Treatment of Levodopa-induced dyskinesia with Vitamin D: A Randomized, double-blind, placebo-controlled trial

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Abstract

Dyskinesia refers to any involuntary movement, such as chorea, dystonia, ballism that affect any part of the body. Levodopa-induced dyskinesia is a neurological disorder that afflicts many patients with Parkinson disease usually 5 years after the onset of levodopa therapy and can cause severe disability. The pathophysiology of this dyskinesia is complex and not fully understood. However, the association between vitamin D and Parkinson disease is interesting. The present study was conducted to evaluate the effect of vitamin D on levodopa induced dyskinesia in patients with Parkinson's disease .In this Double blind clinical trial, 120 patients with PD divided into two groups randomly, vitamin D and placebo group. A dose of 1000 IU/d was selected, Demographic information is registered. In the first visit, three variables have been measured which were the duration, severity of dyskinesia and unified Parkinson's disease rating scale (UPDRS). These variables were measured again after 3 months and the data was analyzed using SPSS 22. There are no differences between two groups after 3 months. This study revealed, vitamin D has no effects on improvement of levodopa induced dyskinesia.

Introduction

Levodopa-induced dyskinesia is one of the most important parameters of Parkinson's disease along with other characteristics such as tremor, rigidity and bradykinesia.[1] The Pathophysiology of dyskinesia is very complex, and yet its basic mechanism is not well defined. Dyskinesia include dystonia, chorea, ballism, myoclonus, tics, and tremor.[2,3] In patients with Parkinson's disease (PD), the treatment with levodopa causes various dyskinetic movements disorder. It usually appear within 5 years of treatment and may be due to depletion of dopaminergic nigrostriatal and pulsatile stimulation of levodopa on dopaminergic receptors.[4,5] The role of vitamin D in Parkinson disease is interesting, the results of animal studies show that vitamin D may has protective effect in dopamine cells.[6] The effect of vitamin D on the levodopa induced dyskinesia has not been studied in any research so far. In this study we aimed to evaluate the effect of vitamin D on levodopa induced dyskinesia in patients with Parkinson's disease.

Materials and Methods

A randomized, double-blind placebo-controlled, parallel group trial was done at the Department of Neurology of Rasoul-Akram Hospitals affiliated with the Iran University of Medical Sciences, Tehran, Iran. The study was approved by Ethical Committee of the University. The study population included the patients with Parkinson disease that have levodopa induced dyskinesia. They were interviewed in the neurology clinic. All participants signed a written informed consent. The 120 patients with PD divided into two groups randomly, vitamin D and placebo and the demographic information registered. The vitamin D3 (1000 IU/d) was administered orally for 3 months to patients. In the first visit, three variables have been measured which are the duration, according to per day by hour and severity of dyskinesia, according to UPDRS IV sub score and also UPDRS. These variables were measured again after 3 months. We used SPSS 22 for statistical analyses and P values <0.05 were considered to indicate significant level. The mean and standard deviation (SD) were used to characterize the study population and a paired t-tests comparing the difference in the means of two groups. We used also the regression analysis to evaluate the overall effect of age, sex, duration of dyskinesia and Parkinson disease (years) on the treatment outcomes.

Results

A total of 120 patients with PD divided into two groups randomly, vitamin D and placebo. 60 patients were assigned to receive vitamin D3, and 60 patients assigned to receive placebo for 3 months and evaluated the duration and severity of dyskinesia before and after treatment. The mean age was 44.02±13.2 in vitamin D group and 49.9±11.4 in placebo group. The Parkinson disease duration in vitamin D group was 7.2 and 7.8 years in placebo group. The duration of dyskinesia was 2.1 years in vitamin D group and 2.4 years in placebo group. The two groups of patients were matched for the age, duration of Parkinson disease and dyskinesia that do not matched for the age in two groups. The results shows, the two variables have significant improvement after treatment with placebo and vitamin D3.The Result of Pearson correlation show that the duration of dyskinesia (years) has positive and significant relationship with severity in two groups of patients and the duration of dyskinesia (years) with dyskinesia duration per day in vitamin D group. But in the placebo group, this relationship only exists before treatment is started. Finally the results of regression analysis showed that age, sex, duration of dyskinesia and Parkinson disease (years) had no effect on the treatment outcomes (Table 1).

Discussion

Dyskinesia is a movement disorder including chorea, ballism, dystonia, tic or combination of these that usually encountered with levodopa therapy. Levodopa induced dyskinesia divided into different forms: peak dose dyskinesia that appear at the high levels of plasma, diphasic dyskine-

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Table 1. Results.

	Vitamin D3	Placebo	P-value
Age	44.02±13.2	49.9±11.4	0.011
Parkinson disease duration (years)	7.2±3.3	7.8±2.9	0.29
Dyskinesia duration (years)	2.1±1.72	2.4±1.61	0.34
Duration (according to per day by hour) Before treatment	3.08±2.1	1.42±0.71	0.001
Duration (according per day by hour) After treatment	2.2±2.1	1.19±0.74	0.008
Severity (according to UPDRS IV sub score) Before treatment	2.6±2.1	2.4±0.9	0.17
Severity (according to UPDRS IV sub score) After treatment	2.2±2.1	1.8±1.1	0.024
UPDRS motor score before treatment	20.52±7.6	21±7.2	0.6
UPDRS motor score after treatment	19.2 ± 7.2	18.02±7.1	0.035

sia that appear at the beginning and end of levodopa effect and finally off dystonia that appear during off period.[7,8] The usual treatment for levodopa induced dyskinesia include decrease the dose of levodopa and use it more frequently with smaller dosages or add the dopamine agonist. We can also use from the amantadine and clozapine.[9,10] The results of our study show that placebos improved Levodopa-induced dyskinesia nearly as much as the vitamin D3 and the difference between them was not significant. As our knowledge our study is the first study that evaluate the effect of vitamin D on levodopa-induced dyskinesia. The associations between vitamin D status and Parkinson's disease (PD) is interesting, the results of meth-analysis study that done by Zheng *et al.* shows that PD patients had lower levels of vitamin D than healthy control and low level of vitamin D increased the risk of Parkinson disease.[11] The results of *in vitro* study shows that vitamin D has protective effect on dopamine neurons. However in another study that done by Meamar *et al.* in Iran show that there is not lower level of vitamin D in patients with parkinsonism in comparison to controls.[12] In our study that assessed the effects of vitamin D on dyskinesia, we cannot find the significant improvement in compared to placebo group and requires further investigation in the future. The results of our study also show that the vitamin D3 has not effect on UPDRS of patients with Parkinson disease.

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