**Harsukh Educational Charitable Society**
**International Journal of Community Health and Medical Research**
Journal home page: www.ijchmr.com doi: 10.21276/ijchmr
Official Publication of "*Harsukh Educational Charitable Society*" [Regd.]

**ISSN E**: 2457-0117 **ISSN P:**2581-5040 **RNI No. -** PUNENG/2017/75049 **Index Copernicus value 2016 =** 52.13

# Original Article

## Evaluation Of Role Of Tocopherol In Treating Epilepsy Patients: A Clinical Study

Deva Lal Kast

Senior Consultant Physician, Department of General Medicine, Krishna Hospital, Ex senior Specialist and Principal Medical Officer, M.G. Government District Hospital, Bhilwara (Raj), India

***ABSTRACT*:**
**Background:** Epilepsy is a vert prevalent and important neurological condition around the world. At least 50 million people around the globe are affected by the disorder and around 100 million people have experienced seizure at least once during their lives. oxidative stress is the chief reason behind the neurodegenerative conditions such as epilepsy.4-11 Vitamin E is found in the roots of wheat and vegetable oils. The most crucial portion of this substance is the α portion because it comprises of 90% of the tocopherol composition of the animal tissues. The present study was conducted with the aim to evaluate the role of tocopherol in the management of epilepsy cases. **Materials and methods**: The present prospective study was conducted in the Department for a period of 1 year. Subjects taking two anticonvulsant drugs in the past 6 months and having 2 seizures per month were included in the study. Patients taking carbamazepine, sodium valproate, levetiracetam, or a combination of them and not taking any Vitamin E supplement were enrolled in the study All the subjects underwent EEG before the beginning of the treatment. Regular follow ups were performed for a period of 6 months and EEG changes and biochemical markers were measured amongst them. Chi square and independent t test were used to compare the results. Probability value of less than 0.05 was considered as significant. **Results:** A total of 60 subjects were enrolled in the present study with 30 subjects in each group. The mean age of cases was 29.8+/-5.1 years and the mean age of controls was 29.6+/-8.2 years. There was no significant difference between the groups. The mean antioxidant capacity of cases before and after treatment was 6.3+/-2.2 mg/dl and 7.7+/-2.3 mg/dl respectively. The mean antioxidant capacity of controls before and after treatment was 7.4+/- 2 mg/dl and 7.3+/-2.2mg/dl respectively. **Conclusion:** Increase in the oxidative stress can be implicated for causing brain damage and hence seizures. There was a considerable improvement in the seizure frequency amongst subjects that were given Vitamin E.

Keywords: Neurological , Oxidative , Tocopherol

**This article may be cited as**: Kast D. Evaluation Of Role Of Tocopherol In Treating Epilepsy Patients: A Clinical Study. HECS Int J Comm Health Med Res 2018;4(2):90-93

**Corrseponding Author :** Dr. Deva Lal Kast, Senior Consultant Physician, Department of General Medicine, Krishna Hospital, Ex senior Specialist and Principal Medical Officer, M.G. Government District Hospital, Bhilwara (Raj), India

## INTRODUCTION

Epilepsy is a vert prevalent and important neurological condition around the world. At least 50 million people around the globe are affected by the disorder and around 100 million people have experienced seizure at least once during their lives. This disease has physical, psychological, social, and economic impact. Its prevalence varies between 5.8/1000 to 10.3/1000 people in developed countries and developing countries respectively.[1] The most common treatments for epilepsy include use of antiepileptic drugs. The most commonly used drugs are valproate sodium, phenytoin, carbamazepine, phenobarbital, and lamotrigine and levetiracetam. Usually combinations of drugs are used to manage epilepsy. The choice of drug depends upon the type of seizures and the portion of brain involved. One of the actions of carbamazepine and sodium valproate and levetiracetam is by the impact on the course of oxidative stress.[2-5] Valproic acid also decreases the concentration of the mitochondrial coenzyme A which is produced by the conversion of the valproate to

valproyl-CoA in the existence of adenosine triphosphate and coenzyme A. This affects fatty acid oxidation and impairs synthesis of ATP. [1,6] Cells of brain are sensitive to reactive oxygen species. This stress can cause damage to the biological molecules of the brain. This oxidative stress is the chief reason behind the neurodegenerative conditions such as epilepsy.[4-11] Vitamin E is found in the roots of wheat and vegetable oils. The most crucial portion of this substance is the α portion because it comprises of 90% of the tocopherol composition of the animal tissues. Vitamin E prevent the negative effects of lipid peroxidation on the brain tissue since it absorbs oxygen free radicals. Various studies have shown the result of Vitamin E on the management of epilepsy. In a recent study Vitamin E was used as adjunctive therapy in the management of epilepsy in children whose seizures were not controlled, and its use resulted in significant improvement. It carries no side effects of risks of toxicity.[6,12,13] The present study was conducted with the aim to evaluate the role of tocopherol in the management of epilepsy cases.

## MATERIALS AND METHODS

The present prospective study was conducted in the Department for a period of 1 year. All the subjects were informed about the study and a written consent was obtained in their vernacular language. The study included subjects between 20-50 years of age. Subjects taking two anticonvulsant drugs in the past 6 months and having 2 seizures per month were included in the study. Patients taking carbamazepine, sodium valproate, levetiracetam, or a combination of them and not taking any Vitamin E supplement were enrolled in the study. The basic demographic information, the frequency of seizures and EEG findings were noted. The venous blood sample was obtained to measure biomarkers involved in the oxidative process of total antioxidant capacity, catalase, and malondialdehyde. Plasma antioxidant capacity was established using Benzie IF method. Catalase activity was assessed using Goth spectrophotometry method. Serum malondialdehyde levels was estimated using the method given by Satoh. The subjects were randomly divided into the cases and the control group. The controls received placebo like those given to the cases. The physician did not know about the medication prescribed. All the subjects underwent EEG before the beginning of the treatment. Regular follow ups were performed for a period of 6 months and EEG changes and biochemical markers were measured amongst them. Interpretation of EEG were randomly carried out by physicians. The before and after treatment values were compared. All the data was arranged in a tabulated form and analyzed using SPSS software. Chi square and independent t test were used to compare the results. Probability value of less than 0.05 was considered as significant.

## RESULTS

A total of 60 subjects were enrolled in the present study with 30 subjects in each group. Table 1 illustrates the baseline characteristics of the study population. The mean age of cases was 29.8+/-5.1 years and the mean age of controls was 29.6+/-8.2 years. There was no significant difference between the groups. There were 43.3% males and 56.7% females amongst the cases and 30% males and 70% females were seen in control group. There were 33.3% of cases with focal seizures and 53.3% subjects with generalized seizures. There were 63.3% controls with focal seizures and 43.3% with generalized seizures. There was no significant difference in the baseline characteristics of the study. Table 2 shows the antioxidant efficacy and seizure frequency of the study. The mean antioxidant capacity of cases before and after treatment was 6.3+/-2.2 mg/dl and 7.7+/-2.3 mg/dl respectively. The mean antioxidant capacity of controls before and after treatment was 7.4+/- 2 mg/dl and 7.3+/- 2.2mg/dl respectively. There was significant difference in the antioxidant levels in cases before and after treatment. The mean catalase levels amongst cases before and after treatment were 14.4+/-5.2 and 16.6+/-4.3 respectively. There was a significant difference in the mean catalase levels before and after treatment. The mean Glutathione levels amongst cases before and after treatment were 14.6+/- 6.2 and 18.4+/-7.3 respectively. There was a significant difference in the mean catalase levels before and after treatment. The seizure frequency amongst cases and controls initially was 2 and after treatment was 1 amongst cases and 2 amongst controls. There was a significant improvement in the seizure frequency amongst the cases.

**Table 1: Baseline characteristics of the study population**

| VARIABLE | CASES (N=30) | CONTROLS (N=30) | P VALUE |
|---|---|---|---|
| **Age** | 29.8+/-5.1 | 29.6+/-8.2 | >0.05 |
| **Gender** | | | |
| **Males** | 13(43.3%) | 9(30%) | >0.05 |
| **Females** | 17(56.7%) | 21(70%) | |
| **Type of seizures** | | | >0.05 |
| **Focal seizures** | 10(33.3%) | 19(63.3%) | |
| **Generalized seizures** | 16(53.3%) | 13(43.3%) | |

## DISCUSSION

In subjects with epilepsy, deficiency of Vitamin E has been seen, this deficiency has been majorly due to antiepileptic therapy, and on the contrary the antiepileptic action of Vitamin E hasn't been confirmed yet.[14,15] In the previous studies, it has been shown that amongst epileptic subjects lipid peroxidation and glutathione peroxidase are parameters of oxidative stress and were significantly higher compared to controls and the levels of Vitamin C, E, and A, i.e. the antioxidant substances were significantly lower amongst the epileptics when compared to

controls, and therefore it was suggested that free radicals may be implicated in epilepsy.[16,17] Vitamin E is able to cross the blood-brain barrier and collect at high concentration in the brain.[18] Therefore, it suggests that in suppression of seizures and neuronal damage, supplementation with Vitamin E could be helpful

**Table 2: Antioxidant efficacy and seizure frequency of the study**

| VARIABLE | | BRFORE TREATMENT | AFTER TREATMENT | P VALUE |
|---|---|---|---|---|
| **antioxidant capacity(mg/dl)** | cases | 6.3+/-2.2 | 7.7+/-2.3 | <0.05 |
| | Controls | 7.4+/- 2 | 7.3+/- 2.2 | >0.05 |
| **Catalase (µ/ml)** | cases | 14.4+/-5.2 | 16.6+/-4.3 | <0.05 |
| | Controls | 17.6+/-4.9 | 17.3 +/- 5.2 | >0.05 |
| **Glutathione** | cases | 14.6+/- 6.2 | 18.4+/-7.3 | <0.05 |
| | Controls | 15.4 +/- 5.5 | 16.4+/-5.6 | >0.05 |
| **Malondialdehyde (nmol/ml)** | cases | 12.5+/-4.2 | 11.6+/-3.7 | >0.05 |
| | Controls | 15.3+/-5.1 | 15.4+/-5.8 | >0.05 |
| **Seizure frequency** | cases | 2 (2-2) | 1 (1-2) | <0.05 |
| | Controls | 2 (2-2) | 2 (2-4) | >0.05 |
| | P value | >0.05 | <0.05 | |

Studies conducted on animals have concluded that Vitamin E has an anticonvulsant effect amongst animal seizure models. [19] According to our study, the mean antioxidant capacity of cases before and after treatment was 6.3+/-2.2 mg/dl and 7.7+/-2.3 mg/dl respectively. The mean antioxidant capacity of controls before and after treatment was 7.4+/- 2 mg/dl and 7.3+/- 2.2mg/dl respectively. There was significant difference in the antioxidant levels in cases before and after treatment. The mean catalase levels amongst cases before and after treatment were 14.4+/-5.2 and 16.6+/-4.3 respectively. There was a significant difference in the mean catalase levels before and after treatment. The mean Glutathione levels amongst cases before and after treatment were 14.6+/- 6.2 and 18.4+/-7.3 respectively. There was a significant difference in the mean catalase levels before and after treatment. The seizure frequency amongst cases and controls initially was 2 and after treatment was 1 amongst cases and 2 amongst controls. There was a significant improvement in the seizure frequency amongst the cases. According to a double-blind study by Raju *et al.* Vitamin E an adjunctive therapy was compared to placebo amongst subjects with uncontrolled epilepsy. After two complete treatment phases no significant difference was observed between the vitamin E and placebo group.[20] Other studies have shown that management with Vitamin E have additional beneficial effects on activity of seizure and neurodegeneration induced by pentylentetrazol[21] or pilocarpine.[22] Moreover, Vitamin E weakened the lipid peroxidation process and elevated catalase activity after pilocarpine-induced seizure and decreased the blood-brain barrier disruption after pentylentetrazol-induced seizure.[21]

## CONCLUSION

Increase in the oxidative stress can be implicated for causing brain damage and hence seizures. In our study, Vitamin E or tocopherol decreased the oxidative load on brain and thus aided in protecting against oxygen free radicals. There was a considerable improvement in the seizure frequency amongst subjects that were given Vitamin E.

## REFRENCES


1. Aguiar CC, Almeida AB, Araújo PV, de Abreu RN, Chaves EM, do Vale OC, *et al.* Oxidative stress and epilepsy: Literature review. Oxid Med Cell Longev 2012;2012:795259.
2. Nemade ST, Melinkeri R. Effect of antiepileptic drugs on antioxidant status epilepsy. Curr Neurobiol 2010;1:109-12.
3. Schulpis KH, Lazaropoulou C, Regoutas S, Karikas GA, Margeli A, Tsakiris S, *et al.* Valproic acid monotherapy induces DNA oxidative damage. Toxicology 2006;217:228-32.
4. Yis U, Seçkin E, Kurul SH, Kuralay F, Dirik E. Effects of epilepsy and valproic acid on oxidant status in children with idiopathic epilepsy. Epilepsy Res 2009;84:232-7.
5. Aycicek A, Iscan A. The effects of carbamazepine, valproic acid and phenobarbital on the oxidative and antioxidative balance in epileptic children. Eur Neurol 2007;57:65-9.
6. Boon NA. Davidson's Principles and Practice of Medicine. 20th ed. USA: Churchill Livingstone, Elsevier; 2006.
7. Fisher RS van Emde Boas W, Blume W, Elger C, Genton P, Lee P, *et al*. Epileptic seizures and epilepsy: Definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). Epilepsia 2005;46:470-2.
8. Ahlen L. The effect of sodium valproat on folat levels, transmethylation, homocysteine and oxidative stress: Is there a link with neurodegeneration and continued seizure? Nutr Pract 2011;12:36-60.
9. Vega Rasgado L, Ceballos Reyes G, Vega-Diaz M. Anticonvulsant Drugs, Oxidative Stress and Nitric Oxide. In Proceeding Western Pharmacology Society; 2011.
10. Thanoon IA, Pachachi OA, Al-Sheikh MM. Effect of carbamazpin on serum leptin, insulin levels and

oxidative stress in epileptic patients. Ann Coll Med Mosul 2012;38:40-5.
11. Ogunmekan AO, Hwang PA. A randomized, double-blind, placebo-controlled, clinical trial of D-alpha-tocopheryl acetate (Vitamin E), as add-on therapy, for epilepsy in children. Epilepsia 1989;30:84-9.
12. Nazıroğlu M. Role of selenium on calcium signaling and oxidative stress-induced molecular pathways in epilepsy. Neurochem Res 2009;34:2181-91.
13. Verrotti A, Scardapane A, Franzoni E, Manco R, Chiarelli F. Increased oxidative stress in epileptic children treated with valproic acid. Epilepsy Res 2008;78:171-7.
14. Asif M. Role of various Vitamins in the patients with epilepsy. IJPR 2013;3:34.
15. Higashi A, Tamari H, Ikeda T, Ohtani Y, Matsukura M, Miyoshino S, et al. Serum Vitamin E concentration in patients with severe multiple handicaps treated with anticonvulsants. Pediatr Pharmacol (New York) 1980;1:129-34.
16. Sudha K, Rao AV, Rao A. Oxidative stress and antioxidants in epilepsy. Clin Chim Acta 2001;303:19-24.
17. Veinbergs I, Mallory M, Sagara Y, Masliah E. Vitamin E supplementation prevents spatial learning deficits and dendritic alterations in aged apolipoprotein E-deficient mice. Eur J Neurosci 2000;12:4541-6.
18. deficits and dendritic alterations in aged apolipoprotein E-deficient mice. Eur. J. Neurosci 2000;12:45414-16.
19. Levy SL, Burnham WM, Hwang PA. An evaluation of the anticonvulsant effects of Vitamin E. Epilepsy Res 1990;6:12-7.
20. Raju GB, Behari M, Prasad K, Ahuja GK. Randomized, double-blind, placebo-controlled, clinical trial of D-alpha-tocopherol (Vitamin E) as add-on therapy in uncontrolled epilepsy. Epilepsia 1994;35:368-72.
21. Kaya M, Cimen V, Kalayci R, Kucuk M, Gurses C, Arican N, et al. Catalase and alpha-tocopherol attenuate blood-brain barrier breakdown in pentylenetetrazole-induced epileptic seizures in acute hyperglycaemic rats. Pharmacol Res 2002;45:129-33.
22. Tomé AR, Feng D, Freitas RM. The effects of alpha-tocopherol on hippocampal oxidative stress prior to in pilocarpine-induced seizures. Neurochem Res 2010;35:580-7.

.

**Source of support:** Nil **Conflict of interest:** None declared



.