RESEARCH ARTICLE

Oxidative Stress in Epilepsy with Comorbid Psychiatric Illness

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ABSTRACT

Background: Free radicals have been implicated in the development of various acute and chronic diseases of brain. The present cross sectional study was designed to illustrate the oxidative stress in epilepsy with co morbid psychiatric illness using malondialdehyde as only few studies were available in this context.

Objective: To evaluate the malondialdehyde (MDA) as a marker of oxidative stress in epilepsy with psychiatric co morbidity.

Materials and Methods: The present cross sectional study had 210 samples which were divided in 5 groups including age and sex matched control. The MDA formation was estimated using the level of thiobarbituric acid reactive substances (TBARS) using spectrophotometry. The statistical analysis was done by using SPSS software and results were described with unpaired T test and p value.

Results: MDA levels were significantly higher in epilepsy with psychiatric co morbidity, psychosis and depression than control. On further comparison, the MDA levels were higher in persons of epilepsy with psychiatric co morbidity than with psychosis or depression.

Conclusion: Level of oxidative stress was significantly higher in epilepsy with co morbid psychiatric illness as compared to control.

KEY WORDS: Epilepsy; Psychosis; Depression; Malondialdehyde (MDA); Lipid Peroxidation Product (LPP)

INTRODUCTION

Epilepsy is a chronic disorder characterized by recurrent unprovoked seizures.[1] An epileptic seizure refers to transient occurrence of signs and or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. All PWE (patient with epilepsy) have seizures but all those who have seizures to not have epilepsy. Seizures occurring in a setting of an acute illness or medical condition like high fever, hypoglycemia etc. are classified as acute symptomatic seizures.[2] The association of epilepsy and psychiatry has a long history. Hippocrate's supposition that "epileptics become melancholics" reflects current thinking of a unidirectional relation between depression and epilepsy, because depression is the most frequent psychiatric co-morbidity in epilepsy.[3] The possible relationship of epilepsy leading to psychosis is development of behavioral abnormality might be due to social stigma, intractable disease, consequence of epileptic activity and treatment of epilepsy or hyperactivity, impulsive behavior or socially maladaptive behavior, increase likelihood of head trauma or drug and alcohol intoxication.

Lipids are an important component of cell membrane. Peroxidation of lipids is implicated in pathogenesis of number of diseases and clinical conditions .These include diabetes, adult respiratory distress syndrome, premature birth disorder, aspects of shock, parkinson 's disease, Alzheimer's disease, preclampsia and eclampsia, various chronic inflammatory conditions, ischemia reperfusion mediated injury to organs including heart brain and intestine, atherosclerosis, organ injury associated with shock and inflammation, fibrosis, cancer, inflammatory liver injury, anthracycline induced cardiotoxicity, silicosis and pneumoconiosis.[4-7] Various studies had evaluated the oxidative stress in epilepsy in several animal models[8,9] and its correlation in human beings[10-12]. The present study had been planned with the aim of studying the level of malondialdehyde in epilepsy patients with psychiatric illness as only few studies regarding this had been known.

MATERIALS AND METHODS

The present cross sectional study was performed in epilepsy and psychiatric patients of attending medicine and neurology clinic of the tertiary care centre in Agra (India) in 2008 to 2009. Informed consent was obtained from all participants and the Institute Ethics Committee approved the study. Each case of epilepsy was subjected to detailed clinical history from patients or from the attendant of the patient or from the witness.

The cases were divided in five groups:
Group I (n-45): Epilepsy with depression
Group II (n-35): Epilepsy with psychosis
Group III (n-25): Depression
Group IV (n-25)-Psychosis
Group V (n-80): Age and Sex matched control.

Inclusion Criteria

1. Age between 10 to 60 years comparable with the standardization samples of the questionnaire used.
2. Diagnosis of epilepsy has been corroborated on the basis of clinical history or definitely abnormal E.E.G.
3. A minimum period of epilepsy with one year, during which five or more epileptic attacks had occurred.
4. Both new and follow up patients were taken for the study.
5. No clinical evidence of drug overdose and post-ictal effect at the time of assessment.
6. Evidence of mental subnormally or psychiatric disorder proceeding the onset of epilepsy, (e.g., depression, psychosis).

Exclusion Criteria

1. Patients beyond more than 60 years and less than 10 years.
2. Patients suffering from any other chronic serious physical illness or organic brain syndrome due to some cause other than epilepsy.

Methods of Psychiatric Assessment

They were given a clinical psychiatric diagnosis according to DSM (IV) criteria (1994).[13] The patients were broadly categorized in two groups

i.e. psychosis or depression. Assessment of psychiatric morbidity was based on (1) Hamilton depression rating scale (HDRS)[14] (2) Brief psychiatric rating scale (BPRS)[15] (3) Middlesex Hospital Questionnaire (MHQ)[16]

Methods Estimation of MDA[17]

MDA was estimated using the level of thiobarbituric acid reactive substances (TBARS). TBARS assay was performed using MDA equivalents derived from tetraethoxy propane. MDA was identified as products of lipid peroxidation that reacts with TBA to give a pink coloured species that absorbs at 532 nm. The method involves heating of separated platelets of patients with TBA reagent containing trichloro acetic acid (TCA), thiobarbituric acid (TBA) and hydrochloric acid. After cooling the solution was centrifuged at 2000 rpm and precipitate obtained was removed .The absorbance of the supernatant was determined at 532 nm against a blank that contained the entire reagent minus the platelets. The MDA equivalents of the sample were calculated using an extinction of 1.56×10^5 M^{-1} cm^{-1}. The level of MDA was read as nmoles MDA per 10^9 platelets.

Data Analysis

The data thus collected was computerized in specific program developed on Microsoft excel 2007 software. The data base so prepared was analyzed with the help of SPSS statistical software. The inferences were drawn from the information and the results were discussed with the available studies. Analysis of Variance test was applied as a test of significance. Level of significance was taken as 0.05.

RESULTS

The total cases included in study were 210 out of which 188 Group I (n=45), 30 (66.67%) were male and 15 (33.33%) were female; Group II (n=35) males were 19 (54.29%) and female were 16 (45.71%); Group III (n=25) males were 17 (68%) and females were 8(32%);Group IV (n=25) males were 17 (68%) and females were 8 (32%) and in Group V (n=80) males were 45 (56.25%) and female were 35 (43.75%). The p value was less than 0.01 in all four groups as compared to control group suggesting increased oxidative stress in E.P.C./psychosis/depression patients than control. (Table 1). In the age range of 10 to 60 years, males (60.95%) were dominated the female by 1.68:1 (Table 2).

The comparison of MDA between Group I (epilepsy with depression) and Group II (epilepsy with psychosis). The p- value between the groups was greater than 0.05 i.e. the level of oxidative stress in two groups were not significantly different (Table 3). Mean MDA level in Group-II was 2.47 and Group-IV was 2.35.On comparison of both groups p value between the groups was less than 0.05 suggestive of greater degree of oxidative stress in epilepsy with depression than in depression alone (Table 3). Comparison between the Group II and Group III ($p< 0.05$) suggested higher degree of oxidative stress in epilepsy with psychosis and then in psychosis alone (Table 3). Comparison of MDA between Group IV (psychosis without epilepsy) and Group III (depression without epilepsy). The mean MDA level in Group IV was 2.35 and Group III was 2.35 and p value between the groups was more than 0.05 suggestive of no significant difference in degree of oxidative stress in psychosis and depression (Table 3).

Table-1: Sex Distribution & MDA among Groups

Group		I	II	III	IV	V
Male	No.	30	19	17	17	45
	Mean	2.47	2.46	2.36	2.36	2.18
	SD	0.17	0.13	0.23	0.24	0.42
	T	4.05	4.04	2.14	2.10	
	P	p<0.01	P<0.01	p<0.01	p<0.05	
Female	No.	15	16	8	8	35
	Mean	2.46	2.46	2.33	2.32	2.11
	SD	0.08	0.07	.24	0.20	0.27
	T	6.98	7.16	2.28	2.49	
	P	p<0.01	P<0.01	p<0.05	p<0.05	
Total	No.	45	35	25	25	80
	Mean	2.47	2.46	2.35	2.35	2.15
	SD	0.16	0.11	0.23	0.21	0.36
	T	6.84	6.99	3.27	3.44	
	P	p<0.01	p<0.01	p<0.01	p<0.01	

Table-2: Age Distribution of Cases

Age		I	II	III	IV	V
10-20	No.	11	6	7	8	20
	%	24.44	17.14	28	32	25.00
21-30	No.	16	9	7	4	26
	%	35.56	25.71	28	16	32.50
31-40	No.	6	11	4	9	17
	%	13.33	31.43	16	36	21.25
41-50	No.	8	4	5	1	16
	%	17.78	11.43	20	4	20.00
51-60	No.	4	5	2	3	1
	%	8.89	14.29	8	12	1.25
Total		45	35	25	25	80
Mean		29.67	32.83	30.89	30.33	29.72
SD		11.64	12.56	11.12	12.27	10.53

Table-3: MDA between Groups

	I &II	I&III	I&IV	II&III	II&IV	III&IV
T	0.331	2.316	2.688	2.395	2.395	0
P	>.05	<.05	<.05	<.05	<.05	>.05

DISCUSSION

The lipid peroxidation product malondialdehyde is commonly used as a measure of oxidative stress in cells. Lipid peroxidation being a free radical reaction occurs when hydroxyl radicals possibly oxygen reacts with the unsaturated lipids of bio-membranes resulting in the generation of lipid peroxide radical (ROO•) lipid hydro-peroxide (ROOH) and fragmentation products such as MDA.[18,19] Nervous system is especially vulnerable to the damaging effect of oxidative stress due to high content of polyunsaturated fatty acids which are susceptible to lipid peroxidation, receive higher percentage of oxygen and relatively deficient in antioxidant enzymes.[20] The present study was conducted to study the oxidative stress in patients of epilepsy with psychiatric illness (psychosis, depression) and comparison of results with age and sex matched controls. The results showed that the level of oxidative stress is higher in epilepsy with psychiatric co-morbidity, psychosis and depression than control. The stress was higher in persons of epilepsy with psychiatric co morbidity than with psychosis or depression. The comparison of oxidative stress in epilepsy without any psychiatric co morbidity by same authors with control had demonstrated that MDA values in epilepsy were significant than control and there was a reduction in the oxidative stress with therapy.[21] The result had been correlated with other studies done in epilepsy and psychiatric illness. Sudha et al showed the role of oxidative stress in their study on 29 epileptic patients, by demonstrating a decrease in various antioxidant defenses and an increase in oxidative stress parameters.[10] Another study reported a 27% reduction in the CSF glutathione level in patients with schizophrenia compared with controls, which coexisted with a 52% glutathione reduction in the medial prefrontal cortex, as measured by magnetic resonance spectroscopy.[22]

CONCLUSION

The present study showed significant level of oxidative stress in epilepsy with psychiatric co morbidity as compared to control. Further studies with large sample number in epilepsy and level of psychiatric co morbidity is needed. The significance of study about the need further research in the role of antioxidant therapy in epilepsy and psychiatric illness.

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