Saudi Journal of Biological Sciences (2016) xxx, xxx–xxx

King Saud University

Saudi Journal of Biological Sciences

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ORIGINAL ARTICLE

Effect of sevoflurane and halothane anesthesia on cognitive function and immune function in young rats

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Received 13 July 2016; revised 13 August 2016; accepted 14 August 2016

KEYWORDS

Sevoflurane;
Halothane;
Immune function;
Cognitive response

Abstract In the current study, we scrutinized the effect of sevoflurane and halothane on cognitive and immune function in young rats. The rats were divided into following groups: sevoflurane, halothane and sevoflurane + halothane groups, respectively. The rats were regularly treated with the pre-determined treatment. We also scrutinized the serum proinflammatory cytokines including IL-10, IL-4 and IL-2; brain level IL-1β; hippocampal neuronal apoptosis concentration were estimated. The water maze test was performed in rats for the estimation of cognitive ability. During the water maze test, on the 1st day the sevoflurane group showed the latency; sevoflurane and sevoflurane + halothane group demonstrated the declined latency gradually as compared to the control group rats after the 3 days. The latency of the control, halothane, sevoflurane + halothane group rats showed the reduced latency and also showed the reduced crossing circle times. The hippocampal neuron apoptosis was significantly increased in halothane and sevoflurane + halothane group as compared to control group rats, respectively. Control group rats demonstrated the increased neuron apoptosis. The proinflammatory cytokines including IL-10 and IL-4 was significantly higher in sevoflurane, halothane and sevoflurane + halothane group rats after anesthesia and the whole brain IL-1β was significantly decrease in the sevoflurane, halothane and sevoflurane + halothane as compared to control group. Sevoflurane can inhibit the anesthesia effect of halothane on the immune and cognitive function of rats.

1. Introduction

Few of the studies showed the intravenous anesthetics does not show effects as analgesic but as having side effects on reducing respiration, which is commonly used in the clinical surgical treatmentv. Several studies revealed that the use of anesthesia can induce mental illness and cognitive destruction and other

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Peer review under responsibility of King Saud University.

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http://dx.doi.org/10.1016/j.sjbs.2016.08.002
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Please cite this article in press as: Qin, J.-H. et al., Effect of sevoflurane and halothane anesthesia on cognitive function and immune function in young rats. Saudi Journal of Biological Sciences (2016), http://dx.doi.org/10.1016/j.sjbs.2016.08.002

adverse effects (Gan et al., 2011; Chen, 2012). Infant's and neonatal central nervous system and immune response are still in the expansion stage and predominantly responsive to the external environment. The mechanism of the action of the anesthesia effect on the immune function and central nervous system is also still unclear (Sun et al., 2010). Moreover, the current experimental study aim was to scrutinize the possible effect of the sevoflurane and halothane on the immune response and cognitive function in young rats.

2. Material and methods

2.1. Experimental study

Swiss Albino (Wistar strain) rats were used for the current study. All the animals were procured from the department animal house. All the animals were kept in the single cage and fed with the normal diet and *ad libitum*. The rats were stored in the standard environmental condition; the rats were stored in the normal temperature 25 ± 2, relative humidity.

2.2. Experimental model

The Wistar rats were divided into the following groups and each group contains 20 rats. Before the experimentation study the rats adopted breeding for one week in animal house. The rats were divided into the following groups: group A, B and C. The rats from the normal control received the intraperitoneal injection of saline (0.9%) 1 mL every 2 h, followed for 3 days. Group A rats received the 1 mL intraperitoneal injection of sevoflurane (80 mg/kg) every 2 h, followed for 3 days. Group B rats received the 1 mL intraperitoneal injection of halothane (80 mg/kg) every 2 h, followed for 3 days. Group C rats received the 1 mL intraperitoneal injection of sevoflurane + halothane (80 mg/kg) every 2 h, followed for 3 days. In the current study, we used the intravenous injection dose 1 mL, if the dose is less than the 1 mL the drug dissolved in the saline. After 15 min of the anesthesia, half of the rats were sacrificed, and rest of the animal was using for the Morris water maze test after 3 weeks. All abandoned or died rats in midway were supplemented via modeling again.

2.3. Estimation of immune parameters

For the estimation of the immune parameters, all group rats' blood samples were collected from puncturing the percutaneous at the point of maximal impulse and collecting in the sterile EP tube. After collecting the blood samples, the blood samples were centrifuged at 3000 rpm for 30 min at 4 °C. The serum samples were separated after the centrifuged; the separated serum samples were stored in the −80 °C. The immune parameters such as IL-10, IL-4 and IL-2 concentration were estimated via using the ELISA.

2.4. Collection, preparation and indicator test of Brain tissue

After collection of blood samples, half of the rats were immediately selected. The rats heart was exposed through thoracotomy and the perfusion needle was inserted into the ascending arota from the left ventricle and fixed. Then the auricle (right) was cut into small pieces and washed using the saline at 4 °C until the right atrium was clean and clear. After that it was fixed into the paraformaldehyde (4%) phosphate buffer. Brain tissue was used for the separation of the hippocampal when the body and the body tissue were hard. The tissue was cut and paraffin embedded. The terminal deoxynucleotidyl transferase mediated nick end labeling (TUNEL) technique was used for the estimation of neuronal apoptosis. The 6 horizons were randomly selected and their average optical density was estimated. The apoptosis index and positive intensity was estimated using the following formula

$$Apoptotic\ index\ (AI) = MOD \times Area\% \times 100$$

where MOD represents the average gray level; the area% denotes the percentage of total positive nucleus area in the total nucleus area. The rest of the rats cerebral were obtained immediately via opening the cranium and tissue of brain was mixed in saline using the homogenizer. The brain tissues (10%) were homogenized and centrifuged at 3000 rpm for 20 min at 4°C. The supernatant samples were stored in the −80 °C for further use. The whole brain IL-1β was estimated via using the ELISA.

2.5. Morris water maze test

Morris water maze test used for scrutinized the behavior of the rats. Morris water maze test contains the four quadrants on the round tanks and at the fourth quadrant was fixed, which was fixed in the underwater 1 cm (Marsden et al., 2010). The rats were randomly selected and put into the water of the selected quadrants, and the camera was used for counting the swim tracks of the rats. The rats were finding the latency, we also calculated. After performing the current test, the platform was successfully removed and rats were dipped into the water till the same point, the time crossing of the rats was also calculated.

2.6. Statistical analysis

The result of the current study was presented as mean ± SD value and graph pad prism software was used for analysis of the data. $P < 0.05$ was considered as the statically significant.

3. Result

3.1. Effect of sevoflurane and halothane on hippocampal neuron apoptosis

The apoptosis assay of the hippocampal neurons was performed on the current study. The experimental group sevoflurane confirms the significantly enhanced hippocampal neuron apoptosis (15.4 ± 7.4%), as compared to the hippocampal neuron apoptosis (2.9 ± 1.3%) of the control group rats. But the halothane group rats showed the hippocampal neuron apoptosis (5.1 ± 2.1%), which was not significant as compared to the control group rats. The sevoflurane + halothane group rats confirm the increased hippocampal neuron apoptosis (11.3 ± 5.7%) as compared to the control group rats and significantly decreased as compared to the sevoflurane group rats.

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