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VITAMIN D DEFICIENCY IN PARKINSONS DISEASE PATIENTS AT A TERTIARY CARE CENTER IN KARACHI, PAKISTAN

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ABSTRACT

Objective: The objective of our study was to identify frequency of 25- Hydroxy vitamin D deficiency in patients with known PD and its possible relationship with activity level and medication use. **Methods & Results:** We analyzed 35 patients. Age range was 41-76 years (mean 55 years). There were 16 women. Mean duration of PD was 6 years (range 4-13 years). 22 patients were active as normal, eight patients were ambulatory with assistance and five patients were wheel chair bound or bed ridden. Only 3 patients were taking Dopamine agonist monotherapy, 16 patients Levadopa monotherapy and 16 patients were taking combination therapy. Vitamin D levels were normal in 7 (20%) patients, mild deficiency 12 (34%), moderately deficient in 10 (29%) and severe deficiency in 6 (17%) patients. There was no statistically significant correlation between activity level and vitamin deficiency states (p=0.95), duration of PD (p= 0.09) and number of medications (P=0.112).
Conclusions: Vitamin D deficiency was common among our PD patients. There was no correlation between Vitamin D deficiency and duration of PD and number of medications.
Key Words: Parkinson's Disease, Vitamin D

INTRODUCTION

The role of vitamin D deficiency in Parkinson's disease has been recently described. Few studies have reported higher prevalence of vitamin D Deficiency in PD patients as compared to control. Evatt and colleagues [1] compared 97 PD patients with 99 age and sex matched controls. Vitamin D deficiency was present in 55% patients as compared to 36% controls. It is hypothesized that chronic low vitamin D levels may be responsible for neuronal death in substantia nigra. [2] Reduced bone mass in Parkinson's Disease is well documented and could be related to vitamin D deficiency. [3] It is thought that high prevalence of Vitamin D Deficiency in these patients is probably related to low sunlight exposure due to reduced activity level. It is unclear that this deficiency is related to patients' activity level, exposure to sunlight or medications use.

Vitamin D is important for maintaining many physiological functions and its deficiency is associated with an increased risk of disease. Vitamin D is also thought to regulate processes which are known to go awry in neurological disorders like multiple sclerosis, Parkinson's disease, Alzheimer's disease and other neurodegenerative disorders.

Humans get vitamin D from exposure to sunlight, from their diet, and from dietary supplements. Vitamin D is primarily produced in the skin on exposure to UV-B radiation. The action of ultraviolet light (UVB) on 7-dehydrocholesterol results in the production of pre-vitamin D which, after thermo-conversion and two separate hydroxylations, gives rise to the active 1,25-dihydroxyvitamin D. Vitamin D acts through two types of receptors: (i) the vitamin D receptor (VDR), a member of the steroid/thyroid hormone superfamily of transcription factors, and (ii) the MARRS (membrane associated, rapid response steroid binding) receptor, also known as Erp57/Grp58. The substantia nigra (the portion of the brain that degenerates in Parkinson's disease) represents the area of the human brain where the VDR is most highly expressed. [4]

Confirmatively, a significant higher prevalence of hypovitaminosis D was observed in patients with Parkinson's disease, when compared to both healthy

controls and patients with Alzheimer's disease[1]. In addition, a positive association between VDR gene polymorphism and Parkinson's disease has been reported. [5] The vitamin D binding protein (VDBP) has been recently shown to be one of eight cerebrospinal fluid biomarkers in Parkinson's disease. [6]

There is no concensus on what is the optimal level of vitamin D in the serum. Generally vitamin D deficiency is defined by most experts as a 25-hydroxyvitamin D level of less than 20 ng per milliliter (50 nmol per litre). [7] Using this figure, approximately one billion people around the world are estimated to have vitamin deficiency or insufficiency. Data from the United States and Europe also show significant prevalence of vitamin D deficiency. Between 40 and 100% of elderly men and women living in the community (not in nursing homes) are deficient in vitamin D. [8] Even in the sunniest areas, vitamin D deficiency is common when most of the skin is shielded from the sun. There are no published population based studies for vitamin D status in Pakistan. Hospital based studies have shown a very high prevalence (more than 70%) among asymptomatic subjects. [9] Possible causes of this deficiency includes genetics, nutritional, environmental or metabolic. [10] The purpose of our study was to identify frequency of 25- Hydroxy vitamin D deficiency in patients with known PD and its possible relationship with activity level and medication use.

MATERIALS AND METHODS

This cross-sectional study was conducted at Neurology Outpatient Clinics, The Aga Khan University Hospital, Karachi during 2008. All patients were seen by a trained neurologist. We checked serum vitamin D level (25 hydroxyvitamin D) in 35 consecutive patients who were diagnosed to have Parkinson's disease. Functional status of the patients was also documented as: normal, assisted ambulation, wheel chair-bound or bed ridden. Patients were divided into 3 groups according to the class of anti-Parkinsonian medications they were taking as: Dopamine agonist monotherapy, Levodopa monotherapy and combination therapy groups.

Vitamin D status was measured by measuring 25OHD concentrations. Electrochemiluminescence immunoassay was used on Elecsys autoanalyzer (Roche Diagnostics). It is a competitive assay in which the binding protein of vitamin D is inactivated during incubation. The assay employs a polyclonal antibody directed against 25-OH vitamin D_3. The within-run CVs were 5.7%, 5.7%, and 5.4% at concentrations of 25.2, 39.9, and 65.6 ng/ml (provided by the assay producer). Inverse relation between 25OHD and PTH will maintain until former reaches 30 to 40 ng per milliliter, at which point PTH levels begin to level off.

Therefore, we used the reference range that most experts now agree.[14] Serum vitamin D levels were defined as mild Vitamin D Deficiency: 15-20 ng/ml, moderate Vitamin D Deficiency: 10-14 ng/ml and severe Vitamin D Deficiency: less than 10 ng/ml. Levels betwenn 20- 30 ng/ml were regarded as Vitamin D insufficiency, levels above 30 ng/ml were considered normal and levels more than 150 ng/ml were labeled as intoxication.

RESULTS

We studied 35 patients whose age range was 41-76 years (mean 55 years). There were 16 women. Mean duration of PD was 6 years (range 4-13 years). Twenty two patients had normal active functional status, eight patients were ambulatory with assistance and five patients were wheel chair bound or bed ridden. Only 3 patients were taking Dopamine agonist monotherapy, 16 patients Levadopa monotherapy and 16 patients were taking combination therapy.

Vitamin D levels were normal in 7 (20%) patients, mild deficiency 12 (34%), moderately deficient in 10 (29%) and severe deficiency in 6 (17%) patients. There was no statistically significant correlation between activity level and vitamin deficiency states ($p=0.95$), duration of PD ($p= 0.09$) and number of medications ($P=0.112$).

DISCUSSION

Vitamin D deficiency was extremely common in our PD patients. Almost all patients complained of aches and musculoskeletal pain. These symptoms are not uncommon among PD patients. Vitamin D deficiency in PD patients may contribute to their suffering and disability. It is important to identify and treat these patients. A low threshold of suspicion is necessary to identify vitamin D deficiency among these patients. These findings have to be confirmed in larger prospective studies with age matched controls. High prevalence of vitamin D deficiency among PD patients indicates need for intervention studies not only looking at symptomatic improvement but disease progression and non-neurological manifestations. These findings are in agreement with published literature.

Low levels of Vitamin D in our patients could be related

to their reduced mobility and minimum exposure to sun light. Alternatively medications used to treat Parkinoson's diseases could affect absorption or metabolism of vitamin D. A cause and effect relationship between vitamin deficiency and PD has not been established.
Larger multi center, interventional studies are needed to address role of vitamin D deficiency in treatment and progression of PD.

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