The Effect of N-Acetylcyctein (NAC) on Antioxidant Indices in Brain Traumatic Patients

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ABSTRACT

Introduction: Due to the various pharmacological effects of NAC and its relative harmlessness, tendency to use NAC has increased for various uses in the recent years. Therefore, the aim of this study was to investigate the effect of N-acetylcyctein (NAC) on antioxidant indices in brain traumatic patients. Method:. 120 patients due to traumatic brain injury with entry criteria were randomly divided into two groups: intervention and control groups. After blood sample was taken, and the initial values of SOD and GPX were recorded in the checklist. One hour after entering to the emergency department , the patients in the intervention group, received 200 mg NAC , diluted with 100 cc of normal saline solution , infused in half an hour. the patients in the control group received only 100 cc of normal saline solution , infusion in half an hour. Six hours after taking medication , re-sampling was done in all the patients and the results were recorded. Results: The results of this study showed that mean of GPX and SOD before the intervention, in two groups of the patients was not statistically significant ($p>0.05$); meanwhile, the mean of GPX and SOD after the intervention was statistically significant in both intervention and control groups ($p < 0.05$). Conclusion: According to the findings of this study, in which the results of the effect of NAC on the traumatic brain injury was evaluated positive and since NAC is a harmless drug, cheap, available and convenient drug.

Key Words: N-acetylcyctein, Antioxidant, Brain Trauma.

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INTRODUCTION

According to the definition of the National Organization of brain injury, traumatic brain injury refers to any brain injury caused by an external force which according to the severity of brain damage, can result in temporary or permanent physical, cognitive and behavioral damages [1]. Also traumatic brain injury is one of the known causes which result in long-term disability in people under the age of 45 [2]. It has been determined that intracranial inflammatory response occurs after brain injuries and it is the cause of secondary brain injuries after traumatic brain injuries [3].

In biological systems, the production of free radicals and active oxygen species is inevitable. Free radicals or oxidants have high chemical activity due to the presence of unpaired electrons and are constantly circulating in the body, and causing damage to macromolecules such as DNA, proteins, lipids, and carbohydrates [4]. In normal circumstances, free radicals are as sideways products of body oxygen metabolism which can destroy cell membranes, and also are able to react with genetic materials that cause the development and progression of many diseases [5].

Post-traumatic processes in the central nervous system are divided into two important phases: acute phase and chronic phase [6]. The acute phase is divided into two stages: the first stage is due to the trauma itself, and the secondary stage results from the release of chemical factors and cytokines.

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Chronic phase beginning depends on the mechanism and the spread of damage, so the more serious the damages, the more harmful cytokines will be produced over time [6, 7]. Damage of the blood-brain barrier, creation of cerebral edema, release of inflammatory cytokines and growth factors are delayed responses to traumatic brain injury [3]. Reducing the amount of cytokines that promote inflammation or vice versa, increasing anti-inflammatory cytokines can be considered as new therapies for reducing brain inflammation [3].

N-acetylcyctein (NAC) is the metabolite of cysteine and the specific antidote to acetaminophen. In fact, this drug is licensed by the FDA only for the treatment of acetaminophen poisoning, although it is commonly used in internal medicine for the treatment of idiopathic pulmonary fibrosis [8]. NAC is traditionally used as mucolytic and has anti microbial effects and vasodilator [9]. Considering the various pharmacological effects of NAC and its relative harmlessness, in recent years, the tendency to use NAC has been increased for various uses. Conducted studies so far on human and animal samples have demonstrated the effect of NAC on reducing free radicals and oxidant factors in brain cells, reducing cerebral edema, apoptosis, and antioxidants, and ultimately improvement of patients with traumatic brain injury [10-13].

Considering the factors such as the impossibility of doing brain biopsy in humans and the failure of repairing nerve cells during brain injury, the aim of this study was to investigate the effect of NAC on brain trauma patients.

METHOD

The study population consists of 120 patients with brain trauma (by using of primary examination and brain CT scan results) who referred to the emergency department of Vali - Asr Hospital in Arak,IRAN in 2017 . This study was approved by the Ethics Committee of Arak Medical University with the code IR.ARAKMU.REC.1395.97 and provided required descriptions about the study to all companions of the patients and written consent was received from all of them. Provisions of the Helsinki treaty were also considered. This study was conducted as a double blind randomized clinical trial. At first, all the patients with inclusion criteria (aged 18 years and more, referred patients with moderate brain trauma, Glasgow coma scale (GCS) between 9-13) were randomly divided into two intervention and control groups. By using a checklist, the patient's underlying information, were recorded.

Then the blood sample taken from the patient and the initial values of SOD and GPX were recorded in the checklist. One hour after entering to the emergency, patients in the intervention group, received 200 mg of NAC, diluted with 100 cc of normal saline solution, infused in half an hour.

The patients of the control group also received only 100 cc of normal saline solution, infused in half an hour.

Six hours after taking medication, re-sampling was done on all the patients and the results were recorded.

During the above period, required actions and routine head trauma were done for all the patients.

Finally, the collected data were analyzed by SPSS 16.

RESULTS

The study population included 120 moderate brain trauma patients.

43 women and 77 men were selected. The age mean of the patients was 37.56 ± 6, 25 years.

The results of the study showed that the vital signs of the patients in both groups were not significantly different before the intervention (p >0.05) (Table 1).

Also, the results of the statistical test showed that there was no significant difference between the mean amount of antioxidant indices of GPX and SOD in both groups before the intervention (p >0.05).

It was also shown that the mean amount of antioxidant indices of GPX and SOD in both groups after the intervention was significantly different (p >0.05) (Table 2).

Table 1: Demographic information

Variable	Intervention group	Control group	P value
age	35.56±3.61	36.26±4.56	.08
Systolic blood pressure	12.31±2.56	12.54±2.24	.09
Temperature	36.02±0/32	36.06±0/47	1
Heart beat	78±8.12	76±7.23	0.27
Number of breaths	16±1.23	17±0.9	0.4

Table 2: Value of GPX and SOD before and after intervention

Antioxidants		Intervention	Control	P value
Before the intervention	GPX	252±11.20	253±10.59	0.52
	SOD	109.51±9.23	107.48±9.08	0.65
After the intervention	GPX	274.02±10.80	253±10.89	0.000
	SOD	132.44±8.13	107.48±8.08	0.000

DISCUSSION

The aim of this study was to investigate the effect of N-acetylcyctein (NAC) in brain trauma patients. In the present study, which was designed as a clinical trial at Vali - Asr Medical Education Center of Arak, Iran in 2017-2018. 120 patients were divided into the intervention and

control groups. The present study indicated that most of the patients in the control and experimental group were between the ages of 21-30 years old (58.3% of the intervention group and 8.51% of the control group) and male were (80% of the intervention group and 78% of the control group). These statistics vary in different societies, but in most studies, such as Taiwan, the most common age group with brain trauma was reported to be 20-29 years old. The results of this study showed that SOD and GPX in brain traumatic patients were not significantly different before the intervention. The results of this study showed that SOD and GPX levels in Brain traumatic patients were significantly different after the intervention, so that in the brain traumatic patients who used N-acetylcyctein, SOD and GPX levels were higher. The antioxidant system of the body includes enzymatic and non-enzymatic agents. For example, it can be pointed to the vitamins of antioxidant enzymes of superoxide dismutase (SOD) and Glutathione peroxidase (GPX) [14]. Superoxide dismutase enzyme, is an enzyme which cleanses superoxide radicals (O2-) or hydrogen peroxide (H2O2). Superoxide dismutase and glutathione peroxidase enzymes confront with created damage by preventing the formation of free radicals and increasing the antioxidant defense [15].

Ewelina (2005) by comparing the SOD and GPX of patients with coronary artery atherosclerosis and patients with hyperlipidemia showed that the antioxidant activity of SOD and GPX in patients with coronary artery atherosclerosis is lower [16]. In a study, Kaynar (1995) measured the GPX and SOD of rates with spinal cord injury in one, four, and twenty-four hours after spinal cord injury, and did not show significant differences in their rates which is not consistent with this study [17]. Chen et al., in a study entitled "The inhibitory effect on the brain inflammatory reactions after a brain trauma in mice: potential neuroprotective mechanism of N-acetylcyctein" which conducted in 2008, showed that after traumatic brain injury, NAC administration can reduce inflammatory reactions in the mouse brain [10]. Nazıroğlu (2014) in a study entitled "Nervous protection with NAC and selenium (se) against brain injury caused by apoptosis and calcium entry in the rat hippocampus", showed that NCA and se have protective effects on oxidative stress, apoptosis, and entering of Ca ion through the activation of the TRPVI channel in the hippocampus of this brain traumatic model [12].

CONCLUSION:

According to the results of this study, the effect of NAC on the traumatic brain injury was evaluated positive and since NAC is a harmless, cheap, available and convenient drug, and since it had no serious complications in the proposed doses, its use is suggested.

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