Abstract. – Oxidative stress is implicated as a major factor for nigral neuronal cell death. Metabolic failure in antioxidant mechanisms could hypothetically facilitate the chemical processes that lead to lipid peroxidation. To elucidate whether elevated lipid peroxidation rates might increase risk of developing Parkinson’s disease (PD), the Authors determined plasma levels of malondialdehyde (MDA) in 80 PD patients and 80 controls. There was a significant difference between the plasma MDA levels of PD patients and controls (7.48 ± 1.55 vs 5.1 ± 1.26 nmol/ml). Plasma MDA levels were inversely related to the age of the PD patients (r=−0.46; p<0.01) and age of onset but in the control group, no such correlation was observed between the plasma MDA and age. However, there was no significant correlation between plasma MDA levels and the duration of disease, Hoehn and Yahr stages and the Unified Parkinson’s Disease Rating Scale (UPDRS). Thus, the results suggest that high plasma lipid peroxidation rates might contribute as a risk factor for PD in West Bengal.

Key Words: Parkinson’s disease, Plasma level, Malondialdehyde, Lipid peroxidation.

Introduction

Parkinson’s disease (PD) is a common, idiopathic, neurodegenerative disorder that produces bradykinesia, muscular rigidity, rest tremor and loss of postural balance. The cardinal pathologic change of Parkinson’s disease is the degeneration of dopaminergic neurons in the substantia nigra pars compacta. The exact cause of nigral neuronal death is still unknown. However, oxidative stress1 and mitochondrial respiratory failure2-4 have been implicated as the major contributors to nigral cell death in Parkinson’s disease. Under conditions of oxidative stress (caused by factors such as inadequate glutathione levels and excess reactive iron concentrations), hydrogen peroxide breakdowns yielding hydroxyl radical, where intracellular components exposed to such conditions result in formation of excessive lipid peroxidation. Thus, free radicals are thought to be produced locally within basal ganglia and lead to progressive degeneration and ultimate death of dopaminergic neurons in susceptible individuals. In support of this hypothesis, many Authors have reported post mortem decrease in glutathione peroxidase activity levels5, catalase and reduced glutathione6,7 in substantia nigra of patients with PD.

Malondialdehyde (MDA) is an intermediate compound and a major indicator of lipid peroxidation process8. In our study, we determined the plasma MDA levels in PD patients and in a large control cohort. The objective of this study was to elucidate whether an increase in plasma lipid peroxidation could be associated with the risk of developing PD in West Bengal. To the best of our knowledge, this is the first biochemical study report on PD in West Bengal.

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Materials and Methods

The patient cohort consisted of 80 sporadic idiopathic PD selected from the Bengali population in West Bengal visiting the out patients Neurology Department of Calcutta Medical College and Hospital and National Neuroscience Centre, Kolkata. Clinical data and detailed family history of each patient are collected with the help of collaborating clinicians. The Unified Parkinson’s Disease Rating Scale (UPDRS)\(^9\) and the Hoehn and Yahr staging\(^10\) were performed for each patient.

The control group consisted of 80 healthy community-based, age and sex-matched volunteers residing in the same areas and from the same ethnic background as the PD patients. None of the control subjects had diagnosable neurological disorders.

Operational Definitions

All the cases have to meet the following symptoms at the time of diagnosis and within the study period:

1. The presence of at least three of the following signs: resting tremor, cogwheel rigidity, bradykinesia and postural reflex impairment, at least one of which must be either rest tremor or bradykinesia\(^11\);
2. No suggestion of a cause for another Parkinsonian syndrome such as drugs, trauma, brain tumor or treatment within the last 12 months with dopamine blocking or dopamine depleting agents and;
3. No atypical features such as prominent oc culomotor palsy, cerebellar signs, vocal cord paresis, severe orthostatic hypotension, pyramidal signs, amyotrophy or limb apraxia.

The following exclusion criteria were applied to the PD patients as well as controls:

a. Hyperlipidemia, diabetes mellitus, coronary heart diseases, arterial hypertension, thyroid diseases, peripheral arteriosclerosis or vascular disorders of the central nervous system;
b. Ethanol intake higher than 80 g/day during the proceeding 6 months;
c. Therapy with vitamin B\(_6\), vitamin E, beta carotene, selenium or zinc during the last 6 months\(^12\).

collection of Blood Samples and Plasma Separation

Approximately 3 ml of peripheral blood sample was collected in K2 EDTA 7.2 mg 4 ml BD Vacutainer. An informed consent was obtained from PD patients, their family members and from normal individuals as controls. Blood was centrifuged at 3000g for 8 minutes. Plasma was separated from the buffy coat carefully and stored at 4°C until analysis. Plasma lipid peroxidation was measured on the basis of the reaction between MDA and Thiobutaric acid\(^13\) and quantification carried out in Perkin Elmer Spectrophotometer (Lambda 25 UV/VIS Spectrometer, Perkin Elmer, Singapore) (wavelength \(\lambda=532\) nm). All analysis was carried out within 3 days of blood collection.

The study protocol was approved by the Ethics Committee of the Institute.

Statistical Analysis

The results are expressed as mean ± SD. Statistical analysis included the two-tailed Student’s \(t\)-test and calculation of correlation coefficient using SPSS v11.5 software.

Results

The age (57.53 ± 12.10 yr), disease onset age (54.3 ± 5.17 yr), duration of the disease (2.9 ± 1.58), Unified Parkinson’s Disease Rating Scale (UPDRS) score (31.2 ± 5.20), Hoehn and Yahr staging (2.43 ± 1.10) and England and Schwab activities of daily living (ADL) (79.80 ± 17.61) are summarized (Table I). More than three-fourths of our patients were males. Most of the

| Table I. Clinical Phenotypes of PD patients and control cohort. |
|-----------------------------|-----------------------------|-----------------------------|
|                             | Patient (n = 80)             | Control (n = 80)             |
| Age (yrs)                   | 57.53 ± 12.10               | 58.32 ± 8.85                |
| Gender                      |                             |                             |
| Male                        | 61                          | 68                          |
| Female                      | 19                          | 12                          |
| Age of Onset of PD (yrs)    | 54.3 ± 5.17                 |                             |
| Duration of PD (yrs)        | 2.9 ± 1.58                  |                             |
| Scores of the UPDRS         |                             |                             |
| Total items\(^{13}\)        | 31.2 ± 5.20                 |                             |
| ADL scale                   | 79.80 ± 17.61               |                             |
| Motor Scale                 | 14.9 ± 2.11                 |                             |
| Hoehn and Yahr stage        | 2.43 ± 1.10                 |                             |
| Lid swelling                |                             |                             |
patients reported an increase in tremor and imbalance during periods of stress. Only four patients were untreated while others are under antiparkinsonian treatment.

Plasma MDA levels were inversely correlated with age of the patients ($r = -0.46; p < 0.01$) (Figure 1). The mean plasma MDA levels in the PD patients and in controls (7.48 ± 1.55 vs. 5.1 ± 1.26 nmol/ml) (Figure 2) differed significantly. Age and sex distribution of patients and controls were similar.

**Discussion**

Mechanisms underlying neuronal death are poorly understood although several in vitro studies have suggested the involvement of oxidative stress\(^1\). The concept that oxidative stress occurs in PD derives primarily from the realization that the metabolism of dopamine, by chemical or enzymatic means, can generate free radicals and other reactive oxygen species via autoxidation and the dopamine oxidation by the monoamine oxidase B. However, Molina et al\(^1\) have shown that lipid peroxidation measured as MDA levels in serum are similar in both the PD patients and controls. Similarly, Poirier and Barbeau\(^1\) reported that MDA levels in the erythrocytes of PD patients had no positive correlation with the members of the control group.

Yoritaka et al\(^1\) reported that 4-hydroxynonenal modified proteins, representing an indicator of increased lipid peroxidation, is found at an elevated level in the nigral neurons of patients who had died of PD. Moreover, the parkinsonism inducing neurotoxin, 1-Methyl-4-Phenyl-1,2,3,6-terahydropyridine (MPTP), induces lipid peroxidation in rodent brains\(^1\). In PD, environment within substantia nigra is conducive to the formation of cytotoxic free radicals. These free radicals react instantaneously with the membrane lipids. Lipid peroxidation of RBC membrane causes them to loose their ability to change the shape and squeeze through the smallest capillaries, thus eventually leading to haemolysis. Brain tissue extracts of PD patients also showed a tenfold increase in lipid peroxides in substantia nigra compared to control subjects\(^2\). Results of the present work indicate that plasma MDA levels are significantly higher in PD patients than in controls and agree with those reported by Kilinc et al\(^3\). Dexter et al\(^4\) have shown that basal lipid peroxidation measured as MDA levels is increased in substantia nigra of PD patients' brain. One report from India by Sudha et al\(^5\) has shown high erythrocyte lipid peroxidation at 0 hour of PD patients. Although the significance of some findings in literature is still unclear and controversial\(^6,7\), our study has speculated that, the increased lipid peroxidation can be considered a risk factor for PD in West Bengal.

**References**


