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Research Article

ROLE OF FREE RADICALS AND ANTIOXIDANTS IN SCHIZOPHRENIA

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ABSTRACT

A disturbance in antioxidant defense system due to free radical induced oxidative injury has been implicated in various neuropsychiatric disorders. Increased generation of free radicals has been supposed to be one of the important causes of schizophrenia. To scrutinize our findings related to possible imbalance in redox status responsible for oxidative damage, parameters for both lipid peroxidation and antioxidant activity were selected and estimated. Blood samples were analysed for Malondialdehyde (MDA), Ascorbic acid and Superoxide dismutase(SOD). Serum TBARS (Thiobarbituric acid reacting substance) was selected as marker for free radical induced lipid peroxidation and plasma ascorbate and plasma SOD were selected as markers of antioxidant status. MDA is a secondary product of lipid peroxidation and our study showed a significant increase in free radicals in cases compared to controls. Further a significant decrease in level of antioxidants Vitamin C and SOD were observed in schizophrenic patients compared to normal controls.

Keywords: Schizophrenia, TBARS (Thiobarbituric acid reacting substances).

INTRODUCTION

Schizophrenia is a psychotic disorder which usually begins before age of 25 and persists thoughout life and affects persons of all social classes[1]. It is characterized by disturbances in thought, verbal behaviour, motor behaviour and interaction withexternal world[1].

Aerobic life is characterized by continuous production of oxidants which is balanced by antioxidants[2]. Antioxidants enzymes like super oxide dismutase (SOD), glutathione peroxidise (GPO) and catalase (CAT) form the first line of defense against free radicals. Vitamin E, Vitamin C etc act as second line of defense. A shift in the balance of the oxidant side may trigger a cascade of reactions leading to formation of highly reactive oxygen metabolites (ROM)[3].

The neural membranes of brain are rich in essential polyunsaturated fatty acids (EPUFA). It has been proposed in several studies that due to impairment of enzymatic and nonenzymatic antioxidant defense the brain EPUFA become susceptible to breakdown by free radicals in schizophrenia. Keeping these facts in mind the present study was undertaken in the Biochemistry, Pathology and Psychiatry departments to analyze the role of free radicals and the antioxidant defense in the diagnosed schizophrenic patients.

Since the neuronal oxidative injury processes and the underlying dynamic molecules regulatory mechanism are reflected in the peripheral blood[4], an effort has been made to investigate the serum MDA level, a thiobarbituric acid reacting substance (TBARS) as indicator of lipid peroxidation. SOD activity in plasma was selected as a marker of antioxidant enzyme status and plasma VitaminC were selected to assay the nonenzymatic antioxidant activities in schizophrenic patients.

AIMS AND OBJECTIVES

To study the role of free radicals and the antioxidants effect in Schizophrenia

MATERIALS AND METHODS

The present hospital based case control study was undertaken in the department of Biochemistry in collaboration with the departments of Psychiatry and Pathology in a tertiary care hospital over a period of two years. The cases were selected from the patients attending the outdoor of Psychiatry Department. The controls were selected from the healthy persons who accompanied the patients from the same region. The controls were not suffering from any psychiatric or metabolic disorder at the time of diagnosis. The cases and controls both were selected by a simple random method. The study was approved by a properly constituted institutional ethical committee.

The study was designed to find the effectof free radicals and antioxidants among the diagnosed schizophrenic patients compared to controls. For the cases the diagnosis of schizophrenia was made by using the ICD-10 criteria[5]. One hundred and fifty cases were diagnosed as schizophrenia by this method. By using a simple random method we selected fifty patients in the study.Whereas fifty healthy controls were selected from the persons accompanying the patients in a simple random method during the same period. None of the cases or controls was under any medication containing vitamin supplementation at the time of diagnosis.

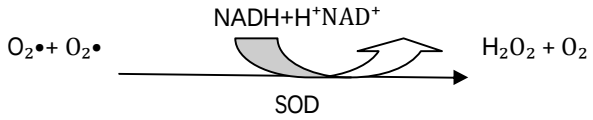
After taking proper consent from the patients sample was collected as follows

- Heparinised blood was collected for plasma SOD (Superoxide dismutase) activity and plasma Ascorbate level.
- Clotted blood without any anticoagulant was collected for assessment of serum TBARS (Thiobarbituric acid reacting substances).

Estimation of plasma Superoxide dismutase (SOD)

Plasma SOD estimation was done as described by P. Kakkar, B. Das and P.N. Vishwanathana[6].

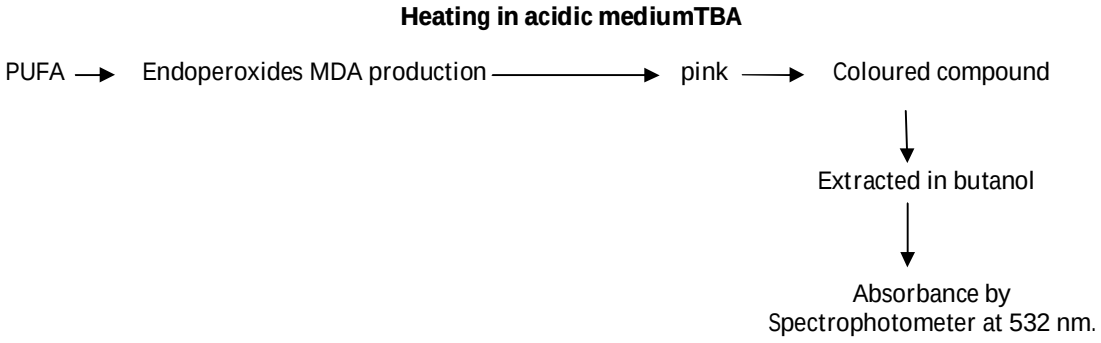
SOD activity was proportional to consumption of $NADH+H^+$.



Estimation of serum Thiobarbituric Acid Reacting Substance (TBARS)

MDA assay based on its reaction with thiobarbituric acid [7].

Polyunsaturated fatty acids react with molecular oxygen to undergo free radical mediated auto-oxidation. During this process various peroxides and aldehyde compounds are formed which decomposed to form MDA on heating in acid medium. These substances then react with thiobarbituric acid to form pink coloured compound[7]. Then the product is extracted in butanol and the absorbance is measured at 532nm.



Estimation of plasma ascorbic acid

Estimation of plasma ascorbic acid was done by photometric method. Ascorbic acid in plasma is oxidized by Cu^2 to form Dehydroascorbic acid which reacts with 2, 4dinitrophenylhydrazine to form a red bishydrazone which is measured at 520nm[8].

RESULTS

Analysis between newly diagnosed schizophrenic patients and controls were done. Table 1 shows the comparison of mean of different parameters between cases and controls.

The lipid peroxidation product serum TBARS was significantly higher in cases whereas the antioxidant SOD, plasma ascorbate showed significantly lower values in cases.

DISCUSSION

Generation of free radicals due to impaired redox balance is supposed to be one of the causes of schizophrenia[9]. Shifting of redox balance towards oxidative stress may occur due to excess generation of free radicals or decreased antioxidant activities as evidenced by several previous and recent studies[10–13].

In our study significant increase in lipid peroxidation, as reflected by increased TBARS was found in newly diagnosed schizophrenic patients whereas the antioxidant parameters (SOD and Vitamin C) were significantly lower. Similar observations were made by Benedicta D Souza et al (2004), Mahadik et al (2001) and Hibbeln et al (2000)[9-11].This indicated that there was increased generation of free radicals which causes lipid peroxidation. As the cases did not suffer from any other systemic or metabolic disorder, the source of free radicals most probably was from the brain cell membrane which has been observed in previous studies as well[9]. Brain membranes are composed of greater than 66% phospholipids by mass versus 33% in peripheral tissues [14,15]. Phospholipids in cell membranes play vital role in receptor mediated signal transduction by generating neurotransmitters[16]. R2 positions in phospholipids are occupied by EPUFAs which are susceptible to breakdown by lipid peroxidation products.Arachidonic acids and Docosahexanoic acids are the key PUFAs in brain and their metabolism is found to be altered selectively in schizophrenia[17]. The most consistent reduction of EPUFA in schizophrenia has been reported in contents ofarachidonic acids and docosahexanoic acids. Increased lipid peroxidation which could not be compensated by body's antioxidant defense became important etiological factor for schizophrenia. Serum TBARS was selected as marker for free radical induced lipid peroxidation and plasma ascorbate and plasma SOD were selected as markers of antioxidant status.

CONCLUSION

Our study showed that free radical induced lipid peroxidation played a significant role in PUFA rich cell membrane damage in newly diagnosed schizophrenic patients who showed compromised antioxidant defense. Human beings cannot synthesize vitamin C due to mutation in gene coding for L gulonolactone oxidase enzyme in glucoronic acid pathway[18]. So in the newly diagnosed schizophrenic patients, significantly reduced level of plasma ascorbate suggests that supplementation of vitamin C may help in management of schizophrenia. It can be concluded that an imbalance in antioxidant defense system occurs in schizophrenia due to persistent oxidative stress [19].

Table 1: Comparison of means of different parameters between newly diagnosed schizophrenic cases and controls

	Serum MDA (nmole/ml)	Plasma SOD (µIU/ml)	VitaminC (mg/dl)
Cases	5.21 ± 0.35	6.98 ± 1.01	0.67 ± 0.003
Controls	2.02 ± 0.76	13.80 ± 1.50	0.91 ±0.007
P value	0.00	0.00	0.00

The SPSS statistical package was used for analysis. Here student t test was done. P value<0.05 was considered as significant

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