

Investigating the Effects of Remimazolam and Propofol on Awakening Quality and Cognitive Function in after Hysteroscopy: A Comparative Study

GUANGMIN FENG, YONG YIN¹ AND JIE ZHANG*

Department of Anesthesiology, Huashan Hospital, Fudan University of Shanghai, ¹Department of Anesthesiology, Civil Aviation Hospital of Shanghai, Shanghai 200336, China

Feng *et al.*: Remimazolam and Propofol on Awakening Quality and Cognitive Function

To explore the differences in awakening quality and cognitive function in patients who received remimazolam vs. propofol anesthesia during hysteroscopy. One hundred patients undergoing laparoscopic surgery at our hospital from March 2022 to August 2022 were randomly allocated to either an observation group or a control group. The control group received anesthesia induction with propofol and remifentanyl, and maintained during surgery, while the observation group received anesthesia induction with remifentanyl and maintained during surgery. Hemodynamic indicators, including heart rate, mean arterial pressure, and respiratory rate were compared between the groups at various time points. The steward recovery score was used to assess patients' recovery quality, and the mini-mental state examination was used to evaluate postoperative cognitive function recovery. In the remazolam group, the changes of mean arterial pressure and respiratory frequency were smaller, the Steward awakening score was higher during awakening, and the cognitive function score was higher after extubation. The performance of remimazolam is better than that of propofol, which indicates that remimazolam may be a better drug choice.

Key words: Remimazolam, propofol, hysteroscopy surgery, awakening quality, cognitive function

With the rapid development of endoscopic technology, hysteroscopy has become the most widely used one in gynecological surgery^[1]. It adopts minimally invasive surgery, which can greatly reduce the time of trauma and recovery, and increase the safety of surgery^[2,3]. However, because the patient needs to maintain a fixed posture during the operation to facilitate the lens entry, the duration of the operation is different, so a certain amount of analgesic drugs are needed to ensure the comfort of the patient during the microscopic examination and the accuracy of the microscopic examination results. Remazolam and propofol are commonly used analgesic drugs, which have good analgesic effect and safety, and are commonly used in hysteroscopy surgery^[4,5]. However, the effects of remazolam and propofol on postoperative recovery of patients are still unclear. Especially, there is a lack of comprehensive research on the influence of awakening quality and cognitive function. Therefore, it is necessary to compare and analyze the effects of remimazolam

and propofol on the quality of recovery and cognitive function of patients after hysteroscopy, so that clinicians can better choose appropriate drugs and improve the clinical treatment effect of patients. At present, there have been some studies on the effects of remimazolam and propofol on the quality of postoperative recovery and cognitive function of patients, but the results of these studies are inconsistent and controversial. This shows that the understanding of this problem is still limited at present, and more in-depth discussion is needed. Therefore, this study intends to compare the application of remimazolam and propofol in hysteroscopic surgery, and to explore its influence on the quality of postoperative recovery and cognitive function of patients, hoping to better select suitable drugs for clinicians and improve the clinical treatment effect of patients. This study randomly assigned 100 patients who underwent hysteroscopic surgery at our hospital from March to August 2022 to an observation group (n=50) or a control group (n=50). The control group had a

*Address for correspondence
E-mail: 15317830096@163.com

mean age of (46.14±6.58) y, with an age range of 20-61 y and consisted of 21 cases of American Society of Anesthesiologists (ASA) grade I and 29 cases of ASA grade II. The observation group had a mean age of 47.31±1.44 y, with an age range of 21-59 y and consisted of 23 cases of ASA grade I and 27 cases of ASA grade II. No significant differences in sex, age or ASA grade were observed between the two groups. This study was approved by the hospital's ethics committee. Inclusion criteria including the 18 y and 65 y old; female patients undergoing hysteroscopy surgery; general anesthesia was used in all patients; patients met the American association of ASA grade II and signed informed consent, and approved to participate in this study. Exclusion criteria including the suffering from obvious heart, liver, lung, kidney and other important organ diseases; allergic to the drugs involved in this study; suffering from mental illness, central nervous system diseases or taking drugs that affect cognitive function; women during pregnancy or lactation; patients who are unable to cooperate with postoperative follow-up and patients who participate in other intervention studies. Two groups of patients chose different medication treatments. In control group; propofol combined with remifentanyl for anesthesia induction and intraoperative maintenance, with 2 mg/kg and 1 mg/kg of two drugs administered respectively (μ) anesthesia induction with 8 mg/kg, 4 mg/(kg/h) and 0.2-0.3 μ g/(kg/min) intraoperative maintenance. In observation group; remimazolam (Hengrui, Batch number: 230224AQ) combined with remifentanyl for anesthesia induction and intraoperative maintenance, with induction doses of 0.4 mg/kg and 1 mg/kg, respectively μ g/kg, with a maintenance dose of 1 mg/(kg/h) and 0.2-0.3 μ g/(kg/min). If the anesthesia is too shallow, the patients in the two groups were given propofol (0.25 mg/kg) or remimazolam benzene sulfonic acid (0.2 mg/kg) intravenously on the basis of the original pump dosage; if the anesthesia is too deep, reduce the dosage of the corresponding drug by 10 % on the basis of the original pump dosage and maintain the Bispectral Index (BIS) value of the EEG at 40-60. Medication stopped immediately after surgery. The Heart Rate (HR), Mean Arterial Pressure (MAP) and Respiratory Rate (RR) of the two groups before anesthesia (T_0), during cervical dilatation (T_1), uterine dilatation (T_2), uterine

cavity observation (T_3), conscious (T_4) were recorded. The patient enters the anesthesia awakening room and is extubated after surgery. After 5 min and 6 h of extubation, the Steward awakening score is used to evaluate their awakening quality^[6], which includes three aspects; awakening degree (0-2 points), respiratory patency (0-2 points), and limb mobility (0-2 points). As the score increases, the patient's awakening degree increases and the awakening quality improves; cognitive function; two groups of cognitive function were evaluated using the simplified Mini-Mental State Examination (MMSE) before anesthesia and during awakening^[7]. MMSE includes memory ability, comprehension ability, computational ability and time orientation, with a total score of 30 points. A score <24 points indicates the possibility of cognitive impairment. MMSE scores were collected 24 h before surgery, 5 min after extubation and 24 h after surgery. The presentation of continuous data was accomplished *via* $x \pm s$ notation. Intergroup comparison was accomplished employing independent sample t-tests, while paired t-tests were implemented to determine any changes within each group. Results with a $p \leq 0.05$ were recognized as statistically significant. Statistician utilized Statistical Package for the Social Sciences (SPSS) 22.0 software. The results indicated that there was no significant difference in MAP and RR between the two groups of patients at T_0 and T_4 ($p > 0.05$). However, at T_1 , T_2 and T_3 , both MAP and RR showed statistically significant differences between the two groups ($p < 0.05$). No significant difference was found in HR between the two groups at any time point ($p > 0.05$) as shown in Table 1. Table 2 illustrates that the observation group outperformed the control group in terms of total score and sub scores of the Steward awakening score, with statistically significant differences, both 5 min after extubation and 6 h after surgery. As shown in Table 3, there was no significant difference between the two groups in terms of MMSE scores 24 h before and 24 h after surgery. But at the 5 min point after extubation, the observation group attained significantly higher MMSE scores than the control group ($p < 0.05$). Hysteroscopy surgery, as an invasive procedure, can easily cause stress reactions in the body and have an impact on the patient's postoperative physical recovery and cognitive function. Therefore, intraoperative

anesthesia should follow the principles of rapid onset, stable sedation and analgesic effects, and quick recovery^[8,9]. Remimazolam benzenesulfonic acid is a new ultra-short acting benzodiazepine drug, and also a derivative of midazolam. Its mechanism of action is similar to midazolam. It can quickly metabolize into a carboxylic acid metabolite with low affinity for Gamma-Aminobutyric Acid Type A (GABAA) receptor through tissue esterase, and has the characteristics of faster onset, faster recovery and higher safety^[5]. Propofol is a rapidly acting intravenous sedative that is also widely used for sedation and anesthesia in surgical patients^[4]. However, the performance of these two drugs may differ in terms of their impact on recovery and cognitive function after hysteroscopic surgery. This study found that the MAP and RR of patients in the remimazolam group had little change during the treatment process, and the Steward's recovery score was higher during the recovery process, as well as the cognitive function score after extubation, which indicated that the remimazolam might be a more effective drug choice in patients after hysteroscopic surgery. In this study, the MAP and RR of patients in the remimazolam group changed slightly during the treatment, indicating that the duration of the treatment was better and the physiological response to patients was more stable, which may be beneficial to the postoperative recovery of patients. In addition, previous studies have found that when the dose of propofol is increased, there is usually a risk of adverse reactions such as decreased blood pressure and respiratory depression^[10,11], consistent with the findings of this study. At the same time, in terms of Steward's awakening score and cognitive function score, the remimazolam group had higher

scores than the propofol group, indicating that remimazolam may be more effective in postoperative patient awakening quality and cognitive recovery than propofol. In addition, remimazolam also has the potential to reduce postoperative cognitive impairment. Surgery and anesthesia have a certain negative impact on cognitive function, especially for elderly patients^[12,13]. Remazolam has a certain sedative effect and may have potential protective effects in reducing the adverse effects of surgery and anesthesia on patient cognitive function. In this study, the cognitive function score of the remimazolam group was higher than that of the propofol group, further supporting this hypothesis. However, this study also has some limitations. Firstly, this study is a single center, small-scale study that did not cover all patients. The number of samples is small, and the results may be influenced by the sample size. Secondly, the study was conducted under certain clinical conditions, so it is necessary to further validate the performance of remimazolam in different clinical practices and patient populations. In addition, the mechanisms of sedative and anesthetic effects of drugs such as remimazolam and propofol also need to be further explored to better understand the potential impact in different patient populations and clinical practices. In summary, when administering medication sedation to patients after hysteroscopic surgery, we need to comprehensively evaluate the effects and side effects of different drugs based on the patient's specific situation. In this study, remimazolam performed better than the propofol group, indicating that remimazolam may be a better drug choice.

TABLE 1: GROUP COMPARISON OF MAP, HR AND RR AT DIFFERENT TIME POINTS

Project	Group	n	T ₀	T ₁	T ₂	T ₃	T ₄
MAP (mmHg)	Control	50	75.21±4.02	74.43±4.06	73.29±3.95	73.76±4.23	74.29±3.84
	Observation	50	74.98±3.88	65.41±4.87	65.12±4.05	64.72±4.63	73.27±3.93
	t		0.736	12.937	13.732	10.635	2.836
	p		0.635	0.005	0.011	0.001	0.972
HR (n/min)	Control	50	74.26±5.73	74.30±5.37	76.37±5.61	74.68±5.19	75.84±5.30
	Observation	50	74.78±5.38	75.23±5.16	75.86±5.89	75.37±5.66	74.91±5.48
	t		0.463	1.374	2.472	2.244	1.084
	p		0.374	0.559	0.736	0.08	0.273

RR (n/min)	Control	50	18.27±1.29	17.84±1.02	17.53±1.37	16.98±1.25	17.82±1.35
	Observation	50	18.10±1.22	13.92±1.29	13.74±1.45	14.02±1.38	17.41±1.27
	t		2.021	8.293	5.837	3.398	1.281
	p		0.283	0.001	0.000	0.018	0.494

TABLE 2: THE QUALITY OF RECOVERY 5 MIN AFTER EXTUBATION AND 6 H AFTER OPERATION WERE COMPARED BETWEEN GROUPS

Group	Time	Sobriety	Airway patency	Limb mobility	Total score
Control (n=50)	5 min after extubation	0.53±0.08	0.94±0.13	0.74±0.09	2.21±0.42
	6 h after surgery	1.16±0.17	1.36±0.40	1.39±0.38	3.91±1.09
Observation (n=50)	5 min after extubation	0.89±0.11*	1.26±0.15*	0.97±0.16*	3.12±0.65*
	6 h after surgery	1.67±0.24*	1.76±0.25*	1.80±0.22*	5.23±0.98*

TABLE 3: GROUP COMPARISON OF MMSE SCORES AT DIFFERENT TIME POINTS (SCORES, $\bar{x}\pm s$)

Group	24 h before surgery	5 min after extubation	24 h after surgery
Control	29.12±0.45	24.87±2.52	28.17±0.81
Observation	29.33±0.49	27.61±2.13	29.15±0.15
t	0.537	2.393	0.682
p	0.487	0.021	0.376

Author's contributions:

Guangmin Feng and Yong Yin have contributed equally to this work.

Conflict of interests:

The authors declared no conflict of interests.

REFERENCES

- Lasmar RB, Lasmar BP. Hysteroscopic management of intrauterine benign diseases. *Minim Invasive Ther Allied Technol* 2021;30(5):263-71.
- Bingol Tanriverdi T, Koceroglu I, Devrim S, Gura Celik M. Comparison of sedation with dexmedetomidine vs. propofol during hysteroscopic surgery: Single-centre randomized controlled trial. *J Clin Pharm Ther* 2019;44(2):312-7.
- Ji X, Sun X, Chen Y. The effect of percutaneous acupoint electrical stimulation assisted with intravenous general anesthesia on postoperative recovery and complications in patients undergoing gynecological hysteroscopic surgery. *Chin J Med* 2020;29(5):4.
- Chen X, Wang D, Shu S. Half effective ventricular target concentration of remifentanyl for inhibiting body movement during hysteroscopy when combined with propofol. *J Clin Anesthesiol* 2020;36(4):2-9.
- Yu W, Li Y, Zhu S. A randomized, single blind, parallel controlled study on the efficacy and safety of remimazolam benzenesulfonic acid and propofol for painless colonoscopy. *Guizhou Med* 2020;44(6):5-7.
- Zhao B, Li D, He L. The effect of sevoflurane combined with remifentanyl on anesthetic effect, hemodynamics and inflammatory factors in patients with acute cholecystitis undergoing laparoscopy. *Mod Biomed Prog* 2022;(3):22-4.
- Lin X, Du Z, Guo C. Anesthesia effect of sevoflurane combined with remifentanyl in laparoscopic hysterectomy. *Chin J Family Plan* 2021;4:5-8.
- Antonik LJ, Goldwater DR, Kilpatrick GJ, Tilbrook GS, Borkett KM. A placebo-and midazolam-controlled phase I single ascending-dose study evaluating the safety, pharmacokinetics, and pharmacodynamics of remimazolam (CNS 7056): Part I. Safety, efficacy and basic pharmacokinetics. *Anesthesia Anal* 2012;115(2):274-83.
- Xiao C. The effect of propofol combined with remifentanyl total intravenous anesthesia on cognitive function and pain after thoracotomy in the elderly. *J Mod Integ Tradit Chin Western Med* 2016(25):3631-3.
- Zhou Y. Adverse reactions of propofol and current research status in forensic pathology. *Chin J Med* 2020;113(6):28-34.
- Jiang C, Huang R, Wang Q. Study on the action and mechanism of propofol. *Guangdong Chem J* 2021;26:7-8.

12. Sun W. Comparative analysis of the effects of general anesthesia and spinal anesthesia on postoperative cognitive function in elderly orthopedic surgery patients. *Chin J Sci Technol Med* 2023;24:3-4.
13. Huang T, Huang C. The application effect of bupivacaine intraspinal anesthesia in elderly orthopaedic surgery patients and its impact on mental cognition, anesthesia recovery and complications. *Clin Med Res Pract* 2023;8(11):4-7.

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms

This article was originally published in a special issue, "New Research Outcomes in Drug and Health Sciences" Indian J Pharm Sci 2023;85(6) Spl Issue "194-198"