ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
Index Copernicus Value: 49. 23

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 3, Issue –4, July - 2018, Page No. : 299 - 303

Serum vitamin D status in Parkinson disease in an Indian population cohort

Dr. Gaurav Gupta, Dr. Anand Ram, Dr. Navneet Kumar

Department of Neurology GSVM Medical College Kanpur, U.P.

Correspondence Author: Dr. Gaurav Gupta, Department of Neurology GSVM Medical College Kanpur, U.P, India.

Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

Objective: Recent accumulating evidence shows that vitamin D deficiency is prevalent in individuals with Parkinson disease and the administration of vitamin D might provide symptomatic benefit and improves quality of life in PD. The purpose of the present study is to perform a meta-analysis on the 25-hydroxyvitamin D (25(OH) D) status in the Indian cohort of patients with PD.

Methods: 150 cases and 200 controls between ages 50 to 80 years who attended neurology OPD from January 2016 to March 2017 at LLR Hospital, Kanpur were selected for analysis.Participants were identified with Parkinson's disease according to MDS Clinical Diagnostic Criteria for PD. Vitamin D levels (25OHD <20 ng/mL: deficient; 20 to 30 electrochemiluminescence immunoassay and intact PTH by immunoradiometric assay. Multivariate logistic regression was used to test for associations between vitamin D and PD after adjustments were made for sex, age, smoking, alcohol use, education, BMI, and vitamin D intake and sunlight exposure.

Results: Deficient and insufficient serum levels of 25-hydroxy-vitamin D3 were associated with PD in multivariate analyses with p values of less than 0.005. Total 25-hydroxy-vitamin D levels were deficient in 22% of patients with PD compared with 12% of controls.The relative risk of developing Parkinson's disease was 67% lower for the quarter of patients with the highest vitamin D levels, compared to the quarter of patients with the lowest vitamin D. Low levels of 25-hydroxy-vitamin D3 levels were correlated with higher total Unified Parkinson's Disease Rating Scale scores at baseline and during follow-up.

Conclusions: Results of our meta-analysis show that PD patients in India had lower mean levels of 25-hydroxyvitamin D than healthy controls.

Introduction

Parkinson's disease (PD) is the very common neurodegenerative disease. It is characterized by degeneration of the dopaminergic neurons in the substantia nigra, resulting in clinical symptoms such as resting tremor, rigidity and bradykinesia [1, 2]. It has been suggested that PD is the result of a complex of nutritional factors, genetic factors, environmental factors and aging [3]; however, the nature of the environmental factors remains largely unclear. Recently, emerging data suggest that vitamin D may play an important role in the progression of the development of PD. It is well established that the vitamin D endocrine system plays a critical role in calcium homeostasis and bone health; however, in recent decades, the broad range of

physiological actions of vitamin D has been increasingly recognized. In addition to its role in proliferation, differentiation and immunomodulation, there is mounting evidence to support an intricate role of vitamin D in brain development and function in health and disease [4]. Optimal balance, muscle strength, and innate immunity require sufficient vitamin D levels, and its deficiency is correlated with increasing risk for a range of adverse health outcomes including cardiovascular diseases [5], stroke [6, 7], multiple sclerosis [8], infectious disease [9, 10] and cancer [11]. Increasing evidence has shown that individuals with PD have lower levels of 25-hydroxyvitamin (25[OH]D) relative to healthy controls and vitamin D deficiency has been proposed to be linked to PD through multiple mechanisms [12]. There is an increasing interest in a range of actions of vitamin D. Low vitamin D status play an important role in the development or pathogenesis of PD [13]. It is reported that the distribution of vitamin D receptors in the substantia nigra is widely known to be affected in PD, and the involvement of this vitamin has been revealed in the regulation of tyrosine hydroxylase gene expression and consequently dopamine biosynthesis [14, 15]. In the present study, we performed a meta-analysis to evaluate comprehensively the vitamin D levels in individuals with PD, which has potential implications for the prevention and treatment of this disease.

Several study has shown that there is an association between Vitamin D and Parkinson's diseases. However very few study have been reported from India. this study have been planned to find out the association between Vitamin D level and Parkinson's disease in Indian population.

Objectives

The purpose of the present study is to perform a meta-analysis on the 25-hydroxyvitamin D (25(OH)D) status in the Indian cohort of patients with PD.

Materials and Methods

Study Design

Cross-sectional, observational, prospective

Selection of cases

150 cases between ages 40 to 84 years who attended neurology OPD from January 2016 to March 2017 at LLR Hospital, Kanpur were selected for analysis. Participants were identified with Parkinson's disease according to MDS Clinical Diagnostic Criteria for PD.

Inclusion Criteria

Patients having age >40years with the Parkinson's disease as per movement disorder society clinical diagnostic criteria for Parkinson disease. The patient must have bradykinesia, resting tremor or rigidity with supportive criteria of clear response to dopaminergic therapy and/or presence of levodopa induced dyskinesia.

Exclusion Criteria

Patients having age <40 years ,patients with co-morbid conditions like CKD, hypothyroidism, sacoidosis, rickets, calcium/phosphorus metabolism disorder, patient already taking/taken vitamin D supplementation and patients having Parkinson plus syndrome were excluded from the analysis.

Selection of control

Normal healthy age and sex matched 200 controls above 40 years of age without any neurological disease were included.

Methodology

Written inform consent was obtained from all participants and detailed history and thorough general and systemic examination was done. Patient were investigated with complete blood count with general blood picture, liver function tests, serum creatinine and blood urea levels, serum electrolytes (Na+/K+/Ca++), blood sugar - fasting/post prandial, glycosylated hemoglobin levels (HbA1C level).Estimation of serum 25-OH vitamin D level measured by quantitative chemiluminescence

immunoassay method. Value categorised as normal (≥30 ng/ml), insufficient (20-29 ng/ml) and deficient (<20 ng/ml). Multivariate logistic regression was used to test for associations between vitamin D and PD after adjustments were made for sex, age, smoking, alcohol use, education, BMI, and vitamin D intake and sunlight exposure .Assessment of severity of Parkinsons disease is done by Unified Parkinson's Disease Rating Scale scores (UPDSR).

Results

Mean age of study population was 64.96±10.0 years in cases and mean age in control was 62.92±10.0 years. Mean serum vitamin D level-20.89±9.23 ng/ml. Deficient and insufficient serum levels of 25-hydroxy-vitamin D3 were associated with PD in multivariate analyses with p values of less than 0.005. Total 25-hydroxy-vitamin D levels were deficient in 22% of patients, insufficient in 40% of patient and normal in 38% of patient with Parkinson's disease compared with 12% of controls were deficient and 28% were insufficient and 60% were normal (Figure 1).The relative risk of developing Parkinson's disease was 67% lower for the quarter of patients with the highest vitamin D levels compared to the quarter of patients with the lowest vitamin D levels. Low levels of 25-hydroxy-vitamin D levels were correlated with higher total Unified Parkinson's Disease Rating Scale scores in our study.

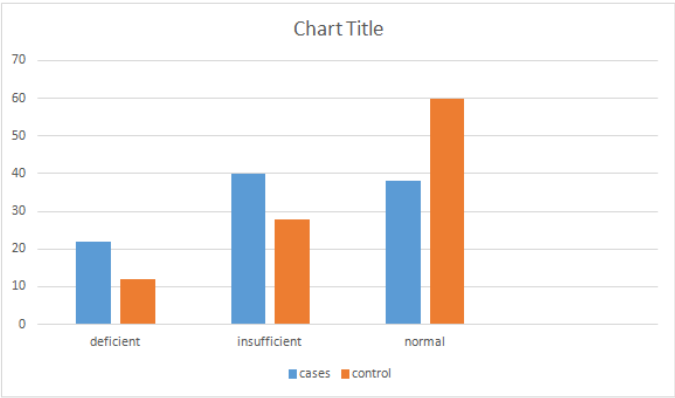

Fig.1 showing prevalence of vitamin D in cases and control

Discussion

The main findings in this meta analysis are that PD patients had lower mean 25(OH)D levels as compared to controls. Vitamin D deficiency is an important condition in the elderly. Prevalence of neurodegenerative disease is also higher in these patients. Vitamin D is produced in body in skin on exposure to UV-B radiation and is found in limited food sources [16]. Some involved factors in vitamin D deficiency are advanced age, avoidance of sun exposure, and darker skin. Serum 25(OH)D is the most useful indicator of vitamin D level of body. A number of biologically plausible mechanisms may explain the associations between vitamin D status and PD. Vitamin D has been shown to exhibit neuroprotective effects through antioxidative mechanisms, neuronal calcium regulation, immunomodulation, enhanced nerve conduction, and detoxification mechanisms. The vitamin D receptors and an enzyme responsible for the formation of the active form 1,25-hydroxyvitamin D have been found in high levels in the substantia nigra, the region of the brain affected most by Parkinson disease [17, 18]. This raises the possibility that chronic inadequacy of vitamin D leads to the loss of dopaminergic neurons in the substantia nigra region and further Parkinson disease. The VDR receptor is an intranuclear receptor. It is encoded by a large gene, over 100 kb, on chromosome 12q12-14 [19]. It is made up of two promoter regions, eight protein-coding exons, and six untranslated exons [19]. An animal study knocking out the VDR resulted in rats with muscular and motor impairments, alopecia, short stature, lower body weight, shorter gait, and impairments on rota rod testing (measures gait and balance) [20]. The mice did not appear to have cognitive impairments there are over 60 identified polymorphisms for VDR. Polymorphisms are mutations with an allele frequency of at least 1% in a given

population. These subtle DNA sequence variation, which occur often in the population, can have a modest but real biological effect. Polymorphisms can effect enhanced/reduced transcription, altered posttranscriptional or posttranslational activity, or the tertiary structure of the gene product [19].

Animal studies have investigated the effects of VDR gene transcription in neuronal cells, and have shown that VDRs and vitamin D are key molecules to brain development, the prevention of anxiety, the induction of glial-derived neurotrophic factor, and the induction of nerve growth factor synthesis [21]. Confirmation of these findings in a large cohort is needed. As well, further research is required to better understand the role of vitamin D in PD associated pathologies. Large multi-center double blinded randomized controlled clinical trials of vitamin D supplementation for the prevention of PD are needed to be conducted to determine the risks and benefits. Such an intervention, if proven safe and effective, could have substantial public health importance.

Conclusion

Results of our meta-analysis show that PD patients in India had lower mean levels of 25-hydroxyvitamin D than healthy controls. These data are certainly helpful in the management of Parkinson disease patients with low Vitamin D levels.

References

1. Dick FD, De Palma G, Ahmadi A, Scott NW, Prescott GJ, Bennett J, Semple S, Dick S, Counsell C, Mozzoni P, Haites N, Wettinger SB, Mutti A, Otelea M, Seaton A, So¨derkvist P, Felice A, Geoparkinson study group (2007) Environmental risk factors for Parkinson's disease and parkinsonism: the Geoparkinson study. Occup Environ Med 64(10):666–672

2. Hancock DB, Martin ER, Mayhew GM, Stajich JM, Jewett R, Stacy MA, Scott BL, Vance JM, Scott WK (2008) Pesticide exposure and risk of Parkinson's disease: a family-based case–control study. BMC Neurol 8(3):6

3. Henchcliffe C, Beal MF (2008) Mitochondrial biology and oxidative stress in Parkinson disease pathogenesis. Nat Clin Pract Neurol 4(11):600–609

4. DeLuca GC, Kimball SM, Kolasinski J, Ramagopalan SV, Ebers GC (2013) Review: the role of vitamin D in nervous system health and disease. Neuropathol Appl Neurobiol 39(5):458–484

5. Zittermann A, Schleithoff SS, Koerfer R (2006) Vitamin D insufficiency in congestive heart failure: why and what to do about it? Heart Fail Rev 11(1):25–33

6. Chaudhuri JR, Mridula KR, Alladi S, Anamika A, Umamahesh M, Balaraju B, Swath A, Bandaru VS (2014) Serum 25-hydroxyvitamin D deficiency in ischemic stroke and subtypes in Indian patients. J Stroke 16(1):44–50

7. Brondum-Jacobsen P, Nordestgaard BG, Schnohr P, Benn M (2013) 25-hydroxyvitamin D and symptomatic ischemic stroke: an original study and meta-analysis. Ann Neurol 73(1):38–47

8. Martinelli V, Dalla Costa G, Colombo B, Dalla Libera D, Rubinacci A, Filippi M, Furlan R, Comi G (2014) Vitamin D levels and risk of multiple sclerosis in patients with clinically isolated syndromes. Mult Scler 20(2):147–155

9. Guzma´n-Fulgencio M, Garcı´a-A´ lvarez M, Berenguer J, Jime´nez-Sousa MA´ , Cosı´n J, Pineda-Tenor D, Carrero A, Alda´miz T, Alvarez E, Lo´pez JC, Resino S (2014) Vitamin D deficiency is associated with severity of liver disease in HIV/HCV coinfected patients. J Infect 68(2):176–184

10. Camargo CA Jr, Manson JE (2014) Vitamin D supplementation and risk of infectious disease: no easy answers. Am J Clin Nutr 99(1):3–4

11. Gorham ED, Garland CF, Garland FC, Grant WB, Mohr SB, Lipkin M, Newmark HL, Giovannucci E, Wei M, Holick MF (2007) Optimal vitamin D status for

colorectal cancer prevention: a quantitative meta-analysis. Am J Prev Med 32(3):210–216

12. Evatt ML (2010) Beyond vitamin status: is there a role for vitamin D in Parkinson disease? Arch Neurol 67(7):795–797

13. Newmark HL, Newmark J (2007) Vitamin D and Parkinson's disease—a hypothesis. Mov Disord 22(4):461–468

14. Evatt ML, DeLong MR, Kumari M, Auinger P, McDermott MP, Tangpricha V, Parkinson Study Group DATATOP Investigators (2011) High prevalence of hypovitaminosis D status in patients with early Parkinson disease. Arch Neurol 68(3):314–319

15. Eyles DW, Smith S, Kinobe R, Hewison M, McGrath JJ (2005) Distribution of the vitamin D receptor and 1 alpha-hydroxylase in human brain. J Chem Neuroanat 29(1):21–30

16. Lawson DE, Paul AA, Black AE, Cole TJ, Mandal AR, Davie M (1979) Relative contributions of diet and sunlight to vitamin D state in the elderly. Br Med J 2(6185):303–305

17. Eyles DW, Smith S, Kinobe R, Hewison M, McGrath JJ (2005) Distribution of the vitamin D receptor and 1 alpha-hydroxylase in human brain. J Chem Neuroanat 29(1):21–30

18. Buell JS, Dawson-Hughes B (2008) Vitamin D and neurocognitive dysfunction: preventing ''D''ecline? Mol Aspects Med 29(6):415–422

19.Kostner K, Denzer N, Muller CS, Klein R, Tilgen W, Reichrath J. The relevanceof vitamin D receptor (VDR) gene polymorphisms for cancer: a review of theliterature. Anticancer Res 2009;29(September (9)):3511–36.

20.Burne TH, McGrath JJ, Eyles DW, Mackay-Sim A. Behavioural characteriza-tion of vitamin D receptor knockout mice. Behav Brain Res 2005;157(February(2)):299–308

21. Han X, Xue L, Li Y, Chen B, Xie A (2012) Vitamin D receptor gene polymorphism and its association with Parkinson's disease in Chinese Han population. Neurosci Lett 525(1):29–33