Perioperative Medicine

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Effects of remimazolam and propofol on sleep rhythm and delirium after spinal surgery in elderly patients

Li Yaqiu[1†], Zhou Heng[2†], Wu Ruimin[1*] and Wang Xuri[1]

Abstract

Objective This study aims to investigate the effects of remimazolam on postoperative melatonin secretion, sleep rhythm, and postoperative delirium (POD) in elderly patients undergoing spinal surgery.

Methods We selected 120 elderly patients scheduled for elective spinal surgery (lumbar interbody fusion via a posterior approach) under general anaesthesia from November 2023 to January 2024. They were divided into 2 groups according to medication, the remimazolam group (R group) and the propofol group (P group), with 60 patients in each group. The R group received an induction dose of remimazolam 0.2 ~ 0.3 mg/kg, followed by a continuous infusion of remimazolam at 0.1–0.2 mg/kg/h for maintenance. The P group received an induction dose of propofol 1.5 ~ 2.0 mg/kg, followed by a continuous infusion of propofol at 4–6 mg/kg/h for maintenance. Melatonin and cortisol concentrations were measured at 04:00 on the day of surgery and postoperative days 1, 2, and 3. The Pittsburgh Sleep Quality Index (PSQI) and resting visual analog scale (VAS) pain scores were recorded on the day before surgery, and on postoperative days 1 and 2, as well as prior to discharge. Additionally, we documented extubation time, PACU stay duration, total and effective button presses on the analgesia pump, instances of supplemental analgesia, and occurrence of complications.

Results Compared to the P group, the R group exhibited significantly shorter extubation time and PACU stay duration ($P < 0.05$). On postoperative days 1 and 2 at 04:00, melatonin concentrations were significantly higher, cortisol concentrations were significantly lower, and PSQI scores were significantly reduced in the R group ($P < 0.05$). The incidence of POD and postoperative sleep disturbance (POSD) was also significantly lower in the R group ($P < 0.05$). Furthermore, on postoperative day 1, the PSQI and resting VAS pain scores in the R group were significantly lower compared to the P group ($P < 0.05$). There were no statistically significant differences between the two groups in terms of surgery duration, anaesthesia duration, total and effective analgesia pump button presses, supplemental analgesia rates, intraoperative hypotension, or incidences of postoperative nausea, vomiting, dizziness, and respiratory depression ($P > 0.05$).

Conclusion The use of remimazolam in elderly patients undergoing spinal surgery has a minimal impact on postoperative melatonin and cortisol secretion rhythms and sleep patterns, and may reduce the incidence of POD and alleviate postoperative sleep disturbances.

Keywords Remimazolam, Spinal surgery, Melatonin, Cortisol, Sleep rhythm, Postoperative delirium

† Li Yaqiu and Zhou Heng contributed equally to this work, as co-first author.

*Correspondence:
Wu Ruimin
1477794587@qq.com
Full list of author information is available at the end of the article

Introduction

Disruption of sleep rhythm presents clinically as sleep deprivation, circadian rhythm disorder, and structural abnormalities (Jamieson et al. 1995). Studies indicate that 15 to 72% of patients may experience sleep rhythm disturbances postoperatively, which can lead to postoperative delirium (POD) and cognitive impairments, and are considered a potential mechanism for POD (Chen et al. 2024). Furthermore, sleep rhythm disturbances may exacerbate acute postoperative pain and delay recovery (Qiu et al. 2022). Elderly patients undergoing spinal surgery are a high-risk group for experiencing sleep rhythm disturbances. The secretion of melatonin and cortisol exhibits a pronounced circadian rhythm, with plasma melatonin serving as a reliable biomarker of endogenous circadian rhythm regulated periodically (Chae et al. 2024; Song et al. 2021). Melatonin induces a hypnotic effect by accelerating sleep onset, improving sleep efficiency, and maintaining normal sleep rhythms. The interference of anaesthetic agents with sleep rhythms is also significant, for example, propofol affects rapid eye movement (REM) sleep, prolongs sleep latency, and decreases postoperative sleep quality (Qiu et al. 2023). The use of remimazolam for sedation during surgery has been shown to improve the Richards-Campbell Sleep Questionnaire (RCSQ) scores after joint replacement surgery (Yang et al. 2022). However, there remains insufficient specific evidence regarding its impact on sleep rhythm (Deng et al. 2023). This study aims to observe postoperative melatonin and cortisol secretion and sleep quality, comparing the effects of remimazolam and propofol anaesthesia on postoperative outcomes in elderly patients, in order to provide insights for reducing the incidence of POD and enhancing perioperative recovery quality.

Materials and methods

General information

The trial was completed in the Department of Anesthesiology, Xinjiang 474 Hospital, and The General Hospital of the Xinjiang Military Region from November 2023 to January 2024. The screening criteria are as follows:

> Inclusion criteria: ① Age between 65 and 85 years; ② Elderly patients undergoing spinal surgery (lumbar interbody fusion, posterior approach) under general anaesthesia; ③ Complete data and follow-up results; ④ ASA II or III classification.
> Exclusion criteria: ① Emergency surgery; ② Preoperative delirium (simple mental status examination score < 27 points or consciousness assessment score ≥ 19 points conducted 1 day before surgery); ③ Parkinson's disease, dementia, multiple injuries, hypoalbuminemia, communication disorders; ④ Preoperative anaemia, haemoglobin levels: < 12 g/dl for females, < 13 g/dl for males; ⑤ Body mass index > 25 kg/m^2; ⑥ Use of melatonin or other related sleep aids.

Patients were randomly allocated into two groups using a random number table: the Remimazolam group (R group) and the Propofol group (P group). The R group received an induction dose of remimazolam at 0.2 ~ 0.3 mg/kg, followed by continuous infusion of remimazolam at a rate of 0.1 to 0.2 mg/kg/h for anaesthesia maintenance. Conversely, the P group was induced with propofol at a dose of 1.5 ~ 2.0 mg/kg, with subsequent continuous infusion of propofol at a rate of 4 to 6 mg/kg/h for maintaining anaesthesia. This research was approved by the Ethics Committee of the Department of Anesthesiology at Xinjiang 474 Hospital. NO. M2025-03. All participants have signed informed consent forms.

Anaesthetic programme

Preoperative fasting was for 8 h and fluid restriction for 2 h. Upon arrival in the operating room, a peripheral venous access was established, and compound electrolyte solution was infused at a rate of 6 to 8 ml/kg/h. Electrocardiogram (ECG), heart rate (HR), blood pressure (BP), pulse oximetry (SpO2), bispectral index (BIS), and body temperature were continuously monitored. For anaesthesia induction, the R group received intravenous remimazolam 0.2 ~ 0.3 mg/kg, sufentanil 0.4 μg/kg, and cisatracurium 0.15 mg/kg, while the P group was given propofol 1.5 ~ 2.0 mg/kg, sufentanil 0.4 μg/kg, and cisatracurium 0.15 mg/kg. Maintenance of anaesthesia involved continuous infusion of remimazolam 0.1 to 0.2 mg/kg/h and remifentanil 0.15 to 0.3 μg/kg/min, with cisatracurium 0.1 mg/kg/h in the R group, and propofol 4 to 6 mg/kg/h, remifentanil 0.15 to 0.3 μg/kg/min, and cisatracurium 0.1 mg/kg/h in the P group. The BIS was maintained between 40 and 60, BP fluctuations were kept within 20% of baseline, end-tidal carbon dioxide (PETCO2) was targeted at 35 to 40 mmHg, and body temperature was maintained at 36 to 37 °C. If HR exceeded 100 beats per minute, esmolol 20 mg was administered; for HR below 45 beats per minute, atropine 0.5 mg was given. For increases in BP above 20% of the baseline, urapidil 20 mg was injected, and for decreases below 20%, dopamine 40 μg was administered.

Thirty minutes prior to the conclusion of surgery, patients were administered 50 mg of flurbiprofen and 2 mg/kg of tramadol. Drug infusion was ceased upon completion of surgery. In Group R, flumazenil at a dose of 0.5 mg was immediately administered intravenously for antagonism, with extubation and transfer to the post-anaesthesia spontaneously and had stable vital signs. All patients were connected to a patient-controlled analgesia (PCA) pump postoperatively, which contained a mixture of 200 mg tramadol, 100 μg sufentanil, and 15 mg tropisetron diluted in 100 ml of saline. The PCA settings included an initial dose of 2 ml, a continuous infusion of 2 ml per hour, and patient-activated boluses of 2 ml with a lockout interval of 15 min. If a patient's Visual Analog Scale (VAS) pain score exceeded 3 upon returning to the ward, and the PCA pump proved insufficient, rescue analgesia was provided via intravenous tramadol 50 mg. For cases of nausea and vomiting, tropisetron 5 mg was administered intravenously.

Outcomes

Primary outcomes

Melatonin and hydrocortisone concentrations were recorded at 04:00 am on the day of surgery, 1, 2, and 3 d postoperatively. Pittsburgh Sleep Quality Index (PSQI) and resting VAS pain scores were recorded 1 day before surgery and 1 and 2 days after surgery, and before discharge. The occurrence of POD (state of consciousness assessment score was recorded from 1 to 7 days postoperatively, and a state of consciousness assessment score of ≥ 22 was considered the occurrence of POD) and postoperative sleep disturbance (POSD) ((PSQI ≥ 7 was considered the presence of sleep disturbance postoperatively) were recorded. The occurrence of adverse events such as intraoperative hypotension (BP < 80% of basal value), postoperative nausea and vomiting, dizziness, and respiratory depression were recorded.

Secondary outcomes

All patients were collected for Preoperative haemoglobin, albumin, duration of surgery, duration of anaesthesia, haemorrhage, extubation time, PACU residence time, total number of analgesic pump compressions, number of effective compressions and remedial analgesia.

Evaluate PACU extubation and discharge:

① Airway status: To assess the patient's airway for patency and for the risk of airway obstruction.
② Respiratory function: Patients need to meet certain respiratory function indicators, such as a steady recovery of spontaneous breathing, respiratory rate, and tidal volume within the normal range.
③ Neuromuscular function: For patients who have used a muscle relaxation agent, the recovery of their neuromuscular function should be assessed.
④ State of consciousness: the patient needs to recover consciousness, can cooperate, and protective cough, swallowing reflex recovery.
⑤Haemodynamic stability: Before extubation, the patient is required to be hemodynamically stable, without obvious active bleeding, and with moderate chest drainage flow.

Statistical analysis

SPSS 26.0 was used for statistical analysis. Continuous variables were expressed as $\bar{x} \pm s$, and the normality of the data was assessed using the Kolmogorov–Smirnov test and the normality plot, and the independent samples *t*-test was used to compare the data that conformed to the normal distribution between the two groups, and the Mann–Whitney test was used for the data that did not conform to the normal distribution. The chi-square test or Fisher's exact test was used for count data. $P < 0.05$ was considered statistically significant.

Results

The comparison of general data

Twenty elderly patients undergoing spinal surgery (lumbar interbody fusion, posterior approach) were included, and they were divided into 2 groups based on medication, 60 in the remimazolam group (group R) and 60 in the propofol group (group P), all of whom were entered into the analysis of outcomes, with no data on dropout (Fig. 1). There were no statistically significant differences in baseline characteristics between the two groups ($P > 0.05$), as shown in Table 1.

Comparison of perioperative indicators in the two groups

The extubation time and PACU residence time of group R were smaller than that of group P, and the difference was significant ($P < 0.05$), as shown in Table 2 and Fig. 2A, D. The preoperative haemoglobin, preoperative albumin, operation time, anaesthesia time, bleeding, total number of presses with analgesic pumps, effective number of presses, and remedial analgesia were compared between patients in the two groups, and the differences were not significant ($P > 0.05$), as shown in Table 2.

Comparison of concurrent melatonin and Hydrocortisone concentrations in the two groups

Compared with group P, melatonin concentration was significantly higher in group R at 04:00 am on the 1 and 2 postoperative days, and cortisol concentration was significantly lower in group R on the 1 postoperative day ($P < 0.05$). The difference in melatonin and hydrocortisone concentrations between the two groups at 04:00 am on the day of surgery, 2 and 3 days postoperatively was not statistically significant. See Table 3 and Fig. 2B, C.

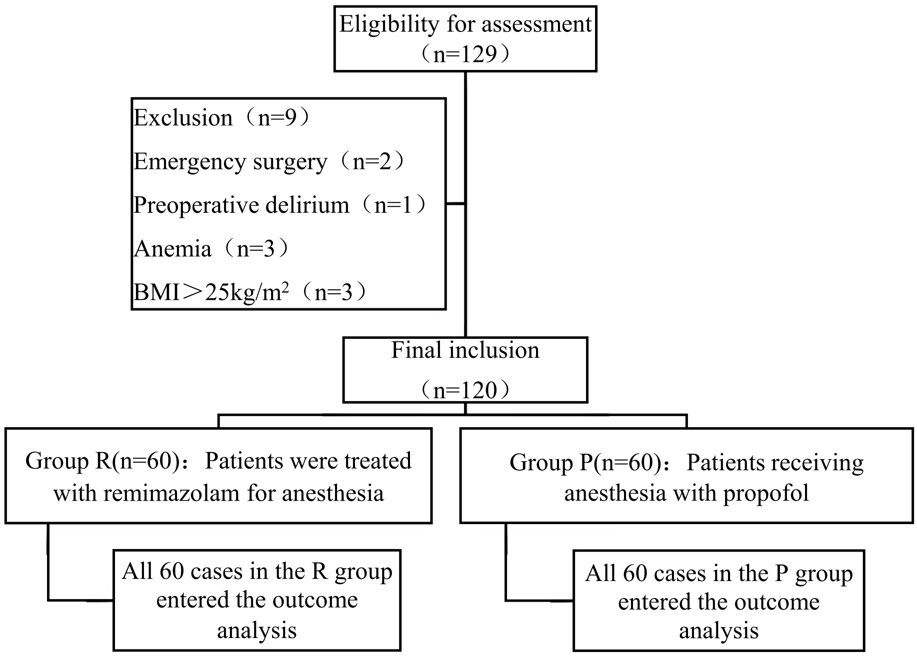

Fig. 1 Flow chart of test grouping

Table 1 Comparison of the preoperative general data between the two groups

Index	Group R (*n* = 60)	Group P (*n* = 60)	*P*
Age (year)	73.96 ± 8.02	72.31 ± 7.13	0.237
Sex (*n*, male / female)	27/33	21/39	0.264
BMI (kg/m^2)	22.63 ± 2.94	21.88 ± 3.01	0.169
Past medical history (*n*/%)			
Hypertension	36/60.0	30/50.0	0.271
Diabetes mellitus	17/28.3	20/33.3	0.553
Coronary disease	10/16.7	15/25.0	0.261
Endocrine system disease	16/26.7	25/41.7	0.083
Metabolic disease	15/25.0	20/33.3	0.315
Smoking history	19/31.7	14/23.3	0.307
Alcohol consumption history	16/26.7	14/23.3	0.673
ASA (*n*/%)			0.323
II	39/65.0	44/73.3	
III	21/35.0	16/26.7	

Values are given as the count or as the mean standard deviation (x ± SD). *ASA* American Society of Anesthesiologists, *BMI* body mass index

Comparison of VAS pain scores without point PSQI and at rest in both groups

PSQI and VAS pain scores at rest were significantly lower in the R group at 1 day postoperatively compared with the P group ($P < 0.05$). The differences in PSQI scores and VAS pain scores at rest at 1 day preoperatively, 2 days postoperatively, and before discharge were not statistically significant between the two groups. See Table 4 and Fig. 2E, F.

Comparison of POD, POSD, and occurrence of adverse effects in the two groups

Compared with group P, the incidence of POD and POSD was significantly lower in group R ($P < 0.05$). The difference in the incidence of intraoperative hypotension, postoperative nausea and vomiting, dizziness and respiratory depression between the two groups was not statistically significant. See Table 5.

Discussion

Postoperative sleep disorder can be defined as the change of postoperative sleep pattern, the change of postoperative sleep time, including the shortening of total sleep time, increasing light sleep time, decreasing or even disappeared deep sleep time, and the increased frequency of postoperative sleep interruption, which is not consistent with patients' preoperative sleep, which affects the of all aspects of patients. Such sleep changes may affect the recovery of body organ dysfunction, especially in brain function (Yu et al. 2021). The duration of postoperative sleep dysfunction is not limited to the hospital period. Studies have reported that sleep during critical recovery, 73% of patients had poor sleep problems during ICU, and more than 57% complained of sleep problems 6 months after discharge. The underlying mechanism of postoperative sleep dysfunction is currently considered

Table 2 Comparison of perioperative blood loss between the two groups

Index	Group R ($n=60$)	Group P ($n=60$)	*P*
Preoperative haemoglobin (g/L)	124..46 ± 21.74	121.35 ± 18.31	0.397
Preoperative albumin (g/L)	40.30 ± 4.66	38.81 ± 5.48	0.112
Operation time (min)	152.16 ± 38.88	149.01 ± 42.58	0.671
Anaesthesia time (min)	166.65 ± 31.17	163.91 ± 37.05	0.661
Bleeding (ml)	197.33 ± 85.52	179.16 ± 77.77	0.226
Extubation time (min)	2.73 ± 0.94	4.20 ± 1.86	0.000△
PACU residence time (min)	15.21 ± 0.93	31.50 ± 9.25	0.000△
Total number of presses with analgesic pumps (second)	5.43 ± 2.93	4.71 ± 2.47	0.141
Effective press times (second)	2.52 ± 0.60	2.37 ± 0.58	0.173
Remedial analgesia (*n*/%)	7/11.7	5/8.3	0.543

Values are given as the count or as the mean standard deviation (x ± SD). △$P < 0.05$

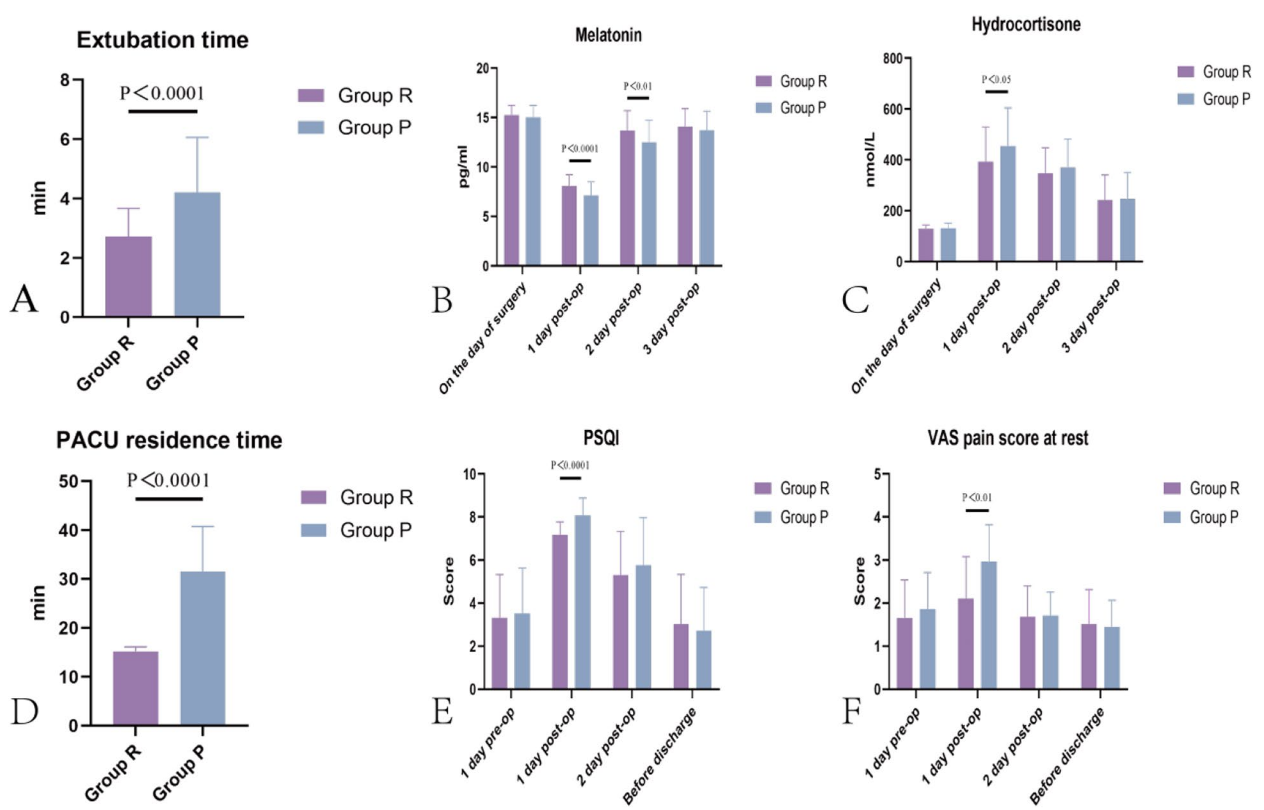

Fig. 2 Comparison of relevant indicators in the R and P group surgery

to be related to postoperative neurological changes and unstable levels of perioperative episodic melatonin and cortisol secretion. With increasing age, melatonin secretion levels decrease by 10 to 15% every 10 years, and may be only about 10% of the peak by age 70 years. In older patients, the circadian rhythm of melatonin may be completely lost, making them more prone to sleep disturbance (Siegel 2005; Anafi et al. 2019).

Remimazolam is a kind of ester-based benzodiazepine; its mechanism is through the specific action on GABA A receptor, enhancing GABA A receptor activity, selective to extracellular chloride ion into the cell, resulting in cell membrane resting potential increased hyperpolarization, excitability decline, thus inhibit neuronal electrical activity, sedation (Wang Chunyan and Yonghao. 2019). Therefore, the amount of anaesthetic drug used and the depth

Table 3 Comparison of concurrent melatonin and hydrocortisone concentrations in the two groups

Index	Follow-up time	Group R (*n* = 60)	Group P (*n* = 60)	*P*
Melatonin (pg/ml)	On the day of surgery	15.24 ± 0.98	15.03 ± 1.21	0.309
	1 day post-op	8.08 ± 1.16	7.13 ± 1.37	0.000△
	2 days post-op	13.68 ± 2.01	12.47 ± 2.25	0.002△
	3 days post-op	14.07 ± 1.83	13.71 ± 1.94	0.305
Hydrocortisone (nmol/L)	On the day of surgery	129.03 ± 14.60	131.70 ± 20.10	0.408
	1 day post-op	392.93 ± 136.09	454.28 ± 150.87	0.021△
	2 days post-op	346.83 ± 101.22	370.26 ± 112.03	0.232
	3 days post-op	241.91 ± 98.81	245.98 ± 104.46	0.827

Values are given as the count or as the mean standard deviation (x ± SD). △*P* < 0.05

Table 4 Comparison of VAS pain scores without point PSQI and at rest in both groups

Index	Follow-up time	Group R (*n* = 60)	Group P (*n* = 60)	*P*
PSQI	1 day pre-op	3.31 ± 2.02	3.51 ± 2.12	0.599
	1 day post-op	7.17 ± 0.59	8.08 ± 0.81	0.000△
	2 days post-op	5.31 ± 2.02	5.76 ± 2.21	0.248
	Before discharge	3.01 ± 2.33	2.72 ± 2.01	0.452
VAS pain scores at rest	1 day pre-op	1.65 ± 0.89	1.86 ± 0.85	0.178
	1 day post-op	2.10 ± 0.98	2.96 ± 0.86	0.009△
	2 days post-op	1.68 ± 0.72	1.71 ± 0.55	0.626
	Before discharge	1.51 ± 0.81	1.45 ± 0.62	0.615

Values are given as the count or as the mean standard deviation (x ± SD). △*P* < 0.05

of sedation it induces are regarded as important factors affecting postoperative sleep rhythms (Dessai et al. 2024). The aim of this study was to compare the effects of remimazolam and propofol on postoperative melatonin and cortisol secretion during anaesthesia maintenance, and thus to investigate their potential effects on postoperative sleep rhythm and postoperative delirium (POD) (Lee et al. 2024). The PSQI scale is a subjective sleep quality assessment tool compiled by Buysse et al. of Pittsburgh Medical Center in 1989. It was translated into Chinese in 1996 and verified its reliability and validity in the Chinese population (Buysse et al. 1989). The results of the study showed that elderly patients receiving both remimazolam and propofol anaesthesia showed reduced peak melatonin concentrations and abnormally elevated cortisol concentrations (Tsukimoto et al. 2024). Melatonin is a neuroendocrine regulator of the sleep-wake cycle that regulates circadian rhythms. Melatonin can improve sleep disorders and restore physiological sleep. Disordered melatonin secretion can have an effect on circadian rhythms. Dispersyn et al. showed that intraperitoneal injection of propofol 10 mg/ml in rats could lead to disturbance of melatonin secretion rhythm, manifested by a significant decrease in melatonin secretion 3 h after anaesthesia and a significant increase in melatonin secretion 20 h after anaesthesia. After 4% isoflurane exposure, the blood melatonin concentration of rats was significantly reduced and the circadian rhythm was significantly destroyed (Dispersyn et al. 2010; Wren-Dail et al. 2017).

In this study, strict pain management was implemented in both groups to exclude disturbances to sleep rhythms. Patients treated with remimazolam had more subdued circadian rhythm hormone fluctuations, lower Pittsburgh Sleep Quality Index (PSQI) scores, and a lower incidence of postoperative somnambulism disorder (POSD) on the first postoperative night compared to elderly patients treated with propofol. This suggests that remimazolam has less of an effect on postoperative sleep in older

Table 5 Comparison of POD, POSD, and occurrence of adverse effects in the two groups

Index	Group R (*n* = 60)	Group P (*n* = 60)	*P*
POD	7/11.7	16/26.7	0.037△
POSD	9/15.0	19/31.7	0.031△
Intraoperative hypotension	4/6.7	11/18.3	0.053
Postoperative nausea and Vomiting	0/0.0	1/1.7	0.315
Dizziness	2/3.3	3/5.0	0.648
Respiratory depression	1/1.7	2/3.3	1.000

patients, possibly related to its metabolic properties. Remimazolam is not dependent on hepatic or renal metabolism, which is particularly important in elderly patients as these organ functions decline with age (Wren-Dail et al. 2017). In contrast, propofol lacks a specific antagonist, resulting in longer retention in the body and persistent inhibition of the supraoptic nucleus (Zhang et al. 2024). In addition, propofol inhibits gamma-aminobutyric acid receptors, which may affect melatonin synthesis in the pineal gland. Remimazolam, on the other hand, is rapidly metabolized by hepatic carboxylesterases to inactive carboxylic acid metabolites and is excreted mainly in the urine within 24 h, with a shorter retention time in the body (White et al. 2024). These rapid metabolism and excretion help to reduce postoperative physiological and cognitive dysfunction in elderly patients and reduce the risk of postoperative delirium, thereby improving treatment outcomes and quality of life (Guo et al. 2023).

The results of the data analysis in this study showed a significant positive correlation between abnormal levels of postoperative hormone secretion, elevated sleep quality scores, and the occurrence of postoperative delirium (POD) in the two groups of patients, which is consistent with the results of the previous study (Zheng et al. 2023). In particular, the circadian rhythms of melatonin and cortisol changed significantly in the postoperative period, with nocturnal melatonin concentrations dropping to a minimum on the first postoperative night, a phenomenon that apparently affected the patients' sleep patterns and led to the abnormalities (He et al. 2022). Further investigation showed that the urinary concentration of 6-hydroxysulfate melatonin (6-SMT) in patients with postoperative POD was significantly decreased. 6-SMT is the main metabolite of melatonin, and the concentration of 6-SMT in urine is closely related to the concentration of melatonin in blood, so the amount of 6-SMT in urine can be used as an indicator of melatonin in blood (Oh and Park 2019). After the operation, the circadian rhythm of melatonin secretion in the patient is changed, and the melatonin level in the patient's plasma is reduced, which affects the sleep quality of the patient, may cause sleep disorder, and change the original sleep pattern. Melatonin can speed up sleep and improve sleep quality and has an important role in regulating the sleep cycle (Leung et al. 2020). On the other hand, anaesthesia maintenance with remimazolam not only reduces the incidence of hypotension in perioperative patients, but also provides a more stable haemodynamic state, which is extremely critical in reducing the incidence of prolonged intraoperative hypotension (Thakur et al. 2024). Studies have shown that intraoperative hypotension lasting longer than 5 min significantly increases the risk of POD in elderly patients, due to the fact that prolonged hypotension leads to ischaemic damage to neuronal cells as well as ischaemia–reperfusion injury, which increases the risk of postoperative cognitive impairment (Porhomayon et al. 2016). The findings of this study therefore highlight the importance of appropriate pre-operative and intraoperative adjustments to medication regimens and enhanced postoperative monitoring of hormone levels to optimize therapeutic outcomes and reduce the risk of complications such as POD. These integrated therapeutic measures are especially critical for elderly patients to significantly improve their postoperative quality of life and overall prognosis.

In this study, elderly patients using remimazolam demonstrated a significantly lower incidence of adverse events compared to those using propofol. More specifically, the use of remimazolam facilitated the rapid awakening of the patients after anaesthesia, allowing them to be extubated earlier and shortening their stay in the postoperative resuscitation unit (PACU). These observations are consistent with the findings of Li et al. (Li et al. 2021) and emphasize the benefits of remimazolam in postoperative management. Furthermore, although there was no significant difference between the two groups in the incidence of common anaesthesia-related complications such as nausea and vomiting, dizziness, and respiratory depression, the performance of remimazolam on other key recovery indicators suggests that it may be useful as a preferred sedative drug for elderly patients. Patients on remimazolam recovered to spontaneous respiration and consciousness more quickly, which had a direct positive impact on reducing the use of postoperative monitoring resources and improving bed turnover. Thus, remimazolam not only results in better postoperative awakening, but may also further reduce the incidence of POD by optimizing sleep quality, which is highly beneficial in improving the long-term prognosis of elderly spinal surgery patients (Yarımoğlu and Basaran 2024).

The article shows that the effects of remimazolam on sleep rhythms and delirium after spinal surgery in elderly patients were compared and summarized, and the results of this retrospective cohort study found that, in terms of clinical safety, remimazolam had a lesser effect on postoperative melatonin and cortisol secretion rhythms and sleep rhythms, with a faster recovery, and reduced the incidence of POD. These results provide some theoretical insights for clinicians regarding the choice of medication for elderly patients undergoing spinal surgery.

Limitations of this study are as follows: ① This trial is a retrospective study, so there may be the possibility of data loss or failure to record data in time, which may bias the results, but the research team to which the authors belonged strictly and carefully recorded the indicators of each group, so that the experimental data to maintain the maximum degree of completeness. ② The inclusion of the sample size is relatively small, the statistical efficacy of insufficient, reporting bias, the results of this study need to be The results of this study require further, multicentre, prospective studies to further elucidate the relationship between clinical outcomes. ③ Melatonin and cortisol levels were measured only once a day for 3 days postoperatively, and this method failed to account for the changes in the secretion rhythms of these hormones over a 24-h period. Future studies could explore the potential effect of exogenous melatonin supplementation at specific time points prior to surgery to observe its potential improvement in postoperative sleep rhythms.④ This research will explicitly acknowledge that the BIS is developed primarily based on the effects of propofol drugs such as propofol and therefore there may be bias in assessing the depth of anaesthesia for benzodiazepines (e.g., reimazolam). We will discuss other possible depth of anaesthesia monitoring methods such as observing patient response, monitoring vital sign changes, using other brain function monitoring techniques, and evaluate the applicability of these methods in our study. In the Discussion section, we will highlight the importance of future studies in developing equivalence assessment tools suitable for different anaesthetic agents to more accurately compare the effects of different anaesthetics.

Conclusion

In conclusion, the use of remimazolam in elderly patients undergoing spinal surgery has less effect on postoperative melatonin and cortisol secretion rhythms and sleep rhythms, results in faster recovery, reduces the incidence of POD, and is worthy of promotion in the clinic.

Authors' contributions

Study design, conception, and critical revision: Li Yaqiu and Zhou Heng. Analysis and interpretation of data: Wu Ruimin and Li Yaqiu. Literature search and drafting of manuscript: Wang Xuri, Li Yaqiu, Zhou Heng.Wu Ruimin and Li Yaqiu contributed to critical revision of the manuscript for important intellectual content and approved the fnal version of the manuscript. All authors read and approved the fnal version of the manuscript.

Funding

Not applicable.

Data availability

To explore the effects of Remazolam on postoperative melatonin secretion, sleep rhythm, and delusion (POD) in elderly patients undergoing spinal surgery, so the dataset analyzed in this study is not publicly available but is available to the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

We confirm that all experiments were performed in accordance with the Declaration of Helsinki. The study was approved by the Ethical Committee of the Xinjiang 474 Hospital NO. M2025-03.

Consent for publication

All patients provided written informed consent.

Competing interests

The authors declare no competing interests.

Author details

[1]Xinjiang 474 Hospital, Xinjiang Uygur Autonomous Region, Urumqi, Xinjiang 830000, PR China. [2]The General Hospital of the Xinjiang Military Region, Xinjiang Uygur Autonomous Region, Urumqi, Xinjiang 830002, PR China.

Received: 26 November 2024 Accepted: 3 February 2025
Published online: 11 February 2025

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