Original Research Paper

Volume - 10 | Issue - 6 | June - 2020 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Biochemistry

CHANGES OF VITAMIN D LEVELS IN PARKINSON'S DISEASE IN LIBYA

Dr. Hatem fawzi Gharour	Department of Biochemistry, Faculty of medicine, University of Benghazi, Benghazi, Libya.
Dr. M. L. Rajeswari*	Associate professor, Department of Biochemistry, Rangaraya Medical College, Kakinada, E.G. Dist, Andhra Pradesh, India. *Corresponding Author
Dr. Andrew J Bennett	School of biomedical sciences, University of Nottingham, Nottingham, UK.
Dr. Deborah j Briggs	School of biomedical sciences, University of Nottingham, Nottingham, UK.
Dr. Salima M Hawda	Department of Biochemistry, Faculty of medicine, University of Benghazi, Benghazi, Libya.
Dr. Abdelhamid El-Zawawi	Neurology department , Benghazi medical centre, University of Benghazi, Benghazi, Libya.
Dr. Peela Jagannadha Rao	Department of Biochemistry and Genetics, School of Medicine, St Matthews University, Grand Cayman, Cayman islands.

ABSTRACT

Background: Parkinson's is one of the major debilitating disorders in elderly people all over the world including Libya especially farmers. The biochemical studies shown that, serum vitamin D concentration was lower among Parkinson's disease cases and it was also associated with age, sex, marital status, education, leisure–time physical activity, smoking, alcohol consumption, body mass index, diabetes, hypertension, and the serum cholesterol. The present study is to see how vitamin D levels in the serum of patients with Parkinson's disease are related to its risk.

Material And Methods: A total 104 subjects, including control, were enrolled in the study and further grouped as, 52 clinically examined Idiopathic Parkinson's disease patients (35 males and 17 females) while remaining 52 were taken as age and sex matched healthy controls.
Serum vitamin D (25(OH)D) was determined from frozen samples, stored at baseline. Estimates of the relationship between serum vitamin D concentration and Parkinson's disease incidence were calculated using Cox's model.

Results: The relative risk of the disease between the highest and lowest quartiles of vitamin D concentration was 0.35 (95% CI 0.15–0.81, p for trend=0.006).

Conclusion: The results are consistent with the suggestion that high vitamin D status protects against Parkinson's disease.

KEYWORDS :

INTRODUCTION

Parkinson's disease (PD) is one of the major debilitating disorders in elderly people all over the world same as in Libya. Prevalence of PD is 44.2/100000 population. Epidemiological data shows farmers are suffering more than general population in Libya. There is a high prevalence of PD in the eastern area mainly in Benghazi, Al-Marg, Beida, Sussa, where the adult residents are agricultural workers. Current study is to investigate whether serum vitamin D level predicts the risk of PD. Serum vitamin D (25(OH)D) was determined from frozen samples, stored at baseline. Estimates of the relationship between serum vitamin D concentration and PD incidence were calculated using Cox's model [1][2]. Vitamin D plays an important role in the pathogenesis of skeletal disorders and calcium homeostasis. Vitamin D inadequacy also predicts increased risk of other chronic conditions e.g. cancer, cardiovascular diseases, and type 2 diabetes [3]. In recent times long term usage of low vitamin D intake was proposed to play a significant role in the pathogenesis of PD. According to the suggested biological mechanism, the PD may be caused by a continuously inadequate vitamin D status leading to a chronic loss of dopaminergic neurons in the brain [4]. The epidemiological evidence of an association between vitamin D and PD is, however, limited to cross-sectional studies, showing lower vitamin D status in patients of PD compared with healthy controls [5].

MATERIAL AND METHODS

A total 104 subjects, including control, were enrolled in the study and further grouped as, 52 clinically examined Idiopathic PD patients (35 males and 17 females) while remaining 52 were taken as age and sex matched healthy controls.

Inclusion Criteria:

1) Male and female patients diagnosed as Idiopathic PD aged between 50 to 70 years. Without any drug therapy.2) Control group included healthy volunteers who were consistent with the patients according to age, sex and body mass index.

Exclusion Criteria:

1) Patients having blood disorders, obvious malignancy, hepatic, renal or cardiac disease and additional history of alcohol or smoking will be excluded from the study.2) Patients with co-existing neurological disorder like Alzheimer's disease, stroke or any kind of neural deficit was also excluded.3) Patients on any concomitant medication such as Lipid lowering drug, antioxidants, vitamins, minerals, herbal treatment, or the substance which may alter our study parameters excluded from study.

10 ml venous fasting blood samples from patients and controls were collected. 4 to 5ml blood was collected in the heparinised vacutainers and remaining 5 to 6 ml blood was collected in plain vacutainers. The samples were centrifuged, the serums were frozen at −20 °C. serum 25(OH)D_3 level were determined using radioimmunoassay method (Immunodiagnostic Systems, Boldon, UK).[6]The sensitivity of the 25 OH-D ELISA test system for Accu-Bind Vitamin D is 0.67 ng / ml. The coefficients of variation between input and titration were 3.95% and 5.62% respectively. Serum vitamin D (25(OH)D) was determined from frozen samples, stored at baseline. Estimates of the relationship between serum vitamin D concentration and PD incidence were calculated using Cox's model [2].

RESULTS

Individuals with higher serum vitamin D concentrations showed a reduced risk of PD. The relative risk between the highest and lowest quartiles was 0.33 (95% CI 0.14–0.80) after adjustment for sex, age, marital status, education, alcohol consumption, leisure-time physical activity, smoking, body mass index.

At baseline, PD cases were more often non-smokers, non–hypertensive, and non–diabetics than subjects who were free from the disease as shown in Table number.1. Serum vitamin D concentration was lower among PD cases and it was also associated with age, sex, marital status, education, leisure-time physical activity, smoking, alcohol consumption, body mass index, diabetes, hypertension, serum cholesterol and the season of measurement as shown in Table number.2.

Table 1. Selected sex– and age–adjusted baseline characteristics by Parkinson's disease.

	Parkinson's disease		p for heterogeneity
	Noncases (N=186)	Cases (N=40)	
Age[1](yrs)	61·8 (8·0)	60·4 (6·5)	0·23
Males[2](%)	43.1	47.2	0.56
education (%)	19.8	23.2	0.55
Married (%)	65.9	68.7	0.66
Regular leisure time physical activity (%)	11.3	7.6	0.42
Smokers (%)	18.7	6.2	0.02
Hypertensive (%)	35.7	21.1	0.03
Body mass index (kg/m2)	26.8 (4.2)	26.5 (3.3)	0.62
Diabetes (%)	8.7	2.7	0.13
Serum total cholesterol (mmol/l)	7.34 (1.37)	7.25 (1.34)	0.65
Serum 25(OH)D (nmol/l)	41.8 (19.5)	36.3 (18.5)	0.05

Table 2. Selected sex– and age–adjusted baseline characteristics by serum 25(OH)D quartiles.

			Serum 25(OH)D mean (SD)		
	1st quartile (N=233)	2nd quartile (N=245)	3rd quartile (N=231)	4th quartile (N=241)	p-value
Age[1](yrs)	63.8 (8.1)	62.2 (8.1)	61.2 (7.8)	60.0 (7.6)	<0.001
Male sex[2](%)	45.1	43.4	42.6	41.8	0.18
education (%)	12.7	18.3	24.6	23.7	<0.001
Married (%)	61.9	65.6	65.8	70.5	<0.001
Regular leisure time physical activity (%)	5.5	10.3	12.9	15.9	<0.001
Smokers (%)	22.3	17.3	18.8	15.6	0.002
Hypertension (%)	37.2	36.6	35.5	32.4	0.04
Body mass index (kg/m^2)	26.7 (4.6)	27.1 (4.3)	27.1 (4.0)	26.2 (3.6)	0.03
Diabetes (%)	11.2	8.9	8.2	6.1	<0.001
Serum total cholesterol (mmol/l)	7.19 (1.41)	7.30 (1.35)	7.39 (1.37)	7.48 (1.32)	<0.001

Quartiles for men 8–28, 29–41, 42–56, 57–159 nmol/l; for women 7–25, 26–36, 37–49, 50–151 nmol/l

A significant inverse association between sex– and age–adjusted serum vitamin D and PD incidence was found as shown in table number 3. The RR of the disease between the highest and lowest quartiles of vitamin D concentration was 0.35 (95% CI 0.15–0.81, p for trend=0.006). After further adjustment for the potential confounders, including body mass index, leisure-time physical activity, smoking, education, marital status, alcohol consumption, the association persisted (RR 0.33, CI 0.14–0.80, p for trend=0.006). Further adjustment for serum cholesterol and hypertension or exclusion of the disease cases occurring during the first two years of follow–up did not notably alter the results either. Inclusion of an interaction term between vitamin D and sex, age, body mass index, serum cholesterol, blood pressure, and the season of measurement did not notably alter the results.

Table 3. Relative risks (Rrs) with 95% confidence intervals (CIs) for Parkinson's disease cases by baseline serum 25(OH)D.

	Serum 25(OH)D				
	1st quartile	2nd quartile	3rd quartile	4th quartile	p-value
Number of cases	17	15	10	8	
Sex–and age–adjusted model	1.00	0.73 (0.36–1.46)	0.47 (0.21–1.03)	0.35 (0.15–0.81)	0.006

Quartiles for men 8–28, 29–41, 42–56, 57–159 nmol/l; for women 7–25, 26–36, 37–49, 50–151 nmol

DISCUSSION

This study shows that low serum vitamin D level predicts an elevated risk of PD incidence. People with a serum vitamin D concentration of at least 50 nmol/l had a 65% low risk than those with values below 25 nmol/l after adjustment for several potential confounders. Accordingly, the mean serum vitamin D level in the present population was about 50% of the suggested optimal level (75–80 nmol/l). Our findings are thus consistent with the hypothesis5 that chronic inadequacy of vitamin D is a risk factor of PD [7][8][9].The vitamin D receptors and an enzyme responsible for the formation of the active form 1,25(OH)2D have been found in high levels in the substantia nigra, the region of the brain affected most by PD[10]. This raises the possibility that chronic inadequacy of vitamin D leads to the loss of dopaminergic neurons in the substantia nigra region and further PD [11]. Concentration of vitamin D is of critical importance for the health of inhabitants who live in the Nordic latitudes where there is decreased exposure to sunlight during the winter. Hence fortification or supplementation of vitamin D is necessary for people living in the northern latitudes during the winter to maintain adequate levels of serum 25(OH)D3 to maintain optimal body function and prevent diseases.[12]

There are, however, some weaknesses to be considered. First, the small number of cases may have caused unstable results. Second, only a single measurement of serum 25-OHD was available which fails to take into account the intraindividual seasonal variation 13]. The major dietary source of vitamin D is fatty fish, whose consumption is also suggested to be beneficial against PD, due to n–3 polyunsaturated fatty acids [14] [15]. The findings are, however, contradictory and vitamin D has several other determinants. Third, the risk factors of PD are not well known, and therefore despite comprehensive adjustments for potential confounders residual confounding may remain.

CONCLUSION

The results are consistent with the suggestion that high vitamin D status protects against PD. It cannot, however, be excluded that the finding is due to residual confounding and further studies are thus needed.

REFERENCES

1. Ma, Chaoran; Liu, Yesong; Neumann, Samantha; Gao, Xiang (2017). "Nicotine from cigarette smoking and diet and Parkinson disease: a review". Translational Neurodegeneration. 6: 18. doi:10.1186/s40035-017-0090-8.
2. Grant WB. Epidemiology of disease risks in relation to vitamin D insufficiency. Prog Biophys Mol Biol. 2006;92(1):65–79.
3. Ahlskog, JE (19 July 2011). "Does vigorous exercise have a neuroprotective effect in Parkinson disease?". Neurology. 77 (3): 288–94.
4. By Caroline M. Tanner, (2011), Environmental Factors and Parkinson's disease; Annual Review of Neurol Neurosurg Psychiatry. 2014;73(5):214–242.
5. Sato Y, Honda Y, Iwamoto J, Kanoko T, Satoh K. Abnormal bone and calcium metabolism in immobilized Parkinson's disease patients. Mov Disord. 2005;20(12):1598–1603.
6. Enko D, Kriegshäuser G, Stolba R, Worf E, Halwachs-Baumann G. Method evaluation study of a new generation of vitamin D assays. *Biochem Med (Zagreb)*. 2015;25(2):203 212. Published 2015 Jun 5. doi:10.11613/BM.2015.020
7. Kilkkinen A, Knekt P, Heliovaara M, et al. Vitamin D status and the risk of lung cancer: a cohort study in Finland. Cancer Epidemiol Biomarkers Prev. 2008;17(11):3274–3278.
8. Evatt ML, Delong MR, Khazai N, Rosen A, Triche S, Tangpricha V. Prevalence of vitamin d insufficiency in patients with Parkinson disease and Alzheimer disease. Arch Neurol. 2008;65(10):1348–1352.
9. Bischoff-Ferrari HA, Giovannucci E, Willett WC, Dietrich T, Dawson-Hughes B. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. Am J Clin Nutr. 2006;84(1):18–28.
10. Eyles DW, Smith S, Kinobe R, Hewison M, McGrath JJ. Distribution of the vitamin D receptor and 1 alpha-hydroxylase in human brain. J Chem Neuroanat. 2005;29(1):21–30.
11. Buell JS, Dawson-Hughes B. Vitamin D and neurocognitive dysfunction: preventing "D"ecline? Mol Aspects Med. 2008;29(6):415–422.
12. Huotari A, Herzig KH. Vitamin D and living in northern latitudes--an endemic risk area for vitamin D deficiency. Int J Circumpolar Health. 2008;67(2–3):164–178.
13. Stamp TC, Round JM. Seasonal changes in human plasma levels of 25-

hydroxyvitamin D. Nature. 1974;247(442):563–565.
14. .van Dam RM, Snijder MB, Dekker JM, et al. Potentially modifiable determinants of vitamin D status in an older population in the Netherlands: the Hoorn Study. Am J Clin Nutr. 2007;85(3):755–761.
15. Bergström L, Kylberg E, Hagman U, Erikson H, Bruce Å. The food composition database KOST: the National Administration's information system for nutritive values of food. Vår Föda 1991;43:439 447.