Am J Transl Res 2021;13(10):12058-12064
www.ajtr.org /ISSN:1943-8141/AJTR0130973

*Original Article*

# The effect of dexmedetomidine combined with epidural anesthesia on post-operative cognitive dysfunction in elderly patients after orthopedic surgery

Yong Zhu[1], Guohui Le[2]

[1]*Department of Anesthesiology, The Sixth People's Hospital of Kunshan City, Kunshan 215321, Jiangsu, China;* [2]*Department of Anesthesiology, Traditional Chinese Medicine Hospital of Kunshan City, Kunshan 215321, Jiangsu, China*

Received January 28, 2021; Accepted March 10, 2021; Epub October 15, 2021; Published October 30, 2021

**Abstract:** Objective: To investigate the effect of dexmedetomidine combined with epidural anesthesia on cognitive dysfunction (POCD) in elderly patients after orthopedic surgery. Methods: A total of 187 elderly patients who needed orthopedic surgery in our hospital from January 2019 to December 2020 were randomly divided into an experimental group (n=95) and a control group (n=92). The patients in the experimental group were administered 1 μg/kg dexmedetomidine hydrochloride injections, and the patients in the control group were administered 0.9% sodium chloride injections, which were infused using a micropump for about 10 minutes. The two groups' cognitive function, VAS scores, and vital signs were compared. Results: There were significant differences in the two groups' mean arterial pressures and heart rates at intubation time (T3), operation start time (T4), and extubation time (T6) ($P < 0.05$). The VAS scores in the experimental group were significantly different from the VAS scores in the control group at 24 hours after the operations, 48 hours after the operations, 72 hours after the operations, and 7 days after the operations ($P < 0.05$). There were no significant differences in the anesthesia times, the average bleeding volumes, or the average operative durations ($P > 0.05$). 48 hours after the operations, the MMSE score in the experimental group was (27.15±1.17), which was significantly different than the MMSE score in the control group (23.11±0.83), and the difference was statistically significant ($P < 0.05$). Conclusion: Epidural anesthesia combined with dexmedetomidine has little circulatory interference in elderly patients; moreover, it can reduce the incidence of postoperative cognitive dysfunction in elderly patients.

**Keywords:** Dexmedetomidine, epidural anesthesia, post-operative cognitive dysfunction, elderly patients, post-orthopedic surgery

## Introduction

With the aging of the global population, about 30%-35% of the elderly need to undergo various surgical treatments [1]. According to a statistical analysis, about 62% of elderly patients need orthopedic surgery, and postoperative cognitive dysfunction (POCD) is a common complication of the central nervous system in elderly patients [2]. The incidence of postoperative POCD in elderly patients over 65 years old is 2-10 times higher than it is in young patients, and the incidence of postoperative POCD in elderly patients over 75 years old is 3 times higher than it is in patients over 65-75 years old, indicating that age is a significant and independent risk factor for the development of POCD [3, 4]. At present, the pathogenesis of POCD is unclear, but it has been proved that the inflammatory reactions caused by anesthesia, surgery, pain, and stress may be closely related to POCD [5, 6]. Determining the correct postoperative analgesia and relieving stress and inflammation are important challenges for reducing postoperative cognitive dysfunction in elderly patients.

Dexmedetomidine can selectively excite the presynaptic membrane $\alpha_2$ receptor, so as to play the negative feedback role of the sympathetic nerve. It has the effects of sedation, the inhibition of anxiety, the reduction of anesthetic drugs, etc., and it can weaken the stress response without causing significant respiratory depression, and it has a potential neuroprotective effect [7]. Some animal studies have found that dexmedetomidine can effectively reduce the post-surgical inflammatory mediators in rats, thus reducing the occurrence of a large bundle of POCD [8, 9]. The purpose of this study is to explore the effect of the perioperative continuous application of dexmedetomidine combined with epidural anesthesia on the early postoperative cognitive function, postoperative analgesia, and vital signs of elderly patients undergoing orthopedic surgery, and we want to provide a strong guarantee for clinical anesthesia.

## Data and methods

### *Clinical data*

187 elderly patients who needed orthopedic surgery in our hospital from January 2019 to December 2020 were randomly allocated into two groups: the experimental group (n=95) or the control group (n=92). The researchers systematically explained the role, purpose, and process of the study to the patients and their families. The patients and their families voluntarily signed the informed consent forms to participate in this study. This study was approved and recognized by the ethics committee of our hospital.

### *Inclusion and exclusion standards*

Inclusion criteria: ① Age: ≥ 65 years; ② ASA grade II-III; ③ No anesthesia contraindications; and ④ The patients were willing to cooperate and help implement the experiment.

Exclusion criteria: ① Patients who had a history of mental illness; ② Patients who had a history of coronary heart disease, diabetes, cerebral infarction, or hypertension; ③ Montreal Cognitive Assessment Scale (MoCA) score ≤ 26 points; ④ Patients who had a serious cardiac disorder, severe liver malfunction, or renal failure; ⑤ Patients with a coagulation dysfunction; ⑥ Patients with a history of using antidepressants or beta blockers; and ⑦ Patients unwilling to participate in our research.

### *Method*

All the patients underwent epidural anesthesia: The operation time was 1.5~2.0 h. The patients were placed in a lateral position and punctured in L2-3 space. After a successful puncture, the catheter was placed at 3 cm, and 2% lidocaine 3 ml was given as a test dose. The patients were asked to change to a supine position, and 0.5% ropivacaine 10 ml was given 5 min later, and 0.5% ropivacaine 5 ml was given again during the operation.

*The control group*: The patients were administered 0.9% sodium chloride injections: before the anesthesia, 1 μg/kg of 0.9% sodium chloride injection was infused using a micropump for about 10 minutes. During the operation, 0.5 μg/(kg/h) of 0.9% sodium chloride injection was continuously pumped.

*The observation group*: The patients were administered dexmedetomidine hydrochloride injection: before the anesthesia, 1 μg/kg dexmedetomidine hydrochloride injection was infused using a micropump for about 10 minutes. During the operations, 0.5 μg/(kg/h) dexmedetomidine hydrochloride injection was continuously pumped.

The infusions of all the drugs were stopped 10 minutes before the end of operations in both groups.

### *Assessing the cognitive function*

The mini mental state assessment scale (MMSE) scores are mainly suitable for screening POCD in the elderly and have become a screening tool for cognitive impairment and other functions. The scores range from 0-30 points, and the higher the score, the better the cognitive function.

### *Vital signs*

The mean arterial pressure (MAP) and HR changes were recorded at 5 minutes before the operations (T1), at the induction time (T2), at the intubation time (T3), at the operation start time (T4), at the operation end time (T5), and at the extubation time (T6).

### *The VAS scores*

*The* VAS scores and the occurrences of adverse reactions such as hypoxemia, laryngeal spasms, agitation, and arrhythmia were recorded [10].

**Table 1.** Comparison of the clinical data between the two groups

| | Experimental group (n=95) | Control group (n=92) | $t/\chi^2$ | *P* |
|---|---|---|---|---|
| Age (years) | 74.1±4.36 | 75.25±6.10 | 1.23 | 0.51 |
| Sex | | | 6.18 | 0.34 |
| Male (n %) | 58 (61.1%) | 51 (55.4%) | | |
| Female (n %) | 37 (38.9%) | 41 (44.6%) | | |
| BMI | 19.5±1.16 | 18.95±1.50 | 3.32 | 0.21 |
| Smoking | 46 (48.4%) | 49 (53.3%) | 4.16 | 0.28 |
| ASA grade | | | 6.79 | 0.36 |
| I | 28 (29.5%) | 21 (22.8%) | | |
| II | 53 (55.8%) | 55 (59.8%) | | |
| III | 14 (14.7%) | 16 (17.4%) | | |
| The average operative duration (min) | 149.1±22.3 | 146.3±18.4 | 2.29 | 0.18 |
| Anesthesia time (min) | 161.2±27.7 | 163.4±24.5 | 1.94 | 0.22 |
| Average bleeding volume (mL) | 211±26.5 | 213±30.3 | 6.39 | 0.48 |

Note: Compared with the control group, a significant difference was P < 0.05.

*Statistical analysis*

All the data were analyzed using SPSS 22.0. The statistical results are expressed as the mean ± standard deviation (M ± SD), the data comparison were conducted using t-tests and the correlation analysis was conducted using the Pearson correlation coefficient, and P < 0.05 was considered a significant difference. The analyses were performed using GraphPad Prism 7 Software (GraphPad Prism, San Diego, CA).

**Results**

*Clinical data*

**Table 1** shows the participants' clinical characteristics. The study included 187 patients, including 95 patients in the experimental group with a mean age of (74.1±4.36) years old, and in the control group, the mean age was (75.25±6.10) years old. The BMI in the experimental group was (19.5±1.16) kg/m$^2$, and in the control group it was (18.95±1.50) kg/m$^2$, and there were no significant differences between two group (P=0.21). There were 46 (48.4%) smokers in the experimental group, and in the control group there were 49 (53.3%). The average operative duration in experimental group was (149.1±22.3) minutes, and in control group it was (146.3±18.4) minutes, and there was no significant difference between the two groups (P=0.18). The average anesthesia time in the experimental group was (161.2±27.7) minutes, and in the control group it was (163.4±24.5) minutes, and there was no significance difference between the two groups (P=0.22). The average bleeding volume in the experimental group was (211±26.5) mL, and the average bleeding volume in the control group was (213±30.3) mL. The number of patients who were ASA grades I, II, or III in the observation group were 28 (29.5%), 53 (55.8%), and 14 (14.7%) cases, respectively. The number of patients who were ASA grades I, II, and III in the control group were 21 (22.8%), 55 (59.8%), and 16 (17.4%), respectively. The two groups were similar in terms of their demographics and clinical characteristics, and there were no statistically significant differences between the two groups.

*Vital signs*

The mean arterial pressure at 5 minutes before the operations (T1) in the experimental group was (87.13±10.24) mmHg, and in the control group it was (89.87±10.02) mmHg. The mean arterial pressures at the induction times (T2), the intubation times (T3), the operation start times (T4), the operation end times, (T5) and the extubation times (T6) in the experimental group were (80.22±14.11) mmHg, (92.44±13.27) mmHg, (88.57±14.27) mmHg, (91.27±11.25) mmHg, and (93.36±8.94) mmHg, and the corresponding values in the control group were (82.14±13.25) mmHg, (99.49±14.56) mmHg, (95.53±13.95) mmHg, (90.53±12.43) mmHg, and (96.61±11.23) mmHg, and there

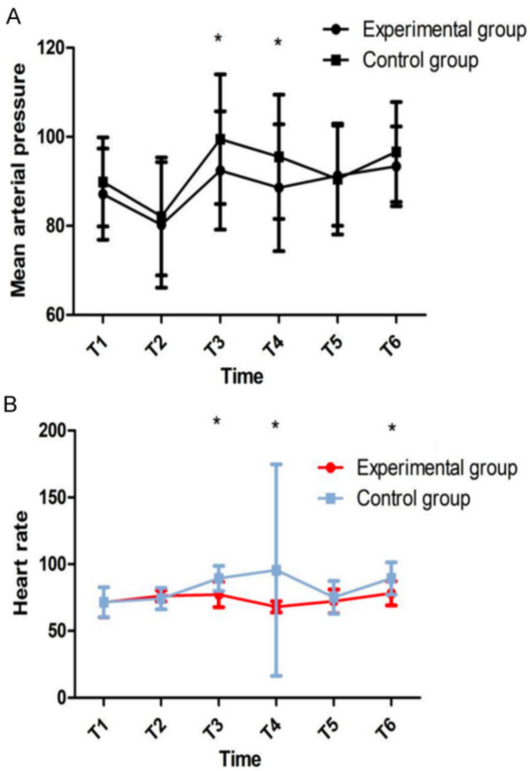


**Figure 1.** Comparison of the vital signs between the two groups. A: Comparison of the mean arterial pressure between the two groups; B: Comparison of the heart rates between the two groups. Note: Compared with the control group, $^{a}P < 0.05$. T1: 5 minutes before Note: Compared with the control group, significant difference as P < 0.05. T1: 5 minutes before the operation; T2: induction time; T3: intubation time; T4: the operation start time; T5: the operation end time; T6: the extubation time.

were significance differences between the two groups at T3, T4, and T6 (P < 0.05). The heart rate at 5 minutes before the operations (T1) in the experimental group was (71.45±11.23) times/min, and in the control group it was (71.57±11.19) times/min. The heart rates at the induction time (T2), intubation time (T3), operation start time (T4), operation end time (T5), and extubation time (T6) in the experimental group were (76.21±4.15) times/min, (77.32±9.51) times/min, (68.14±4.19) times/min, (72.19±8.95) times/min, and (78.19±9.14) times/min, and in the control group the corresponding HR were (74.20±8.03) times/min, (89.36±9.43) times/min, (79.16±6.29) times/min, (75.18±12.25) times/min, and (89.36±12.09) times/min, and there were significance differences between the two groups at T3, T4, and T6 (P < 0.05) (**Figure 1**).

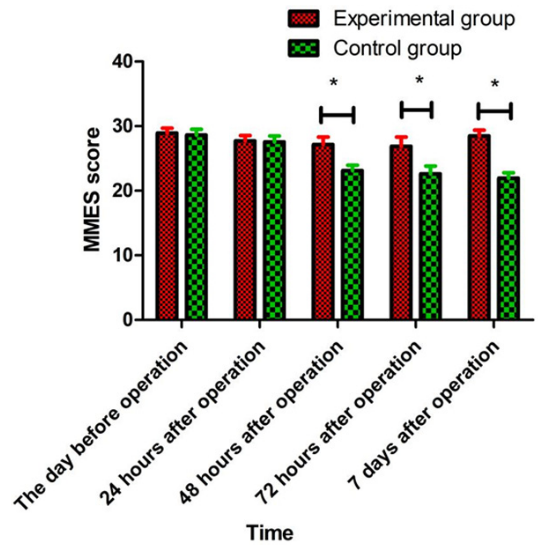


**Figure 2.** Comparison of MMES scores between the two groups. Note: Compared with the control group, $^{*}P < 0.05$.

*Evaluate the cognitive function-MMES score*

The MMES score on the day before the operations in the experimental group was (28.93±0.75) points, and in the control group it was (28.62±0.89) points. The MMES scores at 24 hours after the operations, 48 hours after the operations, 72 hours after the operations, and 7 days after the operation in the experimental group were (27.73±0.83) points, (27.15±1.17) points, (26.89±1.44) points, and (28.49±0.88) points, and in the control group the corresponding values were (27.54±0.94) points, (23.11±0.83) points, (22.61±1.21) points, and (21.96±0.84) points, and there was a significant difference between the two group at 48 hours after the operations, 72 hours after the operations, and 7 days after the operation (P < 0.05) (**Figure 2**).

*Clinical relief of pain-the VAS scores*

As shown in **Table 2**, the VAS score on the day before the operations in the experimental group was (1.19±0.48) points, and in the control group the score was (1.23±0.54) points. The VAS score at 24 hours after the operation, 48 hours after the operation, 72 hours after the operation, and 7 days after the operation in the experimental group were (3.9±0.74) points, (2.54±0.41) points, (2.29±0.48) points, and (1.69±0.54) points, and the corresponding val-

**Table 2.** Comparison of VAS scores between the two groups ($\overline{x}$ ± s)

| group | Number of cases | The day before operation | 24 hours after operation | 48 hours after operation | 72 hours after operation | 7 days after operation |
|---|---|---|---|---|---|---|
| Experimental group | 95 | 1.19±0.48 | 3.9±0.74 | 2.54±0.41 | 2.29±0.48 | 1.69±0.54 |
| Control group | 92 | 1.23±0.54 | 4.02±0.81 | 3.76±0.77 | 3.44±0.51 | 2.51±0.33 |
| t | - | 2.168 | 3.717 | 4.225 | 5.115 | 3.312 |
| *P* | - | 0.312 | 0.009 | 0.007 | 0.006 | 0.003 |

Note: Compared with the control group, a significant difference was P < 0.05.

ues in the control group were (4.02±0.81) points, (3.76±0.77) points, (3.44±0.51) points, and (2.51±0.33) points, and there was a significant difference between the two groups after the operations ($P < 0.05$).

## Discussion

Postoperative cognitive dysfunction (POCD) is a group of neurological complications induced by surgery and anesthesia in addition to the original disease. More common in elderly patients, patient performance of memory, attention, learning ability, abstract thinking, and orientation and other aspects of the disorder, and this is accompanied by a decline in social activity ability, that is, a change in personality, abilities, and skills [11]. It often lasts for weeks or months, and in a few cases lasts for years or a lifetime [12]. This kind of complication has caused an increasingly heavy burden on hospitals, families, and society. According to some studies, the incidence of postoperative cognitive dysfunction occurs mostly in elderly patients, and it may be related to a degeneration of the central nervous system and a decline in neurological function to different degrees [13]. The mechanism of postoperative cognitive impairment involves an imbalance of the nervous, endocrine, and immune systems.

One of the reasons it occurs is that intraoperative stress and hemodynamic changes aggravate neurologic impairment. Different anesthetics can damage cognitive function to varying degrees. Controlling cerebral blood flow and maintaining a balance of the brain metabolism and physiological regulation mechanisms are the measures used to prevent and treat postoperative cognitive dysfunction. α 2-adrenoceptor agonists can inhibit the release of norepinephrine, and have sedative, analgesic and anti-sympathetic effects. During the auxiliary anesthesia, α 2-adrenoceptor agonists can stabilize blood pressure, slow down the heart rate and reduce myocardial oxygen consumption [14]. There is a high density of α 2 receptors in the dorsal motor neuron complex of the medulla oblongata. It has been confirmed that there is also a dense distribution of α 2 receptor in the vagus nerve, the middle lateral cell column, and the substantia nigra colloidal body [15]. Dexmedetomidine can activate this part of the receptor to reduce the blood pressure and the heart rate. Our results showed that the mean arterial pressure and heart rate in the experimental group were significantly lower than they were in the control group at the moment of intubation (T3), the beginning of the operation (T4), and extubation (T6), and the hemodynamics during intubation and extubation were more stable, with statistical significance. It is suggested that dexmedetomidine can reduce the cardiovascular stress response induced by intubation and extubation and maintain patients' hemodynamic stability.

Some studies have shown that postoperative pain can affect patients' postoperative cognitive function, and reducing the postoperative pain has a significant effect on reducing the postoperative cognitive function changes [16, 17]. In this study, the visual analogue scale (VAS) was used. The data showed that the pain score was not higher than 4, in order to reduce the impact of postoperative pain on POCD. This study showed that the VAS scores of the experimental group were more significantly improved than they were in the control group, and the postoperative pain was reduced, suggesting that dexmedetomidine has a protective effect on the early postoperative cognitive function of elderly patients.

There are many clinical methods to evaluate POCD, but they mainly rely on neuropsychological tests, such as WAIS, WMS and MMSE, but other researchers have used Raven test and

MMSE [18]. Among the tests, the memory test is the most sensitive, and the most commonly used method is MMSE. The scale is a screening test, and it can quantitatively evaluate cognitive function by asking patients a series of questions. A MMSE score < 24 is an index to judge cognitive impairment. In this study, MMSE was used to evaluate the cognitive function. The results showed that the MMSE scores in the control group were significantly lower than they were in the same group before the operations, but there was no significant change in the dexmedetomidine group, suggesting that dexmedetomidine has a protective effect on the cognitive function of elderly patients.

The mechanism of dexmedetomidine protecting postoperative cognitive function in elderly patients is unclear. But now it is believed that dexmedetomidine can produce a sympathetic effect, which can effectively reduce the release of inflammatory cytokines and improve the survival rate of septic rats. The stress response occurring during an operation is one of the main causes of perioperative complications, and it is also a key factor leading to POCD [19]. On the other hand, the occurrence of mental disorders is closely related to the function of hypothalamus pituitary adrenal axis and the immune system. Surgical stress and trauma can activate the hypothalamus pituitary adrenal axis hyperfunction and the immune system, increasing the circulating glucocorticoid levels and releasing the inflammatory cytokines (IL-1, IL-2, IL-6, and TNF) in the nervous system, resulting in central serotonin, acetylcholine, and norepinephrine. A disorder of the neurotransmitter system leads to mental disorders and cognitive dysfunction [20]. More importantly, surgical trauma leads to an inflammatory reaction in the central nervous system, which is mediated by inflammatory cytokines, resulting in POCD related to changes in the hippocampal function. The brain tissue of elderly patients with progressive aging is often in a state of chronic inflammatory reaction for a long time. Under normal conditions, the inflammatory reaction of the central nervous system is an important defense mechanism of the central nervous system against external injury factors. However, the aging process and degenerative diseases of the central nervous system put the cerebral glial cells in a highly sensitive state. When they are stimulated by a peripheral inflammatory reaction or injury factors again, the central nervous system will produce an extensive inflammatory reaction [21].

There are some drawbacks to our study. First, in this study, the average hospitalization time of the elderly patients undergoing orthopedic surgery was 5-7 days, so we only observed the patients' cognitive function changes and analgesic effects 7 days after the surgery, and we did not carry out a long-term follow-up of the elderly patients after their discharge. Second, We did not discuss the optimal dose of dexmedetomidine. Therefore, we need to expand the sample size for further clinical observation, and then optimize the anesthesia management through dexmedetomidine and other drugs, so as to improve the perioperative and postoperative prognosis and the prognoses of elderly patients.

In conclusion, dexmedetomidine combined with epidural anesthesia can significantly reduce the incidence of postoperative cognitive dysfunction in elderly patients after general anesthesia, stabilize their hemodynamics, reduce their pain responses, and improve their postoperative quality of life.

## Disclosure of conflict of interest

None.

**Address correspondence to:** Guohui Le, Department of Anesthesiology, Traditional Chinese Medicine Hospital of Kunshan City, No. 189 Chaoyang Road, Kunshan 215300, Jiangsu, China. Tel: +86-18051899158; E-mail: 13773144544@163.com

## References

[1] Urits I, Orhurhu V, Jones M, Hoyt D, Seats A and Viswanath O. Current perspectives on postoperative cognitive dysfunction in the ageing population. Turk J Anaesthesiol Reanim 2019; 47: 439-447.
[2] Alalawi R and Yasmeen N. Postoperative cognitive dysfunction in the elderly: a review comparing the effects of desflurane and sevflurane. J Perianesth Nurs 2018; 33: 732-740.
[3] Kotekar N, Shenkar A and Nagaraj R. Postoperative cognitive dysfunction - current preventive strategies. Clin Interv Aging 2018; 13: 2267-2273.
[4] Damuleviciene G, Lesauskaite V and Macijauskiene J. Postoperative cognitive dysfunc-

tion of older surgical patients. Medicina (Kaunas) 2010; 46: 169-75.
[5] Ho YS, Zhao FY, Yeung WF, Wong GT, Zhang HQ and Chang RC. Application of acupuncture to attenuate immune responses and oxidative stress in postoperative cognitive dysfunction: what do we know so far? Oxid Med Cell Longev 2020; 2020: 9641904.
[6] Liu Y and Yin YQ. Emerging roles of immune cells in postoperative cognitive dysfunction. Mediators Inflamm 2018; 2018: 6215350.
[7] Carr Zyad J, Cios Theodore J, Potter Kenneth F and Swick John T. Does dexmedetomidine ameliorate postoperative cognitive dysfunction? A brief review of the recent literature. Curr Neurol Neurosci Rep 2018; 18: 64.
[8] Wu Y, Dou J, Wan X, Leng Y, Liu XK, Chen LL, ShenN, Zhao B, Meng QT and Hou JB. Histone deacetylase inhibitor MS-275 alleviates postoperative cognitive dysfunction in rats by inhibiting hippocampal neuroinflammation. Neuroscience 2019; 417: 70-80.
[9] Berger M, Oyeyemi D, Olurinde MO, Whitson HE, Weinhold KJ, Woldorff MG, Lipsitz LA, Moretti E, Giattino CM, Roberts KC, Zhou J, Bunning T, Ferrandino M, Scheri RP, Cooter M, Chan C, Cabeza R, Browndyke JN, Murdoch DM, Devinney MJ, Shaw LM, Cohen HJ and Mathew JP; INTUIT Investigators. The INTUIT study: investigating neuroinflammation underlying postoperative cognitive dysfunction. J Am Geriatr Soc 2019; 67: 794-798.
[10] Pratici E, Nebout S, Merbai N, Filippova J, Hajage D and Keita H. An observational study of agreement between percentage pain reduction calculated from visual analog or numerical rating scales versus that reported by parturients during labor epidural analgesia. Int J Obstet Anesth 2017; 30: 39-43.
[11] Monk TG, Weldon BC, Garvan CW, Dede DE, van der Aa MT, Heilman KM and Gravenstein JS. Predictors of cognitive dysfunction after major noncardiac surgery. Anesthesiology 2008; 108: 18-30.
[12] Laalou FZ, Jochum D and Pain L. Postoperative cognitive dysfunction (POCD): strategy of prevention, assessment and management. Ann Fr Anesth Reanim 2011; 30: e49-53.
[13] Lu J, Chen G, Zhou HM, Zhou QH, Zhu ZP and Wu C. Effect of parecoxib sodium pretreatment combined with dexmedetomidine on early postoperative cognitive dysfunction in elderly patients after shoulder arthroscopy: a randomized double blinded controlled trial. J Clin Anesth 2017; 41: 30-34.
[14] Zhang H, Wu ZL, Zhao X and Qiao Y. Role of dexmedetomidine in reducing the incidence of postoperative cognitive dysfunction caused by sevoflurane inhalation anesthesia in elderly patients with esophageal carcinoma. J Cancer Res Ther 2018; 14: 1497-1502.
[15] Zhang XP, Liu YR, Chai M, Yang HT, Wang G, Han M and Li DB. High-fat treatment prevents postoperative cognitive dysfunction in a hyperlipidemia model by protecting the blood-brain barrier via Mfsd2a-related signaling. Mol Med Rep 2019; 20: 4226-4234.
[16] Krupić F, Sadić S, Seffo N, Bišćevic M, Fazlić M, Čustović S and Samuelsson K. Experience of registered nurses in assessing postoperative pain in hip fracture patients with dementia. Med Glas (Zenica) 2018; 15: 75-80.
[17] Ding X, Gao X, Wang ZC, Jiang XL, Lu SM, Xu JJ, Qin GW, Gu ZF and Huang DX. Preoperative chronic and acute pain affects postoperative cognitive function mediated by neurotransmitters. J Mol Neurosci 2020; 71: 515-526.
[18] Bowyer AJ, Heiberg J, Sessler DI, Newman S, Royse AG and Royse CF. Validation of the cognitive recovery assessments with the Postoperative Quality of Recovery Scale in patients with low-baseline cognition. Anaesthesia 2018; 73: 1382-1391.
[19] Chen NP, Chen XF, Xie JP, Wu CL and Qian J. Dexmedetomidine protects aged rats from postoperative cognitive dysfunction by alleviating hippocampal inflammation. Mol Med Rep 2019; 20: 2119-2126.
[20] Zhu YS, Xiong YF, Luo FQ and Min J. Dexmedetomidine protects rats from postoperative cognitive dysfunction via regulating the GABA R-mediated cAMP-PKA-CREB signaling pathway. Neuropathology 2019; 39: 30-38.
[21] Yang W, Kong S, Zhu XX, Wang RX, Liu Y and Chen LR. Effect of dexmedetomidine on postoperative cognitive dysfunction and inflammation in patients after general anaesthesia: a PRISMA-compliant systematic review and meta-analysis. Medicine (Baltimore) 2019; 98: e15383.