

Remimazolam's effect in the anesthesia of elderly hip replacement patients

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Objective: To explore the anesthetic and analgesic effects of remimazolam and propofol in elderly patients undergoing hip replacement and their effects on respiratory and circulatory systems, stress and cognitive function. **Methods** 60 elderly patients undergoing elective hip replacement in the hospital were selected as the research subjects, who were divided into the remimazolam group and the propofol group according to the admission sequence of patients. The remimazolam group was anesthetized with remimazolam, and the propofol group was anesthetized with propofol. The anesthesia-related indicators, perioperative pain degree Visual Analogue Scale (VAS), circulatory indicators heart rate, Mean Arterial Pressure (MAP) before anesthesia (T0), immediately before laryngeal mask insertion (T1), at 5 min after laryngeal mask insertion (T2), at 30 min after laryngeal mask insertion (T3) and at 5 min after laryngeal mask removal (T4), stress response indicators (plasma epinephrine, norepinephrine, cortisol) before anesthesia induction and at 24 h and 72 h after surgery, cognitive function Mini-Mental State Examination (MMSE) and adverse reactions were compared between the two groups.

Results: Among the 60 enrolled patients, only 1 case was excluded due to withdrawal, thus 30 cases in the remimazolam group and 29 cases in the propofol group were included. There were statistically significant differences in the heart rate, MAP, plasma epinephrine, norepinephrine, cortisol and VAS score in the two groups from the aspects of interaction effect and time-point effect ($P < 0.05$). The heart rate and MAP at T1, T2 and T3 in the two

groups were significantly decreased compared with those at T0, but the heart rate and MAP in the remimazolam group at T1, T2 and T3 were significantly higher than those in the propofol group ($P < 0.05$). There were no statistical differences in the anesthesia time, awakening time and extubation time between the remimazolam group and the propofol group ($P > 0.05$). The levels of plasma epinephrine, norepinephrine and cortisol in the two groups were significantly higher at 24 h and 72 h after surgery than those before anesthesia induction, and the above levels were significantly lower in the remimazolam group than those in the propofol group ($P < 0.05$). The VAS scores at each time point in the two groups were significantly reduced compared to before surgery, but there was no statistically significant difference between the two groups after surgery ($P > 0.05$). The MMSE scores of the two groups were significantly lower at 1 d and 3 d after surgery compared with those before anesthesia induction, but the score in the remimazolam group was significantly higher than that in the propofol group ($P < 0.05$). In addition, the incidence rates of adverse reactions were significantly lower in the remimazolam group compared to the propofol group ($P < 0.05$).

Conclusion: Compared with propofol, remimazolam can achieve equivalent anesthetic and analgesic effects in elderly patients undergoing hip replacement. However, the latter one can significantly relieve respiratory and circulatory suppression, stress response and cognitive dysfunction, with good safety.

Key words: Remimazolam; Propofol; Hip replacement; Elderly; Stress response

INTRODUCTION

Hip replacement can effectively relieve the joint pain, correct the deformity and recover and improve the joint motor function of patients, thus it is the most effective surgical intervention for elderly patients with hip diseases [1]. Elderly patients with hip replacement, as a special group, have low body resistance and are often complicated with multiple underlying diseases, so they have high requirements for perioperative anesthesia and most of them prefer general anesthesia [2]. It can be seen that remimazolam and propofol have been clinically studied in the induction and maintenance of general anesthesia, but there is still no clear conclusion about the application effects of the two drugs in elderly patients undergoing hip replacement.

This study adopts remimazolam and propofol to maintain anesthesia of 60 elderly patients undergoing elective hip replacement, and compares the differences in circulatory indicators, stress indicators, anesthetic effects and perioperative pain degree of the two so as to provide more reference for choosing a safe and effective anesthesia regimen for elderly patients undergoing hip replacement.

LITERATURE REVIEW

The circulatory stability of remimazolam

Currently there are many studies of the circulatory stability of remimazolam home and abroad. For instance, Wang, et al. made meta-analysis from all the research in Pubmed before December 2019 and they concluded that remimazolam possesses excellent circulatory stability and safety, which makes it possible to have a better effect on critically ill patients [3]. In addition, Furuta M used remimazolam in a severe aortic stenosis patient and observed its effect in the general anesthesia [4]. He founded that remimazolam has a high safety level during this process and it can preserve cardiac output in this patient. Therefore, Furuta M concluded that remimazolam can be safely used to avoid the risk of cardiac suppression in patients with severe AS. Based on the previous research, we found that remimazolam has high circulatory stability and can improve the safety of general anesthesia in patients with cardiopulmonary insufficiency or circulatory disorders.

Remimazolam in endoscope examination

On the one hand, remimazolam in endoscope examination has good applications, especially in colonoscopy and bronchoscopy. Pastis NJ, et al. used remimazolam and midazolam respectively in two groups of flexible

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bronchoscopies, who discovered that remimazolam, was more effective and safer for moderate sedation [5]. On the other hand, remimazolam has better safety and efficacy in the endoscope examination of high-risk patients. Rex DK, et al. used remimazolam in high-risk colonoscopy to explore its safety and efficacy, discovering that remimazolam is safe and efficient in procedural sedation of high-risk ASA patients undergoing colonoscopy [6].

Application prospect of Remimazolam

Remimazolam does not undergo liver and kidney metabolism, which makes it suitable for general anesthesia in patients with hepatic or renal impairment. Stohr T, et al. used remimazolam in subjects with hepatic or renal impairment and found that neither the pharmacokinetic properties of remimazolam were affected nor dose adjustments are required [7]. Moreover, no unexpected adverse events related to remimazolam were seen in subjects with renal or hepatic impairment. This research indicates that it can be applied to general anesthesia in patients with hepatic or renal impairment. Combined with its antagonist flumazenil, remimazolam can accelerate postoperative recovery and reduce postoperative complications. For the pediatric general anesthesia, most children's recovery time is relatively longer than adults. Remimazolam is suitable for this situation and helpful to accelerate pediatric postoperative recovery. Shioji N, et al. used dexmedetomidine and remimazolam in magnetic resonance imaging and achieved the effect of pediatric sedation [8]. They also noted that although remimazolam was only approved for general anesthesia in adults, four researches into clinical trials of remimazolam are being carried out in pediatric anesthesia in 2021. From our perspective, after the completion of clinical trials, remimazolam may be considered for the pediatric general anesthesia in the future.

DISCUSSION

The main pathological characteristics of elderly patients undergoing hip replacement are degenerative changes of tissues and organs and often accompanied by a variety of underlying factors (such as hypertension, diabetes mellitus, coronary heart disease, etc.) and decreased tolerance to anesthesia and surgery [9]. The respiratory and circulatory inhibitory effects of anesthetics in elderly patients are significantly stronger than those of young patients and the drug eliminated half-life time is longer in elderly patients [10], therefore, how to choose a reasonable and effective anesthesia regimen for elderly patients with hip replacement has become an urgent problem to be solved in clinical application. In addition, this study displayed that there were no significant differences in VAS score, anesthesia time, awakening time and extubation time between the groups, but the awakening time and extubation time of the remimazolam group were slightly shorter than those of the propofol group and the MMSE scores at 1 d and 3 d after surgery were significantly higher than those of the propofol group. Both remimazolam and propofol can satisfy the perioperative analgesic effects and effective anesthesia maintenance time of elderly patients, but during the anesthesia process, remimazolam can avoid the excessive and long-lasting sedation that occurs during propofol anesthesia and can have smaller inhibitory effects on the central nervous system of patients.

Under the dual stimulation of anesthesia and surgery, elderly patients undergoing hip replacement are often in a state of tension and anxiety, in a state of body's stress during perioperative period and abnormal expression levels of plasma epinephrine, norepinephrine and cortisol [11]. Benzodiazepines can significantly inhibit the inflammatory response of mice and effectively inhibit the concentrations of adrenocorticotropic hormone and cortisol during stress [12]. This study showed that norepinephrine and cortisol in the two groups from the aspect of interaction effect, and the heart rate and MAP at T1, T2 and T3 in the two groups were significantly decreased compared with those at T0, and the levels of plasma epinephrine, norepinephrine and cortisol in the two groups were significantly increased at 24 h and 72 h after surgery compared with those before anesthesia induction but the levels were significantly lower in the remimazolam group than those in the propofol group, and the heart rate and MAP at T1, T2 and T3 in the remimazolam group were significantly higher than those in the propofol group, indicating that the

influence of remimazolam on circulation is smaller than that of propofol during induction and remimazolam can maintain a more stable heart rate and MAP after induction and is more conducive to relieving the stress response of elderly patients during anesthesia.

Remimazolam is a new type of ultra-short-acting benzodiazepine, can quickly act on GABA receptor and then generating obvious anesthetic effects [13]. Propofol, as a short-acting intravenous anesthetic drug, plays a role in the induction and maintenance of general anesthesia, but has obvious inhibitory effects on the respiratory system and circulatory system of patients. It has been found that propofol can induce a variety of cardiopulmonary complications (such as hypoxia, hypotension, arrhythmia and respiratory depression, etc.) while exerting sedative effects in clinical application, therefore it has certain limitations in the application for elderly patients [14]. Remimazolam has the advantages of rapid onset of action, fast metabolism, mild influence on circulation and not easy accumulation in long-term application and plays an important role in the induction and maintenance of general anesthesia, and studies have confirmed that remimazolam has milder influence on body's circulation and acts as specific antagonist compared to propofol, and it is more beneficial to reducing the occurrence of postoperative adverse reactions in patients [15]. This study similarly revealed that the total incidence rate of adverse reactions in the remimazolam group was significantly lower than that in the propofol group, suggesting that remimazolam has certain safety on elderly patients with hip replacement.

CONCLUSION

We concluded that in elderly patients' hip replacement, propofol and remimazolam can achieve equivalent anesthetic and analgesic effects; however, remimazolam can significantly relieve respiratory and circulatory suppression, stress response and cognitive dysfunction, more safety.

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