# Effect of Different Doses of Propofol and Nerve block Combined with General Anesthesia on The Intraoperative Anesthesia and Postoperative Awakening and Cognitive Function in Elderly Patients with Knee Osteoarthritis

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**Abstract. Objective.** To explore the effect of different doses of propofol and nerve block combined with general anesthesia on the intraoperative anesthesia and postoperative awakening and cognitive function in elder patients with knee osteoarthritis (OA). **Methods.** According to the inclusion criteria for research object, we selected 98 elderly patients with knee OA who needed surgery and were admitted to our hospital from January 2019 to January 2021 for the study. Patients were divided into the low dose group (given 2 mg/kg propofol by pumping under constant speed during surgery) and the high dose group (given 4 mg/kg propofol by pumping during surgery) by the number table method to compare their indicators including the intraoperative anesthesia effect, with 49 cases in each group. **Results.** No between-group difference was shown in the anesthesia time and postoperative VAS scores, but the awakening time of the low dose group was significantly shorter than that of the high dose group ($P<0.05$); the differences in heart rate (HR) values at various time points between the two groups were not obvious, but the high dose group obtained significantly higher HR values at $T_4$ than the low dose group; the mean arterial pressure (MAP) values of both groups were significantly reduced at $T_1$ and then returned to the level before anesthesia ($P>0.05$); the bispectral index scores (BIS) of both groups experienced a marked drop at $T_1$ and then recovered gradually, but failed to return to the level at $T_0$ till the end, and a between-group difference in BIS indexes presented at $T_1$; the plasma corticosterone (CORT) concentration at $T_1$ of both groups were significantly lowered and then returned to the level at $T_0$, with no between-group difference; and compared with the low dose group, the high dose group achieved slightly lower mini-mental state examination (MMSE) scores at 24-72 h after surgery, with no significant difference between them ($P>0.05$). **Conclusion.** The therapy of different doses of propofol and nerve block combined with general anesthesia has no significant effect on the cognitive function in elderly knee OA patients after surgery. With the nerve block improving the analgesic effect, a low dose of propofol is good for the postoperative awakening of patients. Different doses of propofol inhibited the stress response to a different degree and produced good anesthesia outcomes in elderly patients, but comparatively speaking, a low-dose propofol ensures more smooth indexes and less effect on the intraoperative hemodynamics.

**Keywords:** elderly patients with knee osteoarthritis; postoperative awakening; nerve block; general anesthesia; propofol
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The knee joint is one of the largest joints in the human body for bearing weight, and the joint with the highest morbidity[1-2]. Knee joint diseases usually include the osteoarthritis (OA), rheumatism and rheumatoid arthritis, synovitis and meniscus injury, of which the knee OA is a degenerative disease with joint pain and dysfunction as the main symptoms that are caused by a variety of factors including fibrotic, fissured, ulcerated, and dislodged joint cartilage. The pathogenesis of knee OA is still unclear, but may be related to age, obesity, inflammation, trauma and genetics[3-6]. Knee surgery is generally suitable for patients who fail to respond to nonsurgical treatment, such as joint debridement, cartilage repair, meniscal molding, meniscal suturing, ligament reconstruction, osteotomy, arthrodesis, and knee arthroplasty. Among them, the total knee arthroplasty (TKA) is the most common[7-10]. However, unconventional intraoperative anesthesia is required for elderly patients because of their physiological characteristics, and the aim of this study was to investigate the effect of infusing different doses of propofol during nerve block combined with general anaesthesia in knee OA patients on the intraoperative anaesthesia outcomes, postoperative awakening, and cognitive function, with the results summarized as follows.

## MATERIALS AND METHODS

### General Information

According to the inclusion criteria for research object, we selected 98 elderly patients with knee OA who needed surgery and were admitted to our hospital from January 2019 to January 2021 for the study. Patients were divided into the low dose group and the high dose group by the number table method, with 49 cases in each group. The comparison result of general information of both groups met the study inclusion criteria (P>0.05), see Table 1.

**Table 1 Comparison of general information between the two groups (n=49)**

| Index | Low dose group | High dose group | $X^2$/t | P |
|---|---|---|---|---|
| Age (years old) | 70.56±4.35 | 70.61±4.48 | 0.0560 | 0.9554 |
| Gender | | | 0.6877 | 0.407 |
| Male | 21 (42.86%) | 17 (34.69%) | | |
| Female | 28 (57.14%) | 32 (65.31%) | | |
| ASA grade | | | 0.1667 | 0.683 |
| II | 29 (59.18%) | 27 (55.10%) | | |
| III | 20 (40.82%) | 22 (44.90%) | | |
| Weight (kg) | 57.91±4.45 | 58.34±4.57 | 0.4719 | 0.6381 |

### Inclusion Criteria

① Patients met the clinical diagnosis criteria of knee OA in the *Guidelines for The Diagnosis and Treatment of Osteoarthritis (2018)*; ② patients underwent unilateral surgery; ③ patients had no surgical contraindications; ④ patients had no contraindications to the medicines used in the study; ⑤ the ASA grades were II-III; and ⑥ the study was approved by the Hospital Ethics Committee and patients joined the study of their own volition.

### Exclusion Criteria

① Patients had neural injury of the lower extremity; ② patients had haematological diseases, infectious diseases or immune system disorders; patients had the history of metal disease, ③ knee surgery, or substance abuse; and ④ patients refused to cooperate with the study.

### Methods

All patients were given the knee arthroplasty, and various examinations were conducted before surgery. The surgery and anesthetic procedure were performed by the same team of physicians and anesthesiologists[11-13].

All patients were treated with ultrasound-guided femoral nerve block combined with general anesthesia with the following steps. The patient was positioned supine to expose the unilateral groin, the specific position of the femoral nerve was found and marked by a high-

frequency linear probe of untrasound equipment, the routine disinfection and draping was performed, and the probing angle and scanning depth were adjusted to obtained clearer cross sectional images of the femoral nerve. The needle was punctured with a 22 G nerve stimulator, and the stimulation current was set to 1 mA, frequency to 1 Hz, and time to 1 ms[14-15]. The best position was confirmed by the nerve stimulator during the puncture procedure, the current was reduced properly when the needle tip was close to the target nerve, and the puncture angle and depth were adjusted under ultrasound guidance. If there was still a significant contractile response in the muscle when the current was reduced to 0.2-0.3 mA, needle entry was stopped; and if there was no blood when pumping back, a 5-10 ml mixture of lidocaine (1%) and ropivacaine hydrochloride (0.375%) was injected, the needle kept inserting, and then the aforesaid mixture was injected again. After the successful nerve block was confirmed, the low dose group was given 2 mg/kg of propofol (specification: 10 ml; manufactured: Sichuan Guorui Pharmaceutical Co., Ltd.; NMPA Approval No. H20040079) and 1 μg/kg of fentanyl (specification: 1 mg; manufactured: Jiangsu Nhwa Pharmaceutical Co., Ltd.; NMPA Approval No. H20143314) by intravenous infusion, and the high dose group was given 2 mg/kg of propofol and 1 μg/kg of fentanyl in the same way, and then a laryngeal mask was implanted to inhale the 2% sevoflurane continuously during surgery.

### Observation Indexes

The anesthesia time and awakening time of patients in both groups were counted, and the postoperative pain was evaluated by the VAS pain score, with higher scores indicating stronger pain.

Patients' heart rate (HR), mean arterial pressure (MAP), bispectral index score (BIS), and depth of nasotracheal intubation (NTI) were examined at various time points, namely, before anesthesia ($T_0$), immediately after skin incision ($T_1$), prothesis implantation ($T_2$), suturing ($T_3$), and 15 min after entering the anesthesia recovery room ($T_4$), and 3 ml of central venous blood was collected to determine the plasma corticosterone (CORT) concentration by the ELISA method.

The cognitive function in terms of orientation, memory, concentration and calculation, memory recall, and linguistic competence was evaluated by the mini-mental state examination (MMSE) scoring system before surgery and at 24 h, 48 h and 72 h after surgery. The maximum score was 30 points, and it was considered as cognitive dysfunction if the score after surgery was 2 points less than that before surgery.

### Statistical Processing

In this study, the data processing software was SPSS21.0, the picture drawing software was GraphPad Prism 7 (GraphPad Software, San Diego, USA), items included were enumeration data and measurement data, which were expressed by [n(%)] and ($\bar{x}\pm s$) and examined by $X^2$ test and t-test, respectively, and differences in data of the group were considered statistically significant at $P<0.05$.

## RESULTS

### Comparison of Basic Situations During the Perioperative Period Between the Two Groups

The differences in the anesthesia time and postoperative VAS pain scores between the two groups were not obvious ($P>0.05$), but the awakening time of the low dose group was clearly shorter than the high dose group, which was statistically significant ($P<0.05$), see Table 2.

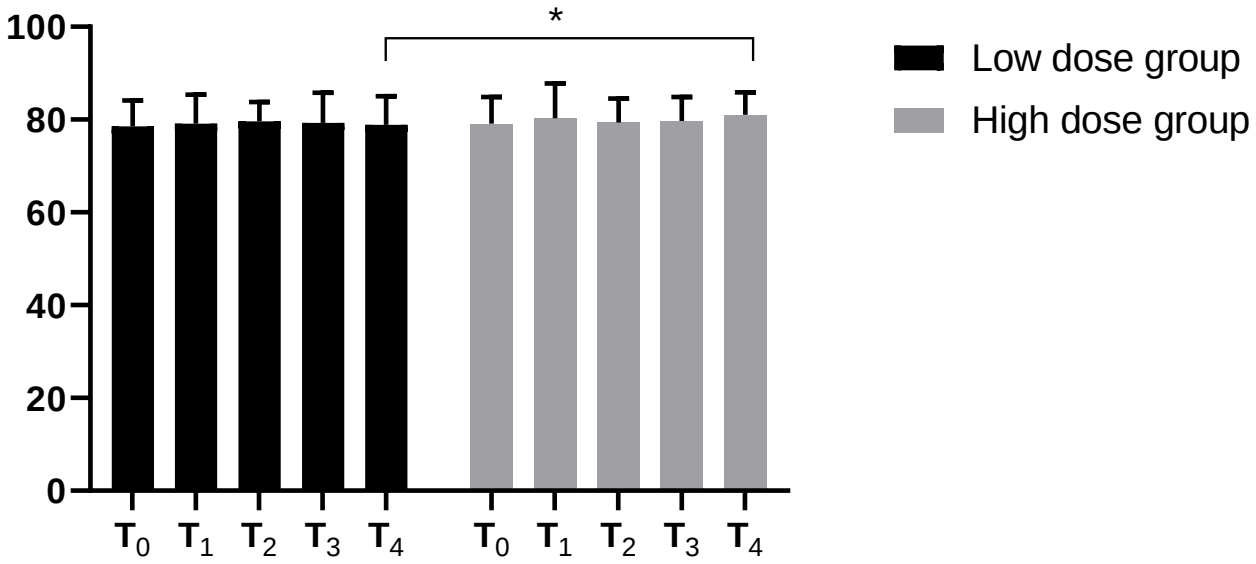
**Table 2 Basic situations during the perioperative period of patients in both groups ($\bar{x}\pm s$)**

| Group | n | Anesthesia time (min) | Awakening time (min) | VAS score |
|---|---|---|---|---|
| Low dose group | 49 | 186.7±10.4 | 6.2±3.2 | 4.6±1.5 |
| High dose group | 49 | 184.5±11.2 | 13.5±3.1 | 4.5±1.4 |
| t | | 1.0076 | 11.4694 | 0.3412 |
| P | | 0.3162 | 0.000 | 0.7337 |

### Comparison of Patients' Hr Values Between the Two Groups

The HR values at various time points of patients in both groups were not significantly different ($P>0.05$), but patients in the high dose group had obviously lower HR values at $T_4$ when compared with the low dose group, see Figure 1.

**Figure 1 HR of both groups ($\bar{x}$±s)**




Note: The horizontal axis indicated the time points, and the vertical axis indicated the HR values in times/min;

The HR values at $T_0$, $T_1$, $T_2$, $T_3$ and $T_4$ of the low dose group were (78.5±5.6), (79.1±6.3), (79.6±4.2), (79.3±6.5) and (78.9±6.1), respectively;

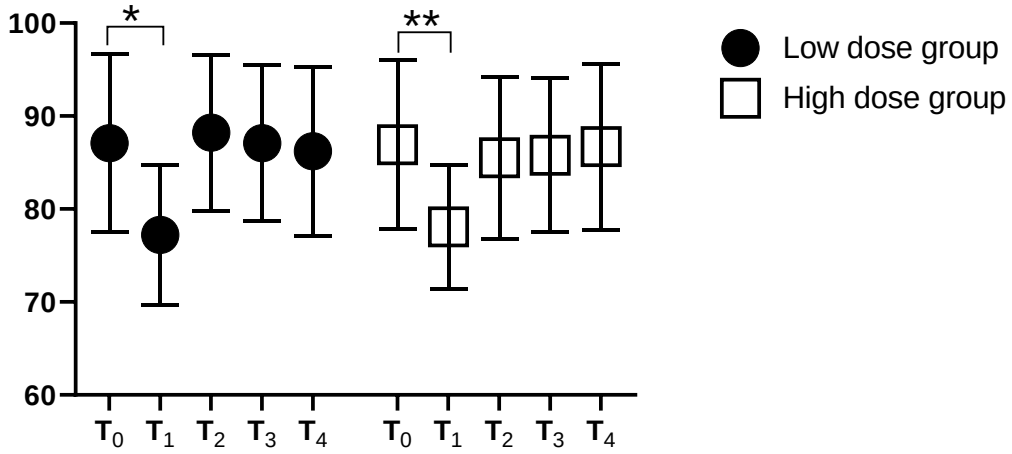
The HR values at $T_0$, $T_1$, $T_2$, $T_3$ and $T_4$ of the high dose group were (79.1±5.8), (80.3±7.5), (79.4±5.1), (79.7±5.2) and (81.0±4.9), respectively; and

* indicated that the difference in the HR values at $T_4$ between the two groups was significant (t=2.3518, P=0.0207).

**Comparison of Patients' Map Values Between the Two Groups**

The MAP values of patients in both groups were significantly reduced at $T_1$, and then returned to the level before anesthesia (P>0.05), see Figure 2.

**Figure 2 MAP values of both groups ($\bar{x}$±s)**




Note: The horizontal axis indicated the time points, and the vertical axis indicated the MAP values in mmHg;

The MAP values at $T_0$, $T_1$, $T_2$, $T_3$ and $T_4$ of the low dose group were (87.1±9.6), (77.2±7.5), (88.2±8.4), (87.1±8.4) and (86.2±9.1), respectively;

The MAP values at $T_0$, $T_1$, $T_2$, $T_3$ and $T_4$ of the high dose

group were (86.9±9.1), (78.1±6.7), (85.5±8.7), (85.8±8.3) and (86.7±8.9), respectively;

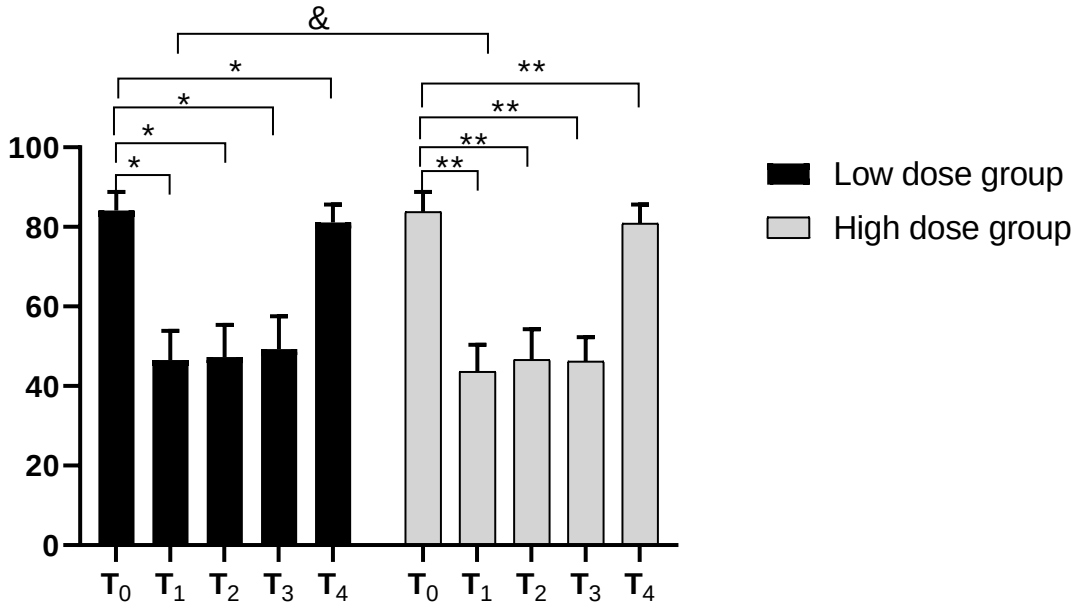
* indicated that the MAP values at $T_0$ and $T_1$ of the low dose group were significantly different (t=5.6886, P=0.000); and

** indicated that the MAP values at $T_0$ and $T_1$ of the high dose group were significantly different (t=5.4511, P=0.000).

**Comparison of Patients' Bis Indexes Between the Two Groups**

The BIS indexes of patients in both groups dropped dramatically at $T_1$ and then recovered gradually afterwards, but failed to returned to the level at $T_0$ till the end. And a between-group difference was seen in the BIS indexes at $T_1$, see Figure 3.

**Figure 3 BIS indexes of both groups ($\bar{x}$±s)**




Note: The horizontal axis indicated the time points, and the vertical axis indicated the values;

The BIS indexes at $T_0$, $T_1$, $T_2$, $T_3$ and $T_4$ of the low dose group were (84.1±4.7), (46.5±7.4), (47.3±8.1), (49.3±8.2) and (81.1±4.5), respectively;

The BIS indexes at $T_0$, $T_1$, $T_2$, $T_3$ and $T_4$ of the high dose group were (83.8±5.0), (43.6±6.8), (46.6±7.7), (46.2±6.1) and (80.9±4.7), respectively;

* from bottom to top indicated that compared with $T_0$, the BIS indexes at $T_1$, $T_2$, $T_3$ and $T_4$ of the low dose group presented significant differences (t=30.0237, 27.5072, 25.7738, 3.2273, and P<0.05 in all cases); and

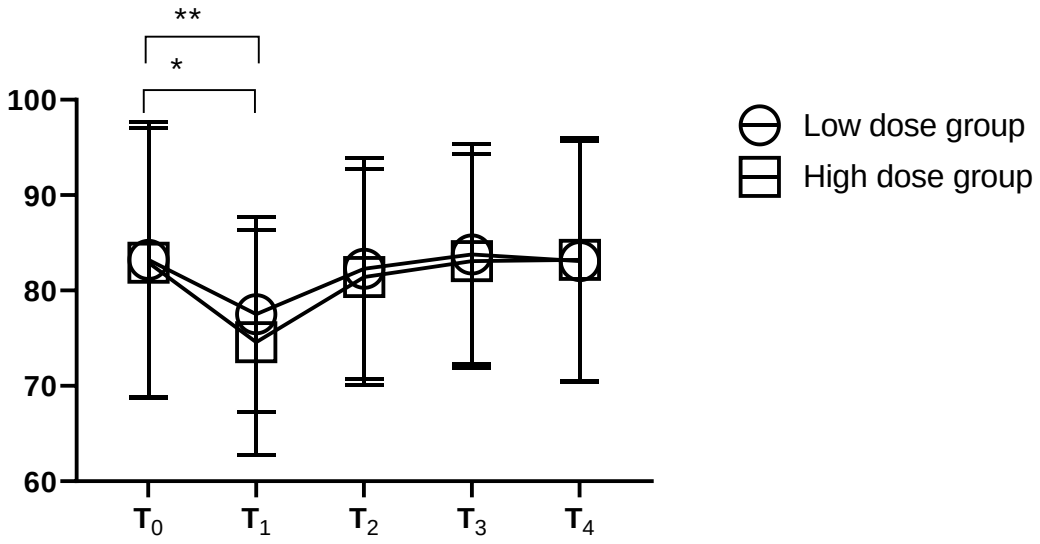
** from bottom to top indicated that compared with $T_0$, the BIS indexes at $T_1$, $T_2$, $T_3$ and $T_4$ of the high dose group presented significant differences (t=33.3397, 28.3631, 33.3700, 2.9582, and P<0.05 in all cases); and

& indicated that the BIS indexes at T1 of both groups were significantly different (t=2.0199, P=0.0462).

**Cort Comparison of Patients' Cort Concentration Between the Two Groups**

The CORT concentration at $T_1$ of patients in both groups were reduced markedly and then returned to the level at $T_0$, with no significant difference (P>0.05), see Figure 4.

**Figure 4 CORT concentration of both groups (x̄±s)**




Note: The horizontal axis indicated the time points, and the vertical axis indicated the concentration in ng/ml;

The CORT concentration at $T_0$, $T_1$, $T_2$, $T_3$ and $T_4$ of the low dose group was (83.2±14.5), (77.5±10.2), (82.3±11.6), (83.8±11.5) and (83.1±12.6), respectively;

The CORT concentration at $T_0$, $T_1$, $T_2$, $T_3$ and $T_4$ of the high dose group was (82.9±14.1), (74.6±11.8), (81.4±11.3), (83.1±11.2) and (83.2±12.8), respectively;

* indicated that the difference in CORT concentration at $T_0$ and $T_1$ of the low dose group was significant (t=2.2506, P=0.0267); and

** indicated that the difference in CORT concentration at $T_0$ and $T_1$ of the high dose group was significant (t=3.1600, P=0.0021).

**Comparison of Patients' Mmse Scores Between the Two Groups**

The MMSE scores at 24-72 h after surgery of the high dose group were slightly higher those of the low dose group, but were not significantly different (P>0.05), see Table 3.

**Table 3 MMSE scores of both groups (x̄±s)**

| Group | n | Before surgery | 24 h after surgery | 48 h after surgery | 72 h after surgery |
|---|---|---|---|---|---|
| Low dose group | 49 | 27.56±1.58 | 23.26±6.91 | 25.42±1.63 | 26.91±8.11 |
| High dose group | 49 | 27.61±1.47 | 25.01±7.92 | 26.96±1.69 | 27.68±7.15 |
| t | | 0.1622 | 1.1655 | 1.2196 | 0.4985 |
| P | | 0.8715 | 0.2467 | 0.2256 | 0.6193 |

## DISCUSSION

According to statistics, age is currently the only identified risk factor in the clinic that can lead to the postoperative cognitive dysfunction in patients undergoing knee arthroplasty, which may be associated with the decrease in the transmitter such as cerebral neuron and acetylcholine, and on the other hand, the imbalance in the anti-inflammatory and pro-inflammatory effects of the central nervous system also increases the probability of elderly patients developing cognitive dysfunction in response to the same surgical stimulus[16-19]. Although knee arthroplasty is a common surgical procedure for the treatment of knee OA in elderly patients, it becomes a clinical problem due to the deterioration of physical function in elderly patients that increases the difficulty in selecting the anesthetic regimen. In the past, intravenous anesthesia was the most

widely applied anesthesia modality in clinical treatment, but it has a great effect on the hemodynamics of patients and is hard to meet the clinical needs. In contrast, nerve block affects the physiological state such as breathing and internal circulation of patients less and thus attracts more attention in the clinic[20-23]. Therefore, elderly patients were selected as the research object in the study to explore the effect of different doses of propofol and nerve block combined with general anesthesia on the postoperative cognitive dysfunction in elderly patients with keen OA, and it was concluded that the anesthesia time and postoperatove VAS pain scores of both groups were not significantly different, but the awakening time of the low dose group was shorter than that of the high dose group; and performing nerve block on the operation side to improve the analgesic effect could greatly inhibit the operative trauma induced stress responses and increase the tolerance level to the laryngeal mask, and a low dose of propofol worked better in the postoperative awakening. In addition, the between-group differences in the HR values at various time points of patients in both groups were not significant, but the HR values at $T_4$ of the high dose group were obviously higher than those of the low dose group; the MAP values of both groups were significantly reduced at $T_1$ and then returned to the level before anesthesia. During the surgical procedure, different doses of propofol would keep patients in various depths of anesthesia, with the depth of the high dose group far lower than that of the high dose group, but the fact that the HR values and MAP values of both groups were close indicated that different dosage would not lead to differences in patients' heart rate and hemodynamics. The study results also presented that the BIS indexes of patients in both groups were obviously reduced at $T_1$ and then recovered afterwards, but failed to return to the level at $T_0$ till the end, and there was a between-group difference in the BIS indexes at $T_1$. It was considered the best anesthesia state in the clinic when the BIS index was at 40-60, and as the patients in both groups obtained the BIS indexes between 40-50, both doses of propofol had better intraoperative anesthesia effect to elderly patients with knee OA, with no obvious difference. In addition, the sudden decrease of BIS values in the high-dose group at $T_1$ was slightly higher than that in the low-dose group, which indicated that the patients in the low-dose group had smoother bispectral indexes. The CORT concentration at $T_1$ of both groups experienced a marked fall and then returned to the level at $T_0$, because when the body was under stress, the hypothalamic-pituitary-adrenal axis (HPA axis) excitement will raise the adrenocorticotropic hormone and then plasma CORT concentration, which is one of the most important stress responses of the body. And the anesthesia induction with propofol led to the decrease of the plasma CORT concentration, explaining why the CORT concentration in both groups was reduced significantly at $T_1$.

The study also found that the MMSE scores at 24-72 h after surgery of the high dose group were slightly higher than those of the low dose group, but such difference was not statistically significant ($P>0.05$). ZHEN-DONG XU[24] and others once found that the anesthesia depth did nothing explicit with the cognitive dysfunction in elderly patients after knee arthroplasty, while the randomized controlled trial conducted by XIAO-WEI DING[25] and other scholars concluded that lighter anesthesia could lower the incidence of cognitive dysfunction within three months after surgery. However, some other scholars considered that the cognitive function of patients underwent deeper anesthesia was recovered in a better way in 4-6 weeks after surgery. It was thus clear that different research objects, research progresses, scales and surgical methods could lead to different clinical study results.[26] In this study, we found under the premise of nerve block improving the analgesic effect, different doses of propofol and nerve block combined with general anesthesia had low impact on the short-term cognitive function in elderly patients underwent knee arthroplasty. However, with the disadvantages including smaller sample and short follow-up period in the study, the fatality rate and long-term prognosis of patients shall be further explored.

To sum up, the postoperative short-term cognitive function in elderly patients with knee OA was not markedly affected by different doses of propofol and nerve block combined with general anesthesia, but with the nerve block promoting the analgesic effect, a low dose of propofol was good for the postoperative awakening. Different doses of propofol presented equivalent better anesthesia effect and inhibited the stress response to a different degree in elderly patients. However, a low-dose propofol ensures more smooth indexes and less effect on the intraoperative hemodynamics.

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