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ORIGINAL RESEARCH

DEPRESSIVE SYMPTOMS AND LEVEL OF 25-HYDROXYVITAMIN D IN FREE-LIVING OLDEST OLD

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Abstract: *Background:* Nowadays, the relation between hypovitaminosis D and depression has been reported and it is estimated that 1 billion people worldwide have vitamin D deficiency or insufficiency. However, the oldest old people are not included or are under-represented in most of the studies. *Objective:* To examine the association between depressive symptoms and 25-hydroxyvitamin D level (25(OH)Vit D) in elderly aged 80 and over who are physically more active and independent. *Design:* Cross-sectional study. *Setting and Participants:* Data collected from 182 oldest old people, aged 80 and over in the Geriatric Division from Federal University of São Paulo. *Measurements:* The functionality was evaluated by the Instrumental activities of their daily living (IADL). The approach of the depressive symptoms was done by the Geriatric Depression Scale (GDS) in its reduced 15 item version. 25-hydroxyvitamin D (25(OH)Vit D) analyses was done in serum sample refrigerated and protected from solar exposition. We considered deficiency serum level of 25(OH)Vit D <10ng/mL, insufficiency between 10 and 30ng/mL and sufficiency >30ng/mL. *Results:* According to blood level of 25(OH)Vit D we found difference between GDS score comparing the groups: "deficiency" (U=144,50; z=-3,126; p=0,002) and "insufficiency" groups (U=975,50; z=-2,793; p=0.005) are different than "sufficiency" group. *Conclusion:* In free-living independent oldest old people the goal of 25(OH)Vit D levels can be higher to avoid depressive symptoms, levels under 30ng/mL can be inadequate. Considering that the costs are low and side effects are not common, 25(OH) Vit D supplementation can be an important public health action.

Key words: Oldest old, aged, 80 and over, vitamin D, depression.

Introduction

The accelerated aging of Brazil has one of its epidemiologic consequences: the increased number of elderly with chronic diseases and incapacities that generate dependency (1). Late-life depression (LLD) affects from 10% to 22% of the growing geriatric population living in the community (2, 3), it´s a risk factor for all-cause mortality in the elderly (4) and adults 85 and older appear to be more vulnerable to depression than other age groups (5). Wu et al. (6) demonstrates that the age-related growth of depressive symptoms occurs wholly in the context of medical comorbidity and does not have an independent effect. Weyerer et al. (7) found that the incidence of depression symptoms, measured using the GDS-15 Geriatric Depression Scale, increases significantly with age in non-demented primary care attenders aged 75 years and older. The presence of depressive symptoms as a risk factor for disability occurs in both genders (8) and it is associated with development of cognitive decline in older patients (9).

Nowadays, the relation between hypovitaminosis D and depression has been reported and it is estimated that 1 billion people worldwide have vitamin D deficiency or insufficiency (10). Hoogendijk et al. (11), in a cohort study, found that the lower levels of vitamin D were associated with higher intensity of depression. Milaneschi et al. (12), in 2010, also in a cohort study (InCHIANTI study), evaluated elderly of ages 65 and up and observed that hypovitaminosis D was a risk factor for the development of depressive symptoms in elderly. On the other hand, Toffanello et al. (13), in a prospectively studied population (Pro.V.A. study), showed that there was no direct effect between vitamin D deficiency and the onset of late-life depressive symptoms.

The oldest old people are not included or are under-represented in most of the studies. Because of that, we want to know if there is association between depressive symptoms and vitamin D in elderly aged 80 and over who are physically more active and independent.

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Table 1
Characterization of elderly aged 80 years and over according to gender

	Men (n=49)	Women (n=133)	p
Age, years, median (CI 95%; IA)	85,0 (85,0-87,0; 6,0)	85,0 (84,0-86,0; 7,0)	p=0,651*
Ethnicity, n (%)			
white	40 (81,6)	87(65,4)	p=0,096&
black and mixed	6 (12,2)	34 (25,6)	
asian	3 (6,1)	12 (9,0)	
25(OH)Vit D, n (%)			
deficiency	5 (10,2)	21 (15,8)	p=0,466#
insufficiency	36 (73,5)	97 (72,9)	
sufficiency	8 (16,3)	15 (11,3)	
Score on MMSE, median (CI 95%; IA)	26,0 (24,0-26,0; 4,0)	24,0 (23,0-25,0; 5,0)	p=0,007**
Score on GDS, median (CI 95%; IA)	3,0 (2,0-4,0; 3,0)	4,0 (3,0-5,0; 3,0)	p=0,009***
BMI[a], kg/m^2, median (CI 95%; SD)	26,7 (25,4-28,0; 4,4)	26,7 (25,9-27,4; 4,4)	p=0,668****
Smoking, n (%)			
current	2 (4,1)	2 (1,5)	p<0,001&
previous	31 (63,3)	22 (16,5)	
never smoked	16 (32,7)	109 (82,0)	

IA: interquartile amplitude; CI: confidence interval; SD: standard deviation; MMSE: Mini–mental state examination; GDS: Geriatric depression scale; BMI: Body mass index; Missing values a=9; *U=3116,50, z=-0,452; **U=2399,00, z=-2,678; ***U=2444, z=-2,605; ****U=2835,50, z=-0,428; #X2=1,505, gl=2; &Fisher's exact test.

Methods

Studied population

The analyzed data is part of a cohort study about free-living independent elderly aged 80 and over. The elderly have been following in the Geriatric Division from Federal University of São Paulo. We didn´t include oldest old people with dementia, cancer, acute disease, dialytic therapy, chemotherapy or radiotherapy.

The studied population included 182 oldest old people evaluated from the period of January 2010 to January 2012. The experimental protocols were approved by the appropriate institutional review committee and meet the guidelines of their responsible governmental agency. Informed consent was obtained from all individual participants included in the study (Federal University of São Paulo Ethical Committee approval number 1532/09).

Clinical assessment

The collected data were sex, age, ethnicity, precedence, smoking history (current, previous or more than one year without smoking, never smoked), alcohol history (drinking any amount of alcohol in the last 10 years), health perception (excellent, good, regular or bad), chronic pain (presence of pain for more than 3 months), and any exposition to sunlight. The neuropsychological evaluation was made by the Mini–mental state examination (MMSE) developed by Folstein and validated in Brazil by Brucki et al. (14). The functionality was evaluated by the Instrumental activities of their daily living (IADL) (15). The nutritional evaluation was made by the means of the Body mass index (BMI) (16), abdominal circumference (AC - we considered as a high AC value in elderly ≥ 102cm in men and ≥ 88cm in women), hip circumference (HC) and waist-to-hip ratio (WHR=CA/HC; WHR > 0,99cm2 in men or > 0,97 in women is associated with an increased cardiovascular risk) (17).

The approach of the depressive symptoms was done by the Geriatric Depression Scale (GDS) in its reduced 15 item version. Paradela et al. (18) validated the Portuguese version of the GDS to track depressive symptoms in ambulatory elderly, with a cut mark at 5/6 showing sensibility of 81% and specificity of 71%.

Biochemical analysis

The biochemical analysis of creatinine, fasting glycemia and serum hemoglobin was measured on a fasting blood specimens (collected after 10-hour fast). 25(OH)VitD analyses was done in serum sample refrigerated and protected from solar exposition. We used the DiaSorin LIAISON® 25(OH)VitD, which one is based on chemiluminescence technology (CLIA).

Table 2
Characterization of elderly aged 80 years and over according to levels of 25(OH)Vit D

	25(OH)Vit D			
	Deficiency	**Insufficiency**	**Sufficiency**	**p**
Age, years, median, (CI 95%; IA)	86,5 (85,0-90,0; 8,3)	85,0 (84,0 - 85,0; 7,0)	86,0 (83,0-87,0; 6,0)	p=0,064*
Female, n (%)	21 (80,8)	97 (72,9)	15 (65,2)	p=0,471#
Score on MMSE, median (CI 95%; IA)	23,0 (20,5-25,0; 6,5)	24,0 (24,0-25,0; 4,5)	24,0 (22,0-26,0; 5,0)	p=0,463**
Score on GDS, median (CI 95%; IA)	4,0 (4,0-5,0; 3,5)	4,0 (3,0-4,0; 3,0)	1,0 (1,0-3,0; 4,0)	p=0,005***
BMI[a], kg/m², average, (CI 95%)	26,2 (24,4-28,0)	26,9 (26,2-27,7)	25,7 (23,9-27,5)	p=0,375****
Abdominal circunference[b] n (%)				
normal	6 (25,0)	57 (44,5)	12 (54,5)	p=0,106##
increased	18 (75,0)	71 (55,5)	10 (45,5)	
WHR[c] n (%)				
normal	15 (62,5)	51 (39,8)	10 (45,5)	p=0,119###
increased	9 (37,5)	77 (60,2)	12 (54,5)	
Smoking, n (%)				
current	1 (3,8)	3 (2,3)	0 (0,0)	p=0,787&
previous	6 (23,1)	39 (29,3)	8 (34,8)	
never smoked	19 (73,1)	91 (68,4)	15 (65,2)	
Alcohol ingestion, n (%)	3 (11,5)	24 (18,0)	5 (21,7)	p=0,629&
Clearance of creatinine[d] mL/min, median (CI 95%; IA)	42,0 (33,4-47,6; 18,0)	47,1 (44,9-51,8; 18,0)	40,4 (37,6-48,2; 11,9)	p=0,011*****
Hemoglobin[e], g/dL, average (CI 95%; SD)	13,0 (12,6-13,4; 1,1)	13,4 (13,1-13,6; 1,2)	13,3 (12,5-14,2; 1,9)	p=0,289******

IA: interquartile amplitude; CI: confidence interval; SD: standard deviation; MMSE: Mini–mental state examination; GDS: Geriatric depression scale; BMI: Body mass index; WHR= waist-to-hip ratio ; Clearance of creatinine: estimated clearance of creatinine. Missing values [a]= 9; [b]= 8; [c]=8; [d]=13; [e]=2. *KW=5,503, gl=2; **KW=1,539, gl=2; ***KW=10,743, gl=2; ****KW=1,954, gl=2; *****KW=9,103, gl=2; ******KW=2,485, gl=2; #X2=1,505, gl=2; ##X2=4,48, gl=2; ###X2=4,249, gl=2; & Fisher's exact test.

We considered deficiency serum level of 25(OH)VitD <10ng/mL, insufficiency between 10 and 30ng/mL and sufficiency >30ng/mL (10).

Statistical analysis

For data processing we used "Statistical Package for the Social Sciences (SPSS) for Windows" (version 13). A measure of central tendency was represented by median and interquartile amplitude (IA) when appropriate. We used the bootstrapping method for assigning confidence intervals from the proportion and median. Levene's test was used to assess the equality of variances for a variable calculated for two or more groups. We also used t Student´s test to determine if two sets of data were significantly different from each other, and the non-parametric tests Mann-Whitney (U) and Kruskal-Wallis (KW). When the Kruskal-Wallis (KW) test leads to significant results, Mann-Whitney (U)´s test was used with Bonferroni-corrected significance level. Chi-square test (X2) was used considering the recommendations of Cochran and the Fisher's exact test when these recommendations were violated.

Results

We studied independent oldest old people, with a IADL median 26,0 (IA 5,0) for men and 24,0 (IA 5,0) for women (p=0,187). Most of them were women and 82% of oldest old women never smoked (Table 1). The women had more depressive symptoms than men. On the other hand, oldest old men had a better performance on MMSE, with a schooling median 4,0 (IA= 5,5) for men and 3,0 (IA 3,3) for women (p=0,09). 83,7% of men and 88,7% of women had insufficiency or deficiency blood levels of 25(OH)Vit D although 52,2% declared sunlight exposition.

We also observed that 66,7% of men and 49,2% of women had excellent or good health perception (p=0,154). 77,6% of men and 62,4% of women did not have chronic pain (p=0,076) and 36,2% of men and 64,6% of women had abdominal circumference increased (X2=11,280; gl=1, p=0,001). There were no differences between serum levels of fasting glycemia of men

compared to women (median 87,0 +/- 16,0 and 88,0 +/- 17,0 respectively). However, the men hemoglobin (average 13,7 +/- 1,6) was greater than for women (average 13,2 +/- 1,5; p=0.005).

According to blood level of 25(OH)Vit D (Table 2) we found difference between GDS score comparing the groups: "deficiency" (U=144,50; z=-3,126; p=0,002) and "insufficiency" groups (U=975,50; z=-2,793; p=0.005) are different than "sufficiency" group; but there was no difference between "deficiency" and "insufficiency" groups (U=1460,00; z=-1.263; p=0,206).

Discussion

In our cross-sectional study, we observed that there was association between worst GDS scores with < 30ng/mL of 25(OH)Vit D in oldest old people. It´s already known that depressive symptoms are associated with clinical 25(OH)Vit D deficiency (levels <10ng/mL) (19) in elderly 65 years of age. This was confirmed in a systematic review and meta-analysis of epidemiological studies: depression risk was found to be inversely associated with serum 25(OH)Vit D in both cross-sectional and cohort studies (20). But it seems that in free-living independent oldest old people the goal of 25(OH) Vit D levels can be higher to avoid depressive symptoms, levels under 30ng/mL can be inadequate. We have to consider that there is a decline of 25(OH)Vit D levels with age and also a gender difference (21) that is going to increase the risk of depression in oldest old age and can compromise functionality.

Low blood levels of 25(OH)Vit D can be related with the inflammatory status observed in depressed patients, because in these conditions, auto-reactive T cells against tissues and synthesis of the interleukins and the pro-inflammatory cytokines (IL-12, interferon gama) are stimulated by the immunologic system (22). Synthesis and metabolism of serotonin (5-hydroxytryptamine) is influenced by cytokine signaling pathways (23). In physiologic conditions, indoleamine 2,3-dioxigenase (IDO) compete by tryptophan hydroxylase (TH) in tryptophan metabolism. The activation of IDO metabolizes the tryptophan in kynurenine and in the end quinolinic acid. It decreases brain tryptophan and the serotonin levels.

The functional reserve decline with age and also the capability to the oldest old to maintain a health life style and independency. It´s interesting to note that these oldest old people are independent, free-living individuals and even so had 25(OH)Vit D levels under 30ng/mL. This was found for others researchers in elderly above 60 years of age (24, 25) despite their high sun exposure during the summer months and regarding the nutritional status (26).

It´s suggested that 25(OH)Vit D supplementation is indicated as a complement of depression treatment (27). Zanetidou et al. (28) demonstrated that administering 25(OH)Vit D to patients 65 years or older as an adjunct to antidepressant therapy was associated with a significant improvement in the depressive symptomatology. Considering that the costs are low and side effects are not common, 25(OH)Vit D supplementation is very cost-effective and can be a good choice to prevent depressive symptoms. This can be an important public health action to avoid depressive humor in oldest old people (29). We already know that to prevent fractures the goal is > 30ng/mL of 25(OH)Vit D (30) and it seems that, in oldest old people these levels are also recommended to avoid depressive symptoms. It´s important to establish if to avoid depressive symptoms in oldest old the goal is also > 30ng/mL of 25(OH)Vit D.

Our study has limitations: selection was by convenience and the GDS is a screening instrument and detect depression symptoms and not the diagnosis of depression. It´s also important to note that 56,9% of the sample had an increased abdominal circumference that can be related with low levels of 25(OH)Vit D and also with a more inflammatory condition.

We conclude that the goal of 25(OH)Vit D levels can be higher to avoid depressive symptoms in free-living independent oldest old people and levels under 30ng/mL can be inadequate. Considering that the costs are low and side effects are not common, 25(OH)Vit D supplementation can be an important public health action.

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Conflict of interest: Márcio Tomita da Rocha Lima, Osvladir Custódio, Patricia Ferreira do Prado Moreira, Lara Miguel Quirino Araujo, Clineu de Mello Almada Filho and Maysa Seabra Cendoroglo have no conflicts of interest to declare.

Ethical standards: This experiment complies with the current laws of the country in which they were performed.

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