Brief Communications

Evaluation of the Neuroprotective Effect of Thiopental and Its Effect on Serum NSE Level in Neurocritical Care Patients

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Abstract

Background: This study aimed to evaluate the neuroprotective effect of thiopental and its effect on serum NSE levels in neurocritical care patients.

Materials and Methods: Patients were divided into two groups (intervention and control). Thiopental administration as the intervention was started at a dose of 3-6 mg/Kg every 30 minutes and continued until 0.3-3 mg/Kg/hour. Sedation with fentanyl and midazolam as control was also performed in 35 patients. After three days, thiopental was discontinued. On the fifth day, the desired indicators were compared between the two groups.

Results: On the third and fifth days, patients in the intervention group had a greater drop in serum NSE levels ($P<0.05$).

Conclusion: The use of thiopental in patients undergoing neurosurgery transferred to the ICU can significantly reduce the NSE of these patients.

Keywords: Thiopental, Neuron-specific enolase (NSE), neurocritical care, ICU

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Introduction

Any damage to the brain, such as trauma or brain injury following brain surgery due to a tumor or bleeding, causes cell damage and the production of brain biomarkers (1). The most important biomarkers currently used to assess brain damage include B100S, Neuro Filament-H, and Neuro Specific Enolase (NSE) (2).

NSE is a common marker in brain injury (3) which is also present in many tissues other than the central nervous system (CNS) (4). Serum concentrations of this biomarker in serum, or cerebrospinal fluid (CSF), often increase dramatically in diseases that lead to relatively rapid degradation (5). On the other hand, measuring the level of this marker may also be useful as a prognostic indicator of nerve damage. For example, there is growing evidence that elevated serum NSE levels are associated with poor coma outcomes, especially when caused by a hypoxic condition.

Thiopental was the first agent of intravenous anesthesia to be tested in clinical trials for intraoperative neuroprotection (6). The ability of thiopental to reduce the consequences of central cerebral ischemia during heart surgery showed that preoperative thiopental administration significantly reduces the rate of persistent postoperative neuropsychological complications (7).

However, humans have conflicting evidence for the neuroprotective effects of thiopental (8). For this purpose, the present study was designed and performed to investigate the neuroprotective effects of thiopental and its effect on NSE in neurocritical patients in Imam Hussein Hospital of Shahid Beheshti University of Medical Sciences, Tehran.

Methods

According to the inclusion (Receiving written consent to participate in the study, neurosurgery 18>age>70 years) and exclusion criteria (History of kidney and liver disease, drug sensitivity (to midazolam, fentanyl, and thiopental), hypotension SBP<90 mmHg and bradycardia HR<60/min, hypertension, chronic patients, anemia, malignancy, inflammatory conditions and systemic infections, pneumonic operations, and emergency video-assisted thoracoscopic surgery (VATS)), patients were divided into two groups. In 35 patients (intervention group) who entered the intensive care unit (ICU) after neurosurgery, after determining the sequential organ failure assessment (SOFA) score and measuring the NSE upon entering the ICU, thiopental sedation was performed for three days. Therefore, thiopental administration was started at a dose of 3-6 mg/kg every 30 minutes and continued until 0.3-3 mg/kg/hr. Sedation with fentanyl and midazolam was also performed in 35 patients (control group). After three days, thiopental was discontinued, and all maintenance treatments were continued during this period. On day 5, NSE blood levels were measured, and the level of consciousness, ventilator dependence, and length of stay in the ICU were compared between the two groups.

The patient's demographic information, including age, sex, and history of previous diseases, was recorded. In patients, blood samples were taken for NSE and sedation level daily for up to five days. Samples were isolated for serum NSE measurement and evaluated at 2-8 ° C for 24 hours.

Student t-test and Mann-Whitney nonparametric test were used to compare the two groups' quantitative variables. All statistical tests were performed in two domains at a significant level of 5%. SPSS 23 software was used to analyze the data.

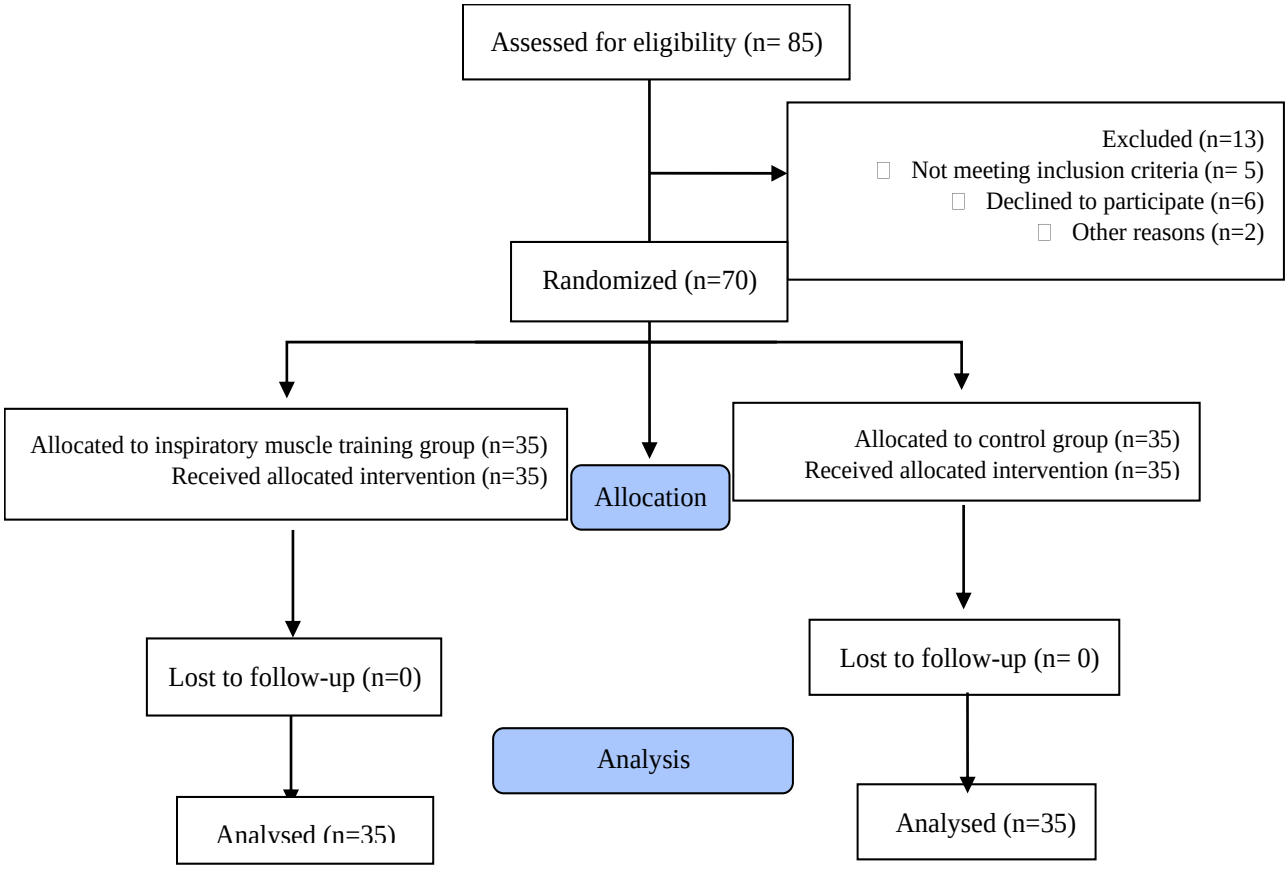

Figure 1. Flow diagram of patients participating and excluded. No harmful complications were reported in the two groups.

The Ethics Committee in Biomedical Research of Shahid Beheshti University of Medical Sciences reviewed the implementation process of this study and declared it applicable following its approved protocols (IR.SBMU.MSP.REC.1398.132).

Results

Of the 70 patients included in the study, 62.85% (44 people) were men, and 37.14% (26 people) were women, while the mean age of participants was 49.07 years (intervention group: 48.02 and Control group: 49.9 years). The two indices of GCS and SOFA scores of patients in the two groups at the time of admission to the ICU were not significantly different.

Examination and comparison of changes in the NSE index in both groups of patients in 5-day periods showed that this index has been declining. Thus, on the third and fifth days, changes in serum levels between the two groups were significantly significant (P <0.05), and patients in the intervention group experienced a greater drop in serum NSE levels (Table 1).

Discussion

Based on the results of the present study, changes in the NSE index showed that this index has been declining over time in both groups of patients. Thus, on the third and fifth days, changes in serum levels between the two groups were significantly significant (P <0.05), and patients in the intervention group (patients receiving thiopental sedation) had a greater drop in serum NSE levels.

Early reports from animal models of ischemia showed that barbiturates prescribed before, during, or after cardiac arrest improved neurological outcomes, while subsequent studies failed to show the neuroprotective effect of barbiturates in ischemic models. A recent study showed that thiopental before or after ischemia reduced nerve damage in gerbils, although post-ischemic thiopental treatment required higher doses than before ischemia (9). However, in comatose survivors, the neuroprotective effects of thiopental use on neurological outcomes have been controversial (10). The neuroprotective effect of barbiturates was initially attributed to their ability to reduce cerebral metabolism. However, electrophysiological doses comparable to different classes of barbiturates (thiopental, methohexital, and pentobarbital) can have different neuroprotective effects in the focal ischemia model (11-13). Barbiturate-mediated neuroprotection has been attributed to redistribution of cerebral blood flow to affected areas, obstruction of the Na channel and glutamate receptors, inhibition of calcium influx, inhibition of free radical formation, and enhancement of GABA-ergic activity.

Zhu et al. (14) showed that thiopental reduced NMDA and AMPA-mediated glutamate toxicity in hippocampal slices in vitro. Kimbro et al. also showed that pentobarbital could reduce AMPA toxicity in vivo rats (15). In addition, thiopental can increase intracellular calcium induced by ischemia in the hippocampus and cortex (16-18); however, the effects of thiopental on the CNS regarding immune system markers are possibly comparable with propofol (19).

However, the small volume of patients, on the one hand, and the small number of indicators studied, on the other hand, can be considered as limitations of our study. Therefore, it is suggested that in future studies, a larger volume of these patients be monitored while examining a larger number of indicators. However, using different doses of thiopental can also

Table 1: Evaluation and comparison of NSE index in the two groups of patients in three time periods at baseline, 3 days later and 5 days after ICU admission.

		Intervention (M±SD)	**Control** (M±SD)	**P.value**
NSE	**first day**	8.36±5.74	8.28±6.31	0.712
	third day	5.28±3.15	7.17±4.14	0.041
	fifth day	4.03±2.98	6.58±3.15	0.007

help to provide comparative results to provide the most effective dose.

Conclusion

The use of thiopental in patients undergoing neurosurgery transferred to the ICU can significantly reduce the NSE of these patients. However, there is no significant change in the SOFA score and Glasgow coma scale (GCS) indices. Therefore, using this drug as a neuroprotective agent in similar patients can be helpful.

Acknowledgment

None.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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