MODULATING EFFECTS OF VITAMIN D₃ SUPPLEMENTATION ON AFFECTIVE-RELATED AND HORMONAL STATUS IN THE PERIMENOPAUSAL WOMEN

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Abstract

Introduction: Perimenopause is an intermediate phase in a woman’s life when physiological changes occur that begin the transition to menopause, such as irregular menstrual periods. Mood disorders in perimenopause period are common and considered as a public health issue. Considering the wide use of complementary and alternative medications such as vitamin supplements in premenopausal patients and our insufficient knowledge about the interaction between hormone replacement therapy and vitamin supplements, investigating the subject from preclinical experimental studies seems very beneficial. This study evaluated the effect of vitamin D₃ supplementation in different doses (low, moderate and high) alone or in a combination with standard hormonal menopausal therapy (HRT) on depression scores and hormonal status for premenopausal women of reproductive age. Results: The women treated with Vitamin D₃ in low (20000 IU) and middle (40000 IU) doses alone or in combination with HRT had greater reduction in depression scores than the control group. The vitamin D₃ groups of patients had significantly higher 25-hydroxyvitamin D concentration and estradiol levels in comparison to the control group (p<0.01). Conclusion: The present trial showed that consuming 20000 and 4000 IU vitamin D3 daily was effective in decreasing depression levels. Furthermore, this is the first clinical study to show a beneficial effect of chronic Vitamin D₃ in low and middle doses administration on depression score in premenopausal women of reproductive age. This work promotes more effective creating of the novel therapeutic targets and strategies for depression-related state treatment in premenopausal women of reproductive age. We suggest further clinical trial in women who are at risk for perimenopausal depression.

Aim. This study evaluated the effect of vitamin D₃ supplementation in different doses alone or in a combination with standard hormonal menopausal therapy (HRT) on anxiety/depression scores and hormonal status for perimenopausal women.

Methods. Subjects. The randomized clinical trial was done on the perimenopausal women of 42,3 ± 2,2 years. **Drugs.** The Vigantol (Vitamin D3, cholecalciferol, Merck KGaA) was administered at three different doses: 20000 IU/day, 40000 IU/day and 60000 IU/day alone or in a combination with standard hormonal replacement therapy (HRT) during 6 months. **Testing of anxiety and depression.** HADS scale. **Hormonal status** was measured by determination of the concentrations for FSH, LH, estradiol, progesterone and DHEA in the serum blood. **VD₃ status** was measured by determination of the concentration for 25-OH-VD₃ in the serum blood. Monoamines turnover was measured by HPLC in daily urine. Statistical processing of the received data was carried out with using SPSS 11.0 with Mann Whitney U test and paired t-test at p<0.05.

VD₃ state in perimenopausal women treated with VD₃ alone or in a combination with HRT in 6 months treatment

Groups of perimenopausal women	25-OH-VD3, µg/l
Control	9,8 ± 0,6
HRT	19,3 ± 0,8
Cholecalciferol 20000 IU/day	31,1 ± 1,2* #
Cholecalciferol 40000 IU/day	32,2 ± 1,6* #
Cholecalciferol 20000 IU/day + HRT	44,5 ± 1,8* #
Cholecalciferol 40000 IU/day + HRT	39,2 ± 1,4* #

* – p<0,05 as compared to the control group, # – p<0,05 as compared to the group of postmenopausal women receiving HRT, ## – p<0,05 as compared to the group of women receiving VD₃ at 20000 IU/day or 100000 IU/day, respectively.

Introduction. Mood disorders in menopausal period are common and considered as a public health issue. A strategy to alleviate the mood disorders associated with perimenopause is hormonal replacement therapy (HRT). However, controversial results related to the effectiveness of such treatment have been frequently reported. There has been longstanding interest in the role of «natural» treatments for depression and mood disorders, such as nutritional and dietary products. Among other nutraceuticals, one of such «natural» substances for treatment of affective-related state could be **vitamin D (VD)**. It then binds to vitamin D receptors in target tissues to regulate gene transcription and to structures within cell membranes to mediate a number of non-genomic responses. VDR are present in most tissues and cells in the body, and within the brain show some specificity to the prefrontal cortex, hippocampus, cingulate gyrus, thalamus, hypothalamus and substantia nigra. This is of relevance as many of those brain regions have been implicated in the physiology of anxiety and depression.

RESULTS

HADS scores in perimenopausal women treated with VD₃ alone or in a combination with HRT in 6 months treatment

Groups of menopausal women	Anxiety, scores	Depression, scores
Control group	19,5 ± 0,8	18,5 ± 0,5
HRT	10,2 ± 0,7*	9,3 ± 0,4*
Cholecalciferol 20000 IU/day	7,7 ± 0,8*	8,2 ± 0,5*
Cholecalciferol 40000 IU/day	8,1 ± 0,8*	8,4 ± 0,8*
Cholecalciferol 20000 IU/day + HRT	3,3 ± 0,2* # ##	4,2 ± 0,7* # ##
Cholecalciferol 40000 IU/day + HRT	3,8 ± 0,4* # ##	3,9 ± 0,5* # ##

5-HT turnover in perimenopausal women treated with VD₃ alone or in a combination with HRT in 6 months treatment in daily urine

Groups of perimenopausal women	5-HT, µg/day	5-HIAA, µg/day
Control group	80,5 ± 7,8	64,5 ± 6,4
HRT	75,2 ± 4,2*	49,3 ± 5,4*
Cholecalciferol 20000 IU/day	52,7 ± 4,8*#	23,2 ± 2,5* #
Cholecalciferol 40000 IU/day	48,1 ± 7,2*	33,4 ± 0,8* #
Cholecalciferol 20000 IU/day + HRT	40,3 ± 8,2* # ##	24,2 ± 4,7* # ##
Cholecalciferol 40000 IU/day + HRT	45,8 ± 4,4* # ##	23,9 ± 6,5* # ##

Hormonal state in perimenopausal women treated with VD₃ alone or in a combination with HRT in 6 months treatment

Groups of perimenopausal women	FSH, IU/l	LH, IU/l	Progesterone, nmol/l	Estradiol, nmol/l	DHEA, µg/ml
Control	22,3 ± 2,4	28,3 ± 2,2	0,5 ± 0,2	0,6 ± 0,2	0,03 ± 0,002
HRT	13,2 ± 2,6*	12,3 ± 2,2*	5,4 ± 0,2*	44,7 ± 3,6*	2,1 ± 0,2*
Cholecalciferol 20000 IU/day	10,1 ± 0,8*	11,2 ± 1,3*	2,4 ± 0,2* #	6,2 ± 0,2* #	6,2 ± 0,2*#
Cholecalciferol 40000 IU/day	9,1 ± 0,3*	10,0 ± 2,2*	2,2 ± 0,2* #	6,1 ± 0,4* #	8,0 ± 0,2*# ##
Cholecalciferol 20000 IU/day + HRT	3,2 ± 0,5* # ##	6,4 ± 0,6* # ##	3,4 ± 0,6* #	56,2 ± 2,8*	3,4 ± 0,3*#
Cholecalciferol 40000 IU/day + HRT	7,0 ± 0,2* # ##	8,0 ± 0,2* # ##	3,0 ± 0,8* #	50,7 ± 4,6* ##	2,1 ± 0,5*# ##

Conclusion. The present trial showed that consuming 20000 and 40000 IU vitamin D3 daily was effective in decreasing depression and anxiety levels in perimenopausal women. Furthermore, this is the first clinical study to show a beneficial effect of chronic Vitamin D₃ in high doses administration on anxiety/depression scores in perimenopausal women. This work promotes more effective creating of the novel therapeutic targets and strategies for affective-related state treatment in perimenopausal women.