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Original Article

Physiology Section

The Effect of Vitamin D3 on Depression in Iranian Women

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ABSTRACT

Introduction: Depression is one of the most common psychiatric illnesses that it associated with a variety of symptoms, high rates of relapse, and many physical and psychological disorders.

Aim: To determine the effect of vitamin D3 supplements on depression in women referred to health centres in Qazvin, Iran.

Materials and Methods: Overall, 374 patients were evaluated with Beck's depression test. A total of 65 patients were included in the study after they were diagnosed with moderate and severe depression. Individuals with moderate depression were divided into two groups: 1) Cognitive Behavioural Therapy (CBT); and 2) CBT plus vitamin D3 (50,000 units of eight tablets for eight weeks). Subjects with severe depression were divided into two groups: 1) drug therapy; and 2) drug therapy plus vitamin D3. Beck's test and vitamin D3 blood sample measurements were performed before and eight weeks after intervention. Independent sample t-test was used to compare the means of control and intervention groups.

Results: Depression scores of patients in post-test stage were significantly lower than depression scores of patients in pre-test stage in all intervention methods ($p<0.01$). Mean depression score (11.4±2.5) of patients in post-test stage of intervention with CBT plus vitamin D3 was significantly lower than the depression score (14.7±2.7) of patients in post-test stage of intervention with CBT ($p<0.05$). The difference of mean depression scores in post-test stage of drug therapy (20.4±3.7) and drug therapy plus vitamin D3 (15.8±3.3) intervention methods was significant ($p<0.05$).

Conclusion: The use of vitamin D3 supplements can be helpful in the treatment of depression in women.

Keywords: Counseling, Drug therapy, Improvement

INTRODUCTION

Depression is the major reason for diseases and disabilities throughout the world. Currently, more than 300 million people are living with depression, with 18% increase from 2005 to 2015 [1].

The prevalence of depression in Iran is 25%, which is reported to be 1.95 times higher in women [2,3]. Depression in women causes the birth of low weight newborn, the birth of a restless baby, a tendency to use cigarettes and drugs, sleep and nutrition disorders, and sometimes suicide [4]. Combining drug therapy with cognitive therapy or behaviour therapy is one of the most effective methods of treating depression [5,6].

Vitamin D is a neuro-steroid and numerous studies have been conducted on the relationship between vitamin D and depression, although they resulted in contradicting outcomes [7-9]. However, there are numerous biological reasons for the probable role of vitamin D in the development and expansion of brain function. Among the reasons for vitamin D effectiveness in depression, the presence of cholecalciferol, the active form of this vitamin in the brain and vitamin D receptors, activating enzymes of this vitamin (1-α hydroxylase) and P450 cytochrome, which catalyses calcidiol hydroxylation to the active form of vitamin D in different regions of central nervous system including amygdala, can be mentioned. The amygdala is responsible for controlling feelings and behaviour of humans [10].

Due to the fact that vitamin D metabolites can pass through blood-brain barriers, and the extensive presence of vitamin D receptors in some regions of the brain, such as the hippocampus, which is related to depression, it can be inferred that it can affect depression [11,12].

The hypothesis of the present study was vitamin D relationship with depression on the base of association of low levels of vitamin D and high prevalence of seasonal mood disorders during winter and at higher latitudes. Due to the limited clinical research conducted in this area, present study aimed to investigate the effect of vitamin D3 supplement on depression among women referred to health centres of Qazvin city, Iran.

MATERIALS AND METHODS

The present analytical study was conducted in 2017. The statistical population of the present study included all women with depression symptom referred to health centres of Qazvin city, during winter, 2017.

Beck's Depression Inventory II (BDI-II) was used to determine the depression status of the samples. The patients with moderate and severe depression and those who scored 2 or 3 in the question 9 on Beck's inventory test were used in the next stage of the experiment. The vitamin D3 serum levels of the selected samples were determined. The samples were then classified in terms of their vitamin D3 serum level as shown in [Table/Fig-1] [13]. Then, those with moderate and severe depression were randomly divided into two groups as follow:

Moderate depression: Group 1) CBT by clinical psychologists, Group; 2) CBT plus vitamin D3 (50,000 units of 8 tablets for eight weeks).

Severe depression: Group 1) drug therapy (fluoxetine, sertraline and citalopram); Group 2) drug therapy plus vitamin D3 (50,000 units of 8 tablets for eight weeks).

Selected individuals provided informed consent to participate in the research project. Then, they underwent two-three months of therapy and CBT based on the predetermined schedule. Vitamin D3 tablet was provided to the women prescribed with vitamin D3 supplement. After the end of the therapy and intervention, the vitamin D3 serum levels of the samples were assessed and BDI was carried out again.

Exclusion criteria: Patients with known malabsorption, other medical or psychological diseases; pregnancy, use of reliable pregnancy prevention methods, pregnancy and breastfeeding

women.

Ethical clearance: This study was conducted with ethical clearance from the Ethical Committee of the Qazvin University of Medical Sciences No.198396, 1395/9/20.

STATISTICAL ANALYSIS

After data collection, the data were entered into SPSS version 22.0 software. Mean and standard deviation were used for descriptive results. Independent sample t-test was used to compare the means of control and intervention groups. Paired sample t-test was used to compare the means of intra-groups.

RESULTS

In the present study, 374 questionnaires were completed in 10 health centres of Qazvin; eight questionnaires were excluded due to incompleteness. Demographic findings are presented in [Table/Fig-2]. Totally, 69.4% (254 persons) of the studied cases had no depression, 12.8% (47 persons) had minor depression, 10.7% (39 persons) had moderate depression and 7.1% (26 persons) suffered from severe depression. Therapy intervention was carried out on 65 patients (moderate and severe depression). In the patients with moderate depression, 25.7% (10 persons) had Vitamin D3 deficiency and 74.3% (29 persons) had inadequate vitamin D3. In patients with severe depression, 57.7% (15 persons) had vitamin D3 deficiency and 42.3% (11 persons) had inadequate vitamin D3 levels.

Level of serum vitamin D (nmol/L)	Result
<10	Deficiency
10-30	Inadequate
30-50	Normal

[Table/Fig-1]: Criteria for grouping individuals in terms of serum vitamin D3 levels.

Variables	Mean±SD	Maximum	Minimum
Age (years)	36.3±10.4	65	18
BMI (kg/m^2)	26.2±4.1	37.8	16
Variables	**Groups**	**Percent**	**Frequency**
Depression status	No depression	69.4	254
	Minor	12.8	47
	Moderate	10.7	39
	Severe	7.1	26
Marital status	Single	15.5	57
	Married	82	300
	Divorcee	2.5	9
Spouse's job	Jobless	2.3	7
	Self-employed	32	96
	Manual worker	24.1	72
	Employee	29.4	88
	Retired	12.2	37
History of systemic disease	Yes	28.4	104
	No	71.6	262
Economic status	Weak(<500 $/month)	11	40
	Moderate(500-1000 $/ month)	48.6	178
	Good(1000-1500 $/ month)	24.6	90
	Excellent(>1500 $/month)	15.8	58
Levels of serum vitamin D	Deficiency	35.2	129
	Inadequate	64.8	237

[Table/Fig-2]: Demographic variable in women under study.

The effect intervention methods on depression score in pre-test and post-test is presented in [Table/Fig-3]. Depression scores of patients in post-test stage were significantly lower than depression scores of patients in pre-test stage in all intervention methods (p<0.01). On the other hand, mean depression score of patients in post-test stage of intervention with CBT plus vitamin D3 was significantly lower than the depression score of patients in post-test stage of intervention with CBT (p<0.05). In addition, the mean depression scores in post-test stage of drug therapy plus vitamin D3 was lower than that in drug therapy [Table/Fig-3].

Depression Severity	Intervention	Number of patients	Pre-test	Post-test	p-value
Moderate	CBT	20	24.4±2.7	14.7±2.7	0.001
	CBT plus vitamin D3	19	25.1±2.9	11.4±2.5	0.001
	p-value	-	0.373	0.01	-
Severe	Drug therapy	13	38.7±7.6	20.4±3.7	0.001
	Drug therapy plus vitamin D3	13	39.1±4.5	15.8±3.3	0.001
	p-value	-	0.155	0.003	-

[Table/Fig-3]: The effect intervention methods on depression score.

Comparison of the effect of vitamin D3 on the depression score, with different levels of serum vitamin D in the pre-test and the post-test stage, is shown in [Table/Fig-4]. The effect of all methods of intervention in two levels of serum Vitamin D (deficiency/inadequate) was significant in the decrease of depression score (p<0.05).

Intervention	Depression severity	Levels of serum vitamin D	Mean±SD		Diff.	p-value
			Pre-test	post-test		
CBT	Moderate	Deficiency	27.3±1.3	16.5±1.7	10.7	0.001
		Inadequate	22.9±1.8	13.7±2.5	9.23	0.001
CBT plus Vitamin D3	Moderate	Deficiency	25±4.3	10.33±0.5	14.66	0.024
		Inadequate	23.4±2.8	12.8±2.5	10.5	0.001
Drug therapy	Severe	Deficiency	39±9.1	20.6±3.8	18.37	0.001
		Inadequate	38.2±5.4	20±3.9	18.2	0.001
Drug therapy plus vitamin D3	Severe	Deficiency	34.8±4.5	16±3.55	18.85	0.001
		Inadequate	35.3±4.9	15.7±3.4	19.6	0.001

[Table/Fig-4]: Comparison of the effect of vitamin D3 in the women's depression score with different levels of serum vitamin D.
Diff: Difference

Depression Severity	Intervention	Age	Marital Status	Spouse's Job	BMI	History of systemic disease	Economic status
Moderate	CBT	0.157*	0.058	0.075	0.661	0.348	0.889
	CBT plus Vitamin D3	0.193	0.283	0.821	0.721	0.415	0.273
Severe	Drug therapy	0.606	0.567	0.66	0.097	0.411	0.799
	Drug therapy plus vitamin D3	0.168	0.287	0.23	0.346	0.945	0.690

[Table/Fig-5]: Depression score mean comparison in intervention methods and demographic variables.
*: Significant p-value

There was no significant difference on the patient's depression scores in different age ranges, marital status, BMI, history of systemic disease, economic condition and spouse's job (p>0.05) among the groups [Table/Fig-5].

The mean of vitamin D3 serum level was 14.7±6.5 nmol/L and the

Stage	Minimum	Maximum	Mean	SD	Skewness	Kurtosis	t	p-value
Before intervention	5	26	14.7	6.5	0.12	-1.3	15.6	0.001
After intervention	16	41	33.03	6.2	-1.15	1.5		

[Table/Fig-6]: Levels of serum vitamin D3 (nmol/L) in women under study.

minimum and maximum values were 5 and 26 nmol/L respectively, before intervention. After the intervention, the mean value was 33.03± 6.2 nmol/L and the minimum and maximum values were 16 and 41 nmol/L, respectively, and this difference was significant (p<0.01) [Table/Fig-6].

DISCUSSION

In the present study [Table/Fig-3], depression score mean of patients in post-test stage in CBT plus vitamin D3 intervention method was significantly lower than depression score mean of patients in CBT method (p<0.01). In addition, depression score mean of patients in post-test stage in drug therapy plus vitamin D3 intervention method was significantly lower than depression score mean of patients in drug therapy method (p<0.01). In other words, intervention methods (CBT and drug therapy) plus vitamin D3 in depression improvement and depression score reduction was more effective than intervention methods without vitamin D3 supplementary. On the other hand, serum levels of vitamin D3 increased significantly after intervention with vitamin D3 supplementation [Table/Fig-5]. This indicates the positive effect of vitamin D3 on depression improvement in women. Results of De-Koning EJ et al., study are in line with that of the present study, which revealed the positive impact of intervention on score reduction of depression and anxiety [14]. Moreover, Schneider KA, indicated that high levels of vitamin D significantly affected the symptoms of depression and anxiety in patients with bipolar depression disorder [15]. Grudet C et al., reported that depressed patients with suicidal tendency had lower levels of vitamin D than depressed patients who were not willing to commit suicide [16]. Jean T and Owens L, showed a significant relationship between the level of vitamin D and adult depression in the USA [17]. The results of Asgari Z, are in line with that of the present study [18]. They showed that treatment-resistant depressed patients completely improved when they received vitamin D. The results of Jamilian HR et al., are also in agreement with that of the present study [19]. They reported that depression has a significant relationship with the reduction of vitamin D serum level and increase of serum level of parathyroid hormones. Vitamin D level and depression severity had a reverse correlation in the study of Mohamed SA et al., more severe depression was associated with lower vitamin D levels [20]. Kerr DC et al., also showed a significant correlation between low levels of vitamin D and clinical symptoms of depression in young women [21]. Jorde R et al., in a study on the effect of vitamin D supplements on depression symptoms of obese and overweight people in Norway reported that people with lower levels of vitamin D had more depression symptoms [9]. Moreover, high consumption of vitamin D can improve these symptoms. The highest effect of vitamin D was observed in people with severe depression symptoms while, Nabizadeh AL et al., Husemoen LL et al., and Yalamanchili V et al., obtained no significant relationship between vitamin D deficiency and severity of depression [13,22,23].

In the present study, demographic variables had no significant difference in terms of depression severity and type of intervention. This shows lack of relationship between these variables and type of therapy. Jean T et al., observed no significant relationship between different levels of vitamin D in adult depression and demographic features (sex, age, smoking condition and marital status) in the USA [17]. Black LJ et al., reported that there was no significant relationship between age and race of western Australian youth with serum level of vitamin D and depression, anxiety and stress symptoms [24]. However, in terms of income and educational level of the participants, there were significant relationships. Different factors such as climate, nutrition and work place can affect vitamin D deficiency. Therefore, further studies are required.

LIMITATION

Timely and correct drug intake was not ensured. The statistical sample of this research is limited to a city and hence, restricts the generalisation of research results at a higher level.

CONCLUSION

The results of the present study showed that the treatment of vitamin D deficiency in women leads to progress in their behavioural function and mood. A significant improvement was observed in the level of depression among women treated with vitamin D for eight weeks. The results of the study suggest that screening patients with depression and prescribing vitamin D for their treatment can be an easy and cost effective way.

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