

No Vitamin D Deficiency in Patients with Parkinson's Disease

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Abstract: Previous trials describe a decrease of vitamin D levels in patients with Parkinson's disease and relationships to clinical disease severity. This case control study found higher but not significant 25-OH-vitamin D plasma levels in patients with Parkinson's disease compared with age- and sex-matched controls and no associations to clinical parameters, such as rating scores of disease severity or assessments of cognitive function. A certain variability of vitamin D concentrations was observed in both cohorts, which were investigated during the same season. These outcomes put into perspective the emerging discussion on the importance of vitamin D in Parkinson's disease. Our results warrant further confirmatory research with a strict matching design of patients and controls, which has not been done in previous investigations. We stress that this case control study does not allow any comment on the putative beneficial effects of vitamin D supplementation, ie, on bone mass or bone mineral density, in patients with Parkinson's disease.

Keywords: vitamin D, blood, case control study

Introduction

Vitamin D is a fat-soluble secosteroid that exerts its effects by binding to the vitamin D receptor (VDR). Activation of vitamin D takes place by enzymatic hydroxylation in the liver and kidney with generation of 1,25-dihydroxycholecalciferol or 1,25-dihydroxyvitamin D₃, (1,25-(OH)₂D₃).¹ Thus, vitamin D may directly and indirectly modulate the expression of hundreds to thousands of genes. A high prevalence of vitamin D deficiency was described in Parkinson's disease (PD).^{2,3} The results and conclusions remain inconsistent.³ The discovery that VDR and 1 α -hydroxylase, the enzyme that converts vitamin D to its active form, are highly expressed in the substantia nigra led to the hypothesis that inadequate levels of circulating vitamin D may lead to dysfunction or cell death within the substantia nigra. Accordingly, reports exist that describe lower vitamin D levels in PD patients compared with healthy controls.⁴ Moreover, a negative association between vitamin D levels with PD risk and severity was shown.⁵⁻⁷ However, outdoor activity and thus exposure to sunlight are also important influencing and confounding factors.⁸⁻¹⁰ Further discussed reasons are reduced mobility in combination with sunlight deprivation, gastrointestinal dysfunction with inadequate vitamin D intake.^{11,12} Generally vitamin D is also well known for its role in the regulation of calcium homeostasis and metabolism. Thus, vitamin D is an essential for the gastrointestinal absorption of calcium, magnesium, phosphate, and zinc.^{13,14} Therefore, the common onset of reduced bone mineral density in PD was also discussed as a consequence of vitamin D insufficiency.^{15,16} Accordingly, vitamin D supplementation has even been suggested for prevention and delay of progression of PD.¹⁷⁻¹⁹ One even postulated that higher vitamin D concentrations predispose for better cognitive function in PD patients.²⁰ However only one study showed the presence of only slight and not significant lower vitamin D levels.²¹ One believes that this outcome may be explained with the harsh climate, frequent cloud cover, high latitude, and the low vitamin content in the common diet of the Faroe Islands, where this trial was undertaken.² Only a few foods contain vitamin D, which is biological inactive similar to the one from skin synthesis. Two prospective studies investigated the association between mid-life vitamin D levels and risk of PD. They produced conflicting results. One

showed an increased risk for PD with lower mid-life vitamin D levels, and the other showed no association between vitamin D and PD risk.³ Another more consistent finding is an inverse association between serum vitamin D level and motor symptom severity in cross-sectional trials.^{3,6,8,22} In view of the emerging aforementioned discussions on the role of vitamin D in PD, we performed a further case control study and determined vitamin D concentrations in PD patients and matched controls.

Materials and Methods

Subjects

Sixty treated PD patients (19 female, 41 male; 72.28±2.98 years) (Table 1) and 60 age- and sex-matched controls (19 female, 41 male; 72.58±3.33) participated.

Design

25-OH-vitamin D levels were determined. Intake of vitamin D, respectively vitamin K containing formulations was an exclusion criterion.²³ Blood was taken during an out-patient visit. Scoring of PD symptoms with the Unified Parkinson's Disease rating scale²⁴ and performance of the Montreal Cognitive Assessment (MoCA) was executed before blood sampling.²⁵ Blood sampling for both patients and controls was performed between March and May.

Methods

Blood samples were drawn in EDTA containing tubes. Vitamin D assessment was performed with LC-MS (company: Chromsystems®), which combines reversed-phase high performance liquid chromatography (HPLC [company: Shimadzu®] with mass spectrometry [AB-Sciex API5000®].

Statistics

The Mann Whitney *U*-test for independent samples was used for comparisons. Spearman rank correlation was employed for the correlation analysis. Data showed no normal distribution. A seasonal adjustment as a time dependent variable of vitamin D was not performed as collection and vitamin D determination for PD patients and controls was done in the same season.²⁶

Ethics

The study protocol and the patient informed consent form were reviewed and approved by the independent ethics committee of the Medical Faculty in the University of Wuerzburg, Germany (sign: 30/17 on 4–19-2017). It complies with the Declaration of Helsinki. Participants gave written informed consent after information on the study protocol.

Table 1 Scored Clinical Characteristics of PD Patients

	Mean	SD	Minimum	Maximum
UPDRS I–IV	40.95	20.44	6	104
UPDRS I	3.08	2.99	0	12
UPDRS II	14.40	8.27	2	42
UPDRS III	19.40	11.57	2	56
UPDRS IV	4.07	4.03	0	19
MOCA	20.68	5.58	8	30

Note: All data are given as mean±standard deviation (SD).

Abbreviations: MOCA, Montreal Cognitive Assessment; UPDRS I, Unified Parkinson's Disease Rating Scale mental behavior; UPDRS II, Unified Parkinson's Disease Rating Scale activities of daily living; UPDRS III, Unified Parkinson's Disease Rating Scale motor examination; UPDRS IV, Unified Parkinson's Disease Rating Scale motor complications; UPDRS I–IV, total UPDRS score.

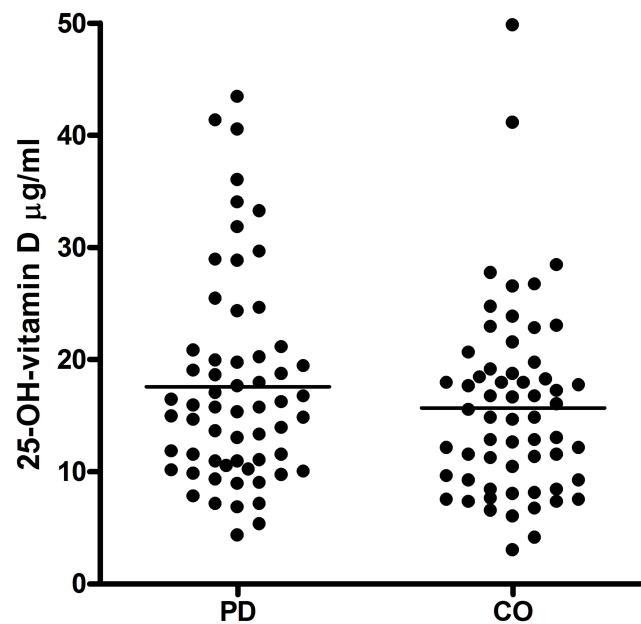


Figure 1 25-(OH)-vitamin D blood concentrations.

Abbreviations: CO, Controls; PD, Parkinson's disease patients, -, mean value.

Data Availability

The data sets generated or analyzed during the current study are available from the corresponding author on reasonable request.

Results

There was no significant difference of 25-OH-vitamin D between PD patients (17.59 ± 9.28 [$\mu\text{g/L}$; mean \pm SD]) and controls (15.69 ± 8.43) (Figure 1). No significant associations between vitamin D levels and clinical parameters were found (Table 2). There was no impact of sex and age (results not shown).

Discussion

We did not find significant higher 25-OH-vitamin D blood concentrations in treated PD patients in comparison with matched controls. No correlation to rating scores for PD and neuropsychological assessments of cognitive function appeared. Our outcomes put into perspective the emerging discussion on the importance of vitamin D in PD to a certain extent. Other investigations report vitamin D deficiency in PD and therefore hypothesize on the role vitamin D in the pathogenesis of PD. We show that a certain variability of vitamin D levels was observed in both cohorts. Our results

Table 2 Correlation Analysis Between 25-(OH)-Vitamin D Blood Concentrations and Clinical Parameters

Variable 1	Variable 2	R	p
25-(OH)-vitamin D	UPDRS	-0.056	ns
25-(OH)-vitamin D	UPDRS I	-0.054	ns
25-(OH)-vitamin D	UPDRS II	-0.08	ns
25-(OH)-vitamin D	UPDRS III	-0.012	ns
25-(OH)-vitamin D	UPDRS IV	0.087	ns
25-(OH)-vitamin D	MOCA	-0.027	ns

Abbreviations: R, correlation coefficient; p, p-value.

warrant further confirmatory research with a strict matching design of patient and controls. We stress that the design of this case control study does not allow any comment on the putative beneficial effects of vitamin D supplementation, ie, on bone mass or bone mineral density in PD patients.^{2,17,27,28} It is known that vitamin D elevation shifts blood flow parameters in a manner that tissue microcirculation is improved.¹ As a consequence, oxygen transport and perfusion of tissue may increase and improve mitochondrial function and defence of oxidative stress, as shown in patients with multiple sclerosis.²⁹ Both mitochondrial impairment and reduction of free radical scavenging capacity also play an essential role in the pathophysiology of chronic neurodegenerative disorders.³⁰ Various trials demonstrated beneficial effects on body function following vitamin D supplementation in disease entities, such as cognitive dysfunction.³¹ Therefore, one may hypothesize that higher vitamin D levels contribute to better coping with symptoms in PD, such as cognitive impairment, and age-related comorbidities, such as diabetes mellitus or cardiovascular disorders.^{6,8,13,22,29,32,33}

There are several limitations. We only assessed once and participants were not taken off PD medication. Therefore, the correlation analysis cannot provide a profound value on the assessments of functional deficits in relation to vitamin D measurement in our PD cohort.

In conclusion, vitamin D levels did not significantly vary between PD patients and matched controls and did not show any relationship to disease severity in contrast to other clinical investigations.

Funding

There was no funding.

Disclosure

The authors have no competing interests in this work.

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