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HIGH SELENIUM LEVELS IN PARKINSON'S DISEASE? A STUDY FROM CENTRAL KERALA

Physiology

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ABSTRACT

Oxidative stress on dopaminergic neurons in the substantia nigra caused by cytotoxic free radicles generated during oxidative metabolism of dopamine is hypothesized to be one of the etiopathogenic mechanisms of Parkinson's disease (PD). Glutathione peroxidase (GPX) plays an important role in reducing peroxide-mediated stress. Selenium, a trace element, is a component of GPX and assists in this process. The aim of this case-control study was to analyze serum Selenium levels among PD patients in central Kerala. Serum selenium was estimated using Inductively Coupled Plasma-Mass Spectrometry in 30 patients and 30 controls. Serum Selenium levels were found to be elevated in PD patients as compared to controls.

KEYWORDS

Parkinson's disease, Dopaminergic neurons, Oxidative stress, Selenium

INTRODUCTION

Parkinson's disease (PD) is a neuro degenerative disorder named after James Parkinson, who first described it in "An Essay on the shaking palsy" (1817).[1] PD affects 1-2 per 1000 of the world population.[2] India ranks 16th in prevalence, but this could be an underestimate as nationwide epidemiological studies are lacking.[3]

A combination of genetic and environmental factors contribute to the etiology and progression of PD. Ageing, dietary habits including intake of sugar, animal fats, vitamins, environmental exposure to toxicants like redox-active transition metals, pesticides, insecticides, neurotoxins and occupations like farming are epidemiologically associated with pathogenesis; less than 1% of PD cases have a pure genetic origin.

Oxidative stress initiated by reactive oxygen species (ROS) and reactive nitrogen species (NOS) is one of the putative mechanisms for neurotoxicity and pathogenesis of PD and other neurodegenerative diseases.[4],[5] Neurons of the substantia nigra (SN) are rich in dopamine (DA); metabolism and auto-oxidation of DA generates oxyradicals and hydrogen peroxide (H_2O_2), which are major causes of oxidative damage and, possibly, of neuronal death. Antioxidants including Glutathione protect against oxidative stress. Glutathione concentrations are reduced in SN of PD patients.[6] This could imply a direct role for low glutathione in PD pathogenesis or it may reflect high levels of oxidative activity in SN leading to greater utilization and depletion of glutathione.[7] Selenium (Se) as selenocysteine, is a component of the enzyme glutathione peroxidase (GPx) which is responsible for reducing and detoxifying H_2O_2. It can therefore reasonably be hypothesized that alteration in Selenium concentrations could affect cellular defenses against oxidative injury and influence the pathogenesis of PD.

This study was designed to test serum selenium concentrations in PD and explore its role in the pathogenesis.

METHODS AND MATERIALS

This is a case- control study conducted at Little Flower Hospital and Research Centre, Angamaly, Kerala. The study was approved by the Institutional Ethics Committee.

Sampling

A total of 60 subjects, 30 cases and 30 controls, were recruited after obtaining voluntary, written, informed consent. The sampling technique used was 'purposive sampling'.

Inclusion Criteria

- Patients in the age group 40-80 years, diagnosed with Parkinson's disease
- Subjects of similar age group not suffering from any major diseases were enrolled as controls

Exclusion Criteria

- Subjects on selenium-containing supplement therapy
- Pregnant or lactating females

Data Collection

Demographic data of patients and controls was entered into a structured proforma.

Blood analysis and estimation: 2 ml of blood was drawn using sterile techniques in EDTA tubes. The blood was centrifuged at 3000 rpm for 15 minutes, serum collected in Eppendorf tubes and refrigerated at -40° C. Serum selenium concentration was assayed using Inductively Coupled Plasma-Mass Spectrometry (ICP-MS).

Statistical Analysis

The data was entered in MS-Excel and analyzed using SPSS 20.0 Version. Independent T test was used for analysis. P<0.05 was considered as significant.

RESULT

Table 1: Comparison of mean serum selenium levels in patients and control

	Parkinson's disease	Controls
Number	30	30
Gender		
• Male	18	18
• Female	12	12
Serum Selenium level (µg/L)		
• Range	60-420	60-280
• Mean	167.3	130.0
• Standard deviation	84.6	59.1
Independent T test T value	1.980	
P value	0.048	

Independent T test, P<0.05 considered as statistically significant

Table 1 shows the comparison of mean serum selenium concentration among the Parkinson's patient group and controls. There were 30 subjects in each group. The mean serum Se was 167.3±84.6 in patients and 130±59.1 in controls. The difference in mean observed was statistically significant (P<0.05).

DISCUSSION

Previous studies of serum Selenium concentrations in PD both from

India and abroad have yielded conflicting results. In the Indian scenario Se levels significantly lower in PD compared to controls was reported by Nikam et al from Belgaum, Karnataka and by Ahmed and Santosh from Delhi.[8],[9] However, Lavanya et al from Visakhapatnam, Andhra found higher selenium concentrations in their patients.[10] Similarly, significantly higher Se concentrations was noted in a large sample of 238 PD patients by Zhao et al from eastern China and replicated by Hemmati-Dinarvand et al from Tabriz, Iran.[11],[12] This was in contrast to an earlier report by Fathi et al from Teheran, Iran where Se concentrations were lower.[13] Younes- Mhenni et al detected no significant difference in serum Se level between PD patients in Tunisia and controls while a prospective study from Norway, revealed that levels of selenium and other trace elements were lower in patients tested 4-12 years after they were diagnosed with PD when compared with their pre-diagnosis levels.[14],[15] Se levels did not correlate with the presence of PD but lower concentrations were associated with poorer performance in tests of coordination among older adults in a large cohort of 1,012 Italian PD participants.[16] High CSF concentrations of selenium have been remarked by Qureshi et al from Pakistan.[17] Ahmed and Santosh found significant variation in 18 other elements apart from Se and postulated that PD was associated with "disturbance in inter-elemental homeostasis".[9]

A meta-analysis of studies reporting trace element concentrations in blood and CSF in patients with PD versus controls was recently published by authors from Italy, Germany and the USA.[18] They retrieved 56 studies reporting data for selenium with a total of 588 patients and 721 controls and could analyse data from 12 studies. Patients showed significantly higher levels of selenium in CSF as compared to controls but levels in serum showed no significant difference. Heterogeneity for serum Se was reported to be very high.

The interpretation of selenium level alterations remains a matter of debate and has often reflected the bias of the investigator. With the underlying premise that Se reduces oxidative stress, high selenium levels have been interpreted as signifying higher requirement in tissues where oxidative damage occurs while lower serum concentrations have been interpreted as suggesting increased usage of Se in combating oxidative stress. In advanced PD, impaired nutritional status and alteration in trace element metabolism have also been postulated to cause low Se levels.[19] Only Adani et al have ventured to suggest based on their meta-analysis that overexposure of the central nervous system to Se, as reflected by high CSF concentrations, may be toxic and a risk factor for PD.[18] This finds support in experimental work in human neuronal cell lines and Caenorhabditis elegans that suggests that high Se levels may not be neuro-protective and could induce oxidative stress in cholinergic neurons respectively.[20],[21]

Although requiring further validation with larger patient samples, our pilot study showed significantly higher levels of Selenium in the serum of patients with PD, compared with controls, which has not previously been reported from Kerala. Dietary sources of Se include sea food, meat and cereals which are abundant in the diet of the population of central Kerala. Low Se levels are, therefore, not a risk factor for PD in this population. Low tissue levels (Sian et al, 1994) coupled with high CSF (Qureshi et al, 2006) and serum levels as in our study would imply greater utilization of Se rather than direct toxicity but any role for Se in causation and progression of the disease has to be investigated further.

CONCLUSION

Selenium levels in the serum of the PD patients studied are higher than in age-matched controls in Central Kerala. Our conclusions need further validation in larger samples and the association between high serum levels and disease progression including a possible role for Se mediated neuro toxicity needs to be explored further.

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