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Original Article

Effect of Edaravone on Postoperative Cognitive Function and Cerebral Oxygen Metabolism in Elderly Patients with Spinal Surgery☆

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SUMMARY

Background: To investigate the effect of edaravone on the postoperative cognitive function and cerebral oxygen metabolism in elderly patients with spinal surgery.
Methods: One hundred and twenty patients undergoing elective thoracolumbar surgery, aged 65–75 years, were randomly divided into two groups: edaravone group (Group E, $n = 60$) and control group (Group C, $n = 60$). At 30 minutes before anesthesia, the patients in Group E received 0.5 mg/kg edaravone, while the patients in Group C received the same volume of normal saline. Mini-mental state examination (MMSE) was performed at 1 day before the operation, and 1 day and 4 days after the operation.
Results: A total of 26 patients in both groups had postoperative cognitive dysfunction. Compared with the preoperative MMSE scores, postoperative MMSE scores decreased significantly in both groups ($p < 0.05$) and the reduction in the 1-day postoperative MMSE scores in Group E was remarkably lower than that in Group C ($p < 0.05$).
Conclusion: Edaravone can reduce the incidence of early postoperative cognitive dysfunction in elderly patients. The underlying mechanism may be related to improvement of cerebral oxygen metabolism.
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1. Introduction

Postoperative cognitive dysfunction (POCD) is an acute mental disorder syndrome caused by multiple-factor-induced deterioration of neurotransmitter system disorder in elderly people on the basis of central nervous system degeneration[1]. More than 200 years ago, it was first reported that postoperative amnesia symptoms occurred in elderly patients undergoing surgery with general anesthesia. And about 100 years ago, postoperative behavior disorder was first reported. However, the term POCD had just emerged and was clearly defined in recent decades[2]. There are many factors that can cause POCD. It has been reported that postoperative mental disorders are often the combined result of many factors, including advanced age, psychological and environmental factors, type and time of anesthesia, intraoperative hypoxemia and hypotension, hypertension, coronary heart disease, and diabetes[3–6]. One study also reported that the occurrence of POCD may be associated with cerebral oxygen metabolism[7]. A multicenter study showed that the incidence of POCD in elderly people undergoing non-heart surgery is as high as 25.8% within 1 week[4]. To date, the drugs used for improving cognitive function include cholinomimetics, cholinesterase inhibitors, calcium antagonists, and alkaloids[8]. As a new type of oxygen free radical scavenger, edaravone has good curative effect when it is used clinically for brain protection[9]. In this study, we aimed to explore the effect of edaravone on postoperative cognitive function and cerebral oxygen metabolism in elderly patients who underwent thoracolumbar surgery in our hospital, so as to provide some references for clinical medication.

2. Methods

2.1. Patients

One hundred and twenty elderly patients undergoing elective thoracolumbar surgery with general anesthesia were enrolled in

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this study. The patients were aged 65–75 years, and no consideration was given to their gender. All patients were American Society of Anesthesiologists Grade I or Grade II, without obvious abnormal preoperative coagulation and kidney function. Patients with severe lung disease, hypertension, abnormal blood sugar, or identified neurological or psychiatric disorders were excluded. Patients with cognitive dysfunction before surgery were also excluded by mini-mental state examination (MMSE). This study was conducted in accordance with the Declaration of Helsinki. This study was approved by the Ethics Committee in our hospital and written informed consent from each patient was also obtained.

2.2. Grouping and treatment

The patients were divided into two groups according to the random digits table method: edaravone group (Group E, $n = 60$) and control group (Group C, $n = 60$). At 30 minutes before anesthesia, the patients in Group E received 0.5 mg/kg edaravone (Nanjing Simcere Pharmaceutical Co., Ltd., Nanjing, China) by intravenous drip, while the patients in Group C received the same volume of normal saline.

2.3. Anesthesia

No premedication was applied to any patient before anesthesia induction. After the patients were sent into the operating room, a peripheral venous pathway was opened and intravenously dripped with lactic acid solution. Under local anesthesia, radial artery puncture and catheterization were carried out to monitor blood pressure and collect blood samples for blood gas analysis (GEM Premier 3000; Instrumentation Laboratory, Bedford, MA, USA). Electrocardiogram, heart rate, and peripheral capillary oxygen saturation of the patients were regularly monitored. After intravenous injection of 0.4 μg/kg sufentanil, 1–2 mg/kg propofol and 0.5 mg/kg rocuronium, the patients received an oral tracheal cannula and mechanical ventilation with an anesthesia machine (Dräger, Hanseatic City of Lubeck, Germany). The tidal volume was 8–10 mL/kg and inspiratory/expiratory volume was 1:2, with a ventilatory frequency of 10–12 times per minute. End tidal CO_2 tension was maintained between 35 mmHg and 40 mmHg (1 mmHg = 0.133 kPa). After intubation, retrograde puncture and catheterization were performed via the right internal jugular vein, leaving the catheter tip in the bulbar zone of the internal jugular vein. The tube was sealed with heparin for subsequent blood collection. Anesthesia was maintained with a trace pump at a speed of 4–6 mg/kg/h of propofol and discontinuous addition of 0.5 mg/kg atracurium for maintaining muscle relaxation. During the operation and according to the hemodynamic changes, 0.1–0.2 mg additional fentanyl could be used. After surgery, the endotracheal tube was withdrawn when the patient awakened and spontaneous breathing recovered (tidal volume > 6 mL/kg and respiratory frequency > 10 times/min). The patients were sent to the anesthesia recovery room with an oxygen mask and routinely monitored.

2.4. MMSE score

MMSE score was measured 1 day before the operation, and 1 day and 4 days after the operation for evaluating the cognitive function of each patient. Cognitive function was quantitatively evaluated by asking each patient a series of problems, including the directive force of the time and place, attention, calculation ability, short-term review of words, immediate memory, and ability to copy a graph. POCD was defined as postoperative MMSE score being reduced by 2 points as compared with the preoperative MMSE score. The highest MMSE score was 30 points, and > 27 points was regarded as normal[10].

2.5. Blood gas analysis

Blood samples were collected synchronously from the radial artery and the bulbar zone of the internal jugular vein immediately after anesthesia induction (T_0), 1 hour after anesthesia induction (T_1), and immediately after the operation (T_2) for blood gas analysis. The speed of blood withdrawal from the internal jugular vein was about 1 mL/min. Arterial oxygen content (CaO_2), internal jugular vein oxygen content ($CjvO_2$), arteriovenous oxygen content difference (Da-jvO_2), and cerebral extraction of oxygen ($CERO_2$) were calculated according to the following formula:

$$CaO_2 = 1.34 \times Hb \times SaO_2 + 0.0031 \times PaO_2; \quad (1)$$

$$CjvO_2 = 1.34 \times Hb \times SjvO_2 + 0.0031 \times PjvO_2; \quad (2)$$

$$Ca - jvO_2 = CaO_2 - CjvO_2; \quad (3)$$

$$CERO_2 = Da - jvO_2 \,/\, CaO_2 \times 100\%. \quad (4)$$

where Hb = hemoglobin; SaO_2 = arterial oxygen saturation; SjvO2 = internal jugular venous oxygen saturation; PaO_2 = arterial oxygen partial pressure; and $PjvO_2$ = internal jugular venous blood oxygen partial pressure.

2.6. Statistical analysis

SPSS version 15.0 statistical software (SPSS Inc., Chicago, IL, USA) was used to process the data in this study. Measurement data were shown as mean ± standard deviation. One-factor analysis of variance was used to compare the data among the groups and unitizing t test was performed for comparison between two groups. Enumeration data were compared using the χ^2 test. A p value < 0.05 was considered to be statistically significant.

3. Results

3.1. General data

The age, gender, weight, American Society of Anesthesiologists grade, anesthesia time, CaO_2, red blood cell count, and hemoglobin did not differ significantly between the edaravone group and control group ($p > 0.05$, Table 1).

3.2. MMSE scores

Compared with the preoperative MMSE scores, the MMSE scores in both groups were significantly reduced at 1 day after the operation ($p < 0.05$). Additionally, the reduction of MMSE scores in Group E was significantly lower than that in Group C ($p < 0.05$, Table 2).

3.3. Incidence of POCD

A total of 26 cases of POCD occurred at 1 day after the operation, including 10 in Group E (16.7%) and 16 in Group C (26.7%), showing a significant difference between the two groups ($p < 0.05$).

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