Correlation Between 25-Hydroxy-Vitamin D and Parkinson's Disease: A Case-Control Study

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Abstract

Background: Previous cross-sectional studies have shown that Parkinson's disease (PD) patients have lower serum 25- hydroxy vitamin D (25(OH)D) concentrations than controls. whether the research in other regions findings are generalizable to China populations remains untested in other studies. In this case-control study we examined the Correlation between 25-hydroxy-vitamin D and Parkinson's disease.

Methods: We establish an association between deficiency of 25-hydroxy-vitamin D and PD in a case-control study of 100 PD patients and 100 control subjects free of neurologic disease in the First Affliated Hospital of Xinjiang Medical University.

Results: Total 25-hydroxy-vitamin D levels, were deficient in 21% of patients with PD compared with 4% of controls. In univariate analyses Plasma levels of 25-hydroxy-vitamin D were associated with PD($p<0.001$), respectively. In multivariate analyses, Vitamin D deficiency(25(OH)D <20 ng/mL) were significant associated with PD ($p=0.008$,OR=17.13,95% CI, 2.082-141.075). Individuals with levels in the lowest quartile of 25(OH)D values had the highest prevalence of PD($p =0.026$,OR=11.786,95%CI,1.342-103.51)compared with individuals with values in the highest quartile.

Conclusions: Our study reveals an association between 25-hydroxy-vitamin D and PD.Patients with incident PD had significantly lower serum 25(OH)D concentrations than age-matched controls, High-risk PD patients with vitamin D deficiency who have not yet developed exercise impairment, these populations should undergo vitamin D measurement and vitamin D treatment as soon as possible.

Background

Parkinson's disease (PD) is a common neurodegenerative disorder that the incidence and disability continue to increase as the population ages[1].Although both genetic and environmental factors have been implicated, its etiological factors are mostly unknown[2]. Recently,among the many pathogenesis of Parkinson 's disease,people found a commonality {25-hydroxy-vitamin D [25 (OH) D]deficiency}, which suggests that there is a correlation between 25 (OH) D levels and Parkinson's.Evatt[3]et al retrospective cross-sectional cohort study found demonstrates a significantly higher prevalence of hypovitaminosis in PD vs both healthy controls and patients with AD.Ding [4]et al study showed that vitamin D deficiency in 17.6% of cases (68/388) compared with 9.3% of controls (26/283; $p =0.002$)Plasma levels of 25-hydroxy-vitamin D3 were associated with the prevalence of PD in both univariate and multivariate analyses ($P=0.0034$P=0.047).The Mini-Finland Health Survey, people in the lowest quartile at baseline had approximately three times the risk of developing PD compared with people in the highest quartile [5].

Sun-light exposure is the major source for vitamin D[6] .The production of vitamin D depends not only on the intensity of ultraviolet rays, but also on the duration of ultraviolet irradiation [7] and there are differences between different regions and races.Wang [8]et al case-control studies found that a significant positive correlation between serum 25(OH)D and sunlight exposure.lower levels of serum 25(OH)D and sunlight exposure are significantly associated with an increased risk for PD.A few case-control studies in Finland ,Iran

,Japan and the United States have reported lower 25(OH)D levels in PD patients compared with age-matched controls[9-11].

Affected by geographical factors, China's annual average sunshine amount is different from other countries in the world.whether the research in other regions findings are generalizable to China populations remains untested in other studies. To address these limitations in previous investigations, in our study, we used immunoassay-based vitamin D measuring assays to investigate an association between deficiency of the 25(OH)D and PD in the First Affiliated Hospital of Xinjiang Medical University from January 2019 to December 2019.

Methods

Study Design and Population

In our study,we collected 100 with PD and 100 control subjects without neurologic disease in the First Affiliated Hospital of Xinjiang Medical University from January 2019 to December 2019.Inclusion criteria for PD cases were conforms to the new standard for clinical diagnosis of Parkinson's disease in China[12].Exclusion criteria for PD cases were diagnosis of endocrine system diseases such as hyperparathyroidism and other diseases of abnormal calcium and phosphorus metabolism，fractures or bone tumors recently (≤6 months);known active ulcer, or active colitis.Inclusion criteria for healthy controls were no current diagnosis or history of a neurologic disease. Exclusion criteria for controls were the same as for cases. Controls were comparable to the PD cases in that they were drawn from the same source population and could be identified as cases, if they had disease.

This study protocol was approved by the institutional review boards of Ethics Committee of First Affiliated Hospital of Xinjiang Medical University. This study is a retrospective study, we don't need to obtain informed consent from eligible patients.

Clinical and Demographic Characteristics Collection

Baseline characteristics of cases and controls were examined (table 1), including factors known to affect vitamin D status such as age, sex, race, smoking status,uric acid,blood calcium,fasting blood glucose,glycated hemoglobin.

25(OH)D Detection

Using immunoassay-based vitamin D measuring assays at the central laboratory of The First Affiliated Hospital of Xinjiang Medical University.

Statistical analysis.

T-test and chi-square test were used to the comparison of Continuous variable and categorical variables. Total 25(OH)D was analyzed categorically, using the established clinical criteria for vitamin D deficiency (25(OH)D<20 ng/mL) , vitamin D insufficiency (25(OH)D 20-29 ng/mL),and vitamin D sufficient(25(OH)D ≥ 30 ng/mL),vitamin D sufficient (25(OH)D ≥30 ng/mL)as the reference.Odds ratios (ORs) and 95% confidence

intervals (CI) were calculated for each quartile individually, using the highest quartile as the reference. Logistic regression analysis was used to evaluate the association between vitamin D concentrations and PD Hoehn and Yahr (HY) stage PD auration, adjusting for age at sample draw. General linear regression models were used for testing associations of vitamin D duration of PD illness. All analyses were performed using the SPSS 26.0 for Mac statistical software(SPSS Inc, Chicago, Illinois, United States), and statistical significance was defined as p 0.05.

Results

Table 1 shows several demographic characteristics of the subjects. The PD cases had a higher age(65.86 ±10.00 years for cases vs 52.88±9.39 years for controls), No significant differences in sex, race, Hepertension,blood calcium,fasting blood glucose low-density lipoprotein-cholesterol(LDL-C) Cystatin C were found between cases and controls. In clinical criteria the PD cases Hoehn and Yahr stage was 2.25±0.07.Compared with the control group, the total plasma 25 (OH)D level in the PD group was lower(32.39± 13.91vs 42.54± 17.72 ng / mL,p <0.001 .

25(OH)D is the vitamin D metabolite that is measured to assess a patient's vitamin D status.Vitamin D deficiency is diagnosed when 25(OH)D <20 ng/mL [13.14], vitamin D insufficiency is defined as 25(OH)D of 21–29 ng/mL, and 25(OH)D >30 ng/mL is considered sufficient[15].In clinical,the average HY stage in the cases was 2.25 ± 0.07.In univariate analysis, the total 25 (OH) D level was lower than that in the control group (32.39 ± 13.91 vs 42.54 ± 17.72 ng / mL, p <0.001).There was vitamin D deficiency in 21%of cases (21/100) compared with 4%of controls (4/100; p = 0.007)). Furthermore, 27% of cases (27/100) were vitamin D insufficient compared with 20% of controls (20/100; p = 0.234).

Multivariate analysis (Table 2) adjusting for baseline of age, Vitamin D deficiency(25(OH)D <20 ng/mL) were Significant associated with PD.The probability of vitamin D deficiency in PD patients is 17.13 times that of the control group (95% CI, 2.082-141.075). Low levels of 25 (OH) D are associated with increased disease prevalence.Individuals with levels in the lowest quartile of 25(OH)D values observed in our population had the highest prevalence of PD with an odds ratio of 11.786 with p =0.026(95%CI,1.342-103.51) compared with individuals with values in the highest quartile(Table 2) . After adjusting for these covariates, deficiency of total 25(OH)D remained enriched in PD with p=0.016.HY stage (3 or≥3) still differences(Figure)

Finally, we examined the relationship between the duration of symptoms and vitamin D levels. Our data shows that the total 25 (OH) D concentration is related to the disease duration (P = 0.002)(Figure)

Discussion

This case-control study of 100 cases and 100 controls in The First Affiliated Hospital of Xinjiang Medical University from January 2019 to December 2019,provides compelling evidence that vitamin D deficiency of PD patients is 17.13 times that in controls of similar ages with-out PD. Individuals with levels in the lowest quartile of 25(OH)D values had the highest prevalence of PD(p =0.026,OR=11.786,95%CI,1.342-103.51)compared with individuals with values in the highest quartile.To the best of our knowledge, this is the first study to investigate the relation between the deficiency of the 25(OH)D and PD in Xinjiang of China.

Several studies have reported an association of PD with lower plasma 25(OH)D concentrations[16-18]. Ding et al [4]study shows that there was vitamin D deficiency in 17.6% of cases (68/388) compared with 9.3% of controls (26/283; p =0.002). After adjusting for for age, sex, race, and vitamin D supplementation,deficiency of total 25(OH)D remained enriched in PD with p =0.03. Wang et al [19]study shows that Vitamin D deficiency (total 25 (OH) D <20 ng / mL) was significantly correlated with PD (P <0.0001).The lowest quartile of 25(OH)D values had the highest prevalence of PD with an OR = 2.66, P <0.0001 (95 %% CI, 1.746-4.03) compared with individuals with values in the highest quartile.Our study also draws results consistent with the above studies，in our case-control study, cases are 11.786 times as likely as controls to be in the lowest quartile compared with the highest quartile.

Suzuki et al[20] conducted a randomized, double-blind, placebo-controlled vitamin D intervention trial,the results showed that vitamin D significantly inhibited the deterioration of the Hoehn-Yahr staging score of PD patients compared with placebo. [difference between groups: P = 0.005; mean±SD change within vitamin D3 group: +0.02 ±0.62 (P = 0.79); change within placebo group: +0.33±0.70 (P = 0.0006)]. It is suggested that vitamin D has a delaying effect on the severity of disease in PD patients, and does not cause adverse reactions such as hypercalcemia.

In our study, it was verified that there is a certain correlation between VD and H-Y classification.Especially for patients who does not yet exist with motor dysfunction (HY grade <3),There was a significant negative correlation between serum VD concentration and H-Y grade.Therefore, it can be inferred that VD can be used as an index to predict the severity of PD before PD sports injury.The lower the serum VD concentration in PD patients, the more likely to be exercise impairment.

Sleemana et al[21]study result showed that mean serum 25(OH)D concentrations were lower in PD than control participants at baseline (44.1±21.7 vs. 52.2±22.1 nmol/L, p<0.05) and 18 months (44.2±23.6 vs. 55.7±28.8 nmol/L, p<0.05). There was a small but significant association between vitamin D status at baseline and disease motor severity at 36 months.

Our study is consistent with previous study results, and there is a certain correlation between VD and disease course.Especially for patients with a long course of disease (course> 6 months), the course of disease is significantly negatively correlated with serum VD concentration. With the extension of the course of disease, the value of VD in the serum of PD patients will decrease accordingly.

A prospective study[22]showed that there are no support to the hypothesis that vitamin D may reduce the risk of PD.In other words, supplementing VD before the disease cannot reduce the incidence of PD. Meamar et al [10] study confirmed that supplementing VD during PD cannot delay the development of the disease.Previous reports indicate that there is a significant difference in the biochemical levels of bone metabolism between PD cases and the control group, this may be due to the impact of PD, not the direct role of PD pathogenesis.

Scherzer et al [23] study pointed out that vitamin D has been produced in rats to improve the toxicity induced by 6-hydroxydopamine.Our study also shows that there is a certain correlation between VD and H-Y classification, but the correlation is not significant (R^2 = 0.4). Studies have shown that there is a certain polymorphism of VDR in the central nervous system, and this polymorphism affects the impact of VD on its

downstream response. However, it is not sufficient to explain the problem only by genetic polymorphism, so further research is needed to confirm it.

There are several limitations in our study.First,our study was conducted on patients and controls in the First Affiliated Hospital of Xinjiang Medical University, not the general Chinese population. The population and ethnic composition of this region and the differences in life are large. It is necessary to evaluate the population lacking vitamin D in other regions of China.Second,because of the relationship between detection methods, our study failed to detect the association between vitamin D from different sources and PD, only to show the correlation between serum VD concentration and PD disease progression, which needs further exploration in the next study.Three,our study is a case-control study and lacks longitudinal clinical evaluation, including multiple vitamin D measurements that fail to assess the relationship between vitamin D status (and its changes over time) and disease progression. In order to provide valuable information, the time window is essential for adequate exposure of vitamin D to prevent or delay the onset of PD. It is necessary to study the longitudinal cohort at different periods to provide valuable information.

Conclusions

In our study,the finding of a high incidence of vitamin D deficiency in the PD.High-risk PD patients with vitamin D deficiency who have not yet developed exercise impairment, these should undergo vitamin D measurement and vitamin D treatment as soon as possible.Particularly in elderly patients, the deficiency is closely related to the content of vitamin D.

Abbreviations

PD:Parkinson disease;25(OH) D:25-hydroxy-vitamin D;HY:Hoehn and Yahr; LDL-C:Low-density lipoprotein-cholesterol.

Declarations

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Authors' contributions

M.X. and W.J.X. conceptualized the current study objectives, analyzed the data, and wrote the manuscript draft.X.X. and Q.J.Z. had responsibility of the final content. All co-authors read and approved the final manuscript and were involved in the conception of the research plan.

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Availability of data and materials

Please contact author for data requests.

Ethics approval and consent to participate

The study protocol was approved by the institutional review boards of Ethics Committee of First Affiliated Hospital of Xinjiang Medical University.

Consent for publication

Not applicable.

Competing interests

The authors declare having no competing interests.

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Tables

Table 1 presents baseline characteristics of the study populations

	PD (100)	Control (100)	P-Value
Age, y	65.86± 10.00	52.88± 9.39	<0.001[a]
Males	54(54)	45(45)	0.203
Race(Han)	73(73)	65(65)	0.221
Hepertension	47(47)	49(49)	0.777
blood calcium	2.26± 0.12	2.27± 0.10	0.523
fasting blood glucose	5.27± 1.31	5.15± 1.61	0.571
LDL-C	2.48±0.82	2.62±0.86	0.221
Cystatin C	0.83±0.21	0.77±0.20	0.057
Clinical criteria			
Age at onset, y	62.15± 1.06		
Duration, y	4.09± 0.48		
Hoehn and Yahr stage	2.25± 0.07		
1	11(11)		
1.5	17(17)		
2	25(25)		
2.5	15(15)		
3	27(27)		
4	5(5)		
25(OH)D	32.39± 13.91	42.54± 17.72	<0.001[a]
<20 ng/mL	21(21)	4(4)	0.007[a]
20-29 ng/mL	27(27)	20(20)	0.234
≥30 ng/mL	52(52)	76(76)	0.033[a]

Abbreviations: 25(OH) D=25-hydroxy-vitamin D;LDL-C=low-density lipoprotein-cholesterol;PD= Parkinson disease;

a Statistically significant.

Table 2 presents multivariate analysis between total 25(OH) D with PD, and HY stage

	PD		HY		Duration	
	OR（95% CI）	P-Value	β	P-Value	β	P-Value
Clinical cutoff analysis						
<20 ng/mL	17.13（2.082-141.075）	0.008[a]	-1.238	0.522	-20.844	<0.001[a]
20-29 ng/mL	0.719（0.230-2.245）	0.570	0.042	0.979	-1.362	0.357
≥30 ng/mL	Ref	Ref	Ref	Ref	Ref	Ref
Quartile analysis						
Total 25(OH) D						
Q1(7.5-19.31 ng/mL)	11.786（1.342-103.51）	0.026[a]	27.849	<0.001[a]	23.223	<0.001[a]
Q2(19.31-30.43 ng/mL)	0.974（0.316-2.998）	0.963	4.195	0.012[a]	2.413	0.087
Q3(30.43-40ng/mL)	0.459（0.138-1.528）	0.204	0.983	0.281	-0.345	0.733
Q4(>40 ng/mL)	Ref	Ref	Ref	Ref	Ref	Ref

Abbreviations: CI =confidence interval; HY= Hoehn and Yahr; 25(OH) D=25-hydroxy-vitamin D;OR =odds ratio; PD= Parkinson disease; Ref. =reference

All relations are statistically adjusted for age.

βindicates regression coefficient.

[a] Statistically significant.

Figures

Figure 1

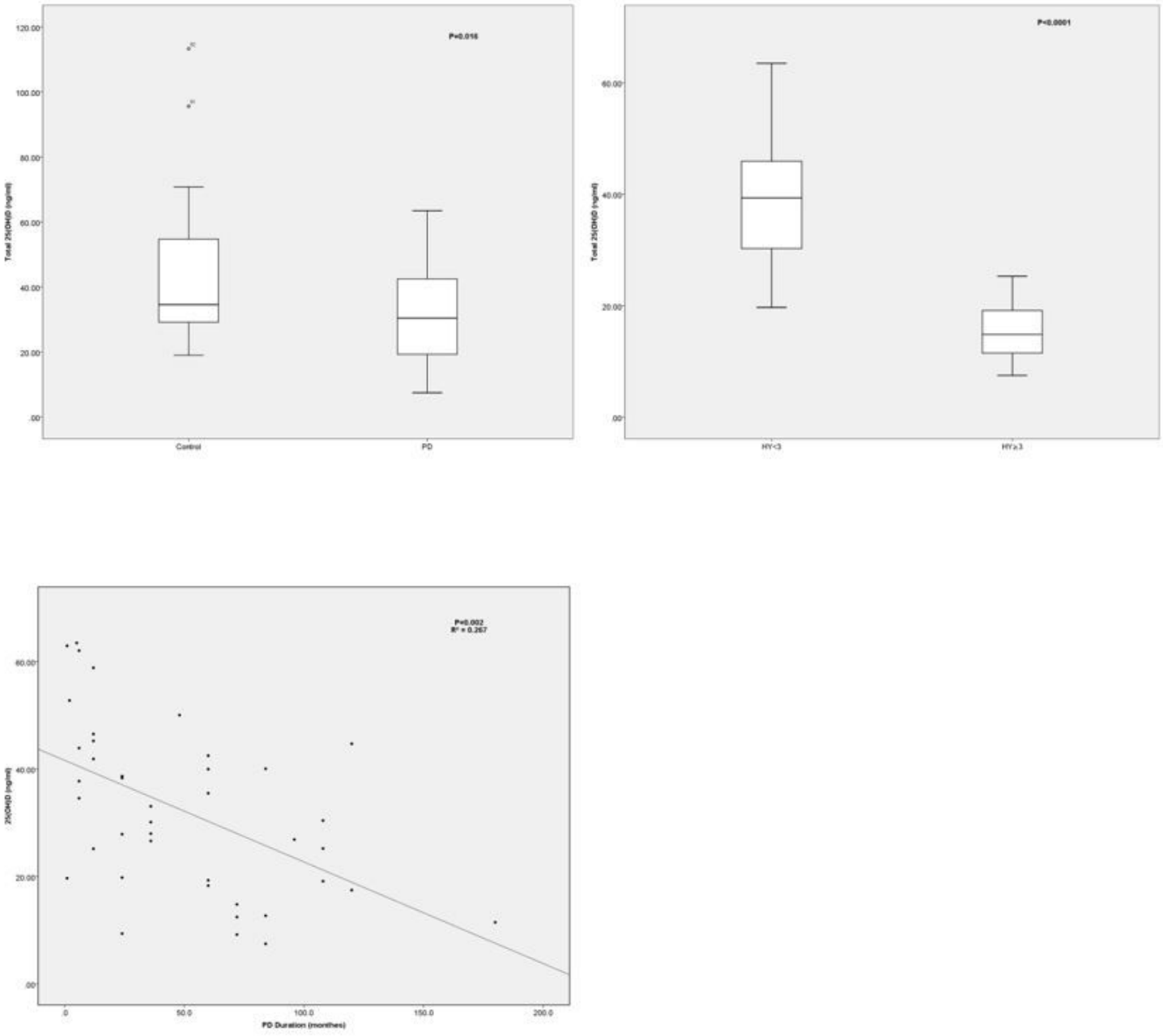

Figure 1

Plasma levels of total 25(OH) D in PD .Relations between total 25(OH) D plasma levels and PD, HY stage (□3 or≥3),and disease duration are visualized. Solid line represents fitted correlation between vitamin D levels and symptom duration, HY= Hoehn and Yahr; 25(OH) D=25-hydroxy-vitamin D;PD= Parkinson disease;