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Study of Oxidative Stress and Antioxidants in Chronic Migraine

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Abstract
Migraine is the most common neurological disorder; on molecular basis it is still not completely understood. An impairment of mitochondrial oxidative metabolism might play a role in the pathophysiology. The aim of this present study was to investigate the differences in oxidative stress status with the measurement of glutathione reductase (GR), glutathione peroxidase (GPx), Superoxide dismutase (SOD), glutathione -s- transferase (GST) and total antioxidant (TAS). There were 110 patients selected in the migraine group and 50 age matched healthy subjects were selected in control group. It shows that the levels of GR, GPx, GST, SOD and total antioxidant were significantly decreased found in migraine patients before treatment compare to normal group as well as after treatment.
Keywords: *Migraine, OS, NO, rTMS, AMT, GST, GSH, MDA, SOD and TAS.*

Introduction

Migraine headache is kind of specific changes in the brain. It causes headache that is associated with the sensitivity of light, sound and smells. Some people having symptoms like nausea or vomiting. In some cases of migraine this type of headache is only one side of the head, are pulsating in nature, and last from two to 72 hours; patients may experience on both sides of head. The pain of a migraine is often described as throbbing or pounding and it may be made worse with physical exertion. Not all headaches represent migraines, and migraine is not the only condition that can cause severe and debilitating headaches. The pain is sometimes described as "drilling," and can be worse than migraine pain in some cases. Cluster headaches are less common than migraine.[1]

Common symptoms include: Eye pain, Sensitivity to light or sound, Nausea, Vomiting, Severe pain, usually on one side of the head that some individuals describe as "pounding"[2]. Globally, approximately 15% of people are affected by migraines.[3]

Migraines are to be due to a mixture of environmental and genetic factors. About two-thirds of cases run in family. Chang in hormone levels may also play an important role, as migraines affect slightly high in boys than girls before puberty and two to three times more women than men. Usually in pregnancy the risk of migraines decreases. They are, however, believed

to involve the nerves and blood vessels of the brain.[4-6]

Initially recommended treatment for chronic migraine is simple pain medication for headache ibuprofen and paracetamol (acetaminophen), for the nausea, and the avoidance of triggers. If simple medications not effective may be specific medications such as triptans or ergotamines are used. A number of medications are useful to prevent attacks including metoprolol, valproate, and topiramate.[7-8]

Oxidative stress occurs during normal metabolism from free radicals and from just about anything that hurts the body, such as pollution, food allergens, or smoke. Oxidative stress may lead to chronic inflammation and inflammation can also raise oxidative stress levels. Both play a large role in headache triggers and chronic diseases that are associated with migraines.

The antioxidant combination appeared to be effective in reducing both the frequency and the severity of migraines. Oxidative stress, which arises because of an imbalance between the production of reactive oxygen species (ROS) and elimination by antioxidant defense mechanisms, has been implicated in various headache disorders.[9] The pathophysiology of migraine is not well known. GR, GPx, GSH, SOD and TAS are the antioxidant enzymes which are known to have critical importance in antioxidant system. These enzymes affect free radicals in metabolic pathways in different places[10]. They have an important role in clearance of free radicals against tissue defect caused by these radicals. The role of antioxidant enzymes in migraine pathophysiology has been reported[11-12].

In this study, we investigate antioxidant enzyme activities which play an important role in the mechanism for clearing the free radicals in migraine and tension type headache.

Materials and Methods

The present study was conducted in the Dept. of Biochemistry in collaboration with Dept. of Medicine at Santosh Medical College Ghaziabad. Total 110 patients having more than five attacks of migraine headache were included in this study and compare with normal controls. Headache severities, frequency of headache and migraine index were noted. Out of 82 patients received repetitive transcranial magnetic stimulation (rTMS) therapy and 28 patients received Amitriptyline (AMT). Oxidative stress and level of antioxidant markers i.e. GR, GPx, GSH, SOD and TAS have been estimated in patients before and after treatment suffer from chronic migraine.

I. Selection of Patients

The study was conducted in the Dept. of Medicine in collaboration with Dept. of Biochemistry at Santosh Medical College Ghaziabad**.** Investigation was carried out in 110 patients suffer from chronic migraine after and before treatment and compared with 50 normal control group composed of age matched healthy subjects.

II. Collection of blood samples

Overnight fasting venous 5ml blood samples were collected from migraine patients before and after treatment and normal healthy control subjects in plain bulb and EDTA bulb. The plasma was separated from plain vacuum tube, aliquoted and stored at -20°C and used for the estimate glutathione reductase (GR), glutathione peroxidase (GPx), Superoxide dismutase (SOD), and total antioxidant (TAS). Serum GR, GPx, SOD and total antioxidant activity were measured by using ELISA and reagents kits will purchased from RANDOX Laboratories Ltd.[13-16]. Estimation of serum glutathione -s- transferase (GST) was carried as per method reported by Habig et.al 1974 [17].

III. Data Analysis

Data were expressed as mean ±SD. Mean values were assessed for significance by paired student –t test. A statistical analysis was performed using the Stastical Package for the Social Science program (SPSS, 23.0). Frequencies and percentages were used for the categorical measures. Probability values $p < 0.05$ were considered statistically significant.

Table no 1 Shows Age and sex wise distribution of Control group and Patients group

Age Group	Sex	Control group	Patients Group
16-20 yrs	Male	7	13
	Female	5	9
21-25 yrs	Male	6	14
	Female	13	13
26-30 yrs	Male	5	15
	Female	3	8
31-35 yrs	Male	4	10
	Female	3	13
Above 36	Male	2	9
	Female	2	6
Total		**50**	**110**

Observations and Results

Following table no 2, 3 and 4 showing the activity of GR, GPx, GST, SOD and TOS in control group, before treatment and after treatment in chronic migraine patients.

Table 2 shows the antioxidant activity in migraine patients and control group

Antioxidants	Control group	Migraine patients (Before Treatment)	'P' Value
GR (µg/HB)	9.27 ±1.74	3.51 ± 1.15	0.001
GPx (µg/HB)	172.34 ±28.49	64.51± 15.11	0.001
GST (µg/HB)	4.98 ± 1.27	1.90±0.26	0.001
SOD (µg/HB)	292.26± 68.40	169.35± 74.21	0.001
Total Antioxidant (umolT/L)	1.37±0.27	1.12±0.19	0.53

Table 3 shows the antioxidant activity before and after treatment in migraine patients

Antioxidants	Before Treatment	After Treatment	'P' Value
GR (µg/HB)	3.51 ± 1.15	8.95 ± 1.38	0.001
GPx (µg/HB)	64.51± 15.11	173.14 ± 29.93	0.001
GST (µg/HB)	1.90±0.26	5.02 ± 1.97	0.001
SOD (µg/HB)	169.35± 74.21	295.44 ±67.95	0.001
Total Antioxidant (umolT/L)	1.23±0.19	1.35±0.28	0.72

Table 4 shows the antioxidant activity in control group and after treatment

Antioxidants	Control group	Migraine patients (After Treatment)	'P' Value
GR (µg/HB)	9.27 ±1.74	8.95 ± 1.38	0.93
GPx (µg/HB)	172.34 ±28.49	173.14 ± 29.93	0.97
GST (µg/HB)	4.98 ± 1.27	5.02 ± 1.97	0.90
SOD (µg/HB)	292.26± 68.40	295.44 ±67.95	0.89
Total Antioxidant (umolT/L)	1.37±0.27	1.35±0.28	0.98

Table 2 shows that the activity of GR, GPx, GST, SOD and total antioxidant in migraine patients, and normal control group. It shows that the levels were significantly decreased found in migraine patients before treatment compare to normal group as well as after treatment. Table no 3 shows that the levels of antioxidant enzymes were significantly increased found after treatment. And table no 4 shows levels of antioxidant enzymes were not significant after treatment and in normal control group.

Discussion

Migraine is a neurovascular disorder that involves spreading cortical depression, neurogenic inflammation, and dysfunction in cranial vascular

contractility[18]. Noxious free radicals produced as a result of metabolic and physiologic processes are normally neutralized by enzymatic and non-enzymatic antioxidant systems. The balance can shift towards a state of oxidative stress due to an increased production of free radicals or a deficiency in antioxidant defense mechanisms[19]. Oxidative stress can damage membrane lipids, nucleic acids, proteins, and extracellular matrix components, including proteoglycans and collagens[20].

Migraines and migraine triggers are associated with oxidative stress. Antioxidants help to stop oxidative stress and migraines. Oxidative stress occurs from free radicals, a normal byproduct of digestion. An excessive amount of free radicals results from things that damage the human body, such as headache triggers. Antioxidants stop oxidative stress by donating themselves to these free radicals that would otherwise attack other stable molecules and cause havoc on the human body.

According to Dr. Mark Hyman glutathione and its isoenzymes were coined the mother of all antioxidants. Migraines are associated with oxidative stress and antioxidants stop oxidative stress. Glutathione recycles boost your glutathione levels to crush oxidative stress and migraines. Unfortunately, headache triggers such as a poor diet, pollution, medications, disease, toxins, and stress can deplete glutathione levels. Low antioxidant levels will not only trigger migraines, but will also leave your immune system wide open to chronic infections and diseases.

Some studies assess activity of antioxidant enzymes in migraine patients are very few and seem to provide divergent results [21-23]. Some researchers have reported changes in platelet SOD in migraine with aura[22] or higher levels of Nitric Oxide (NO) metabolites in migraine[21]. In a group of 28 migraine sufferers, the activities of antioxidant enzymes in erythrocytes were significantly higher as compared to the control group and patients with tension-type headaches [24]. Researchers from India Shukla R et. al., in a group of 55 migrainous patients found no significant differences in the activities of antioxidant enzymes in neutrophils or platelet SOD as compared to the control group[23]. Couch and Hassanein,[25] provided evidence that migraine is a potential risk factor or marker for atherosclerosis-related diseases. SOD protects against vasoconstriction or vasospasm induced by superoxide radicals. The activities of the antioxidant enzymes did not correlate with age, disease duration or the length of time since the last attack. In controversy to our study we showed that the activity of total antioxidant was not significant but the activity of antioxidant enzymes were significantly decreased found as compare to control group.

However, some findings of researcher concerning the oxidant-antioxidants enzyme concentration in migraine are conflicting for many other reasons. Important factors might be age of patients, time of treatment and doses of drugs. Furthermore, some studies assessed the activity of antioxidant enzymes in serum, other in erythrocytes, platelets and neutrophils.

Conclusion

The findings suggest that oxidative stress is increased in the chronic migraine patients and treatment abolishes the stress in part. On the basis of our result and some supportive study we, concluded that antioxidant activity might be helpful for the patients with chronic migraine to prevent oxidant stress.

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