**SHORT COMMUNICATION**

# Vitamin D in Anxiety and Affective Disorders

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**Summary**

Reduced levels of vitamin or its metabolites have been reported in various psychiatric disorders. Insufficient levels of vitamin D in depressive patients have been confirmed by many authors, but there have been conflicting results in subjects with anxiety disorders. In the present cross-sectional study, levels of calcidiol were determined in groups of depressive men and women and in men and women with anxiety disorders and compared with age matched controls. Significantly lower levels of calcidiol were found in men and women with depression as well as in age matched patients with anxiety disorders.

**Key words**

Depression • Anxiety • Calcidiol • Parathormone

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In addition to the long known critical function of vitamin D in calcium metabolism and its role in proliferation, differentiation and immunomodulation, there is a handful of evidence that vitamin D plays an important role for brain and nervous system health and disease (De Luca *et al.* 2013). Fifteen years ago it was suggested that vitamin D was the "forgotten neurosteroid" (McGrath *et al.* 2001). Vitamin D deficiency, diagnosed when the serum 25-hydroxy-vitamin D (calcidiol, $25(OH)D_3$) concentration is less than 20 ng/ml, is highly prevalent worldwide and thought to potentiate a variety of chronic disease states, including diabetes, cancer, and depression.

The association between depressive disorders and vitamin D deficiency from a lack of sun exposure is well established and was first noted two thousand years ago in an ancient literary work by Jordanes *The Origin and Deeds of the Goths* (see Spedding 2014). There are many reports that low levels of vitamin D or calcidiol are associated with major depression (Józefowicz *et al.* 2014) or symptoms of depression (Maddock *et al.* 2013, Black *et al*. 2014, Milaneschi *et al.* 2014, Kerr *et al.* 2015), but no effect on reducing the severity of these symptoms was found with vitamin D supplementation (Kjærgaard *et al.* 2012, Gowda 2015). Current evidence does not definitively demonstrate that vitamin D deficiency is a cause of or risk for developing depression or that vitamin D is an effective therapy for depression (Howland 2011).

In contrast to the reports on vitamin D association with depression, fewer contributions have been published on the association of anxiety disorders with the levels of vitamin D (Armstrong *et al.* 2007). Some of them even deny the relation of vitamin D deficiency with anxiety or stress (Black *et al*. 2014).

In our study, calcidiol levels were investigated in 20 women and 20 men with symptoms of depression and in 20 women and 20 men with anxiety disorders, and compared with the levels of calcidiol in groups of healthy controls (24 women, 12 males). In order to avoid seasonal influences, the patients and control subjects were recruited throughout the whole year. The study sample consisted of three groups of subjects: 1) patients with a depressive disorder (unipolar or bipolar) according to the International Classification of Diseases, 10th Revision (ICD-10; WHO, 2004), 2) patients with a specific anxiety disorder (Phobia, Panic Disorder,



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Obsessive-compulsive Disorder, Generalized Anxiety Disorder, Mixed Anxiety Depressive Disorder, Acute Reaction to Stress, Adjustment Disorder, Post-traumatic Stress Disorder) according to the ICD-10, and 3) healthy matching controls. The diagnosis of psychiatric disorder was confirmed using The Mini-International Neuropsychiatric Interview (M.I.N.I.; Sheehan *et al*. 1998). The interview was performed by an independent clinical psychiatrist. Patients were required to have a minimum symptom severity (depressive or anxiety) of 4 on the Clinical Global Impressions Scale (CGI; Guy 1976), suggesting at least moderately severe illness. The Ethical Committee of the Institute of Endocrinology in Prague approved the protocol of the study, and written informed consent was obtained from all participants.

Calcidiol was detected by the ECLIA method consisting of two main steps: dissolving calcidiol from vitamin D binding protein and followed by heterogeneous electrochemiluminescent immunoassay by analyzer Roche Cobas 6000. Intact parathormone (PTH) serum levels were detected by the same analyzer by using the principle of heterogeneous electrochemiluminescent immunoassay in a sandwich arrangement.

*Statistics*

Since data did not show normal distribution, it was transformed by Box-Cox transformation. Differences between groups were evaluated using one-way ANOVA model followed by Scheffe´s multiple comparison procedure. The statistical software Statgraphics Centurion XVI from Statpoint Inc. (Warrenton, VA, USA) was used for data transformations, ANOVA testing and multiple comparisons.

The results of our study are summarized in Table 1 for men and in Table 2 for women. Groups of patients and controls did not differ in age. The serum levels of PTH were within the normal interval (15-65 ng/l) as in patients and control groups without significant changes.

The levels of calcidiol were significantly lower both in the group of depressive patients and in patients with anxiety disorders in comparison to the group of control persons. It fits both for men (Table 1) and women (Table 2). Calcidiol concentrations indicate the pathophysiological status of patients while in the controls results are in the normal range (30-40 ng/ml).

**Table 1.** Comparison of age, PTH levels and calcidiol levels in 3 groups of men.

| | **GROUP 1 Depressive disorders N=20** | **GROUP 2 Anxiety disorders N=20** | **GROUP 3 Controls N=24** | **p-value** | **Multiple comparisons** |
|---|---|---|---|---|---|
| *Age (years)* | 33.1 (27.2; 39.8) | 29.7 (24.2; 35.9) | 32.4 (27.1; 38.4) | 0.69 | |
| *PTH (ng/l)* | 29.8 (26.2; 34.1) | 35.4 (30.8; 41.2) | 32.1 (27.1; 38.7) | 0.22 | |
| *Vit. D (ng/ml)* | 16.0 (13.4; 18.8) | 19.9 (17.0; 23.1) | 34.4 (30.6; 38.5) | 0.0000 | 1, 2 < 3 |

Data are shown as means and 95.0 percent confidence intervals (in the parentheses) for each group, the levels of significance of the model and multiple comparisons are provided.

**Table 2.** Comparison of age, PTH levels and calcidiol levels in 3 groups of women.

| | **GROUP 1 Depressive disorders N=33** | **GROUP 2 Anxiety disorders N=25** | **GROUP 3 Controls N=28** | **p-value** | **Multiple comparisons** |
|---|---|---|---|---|---|
| *Age (years)* | 33.5 (31.0; 36.0) | 31.5 (28.6; 34.3) | 33.7 (31.0; 36.4) | 0.45 | |
| *PTH (ng/l)* | 36.1 (31.7; 41.3) | 35.8 (30.8; 41.8) | 31.1 (27.0; 35.8) | 0.25 | |
| *Vit. D (ng/ml)* | 20.9 (17.5; 24.5) | 20.2 (16.4; 24.3) | 36.0 (31.3; 41.0) | 0.0000 | 1, 2 < 3 |

Data are shown as means and 95.0 percent confidence intervals (in the parentheses) for each group, the levels of significance of the model and multiple comparisons are provided.

In conclusion, we could confirm that affective disorders are associated with significantly lower levels of calcidiol, the precursor of the active hormone calcitriol, both for men and women. In contrast to the findings of Black *et al*. (2014), the association of vitamin D deficiency was recorded not only for depression but also for anxiety disorders with no significant differences between both studied groups.

## Conflict of Interest

There is no conflict of interest.

## Acknowledgements

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