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Evaluation of the relationship between vitamin D concentration and cognitive performance in community dwelling elderly people

Ocena zależności między stężeniem witaminy D a sprawnością poznawczą u osób w wieku podeszłym nieobjętych opieką instytucjonalną

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Abstract

Introduction: People over the age of 65 are at a significant risk of vitamin D deficiency. This a result of many factors. Based on the studies conducted so far, it can be concluded that there is a relationship between vitamin D deficiency and the elderly age as well as the cognitive efficiency of people in this age group. **The aim of the study** was to assess the levels of vitamin D, the extent of its deficiency and cognitive performance in people over the age of 65. **Material and methods:** The study was carried out in 2014–2015 at the Clinic of Old Age Psychiatry and Psychotic Disorders of the Central Clinical Hospital of the Medical University of Lodz, as part of the DemNutr research project. One hundred eighty-seven people were qualified for the study. Among the research methods used, there were: interview, physical examination, clinical-demographic questionnaire and vitamin D [25(OH) D] concentration in blood serum. **Results:** The mean age of the subjects was 71.3 ± 5.9 years. The majority of the respondents were women – 78.6% (n = 147), men were only 21.4% (n = 40). The mean vitamin D concentrations in the groups of men and women were respectively 23.9 ± 7.46 ng/mL and 24.9 ± 7.21 ng/mL, and were below the norm in both groups. There was a statistically significant difference in the distribution of vitamin D concentration depending on the age of the subjects ($p < 0.05$). It turned out that in all people aged 85 or more the concentration of vitamin D was below 30 ng/mL vs. 78.7% of those surveyed aged 65–74 vs. 61.4% of people aged 75–84. A statistically significant difference in the average vitamin D concentration was also found in people who were examined in the summer (July – August) compared to the subjects in the period from September to June ($p < 0.01$). Significantly higher concentrations of vitamin D_3 were observed in the summer (July – August) than in the remaining months of the year. The respective averages were: 27.2 ± 6.78 ng/mL vs. 23.9 ± 7.24 ng/mL. The mean values in Mini-Mental State Examination (MMSE) were 28.5 ± 1.71 points. There was a statistically significant difference between the number of points obtained in MMSE and age (rank = –0.227, $p = 0.0009$). There was no statistically significant relationship between the MMSE score the sex of the subjects and the vitamin D concentration ($p > 0.05$). **Conclusions:** Among the people over the age of 65, vitamin D deficiency is a common phenomenon. In the study, however, there was no correlation between the vitamin D concentration and the results achieved in MMSE.

Keywords: cognitive functions, dementia, MMSE, vitamin D_3, elderly

Streszczenie

Wstęp: Osoby powyżej 65. roku życia są grupą istotnie narażoną na wystąpienie niedoborów witaminy D. Wpływa na to wiele czynników. Na podstawie przeprowadzonych dotychczas analiz można stwierdzić, że istnieje związek pomiędzy niedoborem witaminy D a wiekiem podeszłym oraz sprawnością poznawczą osób w tej grupie wiekowej. **Celem badania** była ocena stężeń witaminy D, skali występowania jej niedoborów oraz sprawności poznawczej u osób powyżej 65. roku życia nieobjętych opieką instytucjonalną. **Materiał i metody:** Badanie przeprowadzono w latach 2014–2015 w Klinice Psychiatrii Wieku Podeszłego i Zaburzeń Psychotycznych Centralnego Szpitala Klinicznego Uniwersytetu Medycznego w Łodzi w ramach projektu badawczego DemNutr. Do badania zakwalifikowano 187 osób. Wykorzystano następujące metody: wywiad, badanie przedmiotowe, ankieta kliniczno-demograficzna, a także dokonano oznaczenia stężenia witaminy D [25(OH)D] w surowicy krwi. **Wyniki:** Średnia wieku badanych osób wynosiła 71,3 ± 5,9 roku. Większość badanych to kobiety – 78,6% (n = 147), mężczyźni stanowili jedynie 21,4% (n = 40). Średnie stężenia witaminy D w grupie mężczyzn i kobiet wynosiły odpowiednio 23,9 ± 7,46 ng/ml i 24,9 ± 7,21 ng/ml i sytuowały się poniżej normy w obu grupach. Stwierdzono istotną statystycznie różnicę

rozkładu stężenia witaminy D w zależności od wieku badanych ($p < 0,05$). Okazało się, że stężenie witaminy D poniżej 30 ng/ml miały wszystkie osoby w wieku 85 lub więcej lat w porównaniu z 78,7% osób w wieku 65–74 lat i 61,4% osób w wieku 75–84 lat. Wykazano również istotną statystycznie różnicę średniego stężenia witaminy D u osób, które badano latem (lipiec – sierpień), w porównaniu z osobami badanymi w okresie wrzesień – czerwiec ($p < 0,01$). Istotnie wyższe stężenie witaminy D_3 miały osoby badane latem (lipiec – sierpień) niż badani w pozostałych miesiącach roku. Odpowiednie średnie wynosiły 27,2 ± 6,78 ng/ml i 23,9 ± 7,24 ng/ml. Średnie wartości uzyskiwane w Krótkiej Skali Oceny Stanu Umysłowego (Mini-Mental State Examination, MMSE) wynosiły 28,5 ± 1,71 punktu. Stwierdzono istotną statystycznie różnicę pomiędzy liczbą punktów uzyskanych w MMSE a wiekiem (ranga = −0,227, $p = 0,0009$). Nie wykazano zależności istotnej statystycznie pomiędzy wynikiem MMSE a płcią badanych oraz stężeniem witaminy D ($p > 0,05$). **Wnioski:** Wśród osób w wieku podeszłym, powyżej 65. roku życia niedobór witaminy D jest powszechnym zjawiskiem. W przeprowadzonym badaniu nie wykazano jednak korelacji pomiędzy stężeniem witaminy D a wynikami osiąganymi w MMSE.

Słowa kluczowe: funkcje poznawcze, otępienie, MMSE, witamina D_3, wiek podeszły

INTRODUCTION

Vitamin D deficiency is a serious epidemiological problem due to its prevalence, as it affects 50–80% of the human population (Thacher and Clarke, 2011). People over the age of 65 are significantly at high risk of vitamin D deficiency due to insufficient exposure to natural solar radiation, but also to poor nutrition (Arends, 2011; Potyka et al., 2015; Sajkowska et al., 2015).

Vitamin D_3 (cholecalciferol) is a chemical substance belonging to the secosteroids, which is naturally present in animal organisms. Cholecalciferol is a biologically inactive substance, and only after double hydroxylation in positions 1 and 25 it is converted to the active form, calcitriol, the action of which is possible by affecting the vitamin D receptor (VDR) (Haussler et al., 2013; Holick, 2003). The main inducer which stimulates the synthesis of calcitriol is the parathormone (PTH) (Holick, 2003). Both calcitriol and its derivatives may directly or indirectly affect the functioning of cells not related to mineral metabolism. This is done via the enzyme 1α-hydroxylase and the VDR. It is possible to regulate their cell cycle, proliferation, differentiation and apoptosis as well as the expression of growth factors, cytokines, hormones and enzymes (Potyka et al., 2015). Through its action, vitamin D mediates the brain plasticity, neurogenesis, differentiation and the metabolism of neurotransmitters (Eyles et al., 2013). It inhibits neurodegenerative and inflammatory processes and prevents the effects of oxidative stress (Herrmann et al., 2006; Schlögl and Holick, 2014; Streck et al., 2003), which may reduce the risk of developing dementia (Moretti et al., 2017). As demonstrated by numerous studies of the VDR receptor, apart from the osteoarticular system, it is present in the vascular endothelium, myocytes, pancreatic beta cells, the immune system and nervous system cells including depression (Anderson et al., 2010; Holick, 2007; Sajkowska et al., 2015), and dementia (Licher et al., 2017). Research confirms the presence of vitamin D deficiencies in both men and women, more often in the female sex, in people of all age groups ranging from children, young adults to the elderly (Hossein-nezhad and Holick, 2013; Wahl et al., 2012; van der Wielen et al., 1995). Interestingly, vitamin D_3 deficits were more common in the south than in Northern Europe (van der Wielen et al., 1995). The reasons for vitamin D deficiency are seen in the reduced supply of it with food, not enough skin synthesis, disturbed hydroxylation and its increased catabolism (Walicka et al., 2008). There is also a seasonal variation in vitamin D concentrations in the human body as well as a relationship between its level and the time of day, year and latitude, which poses a problem with the interpretation of its serum concentrations. The time spent inside and outside, i.e. exposure to UVB radiation, as well as the use of sunscreens or the type of clothing (Bednarski et al., 2007) are also taken into account. Optimal synthesis and maximum concentrations of vitamin D in our latitude are achieved in the summer months, when exposure to UVB radiation lasts 9 hours a day. In March and September, its synthesis takes place only for 3 hours, and in the winter period for a shorter time (Tuchendler and Bolanowski, 2010). In 2013, due to the widespread problem of vitamin D deficiency in the Central European population, including Poland, in various age groups – also the elderly – a Team of Experts representing various fields of medicine developed recommendations for vitamin D supplementation for healthy people, people at risk for its deficiencies and those in whom deficits of vitamin D are already present (Płudowski et al., 2013).

The aim of the study was to assess the level of vitamin D_3 in elderly people and to analyse the relationship between the obtained result and the level of cognitive performance assessed by the Mini-Mental State Examination (MMSE) clinical screening.

MATERIAL AND METHODS

The study was carried out in 2014–2015 at the Clinic of Old Age Psychiatry and Psychotic Disorders of the Central Clinical Hospital of the Medical University of Lodz as part of the DemNutr research project (Dementia and Nutrition) realised in the HARC consortium – Healthy Ageing Research Centre, HARC FP7 RegPot. The study enrolled 187 people who met the inclusion criteria: age >65, elderly people living in the community, not hospitalised, not in care facilities, without declared cognitive impairment, confirmed cognitive impairment without dementia or diagnosed dementia (according to International Statistical Classification of Diseases and Related Health Problems, 10th revision, ICD-10 diagnostic

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criteria), result in the MMSE >18 points, presence of a carer allowing for an accurate evaluation of the interview data. The exclusion criteria were: diagnosed dementia syndrome of moderate and severe intensity, no caregiver present during the interview and the examination, presence of somatic illness that could significantly affect the assessed parameters (e.g. cancer), chemo- and radiotherapy, connective tissue diseases, chronic and acute inflammation, decompensated chronic diseases, e.g. diabetes. The study included an interview, a physical examination, a questionnaire – clinical-demographic survey – and a panel of laboratory tests of blood serum collected on an empty stomach. The level of vitamin D [25(OH)D] was measured in the hospital laboratory of the Central Clinical Hospital of the Medical University of Lodz, in accordance with the standards applicable at the centre (reference values of vitamin D level are 30–100 ng/mL). In order to exclude the factor confounding the obtained results, that is, the impact of the season of the year in which the measurement was made, a separate analysis was performed including the above variable. The collected data were analysed using the STATISTICA 9.1 program. $p < 0.05$ was assumed to be the statistically significant level. Statistical parameters were calculated: the arithmetic mean and the median as average measures, the standard deviation and the coefficient of variation as a measure of differentiation. The minimum and maximum values were also given. In the case of the distribution of vitamin D_3 concentration analysed in subgroups of demographic variables – normal, below the norm – stratum weights were calculated (expressed in %). To compare the average level of vitamin D_3 in the two subgroups analysed, the non-parametric Mann–Whitney test was used. However, when there were three subgroups (education, age), ANOVA Kruskal–Wallis test was used, which is a nonparametric equivalent of variance analysis. The Chi-square distribution compatibility (χ^2) was also used. Non-parametric tests were selected due to the nature of the variable – a vitamin D_3 concentration significantly different from the normal distribution. The study was positively evaluated by the Bioethics Committee of Medical University of Lodz (No. RNN/736/14/KB from November 25, 2014).

RESULTS

One hundred eighty-seven people were enrolled in the study, whose average age was 71.3 ± 5.9 years. The majority of the respondents were women, 78.6% (n = 147), only 21.4% of them were men (n = 40) (Tab. 1). The mean vitamin D concentrations in the groups of men and women were respectively 23.9 ± 7.46 ng/mL and 24.9 ± 7.21 ng/mL, which is below the norm in both groups. There was a statistically significant difference in the distribution of vitamin D concentration depending on the age of the subjects ($p < 0.05$). It turned out that the concentration of vitamin D below 30 ng/mL was found in all people aged 85 or more vs. 78.7% of those aged 65–74 vs. 61.4% in those aged 75–84. It was also found that there was a statistically significant difference in the average vitamin D concentration in people who were examined in the summer (July – August) in comparison with the subjects in the period from September to June ($p < 0.01$). Significantly higher concentrations of vitamin D_3 were observed in the summer (July – August) than those in the remaining months of the year. The respective averages were: 27.2 ± 6.78 ng/mL vs. 23.9 ± 7.24 ng/mL (Tab. 2). The mean values in MMSE were 28.5 ± 1.71 points. There was a statistically significant difference between the number of points obtained in MMSE and age (rang = –0.227, $p = 0.0009$). There was no statistically significant relationship between the MMSE score, the sex of the subjects, and vitamin D concentration ($p > 0.05$) (Tab. 3).

DISCUSSION

There was a general deficiency of vitamin D in the study group. Only 24.6% of respondents had normal concentrations 25(OH)D, in the range of 30–43.8 ng/mL. Numerous studies that have been carried out so far confirm shortage of this vitamin present in Poland on a large scale. Age is considered to be one of the most important causes leading to vitamin D deficiency, because changes related to the ageing process taking place in the human body can result in insufficient levels of this vitamin. Researchers report that as a result of ageing, there is a reduction in its synthesis in the skin compared to younger people. This is due to the limited exposure to solar radiation, caused by spending a significant amount of time in enclosed spaces (Kupisz-Urbańska and Galus, 2011; Nowak et al., 2016). The synthesis of vitamin D in the human body is correlated with the degree of exposure to UVB radiation and is variable depending on the latitude and the time of day and season, age and skin pigmentation (Bednarski et al., 2007). The author's own results obtained in the present study regarding seasonality of vitamin D concentrations are consistent with the previous studies confirming that only the measurement of vitamin D concentrations in the summer (July – August), giving higher vitamin D concentrations as compared to the respondents' time in winter, is statistically significant ($p < 0.01$). This may

	Number of respondents	%
Sex		
Male	40	21.4
Women	147	78.6
Sum	187	100.0
Age (years)		
65–74	136	73.1
75–84	44	23.9
85 or more	6	3.2
Sum	186*	100.0

* One of the persons included in the study failed to provide their age in the clinical demographic survey.

Tab. 1. Characteristics of the study group in terms of sex and age

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	Vitamin D_3 (ng/mL)				Sum	Sum (%)	Chi² test	*p*
	Below 30		30–43.8					
	n	%	*n*	%				
Sex								
Male	30	75.0	10	25.0	40	100	0.004	0.947
Women	111	75.5	36	24.5	147	100		
Sum	*n* = 187							
Age (years)								
65–74	107	78.7	29	21.3	136	100	7.390	0.0249
75–84	27	61.4	17	38.6	44	100		
85 or more	6	3.2	-	-	6	100		
Sum	*n* = 186*							
Season								
VII and VIII	32	71.1	13	28.9	45	100	0.588	0.443
IX–VI	109	76.8	33	23.2	142	100		
Sum	*n* = 187							
* One of the persons included in the study failed to provide their age in the clinical demographic survey.								

Tab. 2. Distribution of vitamin D_3 concentration depending on the demographic variables and the test season

indicate the highest intensity of ultraviolet radiation and the longest exposure time to solar radiation during strictly holiday periods. Hungarian explorers assessed the influence of latitude on the intensity of vitamin D production. They confirmed that the maximum UVB ultraviolet radiation levels are in July, and the minimal ones are in December, so only in the summer months it is possible to obtain optimal concentrations of vitamin D (Bakos and Mikó, 2007), which is compatible with the results we obtained. The studies also found out that the higher the geographical latitudes. As compared to the lower ones, the significantly higher dose of the radiation is needed to synthesise the same amounts of vitamin D under the influence of exposure to the sun. In addition, in lower latitudes, the degree of vitamin D synthesis is independent of the season, and is even comparable in summer and winter (Kimlin et al. 2007; O'Neill et al., 2016). Other researchers also observed the dependence of changes in vitamin D concentrations on the season in postmenopausal women, obtaining significantly higher levels in the summer than in the winter ($p < 0.001$) (Hill et al., 2007).

Vitamin D_3 (ng/mL)	MMSE						Sum
	Norm		MCI		Dementia		
	n	%	*n*	%	*n*	%	
Below 30	129	76.8	11	61.1	1	100.0	141
30–43.8	39	23.2	7	38.9	-	-	46
Sum	168	100.0	18	100.0	1	100.0	187
Chi² = 2.482; *p* = 0.479.							

Tab. 3. Distribution of vitamin D_3 depending on MMSE

Similar results were obtained by examining the population of people in a subtropical climate latitudes, where in both women and men vitamin D concentrations were significantly higher in summer than in winter (Carnevale et al., 2001). Investigating the relationship between vitamin D concentration and the season of the year in tropical climate and bone mineral density as well as the VDR genotype, the authors similarly stated that the lowest serum vitamin D values are present in the winter and the highest in the summer season (Saadi et al., 2006). Other researchers report that both women and men were deficient in vitamin D, and the seasonal variation in its levels was observed in both sexes, but lower in women than in men. The maximum values of 25(OH)D were obtained in the measurements carried out in August (Katrinaki et al., 2016). The dermal synthesis of vitamin D as a result of exposure to UVB radiation with a wavelength of 290–315 nm provides 90% of the body's need for this vitamin, taking into account factors such as geographical latitude, season and day, weather conditions, environmental factors, the degree of skin saturation with melanin, the percent of exposed body surface or the use of UVB filters (Holick, 2007; Kupisz-Urbańska and Galus, 2011; Żukowska-Szczechowska and Kiszka, 2011). In the autumn – winter period, from October to March there are no optimal solar conditions in Central Europe for the synthesis of vitamin D which would ensure its proper concentration in the human body. The best UVB exposure period is April – September, for a minimum of 15 minutes everyday, with at least 18% of the body surface exposed between 10 am and 3 pm, without the use of sunscreens (Płudowski et al., 2013). In a Polish study conducted on a group of 92 people, insufficient intake of vitamin D with diet was demonstrated,

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resulting in its low serum concentrations. The percentage of its consumption in food rations was only 57.1% of the recommended norm (Tokarz et al., 2008). In the PolSenior study, in which 3,910 people over the age of 65 participated, a decrease in the concentration of vitamin D was observed along with an ageing process. There were significant differences in the incidence of its deficiencies in different age groups (55–59 years vs. 65 and more). The reason for this massive and decrease in the concentration of calcitriol, exacerbating with age, is primarily the deterioration of renal function, accompanied by the lowering in the concentration of cholecalciferol, as a result of its insufficient intake with food and reduced skin photosynthesis (Napiórkowska et al., 2012). The results of our study also confirm the tendency for decreasing vitamin D concentration related to age, where the lowest concentrations were obtained in people over the age of 85 and the mean values in this group were 22.2 ± 3.27 ng/mL. The study did not show a statistically significant relationship between the MMSE score and the vitamin D concentration ($p > 0.05$), as confirmed by numerous data in the analysed literature. However, a statistically significant relationship between the level of cognitive functioning, the number of points obtained in MMSE and the age of the respondents was confirmed (rank = –0.227, $p = 0.0009$). The aim of the Lau et al. (2017) study was to identify the neuroprotective factors in the elderly. According to them, numerous previous reports suggest that both vitamin D, telomere length, and brain-derived neurotrophic factor (BDNF) are associated with cognitive functions. They proved that supplementation with vitamin D ($p < 0.05$), high concentrations of BDNF ($p < 0.05$) and long telomeres ($p < 0.001$) reduce the risk of developing mild cognitive impairment (MCI), and people with the above parameters are more likely to age well (Lau et al., 2017). As it is known from the literature, MCI increases the risk of conversion to dementia within 4 years of the diagnosis by 5–15% (Bilikiewicz and Parnowski, 2011). SanMartin et al. (2018) studied the influence of selected metabolic factors on the state of cognitive functioning. They assessed the relationship of vitamin D, the amyloid beta concentration in the brain and lymphocytosis as well as its influence on the sensitivity of brain cells to oxidative stress, due to the action of hydrogen peroxide (H_2O_2), in patients with Alzheimer's disease (AD). As a result, they found out that the higher the levels of leucocytosis in people with MCI and AD, the greater the susceptibility to oxidative stress and neuronal apoptosis. In people with MCI, but not with AD, the sensitivity of lymphocytes to H_2O_2 and amyloid beta concentration improves as a result of 6-month supplementation with vitamin D. In addition, the level of cognitive functioning improves after 18-month supplementation with this vitamin (SanMartin et al., 2018). Metabolic syndrome and vitamin D deficiency are common among the elderly, constituting risk factors for the deterioration of cognitive functions. This dependence was studied by Lee et al. (2017) among the population of Korean seniors. The participants in the study who suffered from cognitive impairment assessed on the MMSE scale were more likely to have metabolic syndrome and low vitamin D levels than those in whom no cognitive impairment was diagnosed (Lee et al., 2017). Studying the population of older people in Japan, Sakuma et al. (2018) also showed in their project that low levels of vitamin D are independently associated with a greater likelihood of cognitive deterioration – just as was the age of the subjects. The participants of the study achieved worse results ($p = 0.0110$) in the MMSE-J questionnaire (Mini-Mental Scale Examination Japanese). The results of a study conducted by Song and Wu (2018) in elderly people with heart failure indicate a relationship between vitamin D intake, sleep quality, and the cognitive state. They found out that an increased daily intake of vitamin D ($p < 0.001$) and poorer quality of sleep ($p < 0.001$) affected cognitive functioning. In the analysis, there was an evident link between vitamin D deficiency and poor sleep quality ($p = 0.033$) and the cognitive status of seniors with circulatory insufficiency (Song and Wu, 2018).

CONCLUSIONS

Vitamin D deficiency is a common phenomenon among the elderly above 65. Therefore, special attention should be paid to the reasons for this condition and appropriate prophylaxis and supplementation of vitamin D should be implemented in accordance with the current standards to compensate for its shortages. The study also failed to confirm the relationship between vitamin D, the results achieved in MMSE and the state of cognitive functioning. When constructing subsequent tests, it would be necessary to take into account other parameters which may influence the results obtained, such as comorbidity, pharmacotherapy or addiction.

Conflict of interest

The authors do not report any financial or personal affiliations to persons or organisations that could negatively affect the content of or claim to have rights to this publication.

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