7%)	9 (20.9%)	0.024
Bradycardia, n (%)	2 (4.7%)	4 (9.3%)	0.672
Tachycardia, n (%)	9 (20.9%)	12 (27.9%)	0.136
PONV, n (%)	4 (9.3%)	2 (4.7%)	0.672
Laryngospasm, n (%)	0 (0%)	2 (4.7%)	0.494
Grade of cough, n (%)	1 (0 to 2)	2 (1 to 2)	0.008
POD, n (%)	0 (0%)	0 (0%)	NT
Hypoxemia, n (%)	0 (0%)	0 (0%)	NT

Data presented as number (%) were analysed using chi-square test or Fisher exact test.Data presented as median (IQR) were analysed using the Mann-Whitney test.PONV, postoperative nausea and vomiting; POD, postoperative delirium

being a prospective, double-blind randomized controlled trial, the participants were selected from a specific group and standardized anesthesia methods were used, which improved the validity and credibility of the results.

Conclusion

After nasal surgery, the incidence of EA and severe EA in adults can be effectively reduced by intravenous injection of 0.1 mg/kg remimazolam. In addition, such intervention measures will not lead to extension of the extubation time and the length of the PACU stay, nor increase the risk of postoperative adverse events. For nasal surgery, this is a safe and effective intervention strategy.

Abbreviations

EA	Emergence agitation
MAP	Mean arterial pressure
HR	Heart rate
ASA	American Society of Anesthesiologists
NYHA	New York Heart Association
BIS	Bispectral index
PACU	Post-anesthesia care unit
NRS	Numeric rating scale
SAS	Riker sedation agitation scale
PONV	Postoperative nausea and vomiting
POD	Postoperative delirium
SD	Standard deviation
IQR	Interquartile Range
ENT	Ear, nose, and throat

Acknowledgements
We thank the patients who participated in this study.

Author contributions
Dr Duan had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Drs Lu and Dr Xu are co–first authors and contributed equally to the article.concept and design: Duan, Lu, Xu.Acquisition, analysis, or interpretation of data: Duan, Lu, Xu, Dai, Wu, Ai, Lan, Dong.Drafting of the manuscript: Duan, Lu, Xu.Critical revision of the manuscript for important intellectual content: Lu, Duan, Xu.Statistical analysis: Lan, Ai, Dai, Lu.Administrative, technical, or material support: Wu, Xu.Supervision: Duan, Xu.

Funding
None.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This trial was performed in accordance with the Declaration of Helsinki and the Chinese Clinical Trial Specifications. The study was approved by the Medical Ethics Committee of Lishui People's Hospital (Wenzhou Medical University Lishui Hospital) (approval No. 2023 – 137), and was registered in the Chinese Clinical Trial Registry (www.chictr.org.cn; registration number: ChiCTR2300075300). Written informed consent was obtained from all participants. The study protocol followed the CONSORT guidelines. The study protocol was performed in the relevant guidelines.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Center for Rehabilitation Medicine, Department of Anesthesiology, Affiliated People's Hospital, Zhejiang Provincial People's Hospital, Hangzhou Medical College, Hangzhou, People's Republic of China
[2]Department of Anesthesiology, Lishui People's Hospital, The First Affiliated Hospital of Lishui University, Wenzhou Medical University Lishui Hospital, No. 1188, Liyang Street, Lishui 323000, Zhejiang, People's Republic of China

Received: 8 November 2024 / Accepted: 23 December 2024
Published online: 07 January 2025

References

1. Lepousé C, Lautner CA, Liu L, et al. Emergence delirium in adults in the post-anaesthesia care unit. Br J Anaesth. 2006;96(6):747–53. https://doi.org/10.1093/bja/ael094.
2. Munk L, Andersen G, Møller AM. Post-anaesthetic emergence delirium in adults: incidence, predictors and consequences. Acta Anaesthesiol Scand. 2016;60(8):1059–66. https://doi.org/10.1111/aas.12717.
3. Liang C, Ding M, Du F, et al. Sevoflurane/propofol coadministration provides better recovery than sevoflurane in combined general/epidural anesthesia: a randomized clinical trial. J Anesth. 2014;28(5):721–6. https://doi.org/10.1007/s00540-014-1803-0.
4. Yu D, Chai W, Sun X, et al. Emergence agitation in adults: risk factors in 2,000 patients. Can J Anaesth. 2010;57(9):843–8. https://doi.org/10.1007/s12630-010-9338-9.
5. Mo JH, Han DH, Shin HW, et al. No packing versus packing after endoscopic sinus surgery: pursuit of patients' comfort after surgery. Am J Rhinol. 2008;22(5):525–8. https://doi.org/10.2500/ajr.2008.22.3218.
6. Lee A, Shirley M, Remimazolam. A review in Procedural Sedation. Drugs. 2021;81(10):1193–201. https://doi.org/10.1007/s40265-021-01544-8.
7. Yang X, Lin C, Chen S, et al. Remimazolam for the prevention of emergence delirium in children following tonsillectomy and adenoidectomy under sevoflurane anesthesia: a randomized controlled study. Drug Des Devel Ther. 2022;16:3413–20. https://doi.org/10.2147/DDDT.S381611.
8. Aldrete JA. The post-anesthesia recovery score revisited. J Clin Anesth. 1995;7(1):89–91. https://doi.org/10.1016/0952-8180(94)00001-k.
9. Lee S, Sohn JY, Hwang IE, et al. Effect of a repeated verbal reminder of orientation on emergence agitation after general anaesthesia for minimally invasive abdominal surgery: a randomised controlled trial. Br J Anaesth. 2023;130(4):439–45. https://doi.org/10.1016/j.bja.2022.12.009.
10. Amin SM, Hasanin A, ElSayed OS, et al. Comparison of the hemodynamic effects of opioid-based versus lidocaine-based induction of anesthesia with propofol in older adults: a randomized controlled trial. Anaesth Crit Care Pain Med. 2023;42(4):101225. https://doi.org/10.1016/j.accpm.2023.101225.
11. Flanagan NM, Spencer G. Informal caregivers and detection of delirium in postacute care: a correlational study of the confusion assessment method (CAM), confusion assessment method-family assessment method (CAM-FAM) and DSM-IV criteria. Int J Older People Nurs. 2016;11(3):176–83. https://doi.org/10.1111/opn.12106.
12. Barreto ACTP, Rangel da Rocha Paschoal AC, Barbosa Farias C, et al. Fatores De Risco associados a delírio no despertar Da anestesia em crianças submetidas à Cirurgia ambulatorial [Risk factors associated with anesthesia emergence delirium in children undergoing outpatient surgery]. Braz J Anesthesiol. 2018;68(2):162–7. https://doi.org/10.1016/j.bjan.2017.11.002.
13. Kanaya A. Emergence agitation in children: risk factors, prevention, and treatment. J Anesth. 2016;30(2):261–7. https://doi.org/10.1007/s00540-015-2098-5.
14. Kim HC, Kim E, Jeon YT, et al. Postanaesthetic emergence agitation in adult patients after general anaesthesia for urological surgery. J Int Med Res. 2015;43(2):226–35. https://doi.org/10.1177/0300060514562489.
15. Kim HJ, Kim DK, Kim HY, et al. Risk factors of emergence agitation in adults undergoing general anesthesia for nasal surgery. Clin Exp Otorhinolaryngol. 2015;8(1):46–51. https://doi.org/10.3342/ceo.2015.8.1.46. Epub 2015 Feb 3. PMID: 25729495; PMCID: PMC4338091.
16. Kim SY, Kim JM, Lee JH, et al. 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.
17. Dahmani S, Stany I, Brasher C, et al. Pharmacological prevention of sevoflurane- and desflurane-related emergence agitation in children: a meta-analysis of published studies. Br J Anaesth. 2010;104(2):216–23. https://doi.org/10.1093/bja/aep376.
18. Cho EJ, Yoon SZ, Cho JE, et al. Comparison of the effects of 0.03 and 0.05 mg/kg midazolam with placebo on prevention of emergence agitation in children having strabismus surgery. Anesthesiology. 2014;120(6):1354–61. https://doi.org/10.1097/ALN.0000000000000181.
19. Jo JY, Jung KW, Kim HJ, et al. Effect of total intravenous anesthesia vs volatile induction with maintenance anesthesia on emergence agitation after nasal surgery: a randomized clinical trial. JAMA Otolaryngol Head Neck Surg. 2019;145(2):117–23. https://doi.org/10.1001/jamaoto.2018.3097.
20. Duan J, Ju X, Wang X, et al. Effects of remimazolam and propofol on emergence agitation in elderly patients undergoing hip replacement: a clinical, randomized, controlled study. Drug Des Devel Ther. 2023;17:2669–78. https://doi.org/10.2147/DDDT.S419146.
21. Deng Y, Qin Z, Wu Q, et al. Efficacy and safety of remimazolam besylate versus dexmedetomidine for sedation in non-intubated older patients with agitated delirium after orthopedic surgery: a randomized controlled trial. Drug Des Devel Ther. 2022;16:2439–51. https://doi.org/10.2147/DDDT.S373772.
22. Yang JJ, Lei L, Qiu D, et al. Effect of remimazolam on postoperative delirium in older adult patients undergoing orthopedic surgery: a prospective randomized controlled clinical trial. Drug Des Devel Ther. 2023;17:143–53. https://doi.org/10.2147/DDDT.S392569.
23. Lee HJ, Lee HB, Kim YJ, et al. Comparison of the recovery profile of remimazolam with flumazenil and propofol anesthesia for open thyroidectomy. BMC Anesthesiol. 2023;23(1):147. https://doi.org/10.1186/s12871-023-02104-1.
24. Ko CC, Hung KC, Illias AM, et al. The use of remimazolam versus propofol for induction and maintenance of general anesthesia: a systematic review and meta-analysis. Front Pharmacol. 2023;14:1101728. https://doi.org/10.3389/fphar.2023.1101728.

25. Liao YQ, Min J, Wu ZX, et al. Comparison of the effects of remimazolam and dexmedetomidine on early postoperative cognitive function in elderly patients with gastric cancer. Front Aging Neurosci. 2023;15:1123089. https://doi.org/10.3389/fnagi.2023.1123089.

Publisher's note