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SHORT COMMUNICATION

Recovery of postoperative cognitive function in elderly patients after a long duration of desflurane anesthesia: a pilot study

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Abstract Postoperative cognitive dysfunction (POCD) increases morbidity and mortality. The mechanisms underlying POCD remain elusive; however, systemic responses induced by anesthesia and surgery might trigger neuroinflammation and POCD. Desflurane is a preferable volatile anesthetic agent for elderly patients because it facilitates shorter recovery from general anesthesia. The aim of this study was to determine whether quality of emergence and cognitive function in elderly patients undergoing a long duration desflurane anesthesia are better than those in the case of sevoflurane anesthesia. Forty-two patients who were older than 65 years of age and scheduled for surgery of more than 4 h in duration were enrolled in this study. Patients were randomly assigned to a desflurane anesthesia group (D group) and sevoflurane anesthesia group (S group). General anesthesia was maintained with 3.5 % desflurane (D group) and 1.0 % sevoflurane (S group). The Mini-Mental State Examination (MMSE) was used for assessing cognitive function 24 h before and after surgery. Postoperative MMSE score in the D group was significantly improved compared to that in the preoperative period. In conclusion, elderly patients undergoing desflurane anesthesia have significantly better quality of emergence and may have better cognitive function than those in elderly patients undergoing sevoflurane anesthesia.

Keywords Desflurane · Geriatric surgery · Postoperative cognitive dysfunction

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Introduction

Postoperative cognitive dysfunction (POCD) increases morbidity and mortality, and advanced age is an independent risk factor for POCD [1]. The mechanisms underlying POCD remain elusive; however, it has been reported that a peripheral surgery-induced innate response triggered inflammation in the hippocampus and memory impairment [2]. It has also been reported that volatile anesthetics triggered POCD via neuroinflammation in the central nervous system [3]. These reports suggested that surgery and general anesthesia per se potentiated reversible and/or irreversible neuronal degradation and POCD. It has been reported that volatile anesthetics, isoflurane, sevoflurane and desflurane, at high concentrations demonstrated similar neurotoxic profiles in neonatal mice [4]. Thus, bispectral index-guided anesthesia has been reported to decrease the incidence of POCD by optimizing the dosage of anesthetic agents in clinical settings [5].

Desflurane is a preferable volatile anesthetic agent for elderly patients because it facilitates shorter extubation and recovery from general anesthesia as compared to sevoflurane [6, 7]. Desflurane has a low blood/gas partition coefficient and a property of undergoing rapid washing and washout [8]. Moreover, desflurane has been reported to augment laryngeal C-fiber inputs to nucleus tractus solitarii neurons by activating transient receptor potential-A1 [9]. These properties are likely to contribute to protective airway reflexes after general anesthesia and might contribute to better quality of emergence from general anesthesia than that of sevoflurane anesthesia [10].

Mini-Mental State Examination (MMSE) score is used to examine cognitive function frequently because it is useful for screening for dementia and delirium [11] and it can also be used for assessing the incidence of POCD [12].

However, POCD has only been evaluated in elderly patients who underwent general anesthesia for less than 2.5 h [12]. Since general anesthesia per se might potentiate neuronal inflammation, a long duration of surgery might be harmful for cognitive function. For emergence from general anesthesia, desflurane has been shown to have a great advantage over other anesthetics when the duration of surgery is more than 3 h [13].

The aim of this study was to determine whether quality of emergence and cognitive function in elderly patients undergoing a long duration of desflurane anesthesia are better than those in elderly patients undergoing a long duration of sevoflurane anesthesia.

Methods

After approval for the protocol of the present study by the ethics committee of our institution, informed consent was obtained in writing from all participating patients or their legal representative. Forty-two patients who were ASA physical status 1–2, older than 65 years of age and scheduled for surgery of more than 4 h in duration were enrolled in this study. Exclusion criteria were cardiovascular surgery, neurosurgery, pre-existing dementia, neurological disturbance, liver deficiency, renal deficiency, and psychiatric deficiency. This study was registered in the ClinicalTrials.gov database (NCT01700907). Using an electronically randomized method, patients were randomly assigned to a desflurane group (D group, $n = 21$) or sevoflurane group (S group, $n = 21$). Anesthesia was induced with propofol at 1.5–2.0 mg/kg and remifentanil at 0.25 μg/kg/min and was maintained with desflurane at 3.5 % (D group) or sevoflurane at 1.0 % (S group). Desflurane or sevoflurane was started from dialed concentration 3 or 2 %, respectively. The concentration of desflurane was gradually achieved an end tidal concentration of 5.2 % during 2 min. Tracheal intubation was facilitated when the end tidal concentration of desflurane or sevoflurane reach 5.2 or 1.5 %, respectively. The end tidal concentration of desflurane or sevoflurane was decreased to 3.5 or 1.0 %, respectively. After tracheal intubation, the infusion rate of remifentanil was adjusted to maintain systolic blood pressure in the range of 80–120 mmHg or to maintain systolic blood pressure when the anesthesia started ranging from more than 80 % to less than 120 %. Patients were mechanically ventilated with an inspired mixture of air and oxygen (3:1) at a fresh gas flow rate of 4-L/min. When surgery ends, the fresh gas flow rate was increased to 6-L/min (100 % oxygen). Extubation criteria was defined as follows: respiratory rate ≥8 times/min, tidal volume ≥5 mL/kg, systolic blood pressure ranging from 80 to 150 mmHg, body temperature ≥36.0 °C, recovering cough reflex, train-of-four ratio ≥0.9, and SpO_2 ≥97 %. Patients who had an epidural analgesia were administered as a continuous 4 mL/h infusion of 0.2 % ropivacaine and fentanyl (2 μg/mL). No opioids was added postoperatively, 50 mg flurbiprofen was administered at least every 6 h when patients required an additional analgesia agent. Patients' demographic data including gender, age, height, weight, and duration of surgery were recorded. The times from discontinuation of the administration of anesthetics to eye opening, to response to verbal commands, and to extubation were recorded for assessing emergence from anesthesia. Recovery system profiles of postoperative consciousness were evaluated by the modified Aldrete scoring system immediately after extubation and 6 h after surgery [14, 15]. MMSE was used for assessing cognitive function 24 h before and after surgery. The theoretical sample size needed for the present study was designed to have a power (1-β: >0.8) to detect an anesthetic effect based on the previous data that of a 60 % change of a SD in the MMSE score ($\alpha < 0.05$). Statistical comparisons were performed by using the unpaired t test, Wilcoxon signed-rank test, Mann–Whitney U test, and two-way ANOVA with Dunn's multiple comparison. $P < 0.05$ was considered statistically significant. Data are presented medians [25–75 percentile]. All statistical comparisons were performed with the use of GraphPad PRISM 6 software (GraphPad Software, Inc., CA, USA).

Results

The patients' demographic data are presented in Table 1. There was no significant difference between the groups. Assessment of the time to emergence from general anesthesia was based on the times from discontinuation of the administration of anesthetics to eye opening, to response to verbal commands, and to extubation. Figure 1 shows the times of emergence from general anesthesia. The times to eye opening, to response to verbal commands, and to extubation in the D group and S group were 187 [156–275] s (D group) and 315 [285–450] s (S group),

Table 1 Characteristics of surgical patients

	D group	S group
Female/male	11/10	12/9
Age (years)	74 ± 5	73 ± 6
Height (cm)	159 ± 10	157 ± 11
Weight (kg)	55 ± 9	59 ± 10
Duration of surgery (min)	313 ± 165	251 ± 151

Data are presented as number or mean ± SD

D group patients who underwent general anesthesia with desflurane

S group patients who underwent general anesthesia with sevoflurane

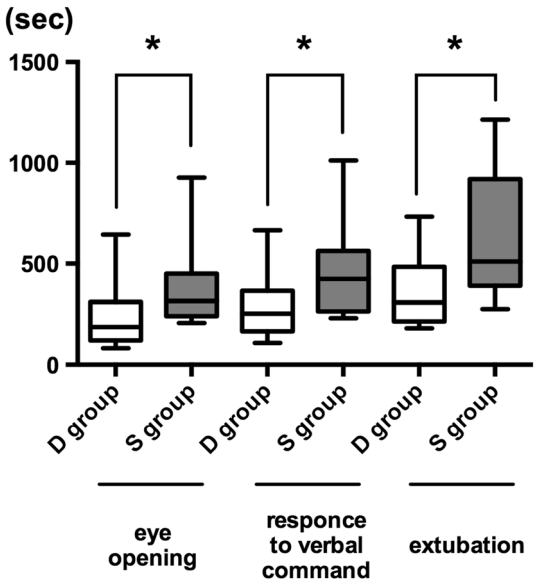

Fig. 1 Times from discontinuation of anesthesia to eye opening, to response to verbal commands, and to extubation. *D group* patients who underwent desflurane anesthesia, *S group* patients who underwent sevoflurane anesthesia. *$p < 0.05$

253 [193–363] s (D group) and 424 [395–558] s (S group), and 308 [221–464] s (D group) and 510 [416–801] s (S group), respectively ($P < 0.05$ in all groups). The modified Aldrete score and MMSE score are presented in Table 2. Figure 2 shows MMSE scores before and after surgery. The MMSE score in the D group in the preoperative period was significantly lower than that in the postoperative period.

Discussion

We demonstrated shorter emergence from general anesthesia in the D group than in the S group after a long surgery in elderly patients. Desflurane has been reported to be a preferable for elderly patients because of its small blood/gas partition coefficient [8]. Since desflurane has also been reported to increase sympathetic nerve activity, this sympathetic nerve activation might also contribute to rapid emergence from general anesthesia [16, 17]. The time for extubation from discontinuation of the anesthetic agent was approximately 200 s faster in the D group than in the S group in this study, and this result might indicate the protective effects of airway reflexes. Moreover, the modified Aldrete score in the D group was significantly higher than that in the S group after extubation, and our results suggest that desflurane anesthesia is superior to sevoflurane anesthesia in terms of quality of emergence from general anesthesia after long surgery. It has been reported that recovery from desflurane anesthesia was significantly faster than that from sevoflurane anesthesia in bariatric surgery [18]. As mentioned above, desflurane has been reported to have a protective effect for airway reflex and this property might contribute to the better quality of emergence from general anesthesia than that of sevoflurane.

In the present study, the MMSE scores in the D and S groups before and after surgery were comparable. Isoflurane, sevoflurane, and desflurane showed similar properties of neuronal toxicitiy in neonatal mice, [4] and neuroinflammation influences neuronal functioning either directly or through modulation of intraneuronal pathways such as the brain-derived neurotropic factor-mediated pathway [19]. On the other hand, desflurane has been reported to have protective effects for the neurologic outcome after cardiopulmonary bypass and hypoxic neuronal damage [20, 21]. Since the preoperative MMSE score in the D group was significantly lower than that in the postoperative period in the present study, our results indicated that desflurane anesthesia did not inhibit learning by repeat testing. Neither desflurane nor sevoflurane aggravate cognitive function after long surgery in elderly patients; however, desflurane anesthesia might be better for elderly patients in terms of quality of emergence.

Table 2 Numerical parameters of modified Aldrete scores and MMSE scores

Test	Time	D group	S group	*P* value
Modified Aldrete score	After extubation	9.0 [9.0–10.0]	8.8 [8.0–9.1]	0.049
	6 h after surgery	10 [10.0–10.0]	10 [10.0–10.0]	Not applicable
MMSE score	24 h before surgery	28.0 [26.0–29.0]	29.0 [25.1–30.0]	0.048
	24 h after surgery	29.0 [23.0–30.0]	28.0 [25.1–30.0]	

Data are presented as median [25–75 percentile]

D group patients who underwent general anesthesia with desflurane

S group patients who underwent general anesthesia with sevoflurane

MMSE Mini Mental State Examination

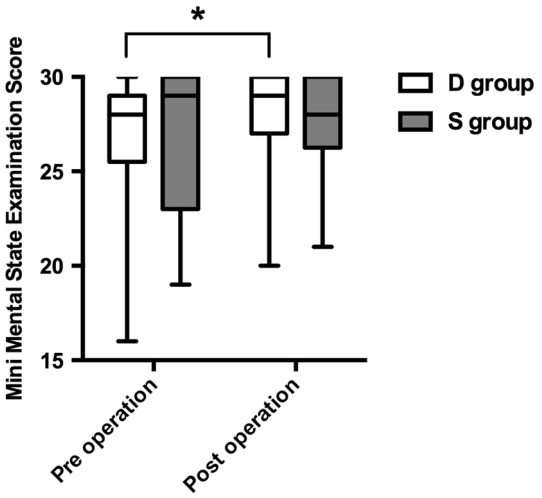

Fig. 2 Comparison of Mini-Mental State Examination score between before and 24 h after surgery. *D group* patients who underwent desflurane anesthesia, *S group* patients who underwent sevoflurane anesthesia. $*p < 0.05$

Conclusions

In the present study, we investigated the quality of emergence and cognitive function in elderly patients undergoing a long duration of desflurane or sevoflurane anesthesia. Increase in the MMSE score related to learning by repeat testing was inhibited by sevoflurane anesthesia but not by desflurane anesthesia. Elderly patients undergoing desflurane anesthesia have significantly better quality of emergence and may have better cognitive function than those in elderly patients undergoing sevoflurane anesthesia even with a long period of surgery.

Conflict of interest This work was financially supported by Baxter US.

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