Journal of Aging Research & Clinical Practice©
Volume 2, Number 1, 2013

ALARMING VITAMIN D DEFICIENCY IN OLDER PSYCHIATRIC INPATIENTS

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Abstract: *Objectives:* To explore vitamin D levels in older persons admitted to a psychiatric ward, acknowledging its potential relationship with a variety of psychiatric disorders and high prevalence rates of inadequate vitamin D levels in later life. *Design:* Consecutive case-series. *Setting:* Old age psychiatry ward of a secondary mental health centre in the Netherlands. *Participants:* 159 patients aged 52 to 94 admitted at the old age psychiatry ward. *Measurements:* Serum vitamin D3 (25(OH)D) levels were determined by taking a fasting blood sample within two days of admission and classified in five categories, i.e. severe deficient (< 10 nmol/l), deficient (10-24 nmol/l), insufficient (25-49 nmol/l), hypovitaminosis (50-74) and adequate (≥75 nmol/l) serum levels. Psychiatric diagnosis was made according to DSM-IV-TR criteria and classified in five overarching categories, i.e. depressive disorders, bipolar disorder, cognitive disorder no delirium, psychotic disorders and other psychiatric disorders. *Results:* Only 4/159 (2.5%) patients had adequate vitamin D levels. In 35 (22.0%) patients we found hypovitaminosis, vitamin D insufficiency in 69 patients (43.4%) and deficiency in 51 patients (32.0%) of which 15 patients (9.4%) had a severe deficiency. Although the prevalence of insufficiency and deficiency did no differ across diagnostic groups, patients with psychotic disorders had lower levels of vitamin D compared to the other diagnostic groups. *Conclusion:* The high prevalence of inadequate vitamin D levels argues for screening of vitamin D levels in older persons admitted to a psychiatric ward enabling an optimal vitamin D supplementation. The wide range of inadequate levels supports vitamin D assessment to determine the appropriate supplementation dosage regime.

Key words: Vitamin D deficiency; aged; psychiatric disorders.

Introduction

Although the role of vitamin D in bone growth and remodelling has been widely acknowledged (1), recent studies also suggest a role for vitamin D deficiency in multifactorial disorders particularly as they relate to aging (2, 3). The main sources of vitamin D for humans are dietary consumption or endogenous production in the skin after sunlight exposure (4). Older people often suffer from vitamin D deficiency, because the capacity of the skin to synthesise vitamin D and renal functioning decreases with age and less sunlight exposure due to decreased outdoor activity. The prevalence of vitamin D deficiency in independently living older people in North-Western countries ranges from 25 to 75% and 60-80% of institutionalised older people do have a vitamin D deficiency (5, 6). To our knowledge only one study has examined independent living patients recently admitted to a mental health hospital. Among 107 consecutive admissions to a psychiatric inpatient service in New York City in winter, 52.3% of the patients were classified as deficient in vitamin D (<50 nmol/l), with, as opposed to expectations, higher prevalence rates in younger versus older patients (resp. 71.1% vs 37.9%) (7).

Vitamin D plays a role in brain functioning as evidenced by vitamin D2 and D3 receptors and 1α-hydroxylase (see below) in the central nervous system (4, 8). Low vitamin D levels have been reported in several psychiatric disorders when corrected for food intake and proxies for sunlight exposure (9-13). Strongest evidence has been reported for cognitive disorders, as two large prospective studies show the relation between vitamin D deficiency and cognitive impairment (14, 15). Recently a systematic review provides evidence for the relationship between low serum vitamin D levels and Alzheimer's disease (16). However, a clear link between vitamin D level and cognition has not yet been established and in many cases the role of vitamin D deficiency as a causal or circumstantial factor is still debated (17). Epidemiologic evidence for the relationship between vitamin D and depression comes primarily from cross-sectional studies, but include both community-dwelling elderly (3, 9) as

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Received November 9, 2012
Accepted for publication December 3, 2012

well as clinical samples (18, 19). Low vitamin D has been prospectively linked to the onset depression in later life (20). Recently, however, two intervention studies found low vitamin D levels in depressed patients, but no effect was seen of supplementation vitamin D on depressive symptoms (21, 22). Involvement of vitamin D in schizophrenia has been postulated by several studies (11, 12). As most studies focused on maternal hypovitaminosis D prenatal and vitamin D supplementation during the first year of life, the relevance for psychotic disorders in later life remains elusive. As far as we know there are no studies that focus on a relationship between vitamin D deficiency and bipolar disorder.

The aim of this study is to determine the prevalence of vitamin D deficiency and insufficiency by psychiatric diagnosis in older patients admitted to an old age psychiatry ward.

Methods

Sample

The domain population consisted of all patients (N=238) admitted to the inpatient ward of the old age psychiatry department of Pro Persona Mental Health Care Institute (Arnhem, The Netherlands) between July 2008 and March 2010. If a patient was admitted several times in the period of research, only the first admittance was included. Excluded were those patients who underwent already a vitamin D supplementation.

Primary outcome measures

Psychiatric diagnoses - The psychiatric diagnosis or diagnoses were ascertained by an experienced resident and old age psychiatrist and classified according to DSM-IV-TR-criteria. Psychiatric diagnoses were reclassified within the following categories: depressive disorder (major depressive disorder, dysthymia), bipolar disorder, psychotic disorders (schizophrenia, schizoaffective disorder), cognitive disorders (cognitive disorder NOS, dementia) and other (e.g. somatoform disorder, delirium, adjustment disorder, anxiety disorder, personality disorder, psychiatric disorder due to a medical condition). In case of more than 1 diagnosis, a primary and secondary diagnosis were ascertained.

Vitamin D - The vitamin D status was measured by 25-hydroxy-vitamin D (25(OH)D) within 2 days of hospitalisation by taking a fasting blood sample. 25(OH)D is a precursor for the biologically active form of vitamin D (1,25-dihydroxy vitamin D) and generally used to asses an individual vitamin D status, as it well reflects both dietary intake as sunlight exposure (4). The serum 25(OH)D concentration was determined using a competitive chemiluminescentie immunoassay (Diasorin, serial 2229002691, software 2.30), with a detectionrange from 10 nmol/l to 100 nmol/l. Levels were classified in categories, i.e. severe deficient (< 10 nmol/l), deficient (10-24 nmol/l), insufficient (25-49 nmol/l), hypovitaminosis (suboptimal (50-74) and optimal (≥75 nmol/l) serum levels) (1, 23).

Covariates

In addition to usually included covariates age, sex, season of blood withdrawal and chronic comorbid diseases (3), we also included smoking status, renal functioning (GFR), use of vitamin D affecting drugs (anti-inflammatory medications, anticonvulsant medications, cholesterol-lowering medication, antibiotic medications, ulcer medications and laxatives like mineral oil) (9).

The smoking behaviour was defined as current smoker (yes/no). The meteorological season of admission was defined as winter (December, January, February), spring (March, April, May), summer (June, July, August) or autumn (September, October, November). Chronic comorbid diseases and medication use were extracted from the medical dossier. Initially self-reported data on comorbid disease status and drug use, are always checked by the electronic medical dossier of the referring general practitioner (in the Netherlands all patients are linked to only one GP), and the pharmacy records.

Although psychotropic drug use may affect vitamin D levels, we did not a priori adjust for the use of antidepressants, lithiumcarbonate, antipsychotics, and benzodiazepines as these drugs are intrinsically related to the psychiatric diagnosis and may led to overcorrection of the model.

Statistical Methods

All variables showed a normal distribution, except for the number of chronic somatic diseases. The number of chronic somatic diseases were reclassified in no, 1 or 2 or more diseases and added as dummies in the analyses (only 7 patients had 3 diseases and 2 patients had 4 diseases). Season of blood withdrawal were also included as dummies.

Univariate associations between vitamin D serum levels and all covariates were analysed by means of Student's t-test or chi-square tests.

In order to examine vitamin D levels across diagnostic groups, ANOVA was applied adjusted for covariates. Nonetheless, as a substantial number of patients had a secondary psychiatric diagnosis, we subsequently performed linear regression with vitamin D level as the dependent variable. In the first block, we entered all covariates, where after in a second block all diagnostic groups (primary or secondary diagnosis combined) were entered as the independent variables of interest.

Subsequently, we checked whether results changed after additional correction for psychotropic drug use (see above).

All analyses were carried out using the Statistical Package for the Social Sciences (SPSS) version 19.0 (Inc. Chicago)

Results

Sample - Of the 238 admissions, 45 were re-admissions for a second or third time in the period, resulting in a domain population of 193 patients. Of these 193 patients, 7 patients were excluded as they already received vitamin D supplementation and another 27 refused consent for blood withdrawal, leaving a final study population of 159 patients. Table 1 presents the characteristics of the final study population (n=159).

Table 1
Baseline characteristics (n=159)

Characteristics:	Descriptives	Values
• Age (years)	mean (SD)	71.3 (8.6)
• Female sex	n (%)	106 (66.7)
Smoking Current (yes)	n (%)	61 (38.4)
Glomerular Filtration Ratio (GFR)	mean (SD)	73.1 (19.5)
Number of comorbid chronic diseases		
• None	n (%)	57 (35.8)
• One	n (%)	67 (42.1)
• Two or more	n (%)	35 (22.0)
Season of admission:		
• Winter	n (%)	39 (24.5)
• Spring	n (%)	25 (15.7)
• Summer	n (%)	37 (23.3)
• Autumn	n (%)	58 (36.5)
Drug use:		
• Vitamin D affecting drugs	n (%)	10 (6.3)
• Antidepressants	n (%)	66 (41.5)
• Antipsychotics	n (%)	74 (46.5)
• Lithiumcarbonate	n (%)	23 (14.5)
• Benzodiazepines	n (%)	100 (62.9)

Abbreviations: SD, standard deviation; N, number of participants

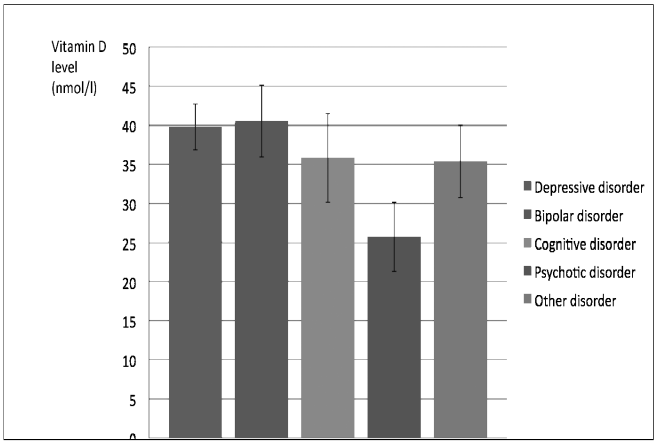
Psychiatric diagnoses – Primary diagnoses were (in decreasing order): depressive disorder (n=58, 36.5%), psychotic disorder (n=30, 18.9%), bipolar disorder (n=25, 15.7%), cognitive disorder/dementia (n=17, 10.7%), and other (n=29, 18.2%). A total of 47/159 (29.6%) were classified with a secondary diagnoses, especially a cognitive disorder. Prevalence rates after combining the primary and secondary diagnoses were: depressive disorder (n=61, 38.4%), cognitive disorder/dementia (n=54, 34%), psychotic disorders (n=34, 21.4%), bipolar disorder (n=26, 16.4%) and other (n=31, 19.5%).

Vitamin D levels – Mean vitamin D (25(OH)D) level at admission was 35.71 (SD 21.9) nmol/l. Only 4/159 (2.5%) patients had adequate vitamin D levels. In 35 (22.0%) patients we found hypovitaminosis (suboptimal) 25(OH)D serum, vitamin D insufficiency in 69 patients (43.4%) and deficiency in 51 patients (32.0%) of which 15 patients (9.4%) had a severe deficiency.

Based on these alarming results, we also measured vitamin D in the 7 patients receiving vitamin D supplementation; the mean vitamin D level was 50.4 (SD 18.5) nmol/l, of which none had an adequate level (deficient, n=1; insufficient, n=2; hypovitaminosis (suboptimal, n=4).

Neither the prevalence of insufficient and deficient vitamin D levels combined ($X2$=6.4, df=4, p= .17) nor the prevalence of deficient vitamin D levels ($X2$=3.0, df=4, p= .55) differed between diagnostic groups. The mean vitamin D levels, adjusted for covariates, did also not significantly differ between the primary diagnostic groups (ANOVA: F=2.02,df=4, p=.096) (see figure 1).

Figure 1
Estimated marginal mean (SE) serum vitamin D levels adjusted for covariates per diagnostic group based on primary diagnoses



Linear regression analysis combining primary and secondary diagnoses and adjusted for all covariates except psychotropic drug use, showed that only patients with psychotic disorders differed significantly from the other groups (β= -.27, p= .036; model R2=0.30; see table 2).

Adding psychotropic drug use to this linear regression modelled to an increase of explained variance (R2=0.39; antidepressants, β=0.18, p= .080; antipsychotics, β= 0.19; p=.025; lithium, β=-0.20, p=.021; benzodiazepines, β=-0.14, p=.094), but did not change the results with respect to diagnostic groups. Only psychotic disorders remained significant (β= -0.25, p= .050).

Discussion

Main findings

Three out of four older persons admitted to an old age psychiatric ward do have insufficient or deficient vitamin

D levels. Although the proportion of patients with insufficient or deficient vitamin D level did not differ across groups, adjustment for confounders revealed the lowest levels in patients suffering from psychotic disorders. Furthermore, we found that the effect of age, season of admission and use of medication on the level of 25(OH)D3 is far more important than the underlying psychiatric disorder.

Table 2
Determinants of serum vitamin D levels in older patients recently admitted at an inpatient clinic for old age psychiatry

Determinant	B	beta	p
Age (in years)	-0.71	-0.27	.007
Sex (1=male, 2=female)	-6.64	-0.15	.087
Smoking (0=no, 1= yes)	-7.57	-0.17	.057
Glomerular Filtration Ratio	-0.05	-0.05	.602
Comorbid somatic diseases:			
• One disease (dummy)	2.66	0.06	.531
• Two or more diseases (dummy)	-4.64	-0.09	.357
Season of admission:			
• Winter (dummy)	-17.56	-0.35	.002
• Spring (dummy)	-1.13	-0.02	.860
• Autumn (dummy)	-4.49	-0.10	.371
Vitamin D affecting drug use (0=no, 1=yes)	-12.19	-0.15	.103
Psychiatric diagnostic group			
• Depressive disorder (0=no, 1=yes)	-0.56	-0.01	.932
• Bipolar disorder (0=no, 1=yes)	1.85	0.03	.813
• Cognitive disorder (0=no, 1=yes)	-5.84	-0.13	.176
• Psychotic disorder (0=no, 1=yes)	-14.79	-0.27	.036
• Other disorder (0=no, 1=yes)	-4.16	-0.07	.554

Methodological considerations

For interpretation of our data it is important to bear in mind that we were not able to correct for all potential confounders. Outdoor activities, sun light exposure per day, obesity, vitamin D intake per day and ethnicity were not taken into account (24). Some of these factors, like obesity, outdoor activity and vitamin D intake, may be directly related to the psychiatric disorder (25), so even if we had measured these factors, causal interpretation was still hampered due to the cross-sectional design. No control group has been studied to better understand the role of the many factors involved in vitamin D concentration. The importance of our results therefore is noticing the alarming high prevalence of vitamin D insufficiency and deficiency among older people with psychiatric disorders requiring hospitalisation.

Clinical relevance

To our knowledge this is the first study that looks for prevalence rates of vitamin D deficiency and insufficiency in elderly patients admitted from their home-situation to an old age psychiatric ward. Although we did not include a control group with older persons without any psychiatric disease, the results are comparable to figures of vitamin D deficiencies of institutionalised older people (26-28), but not to community-dwelling older persons. Moreover, acknowledging that the optimal level of 25(OH)D3 in older persons is even higher compared to younger people, due decreased sensitivity to the biological active form of vitamin D, i.e. 1,25(OH)2D3, as well as a decreased capacity of the kidney to hydroxylate 24-OH vitamin D3 to 1,25-diOH vitamin D3 (3, 39).

Clinical implications

Since optimal vitamin D levels (≥ 75 nmol/l) are important to prevent complications of osteoporosis, muscle weakness, vascular disease and potentially frailty and psychiatric disorders (20) and prevalence of inadequate vitamin D levels in older persons is high, our results argue for screening all older persons admitted to a mental hospital. First, the assessment of common clinical risk factors in general fails to identify the majority of patients with hypovitaminosis D (30). Secondly, only 2.5% of our sample had optimal vitamin D levels, and even none of the 7 patients who were substituted with vitamin D. Thirdly, the amount of substitution of vitamin D depends on the actual vitamin D level, whereas these assays are quite cheap nowadays (around 9 euro per patient). Supplementation of suboptimal vitamin D levels is necessary, but international consensus on how to achieve this level rapidly is missing. Different dosage regimens are described in literature. Although vitamin D supplementation is described as safe with only toxic effects at serum levels above 220 nmol/l (31), 1-yearly dosage of 500.000IU increased fracture risk in postmenopausal women (32). To achieve an optimal level the following formula can be used to determine the total loading dose: colecalciferol dose (IU)= 40x (75-serum 25-OH D (3)) x body weight. This can be given in doses of 25.000- 50.000 IU colecalciferol per week (33). After loading, a maintenance dose is advised of 1000-2000 IU per day (23).

Future perspective

As low serum vitamin D levels can easily be substituted and are considered a universal risk factor for several ageing related disorders (34), future research should also take into account older patients admitted to a general hospital, exploration of the association between inadequate vitamin D levels and psychiatric disorders, international consensus on dosage regimes and cost-effectiveness of screening and substitution.

Disclosures and acknowledgments: R.C. Oude Voshaar is research fellow of the Dutch Scientific Organisaton (ZonMW) (research grant 90700231)

Conflict of interest: The authors have no financial or any other kind of personal conflicts with this paper.

Author contributions: All authors had substantial contributions to conception and design or analysis and interpretation of the data. All authors had substantial contributions to drafting the article and revising it critically for important intellectual content. All authors approved the final version.

Sponsor's Role: The authors maintained full independence in the conduct of this work. The sponsors had no role in design, methods, subject recruitment, data collections, analysis or preparation of the manuscript.

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