

## ORIGINAL RESEARCH

**Assessment of Role of Tocopherol in Treating Epilepsy Patients**Kanhaiya Prasad<sup>1</sup>, Vidyasagar Ram<sup>2</sup>, Ashish Gautam<sup>3</sup>**ABSTRACT**

**Introduction:** Tocopherol inhibits the effects of oxidation in brain tissues (antioxidant) and is a free radical scavenger. Free radical scavengers have been implicated in the epileptic brain injury caused by prolonged seizures due to hyperoxia. Aim: assessment of role of tocopherol in treatment of epilepsy.

**Material and methods:** The present study was conducted in the department of psychiatry of medical institution. The selection of patients was done from the list of patients reporting to the outpatient department. In the present study, patients aged between 16-65 years who reported to outpatient department with prediagnosis of epilepsy were selected. For control group we selected 50 healthy individuals who self volunteered to participate in the study. The demographic characteristics of the patients were collected using a questionnaire. For the measurement of MDA levels in blood platelets, 5 ml of blood was drawn from each patient and sent to laboratory for evaluation.

**Results:** Out of 250 patients, 85 patients belonged to Epileptic group, 66 to Epileptic with psychiatric group, 49 to Psychiatric group and 50 to control group. The level of MDA was statistically significantly much increased in patients having epilepsy with psychiatric co-morbidity. The average values of SOD were significantly lower in epilepsy patients, epilepsy with psychiatry patient, psychiatry patients in the comparison with the control group.

**Conclusion:** The levels of MDA are significantly higher in epileptic patients and thus, antioxidant therapy is significantly helpful in epileptic patients.

**Keywords:** antioxidant, epilepsy, MDA, oxidative stress, tocopherol

**How to cite this article:** Kanhaiya Prasad, Vidyasagar Ram, Ashish Gautam. Assessment of role of tocopherol in treating epilepsy patients. *International Journal of Contemporary Medical Research* 2015;2(5):1428-1431.

<sup>1</sup>Associate Professor, Department of Medicine, GCRG Medical College, Lucknow, <sup>2</sup>Assintant Professor, Department of Medicine, Uttar Pradesh University of Medical Sciences, Saifai, Etawah, UP, <sup>3</sup>Associate Professor, Department of Medicine, S N Medical College Agra, UP, India

**Corresponding author:** Dr. Vidyasagar Ram, Assintant Professor, Department of Medicine, Uttar Pradesh University of Medical Sciences, Saifai, Etawah, UP, India

**Source of Support:** Nil

**Conflict of Interest:** None

**INTRODUCTION**

Epilepsy, a psychological disorder is a chronic disease and recurrent unprovoked seizures are characteristic to epilepsy.<sup>1</sup> An epileptic seizure alludes to transient event of signs and additionally side effects because of abnormal intemperate or synchronous neuronal action in the cerebrum. All PWE (persistent with epilepsy) have seizures however every one of the individuals who have seizures do not have epilepsy.<sup>2</sup> Numerous hereditary, radiological, and biochemical inquires have been performed to decide the etiology of this disorder. The inhibition of gamma-amino butyric acid (GABA) excitation of neurons is weakened, and raised excitatory neurotransmitters are most contributory to the pathophysiology of epilepsy.<sup>3,4</sup> Production of free radicals has a part in the direction of organic capacity and harm to cell structures, and in addition in the pathogenesis of neurodegenerative maladies, for example, Parkinsonism, stroke, epilepsy, and dementias, in the focal sensory system. Most likely, the oxidative stress has an important role in the pathophysiology of epilepsy. Tocopherol represses the impacts of oxidation in mind tissues (cell reinforcement) and is a free radical forager.<sup>5</sup> The brain injury of an epileptic patient due to delayed seizures occurs because of hyperoxia and this can be stabilized by free radical scavengers. An anticonvulsant activity of Vitamin E has been exhibited in the intracerebral ferrous chloride model of epilepsy.<sup>6</sup>

Hence, the present study was planned to assess the role of tocopherol in treatment of epilepsy.

**MATERIALS AND METHOD**

The present study was conducted in the department of psychiatry of medical institution. The ethical approval for the protocol of the study was obtained from ethical committee of institute prior to starting the study. The selection of patients was done from the list of patients reporting to the outpatient department.

**Inclusion criteria were:**

- Age ranging between 18-65 years
- Prediagnosed epilepsy for 5 years or more
- Negative history of systemic illness
- Negative history of taking medication for epilepsy

**Exclusion criteria were:**

- Significant pathology in MRI
- Pregnancy
- Cardiac disorders

- Previous history of using antioxidant drugs
- Diabetes mellitus

In the present study, patients aged between 16-65 years who reported to outpatient department with prediagnosis of epilepsy were selected. For control group we selected 50 healthy individuals who self volunteered to participate in the study. An informed signed consent was obtained from all the patients after explaining to them about the procedure of the study. A total of 250 patients participated in the study. The patients were divided into 4 groups based on their condition. The patients were grouped into Epileptic group, Epileptic with psychiatric group, Psychiatry group and Control group. In the Epileptic group, the number of patients was 85; in Epileptic with psychiatric group, the number of patients was 66; in Psychiatry group, the number of patients was 49 and in Control group, the number of patients was 50. The demographic characteristics of the patients were collected using a questionnaire. A questionnaire was given to all the patients and instructions were given to fill the questionnaire.

For the measurement of MDA levels in blood platelets, 5 ml of blood was drawn from each patient and sent to library for evaluation. The serum was extracted from the blood and MDA levels were determined using Northwest MDA assay kit according to manufacturer’s instructions. The determined levels of MDA for each patient were recorded and data stored for analysis.

**STATISTICAL ANALYSIS**

The statistical analysis of the data was done using Statistical Package for Social Sciences (SPSS) program for windows. The significance of the data was checked using Chi-square test and Student’s-t-test. A p-value<0.05 was predefined to be statistically significant.

**RESULTS**

A total of 250 patients were included in the study. Out of 250 patients, 85 patients belonged to Epileptic group, 66 to Epileptic with psychiatric group, 49 to Psychiatric group and 50 to control group. Table 1 shows the average levels of MDA in patients in epileptic patients, epilepsy with psychiatric patients, only psychiatric patient and control group. On comparing, we observed that the level of MDA was statistically significantly much increased in patients having epilepsy with psychiatric co-morbidity (p<0.001), rather than isolated pure epilepsy and pure psychiatric patients in both the sexes. Table 2 shows the average levels of SOD in platelets of epileptic patients, epileptic with psychiatric patients and control group according to sex. We observed that the average values of SOD were significantly lower in epilepsy patients, epilepsy with psychiatry patient, psychiatry patients in the comparison with the control group. The results are statistically significant (p<0.001). The values of SOD were much lower in epileptic patients when they are associated with psychiatric illness (p<0.001) in male and female sexes.

**DISCUSSION**

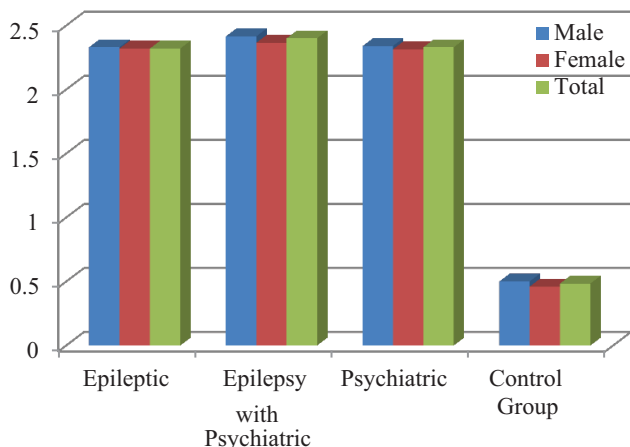
The membrane integrity is disturbed due to peroxidation of membrane lipids because the membrane lipids containing unsaturated fats are especially delicate to oxidative stress.<sup>7,8</sup> The regularly harmed layers are repaired and one essential repair system is reacylation of the phospholipids in the film. There are reports that lipid peroxidation hinders this reacylation process.<sup>9</sup> Because of elevated content of polyunsaturated unsaturated fats, the nervous system is more susceptible to damaging effects of oxidative stress.<sup>10</sup> It gets an extensive level of oxygen and is moderately lacking in cell reinforcement chemicals. It has been recommended that an expansion in the free radicals may cause neuronal degener-

Groups			Epileptic	Epilepsy with psychiatric	Psychiatric	Control group
Sex	Male	No.	59	43	34	29
		Mean	2.33	2.415	2.34	0.50
		SD	0.30	0.225	0.225	0.169
		t	30.529	39.475	36.104	-
		p	<0.001	<0.001	<0.001	-
	Female	No.	26	23	15	21
		Mean	2.32`	2.365	2.315	0.460
		SD	0.22	0.19	0.22	0.111
		T	35.340	40.078	33.27	-
		p	<0.001	<0.001	<0.001	-
	Total	No.	85	66	49	50
		Mean	2.32	2.40	2.33	0.484
		SD	0.27	0.215	0.22	0.145
		t	44.477	55.918	50.018	-
p		<0.001	<0.001	<0.001	-	

**Table-1:** Showing average levels of MDA in platelets in epileptic patients, epilepsy with psychiatric patients and only psychiatric patient and control group

Groups			Epileptic group	Epileptic with psychiatric group	Psychiatry group	Control group
Sex	Male	No.	59	43	34	29
		Mean	3.40	3.36	3.41	4.41
		SD	0.42	0.42	0.49	0.23
		t	12.090	12.278	11.083	-
		p	<0.001	<0.001	<0.001	-
	Female	No.	26	23	15	21
		Mean	3.39	3.28	3.37	4.37
		SD	0.49	0.44	0.43	0.24
		t	8.377	10.061	8.918	-
		p	<0.001	<0.001	<0.001	-
	Total	No.	85	66	49	50
		Mean	3.40	3.33	3.41	4.39
		SD	0.42	0.48	0.40	0.236
		t	15.367	14.412	14.980	-
		p	<0.001	<0.001	<0.001	-

**Table-2:** Showing average levels of SOD in platelets of epileptic patients, epileptic with psychiatric patients and control group according to sex



**Figure-1:** Showing Average level of MDA in different groups

ation through per-oxidation and reduction in the glutathione peroxidase levels. These free radicals have been ensnared in the advancement of numerous intense and constant infections of the cerebrum, similar to epilepsy, cerebrovascular disease, Alzheimer's illness, and so forth. In the human cerebrum, there is an unmistakable provincial dissemination of thio-barbituric-corrosive (TBA) positive materials in the endogenous pool, with larger amounts in the cerebellar vermis and lower levels in the thalamus, cortical areas, substantia nigra, caudate core, pallidum, putamen, thalamus and the pineal organ. Oxidative anxiety worsens the etiology of epilepsy.<sup>10,11</sup>

The present study was planned to assess the role of tocopherol in treatment of epilepsy. We observed that the level of MDA was statistically significantly increased in patients having epilepsy with psychiatric co-morbidity. The average values of SOD were significantly lower in epilepsy patients, epilepsy with psychiatry patient, psychiatry patients in the comparison with the control group. Similar results were found in studies by other authors. Dönmezdil N et al

assessed regardless of whether an expansion in oxidative markers is connected specifically with the confusion, autonomous of epileptic medicament. Thirty individuals healthy and 30 recently determined to have epilepsy and who got mobile treatment in the polyclinic of the Neurology Department partook in the examination. The tests identifying with serum malondialdehyde (MDA) levels and paraoxonase 1 (PON1) action were completed in the natural chemistry research facility. Despite the fact that the levels of MDA in the patient gathering were observed to be high contrasted with those of the control gathering, which comprised of individuals healthy, there was no factually huge distinction. PON1 action in the serum taken from individuals in the patient gathering was bring down in contrast with that saw in the serum of the control gathering. In any case, it was not all that low as to have noteworthiness from a factual perspective. The creators reasoned that such an abnormal state of oxidative parameters ought to have been identified with the malady and that factually huge discoveries that developed in some different investigations could have been identified with an antiepileptic treatment. Pandey MK et al assessed malondialdehyde (MDA) as a marker of oxidative worry in epilepsy with psychiatric co morbidity. The study had 210 examples which were separated in 5 bunches including age and sex coordinated control. The MDA development was assessed utilizing the level of thiobarbituric corrosive receptive substances (TBARS) utilizing spectrophotometry. The measurable examination was finished by utilizing SPSS programming and results were portrayed with unpaired T test and p esteem. MDA levels were fundamentally higher in epilepsy with psychiatric co grimness, psychosis and misery than control. On assist examination, the MDA levels were higher in people of epilepsy with psychiatric co bleakness than with psychosis or depression. The creators presumed that the level of oxidative stress was fundamentally higher in

epilepsy with co horrible psychiatric disease when contrasted with control.<sup>12,13</sup>

Sudha K et al decided the exercises and groupings of erythrocyte film lipid peroxidation, the rate hemolysis, erythrocyte compounds superoxide dismutase (SOD), glutathione peroxidase (GP), glutathione reductase (GR), catalase, and plasma vitamin C, vitamin E, vitamin An and ceruloplasmin in 29 epileptic patients and 50 typical controls. Ten patients who were treated with phenobarbital and who did not get shakings for 1 year were considered for followup. Lipid peroxidation and rate hemolysis in patients with epilepsy was altogether higher when contrasted with controls. In addition, plasma ceruloplasmin fixations were additionally uniquely expanded in these cases. Erythrocyte GR and plasma vitamin C and A focuses were altogether lower in epileptics when contrasted with controls. In the followup patients, the erythrocyte GR was altogether higher than their pre-treated condition. Besides, the plasma vitamin An, E and C focuses had accomplished the ordinary range. This examination showed that the cancer prevention agent status in blood of epileptic patients which was low contrasted with controls, enhanced after treatment, recommending that free radicals might be involved in epilepsy. Pandey MK contemplated the level of the lipid peroxidation items i.e. malondialdehyde (MDA) as a marker of oxidative worry in epilepsy patients. This case control think about had 170 examples which involved Group I(n-90) patients of epilepsy as the cases, which were contrasted and Group II (n-80) which were age and sex coordinated controls. The lipid peroxidation item i.e. MDA development was evaluated by surveying the levels of thio-barbituric corrosive responsive substances (TBARS) by utilizing spectrophotometry. The mean MDA esteem in Group I ( $2.38 \pm 0.31$ ) was essentially brought than up in Group II, in this manner proposing that the MDA esteems were brought up in epilepsy. The mean MDA level following 1 year of treatment was  $2.25 \pm 0.25$ , with a p estimation of  $<0.05$ , along these lines recommending a lessening in the oxidative worry with treatment. This presumes the level of the lipid peroxidation is fundamentally higher in epilepsy when contrasted with the control and oxidative anxiety builds which were found with the term of the epilepsy. The oxidative anxiety had no huge distinction in the guys and females. The oxidative anxiety was found to decrease on sufficient antiepileptic therapy.<sup>14,15</sup>

## CONCLUSION

From the results of present study, we conclude that levels of MDA are significantly higher in epileptic patients and thus, antioxidant therapy is significantly helpful in epileptic patients.

## REFERENCES

1. Epilepsy and Related Disorders. In: Ropper A, Brown RJ (Eds.). Adams and Victor –Principle of Neurology.,

- 8th Ed, Boston: McGraw-Hill Professional, 2005. p. 271-278.
2. Aguiar CC, Almeida AB, Araújo PV, et al. Oxidative stress and epilepsy: literature review. *Oxid Med Cell Longev.* 2012;2012:795259.
3. Kong Q, Lin CL. Oxidative damage to RNA: mechanisms, consequences, and diseases. *Cell Mol Life Sci.* 2010;67:1817–1829.
4. Chang S-J, Yu B-C. Mitochondrial matters of the brain: mitochondrial dysfunction and oxidative status in epilepsy. *J Bioenerg Biomembr.* 2010;42:457–459.
5. Soderfeldt B, Blennow G, Kalimo H, et al. Structural changes accompanying bicuculline induced seizures in rats following manipulations of tissue oxygenation or alpha-tocopherol levels. *Acta Neuropathol.* 1983;60:80-91.
6. Willmore J, Watson RR, Jackson JC, et al. The role of iron induced hippocampal peroxidation in acute epileptogenesis. *Brain Res.* 1986;382:422-26.
7. Zaleska MM, Wilson DF. Lipid hydroxyperoxides inhibit the reacylation of phospholipids in the neuronal membranes. *J. Neurochem.* 1989;52:255-260.
8. Kaneko M, Panagia V, Paolillo G, Majumder S, Ou C, et al. Inhibition of cardiac phosphatidyl ethanolamine-N-methylation by oxygen free radicals. *Biochim. Biophys. Acta.* 1989;1021:33-38.
9. Coyle JT, Puttfarcken. Oxidative stress, glutamate and neurodegenerative disorder. *Science.* 1993;262:689-93.
10. Boehme DH, Kosecki R, Carson S. Lipid peroxidation in human and rat tissue. *Brain Research.* 1977;136:11-21.
11. Oliver CN, Starke-Reed PE, Stadtman ER, Lin GJ, Correy JM, Floyd RA. Oxidative damage to the brain proteins, loss of the glutamine synthetase activity and production of free radicals during ischaemia/ reperfusion induced injury to the gerbil brain. *Proc Natl Acad Sci USA.* 1990; 87:5144–47.
12. Dönmezdil N, Çevik MU, Özdemir HH, Taşın M. Investigation of PON1 activity and MDA levels in patients with epilepsy not receiving antiepileptic treatment. *Neuropsychiatric Disease and Treatment.* 2016;12:1013-1017.
13. Pandey MK, Mittra P, Maheshwari PK. Oxidative stress in epilepsy with comorbid psychiatric illness. *Natl J Physiol Pharm Pharmacol.* 2013;3: 92-96.
14. Sudha K, Rao AV. Oxidative stress and antioxidants in epilepsy. *Clinica Chimica Acta.* 2001;303:19-24.
15. Pandey MK, Mittra P, Maheshwari PK. The lipid peroxidation product as a marker of oxidative stress in epilepsy. *Journal of Clinical and Diagnostic Research.* 2012; 6:590-592.