

The Effect of Dexmedetomidine Pre-treatment on Postoperative Cognitive Dysfunction in Elderly Patients Undergoing General Anesthesia for Orthopedic Surgery

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Introduction. To investigate the intervention effect of edaravone pretreatment before general anesthesia and its effect on the incidence of postoperative cognitive dysfunction (POCD) in elderly patients undergoing orthopedic surgery.

Methods. A total of 94 elderly patients undergoing orthopedic surgery from June 2021 to June 2023 were selected and divided into a control group and an observation group by envelope method, with 47 cases in each group. The control group was injected with the same amount of normal saline before anesthesia induction, and the observation group was intravenously injected with edaravone before anesthesia induction. The effect of the two groups was evaluated 5 days after anesthesia, and the patients were followed up for 3 months. The Mini-mental State Examination (MMSE) score, visual analogue scale (VAS) score, inflammatory response, postoperative cognitive dysfunction (POCD) and incidence of adverse reactions were compared between the two groups.

Results. Both groups were accompanied by different degrees of cognitive impairment at different time points after operation. The MMSE scores of the observation group on the 1st, 3rd and 5th day after operation were higher than those of the control group ($P<0.05$). The VAS scores of the observation group at different time points after operation were lower than those of the control group ($P<0.05$). Both groups were accompanied by varying degrees of

inflammation and pain mediators after operation. IFN- γ in the observation group was higher than that in the control group ($P < 0.05$). The levels of IL-4, SP and β -EP were lower than those in the control group ($P < 0.05$). The incidence of POCD in the observation group was lower than that in the control group ($P < 0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P > 0.05$).

Conclusion. Edaravone pretreatment before general anesthesia in elderly patients undergoing orthopedic surgery can help reduce the impact on the cognitive level of patients, relieve pain and inflammatory response, and reduce the incidence of POCD, with high drug safety, which is worthy of promotion and application.

Keywords. Edaravone pretreatment; General anesthesia; Orthopedic surgery; Elderly patients; Postoperative cognitive dysfunction; Inflammatory response; Adverse reactions

INTRODUCTION

Orthopedic surgery accounts for a relatively high proportion of the elderly population. Due to the older age of patients, bone loss, and the fact that patients are often accompanied by chronic diseases such as osteoporosis and diabetes, the incidence of bone-related diseases in patients is high [1]. According to Wang Yating et al. [2], compared with conservative treatment, surgical treatment has the advantages of shorter time and faster postoperative recovery, and most patients can benefit from it. General anesthesia is widely used in elderly patients undergoing orthopedic surgery, which can ensure the smooth completion of the operation, help to strengthen the pain of patients, and reduce the perioperative stress response [3]. Postoperative cognitive dysfunction (POCD) has a high incidence in elderly patients after surgery. The main clinical manifestations are confusion and memory impairment, which increase the incidence of postoperative complications and affect the prognosis of patients [4]. Edaravone, as the preferred oxygen free radical scavenger, plays an important role in brain protection applications and can reduce neurological dysfunction [5]. This study mainly investigated the intervention effect of edaravone pretreatment before general

anesthesia in elderly patients undergoing orthopedic surgery and is reported as follows.

1 MATERIALS AND METHODS

1.1 General Information

A total of 94 elderly patients undergoing orthopedic surgery from June 2021 to June 2023 were selected and divided into two groups. There were 47 patients in the control group, 29 males and 18 females, aged (61-84) years, with an average age of (71.71±4.84) years. There were 9 cases of cervical spine surgery, 21 cases of lumbar spine surgery, 10 cases of femoral neck fracture surgery and 7 cases of femoral shaft fracture surgery. There were 47 patients in the observation group, 29 males and 18 females, aged (61-82) years, with an average age of (71.61±4.77) years. There were 6 cases of cervical spine surgery, 22 cases of lumbar spine surgery, 8 cases of femoral shaft fracture and 11 cases of femoral neck fracture surgery. There was no significant difference in general data between the two groups ($P>0.05$).

1.2 Inclusion and exclusion criteria

Inclusion criteria: (1) All patients were admitted to our hospital for orthopedic surgery [6] and underwent general anesthesia; (2) age ≥ 60 years, American Society of Anesthesiologists physical status I-III; (3) There was no history of allergy to anesthetics and edaravone. Exclusion criteria: (1) patients with respiratory diseases or abnormal preoperative cognitive function; (2) the presence of other central nervous system diseases, such as a history of cerebral infarction.

1.3 Methods

Both groups underwent general anesthesia, preoperative examinations were completed, detailed surgical methods were formulated, patients were treated with intravenous inhalation combined with tracheal intubation general anesthesia, intravenous infusion of midazolam (Jiangsu Enhua Pharmaceutical Co., LTD., Chinese medicine approval number H20031037, Specifications: 2ml:2mg) 0.1-0.15mg/kg, propofol (Henan Sinophasic Pharmaceutical Group Co., LTD.,

Sinophasic approval number: H20010368, Specification: 10ml: 100mg*5 / box *40 boxes/piece) 0.5-1.0mg/kg, sufentanil (Yichang Renfu Pharmaceutical Co., LTD., Chinese Medicine approval number H20054171, Specification: 1ml: Anesthesia was induced with 50 μ g (as sufentanil) 0.5 μ g/kg and cisatracurium (Shaanxi Xilicai Pharmaceutical Co., LTD., Chinese Medicine license H20213984, size: 5mg(as cisatracurium) 0.2mg/kg. After successful tracheal intubation, the anesthesia machine was connected and the patient's breathing was controlled. During the operation, according to the patient's body movement and stress response, sevoflurane (Lunan Pharmaceutical Group Shandong New Era Pharmaceutical Co., LTD., Chinese Medicine approval number H20233956) 0.6-1.5MAC, continuous infusion of propofol 20-50 μ g/ (kg·min), remifentanyl (Lizhu Pharmaceutical Group Co., LTD., Chinese Medicine approval number H20030197, Chinese Medicine approval number H20233956) were selected. Standard: 2mg) 0.1-0.2 μ g/ (kg·min), cisatracurium 0.1mg/kg was intermittently infused according to the patient's body movement and stress response. The control group was injected with the same amount of normal saline before general anesthesia induction, and the observation group was pretreated with edaravone intravenously before anesthesia induction. Edaravone (Hubei Tang Ren Pharmaceutical Co., LTD., Chinese Medicine approval number H20080495, specification: 20ml:30mg) 0.5mg/kg mixed with 100mL normal saline, intravenous drip, two groups of patients were evaluated 5 days after anesthesia, and completed 3 months of follow-up.

1.4 Indicators of observation

(1) Mini-Mental State Examination (MMSE) score; The cognitive level of patients in the two groups was evaluated by MMSE scale before operation and 1, 3 and 5 days after operation, and the higher the score, the better [7]. (2) Visual analogue scale (VAS) score. The VAS scale was used to evaluate the pain of patients at different time points before operation, 1 day, 3 days and 5 days after operation. The total score was 10 points, and the lower the score, the better [9]. (3) inflammatory response. The

levels of interferon- γ (IFN- γ), interleukin-4 (IL-4), substance P (SP) and endorphin (β -EP) were detected by enzyme-linked immunosorbent assay before and after operation in the two groups [9-10]. (4) postoperative cognitive dysfunction (POCD) and adverse reactions. The incidence of postoperative POCD, nausea and vomiting, respiratory depression, hypotension and tachycardia in the two groups were recorded.

1.5 Statistical Analysis

SPSS26.0 software was used to process the data. The enumeration data were analyzed by χ^2 test, expressed by n (%), and the measurement data were analyzed by t test, expressed by $(\bar{x} \pm s)$, $P < 0.05$ was statistically significant.

2 RESULTS

2.1 Comparison of MMSE scores between the two groups

Both groups were accompanied by different degrees of cognitive impairment at different time points after operation. The MMSE scores of the observation group at different time points after operation were higher than those of the control group ($P < 0.05$), as shown in Table 1.

Table 1 Comparison of MMSE between the two groups (score, $\bar{x} \pm s$)

Groups	Number of cases	Before surgery	One day after surgery	3 days after surgery	5 days after surgery
Observation group	47	28.42±1.51	27.89±1.16 [#]	26.61±0.98 [#]	26.02±0.79 [#]
Control group	47	28.45±1.54	26.32±0.98 [#]	25.01±0.78 [#]	24.43±0.63 [#]
T	/	0.063	2.551	3.312	4.098
P	/	0.615	0.031	0.029	0.000

Compared with preoperative, [#] $P < 0.05$.

2.2 Comparison of VAS scores between the two groups

Both groups were accompanied by different degrees of pain after operation, but with the extension of time after operation, the effect of anesthesia was reduced, the pain was increased, and the pain was the highest at 3 days after operation. The postoperative VAS score of the observation group was lower than that of the control group ($P<0.05$), as shown in Table 2.

Table 2 Comparison of VAS scores between the two groups (score, $\bar{x} \pm s$)

Groups	Number of cases	Before surgery	One day after surgery	3 days after surgery	5 days after surgery
Observation group	47	0.98±0.12	1.32±0.32 [#]	2.21±0.65 [#]	1.42±0.37 [#]
Control group	47	1.00±0.14	2.51±0.48 [#]	3.43±0.72 [#]	2.51±0.42 [#]
T	/	0.724	3.996	4.323	3.029
P	/	0.381	0.000	0.000	0.000

Compared with preoperative, [#] $P<0.05$.

2.3 Comparison of inflammatory responses between the two groups

Both groups were accompanied by varying degrees of inflammation and pain mediators after operation. IFN- γ in the observation group was higher than that in the control group ($P<0.05$). The levels of IL-4, SP and β -EP were lower than those in the control group ($P<0.05$), as shown in Table 3.

Table 3 Comparison of inflammatory responses between the two groups ($\bar{x} \pm s$)

Groups	Point of time	IFN- γ (ng/L)	IL-4 (ng/L)	SP (pg/mL)	β -EP (pg/mL)
Observation group (n=47)	Before intervention	11.62±0.94	5.36±0.84	41.25±4.69	94.31±6.45
	After the intervention	9.58±0.71 ^{#*}	6.71±0.91 ^{#*}	52.17±6.96 ^{#*}	112.15±7.93 ^{#*}

Control group (n=47)	Before intervention	11.64±0.96	5.41±0.86	41.27±4.71	94.34±6.59
	After the intervention	8.13±0.57*	8.47±0.98*	73.48±8.34*	132.89±10.26*

Compared with the control group, #P<0.05; Compared with that before intervention, *P<0.05
 2.4 POCD and safety were compared between the two groups

The incidence of POCD in the observation group was lower than that in the control group (P<0.05). There was no significant difference in the incidence of adverse reactions between the two groups (P>0.05), as shown in Table 4.

Table 4 Comparison of POCD and safety between the two groups [n (%)]

Groups	Number of cases	POCD	Drug safety				Incidence rate
			Depression of respiration	Nausea and vomiting	Low blood pressure	Tachycardia	
Observation Group	47	1 (2.13)	0 (0.00)	1 (2.13)	1 (2.13)	0 (0.00)	2 (4.26)
Control Group	47	7 (14.89)	2 (4.26)	1 (2.13)	1 (2.13)	1 (2.13)	5 (10.64)
χ^2	/	5.562	/	/	/	/	0.945
P	/	0.037	/	/	/	/	0.441

3 DISCUSSION

For general anesthesia cases, the incidence of POCD one week after surgery is 19.0%. For elderly fracture cases, due to the older age of patients, often accompanied by a variety of underlying diseases, and long-term immobilization and bed rest after fracture surgery, the incidence of POCD will increase [11]. In this study, both groups were accompanied by different degrees of cognitive impairment at different time

points after operation. The MMSE scores of the observation group on the 1st, 3rd and 5th day after operation were higher than those of the control group ($P < 0.05$). Both groups were accompanied by different degrees of pain after operation, but with the extension of time after operation, the effect of anesthesia was reduced, the pain was increased, and the pain was the highest at 3 days after operation. The postoperative VAS score of the observation group was lower than that of the control group ($P < 0.05$). The results showed that edaravone pretreatment for elderly patients undergoing orthopedic surgery under general anesthesia was helpful to improve the cognitive level of patients, consolidate the anesthesia effect, reduce the pain of patients, and facilitate the recovery of patients. Analysis of the reasons: Edaravone pretreatment, as a commonly used oxygen free radical scavenger, plays an important role in brain protection. Modern pharmacological results show that [12] edaravone has a strong inhibitory effect on free radical damage, reduces oxidative stress damage caused by anesthetic drugs during the perioperative period, helps to reduce the apoptosis rate of nerve cells, and thus reduces neurological dysfunction. In this study, both groups were accompanied by varying degrees of inflammation and pain mediators after operation. IFN- γ in the observation group was higher than that in the control group ($P < 0.05$). The levels of IL-4, SP and β -EP were lower than those in the control group ($P < 0.05$). The incidence of POCD in the observation group was lower than that in the control group ($P < 0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P > 0.05$). According to the results, edaravone can reduce the incidence of POCD and reduce the inflammatory stress response of the body produced by anesthesia, and most patients can benefit from it. Analysis of reasons: The use of edaravone can reduce vascular cognitive impairment, reduce inflammatory factors such as IL-4, SP and β -EP and pain levels, help to increase the expression of vascular endothelial growth factor, inhibit the inflammatory reaction of vascular cognitive impairment, improve vascular repair effect, and maximize the protection of the body's brain function, so as to reduce vascular cognitive impairment

[13-14]. Geng Ying et al. [15] showed that edaravone can help reduce cerebral oxygen consumption, improve cerebral blood flow and reduce energy metabolism disorders in elderly patients undergoing orthopedic surgery under general anesthesia. The drug can inhibit the expression of inflammatory factors during the perioperative period and play a good neuroprotective effect.

In conclusion, edaravone pretreatment before general anesthesia in elderly patients undergoing orthopedic surgery can help reduce the impact on the cognitive level of patients, relieve pain and inflammatory response, and reduce the incidence of POCD, with high drug safety, which is worthy of promotion and application.

ACKNOWLEDGEMENT

Conduct subregional, age-appropriate, real-world pain epidemiology studies

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