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Vitamin D and the Selected Diseases of the Nervous System

Witamina D a wybrane schorzenia układu nerwowego

Monika Biercewicz¹, Łukasz Pietrzykowski², Kornelia Kędziora-Kornatowska¹

¹Clinic of Geriatrics, Collegium Medicum Nicolaus Copernicus University, Torun, Poland

²Scientific Circle Neurological and Neurosurgical Nursing Department,
Collegium Medicum Nicolaus Copernicus University, Torun, Poland

Abstract

Interest in the role of vitamin D in the human body has greatly increased in the last decade. Many scientific studies provide the evidence of vitamin D deficiency, which is considered to be one of the most serious health problems in children, young people as well as those middle-aged and older people. The effects of vitamin D deficiency in the prenatally period can affect the health condition at later age, and can be related to diseases of chronic and progressive nature. Nowadays, vitamin D is seen rather as a hormone and is said to have pleiotropic effect. Apart from its classical effect on calcium and phosphate metabolism, vitamin D is also applied in the prophylaxis and treatment of the cardiovascular system and metabolic diseases, cancer or autoimmune diseases. Taking into account scientific reports on certain diseases of the nervous system, there is an indication regarding a relationship between their occurrence and the deficit of vitamin D. Therefore, this vitamin can be seen as a potential “candidate” to support the prevention as well as treatment of these diseases. It should be emphasized however, that not everything in this matter is absolutely certain and clear; further studies are still required in this area. (JNNS 2015;4(2):85–90)

Key Words: vitamin D, diseases of the nervous system

Streszczenie

Zainteresowanie rolą witaminy D w organizmie człowieka znacznie wzrosło w ostatnim dziesięcioleciu. Faktem udokumentowanym przez wiele badań naukowych jest deficyt witaminy D, uważany za jeden z poważniejszych problemów zdrowotnych u dzieci, młodzieży oraz osób w średnim i podeszłym wieku. Skutki niedoboru witaminy D w okresie prenatalnym mogą wpływać na stan zdrowia w późniejszym wieku i mieć związek z występowaniem chorób o charakterze przewlekłym i postępującym. W dzisiejszych czasach witamina D postrzegana jest bardziej jako hormon i mówi się o jej działaniu plejotropowym. Oprócz klasycznego wpływu na gospodarkę wapniowo-fosforanową witamina D znajduje zastosowanie w profilaktyce i leczeniu schorzeń układu sercowo-naczyniowego, metabolicznych, nowotworów, czy autoimmunologicznych. Biorąc pod uwagę doniesienia naukowe dotyczące niektórych chorób układu nerwowego wskazywane jest istnienie związku ich występowania z deficytem witaminy D. Dlatego też witamina ta może być postrzegana jako potencjalny „kandydat” do wspomagania profilaktyki i leczenia także tych schorzeń. Należy jednak podkreślić, że nie wszystko w tej kwestii jest do końca pewne i wyjaśnione; wymagane są jeszcze dalsze badania w tym obszarze. (PNN 2015; 4(2):85–90)

Słowa kluczowe: witamina D, schorzenia układu nerwowego

Introduction

In recent years, there have appeared numerous interesting scientific reports on vitamin D and its impact on the human body. One can say that the studies focused on this matter are experiencing a kind of renaissance.

Although vitamin D is most often associated with its effect on metabolic processes in the bones, numerous studies indicate that it also plays an important role in the human extraosseous system. Since Stumpf's studies carried out in the 70s of the last century its pleiotropic effect has been referred to [1]. A breakthrough

in research on vitamin D was the discovery by Brumbaugh and Haussler of nuclear vitamin D receptor — VDR (vitamin D receptor) contained in cells of most tissues and organs [2,3]. These receptors are also found in nerve and glial cells [4]. Currently, the possibilities of using vitamin D (considered as a pro-hormone) are believed to be both in the prevention and in the treatment of a variety of diseases including diabetes, rheumatoid arthritis, cancers, asthma [5–15]. Also, in the literature we can find works linking vitamin D with lowering blood pressure value, it should be noted however, that the position of scientists in this matter is not entirely consistent [16–18]. Its influence is also studied in the case of diseases related to the nervous system. Neuroprotective and immune-modulatory effect of this hormone has been described in several experimental models, indicating the potential value of 1.25 (OH)₂D₃ (calcitriol — the active form of vitamin D₃), pharmacological analogs in neurodegenerative and neuro-immunological diseases [4]. Many studies confirm the relation of vitamin D to Alzheimer's disease (AD), Parkinson's disease (PD), whereas numerous scientific reports also refer to multiple sclerosis (MS), epilepsy or strokes. The aim of this paper is to review the reports regarding vitamin D in relation to selected diseases of the nervous system.

Review

Parkinson's Disease — PD

Parkinson's disease is one of major reasons for disability in elder people. The disease affects on average approximately 0.3% of the overall population in the industrialized countries, however in the older age groups that percentage is much higher. For example, the Pol-Senior study, where a multi-faceted assessment of the everyday functioning of Poles in various periods of old age was carried out, the symptoms of the disease were observed in 0.56% of respondents from the foreground of old age — between 55 and 59 years old, and as many as in 2.6% of patients in the group of over 65 years of age [19]. In 2007 there was released a publication, including for the first time a hypothesis that long-term vitamin D deficiency may possibly relate to pathogenesis, progression and clinical manifestation of the disease [20]. A year later a report of a comparative study was released, in which participated patients with Parkinson's disease, Alzheimer's disease as well as healthy persons. This study confirmed the largest deficit of 25 (OH) D₃ ≤30 ng/mL at the level of 55% in the case of Parkinson's disease [21]. The Finnish studies obtained from a 29-year observation, carried out within the period from 1978 to 2007 (3173 people initially healthy — without PD) showed that too low levels of vitamin D

in the body may increase the risk of developing PD. In the group of those with the lowest levels of vitamin D in the blood, Parkinson's disease risk was three times higher than in the case of those having the largest amount of this vitamin [22]. Another research confirming the relation of PD progression with 25 (OH)D was carried out by Suzuki et al., conducted on 137 patients [23]. The degree of the disease progression was evaluated by means of the HY (Hoehn & Yahr) scale as well as with the use of the UPDRS (Unified Parkinson's Disease Rating Stage). In this study, measurements were made of 25-hydroxyvitamin D (25(OH)D), and 1.25-dihydroxyvitamin D (1.25(OH)D). Almost half of respondents (49%) showed a deficit of 25 (OH)D <20 ng/mL; whereas it was not observed in the case of 1.25 (OH)D. There were observed statistically significant differences between the progression of the disease measured by means of the H&Y scale and the 25 (OH)D (p=0.002) level, such differences were not observed in reference to 1.25 (OH)D (p=0.78). Additionally, this research implicated a connection between the occurrence of FokI genotype CC of vitamin D receptor with a milder course of the disease. Another research by Suzuki et al., carried out in Japan on 114 patients with the PD regarded the effect of annual supplementation of vitamin D₃ on the progression of the disease. The patients were divided randomly into two groups (placebo n=58), and those supplementing vitamin D₃ 1200 IU/day (n=56). It was concluded on the basis of the research that supplementation is beneficial and can stabilize the PD for a short period of time, however, in patients with genotype FokI TT or CT without inducing hypercalcemia. Such an effect was not observed in the case of patients with FokI CC [24].

Dementia

Dementia is a syndrome resulting from brain disease, usually of a chronic or progressive nature, in which cognitive functions such as memory, thinking, orientation, comprehension, counting, learning ability, language and evaluation are disrupted. The most common form of dementia is Alzheimer's disease, constituting according to various data even 50–70% of all dementias [25]. They are identified mainly in elderly patients (in approximately 10% of the geriatric population); it is emphasized that a considerable increase of the frequency of dementia occurrence appears with age, particularly between 65 and 85 years of age [26]. Dementia is a serious medical problem due to the progressive nature of the disease, leading to the total dependence of the patient on the assistance from other people.

Currently, there are quite a lot of studies regarding the issue of vitamin D deficiency as well as the possibi-

lity of its effect on cognitive functions. In 2010, a prestigious journal *Neurology* published the results of studies evaluating the relation between vitamin D concentration and the risk of cognitive disorders. The research carried out by Annweiler et al., evaluated the concentration of 25 (OH)D in 752 women aged over 75 years who participated in the osteoporotic EPIDOS programme. For the assessment of cognitive functions in older patients there was applied Pfeiffer's SPMSQ questionnaire (Short Portable Mental Status Questionnaire), consisting of 10 questions. The research proved a significant relation between low values of vitamin D (<10 ng/ml), and worse results in tests assessing memory compared to women with appropriate amounts of this vitamin ($p=0.006$) [27]. Another research conducted by Buell et al., and carried out in the group of 318 patients using home care services (women and men, both white and black) aged over 60 years, regarded the correlation between lowered vitamin D values (25 (OH)D) and dementia as well as vascular changes. The results of the research indicated the occurrence of a lower concentration of 25 (OH)D in patients with dementia (16.8 vs 20.0 ng/ml $p<0.01$) [28]. Litteljohns observations lasting almost six months and covering 1658 patients under the care of ambulatory — without dementia, cardiovascular disease or strokes, showed that the lowered values 25 (OH)D<50 nmol/L are connected with an increased risk of dementia [29]. In Italian studies INCHIANTI carried out on the population of 858 elder people (with the health condition assessed every three years) the relationship of 25 (OH)D with the deterioration of cognitive functions was investigated. The MMSE scale (Mini Mental State Examination) as well as the test of linking letters A and B (Trail-Making Test) were applied in the research. The authors proved that low levels of 25 (OH)D<25 nmol/L were connected with the deterioration of cognitive functions when compared to persons with the levels ≥ 75 nmol/L. In the patients with a lower level of 25 (OH)D<25 nmol/L there was observed a gradual deterioration of cognitive functions assessed by means of the MMSE scale by approximately 0.3 points/a year as well as in the Trail-Making Test B [30].

To similar conclusions came German researchers who were carrying out observation studies ESTHER on the group of 1639 older people [31]. Also, the results of the Chinese research on the population of older people indicate a lower concentration of 25 (OH)D in the patients with cognitive functions disorders (<18 points on the MMSE scale) compared to those meeting the standard and assessed by the same scale (25 (OH)D 31.9 versus 45.6 nmol/L) [32].

Sclerosis Multiplex — SM

Multiple sclerosis is a chronic, inflammatory, demyelinating disease of the central nervous system (CNS), wherein there is a multifocal damage (demyelination and axonal disintegration) of the nerve tissue. The disease has most commonly a phase course with periods of exacerbation and remission, usually concerns young people, with a slight predominance of cases in women. The etiology of MS is not known, but there are many hypotheses saying that the reason for it might be a virus, previously unknown antigen, also vitamin D deficiency, particularly in the period of childhood, is taken into consideration. MS can give rise to a variety of symptoms and syndromes; these most often consist in movement, sensory, cerebellar (imbalance) disorders, visual disturbances, autonomous, pain syndromes and psychiatric symptoms: cognitive dysfunction and mood disorders. A common symptom is also the chronic fatigue. Multiple sclerosis is one of the most common reasons for disability in young people, although many patients may experience the mild nature of its course [33].

As it has already been mentioned, based on years of observing the occurrence of new MS relapses is also linked with vitamin D deficiency. There are also opinions that exposure to sunlight during an early period of childhood increases the synthesis of cholecalciferol in the skin, which may reduce the risk of developing MS [34]. One of the many studies proving this hypothesis is a study conducted on 22 patients with MS with relapsing course (12 women and 10 men) aged 18–32 years [35]. The study was conducted in Dubai during within the period from February 2011 to September 2012. Each patient was evaluated every second month for a year. Apart from the 25 (OH)D level, there was also performed evaluation of the functional condition by means of the Kurtzke's Extended Disability Status Scale — EDSS, and neuro-imaging examination of the brain MRI (Magnetic Resonance Imaging). It was concluded based on the research that Vitamin D plays an important role in the course and severity of the disease. In patients with relapses of the disease, there occurred significantly lower levels of vitamin D in serum than in the case of patients without recurrences (28.4 vs 53.8 nmol/L; $p=0.000$). The amount of vitamin D in the plasma was inversely correlated with the clinical stage of the disease; the mean value on the EDSS scale in patients with relapses was higher than in patients without them (3.2 vs 2.3; $p=0.034$). Another research — Dutch, included both patients suffering from MS ($n=103$) as well as healthy people/control group ($n=110$) [36]. In people participating in the research the level of vitamin D (25 (OH)D and 1.25 (OH)₂D) was marked in the summer and winter period. The research indicated reduction of the MS risk in women by 19% with the

rise of 25 (OH)D/1.25 (OH)₂D concentration by 10 nmol/l /10 pmol/. In addition, a correlation has been observed between the condition of women assessed by EDSS scale and the concentration of 25 (OH)D in the serum, both in summer ($r=-0.25$, $p=0.044$) as well as in winter ($r=-0.29$, $p=0.020$). Whereas, in the American comparative studies conducted on people with MS as well as on healthy ones/control group (Whites, Blacks and Latinos), the level of 25 (OH)D was marked, there was found an inverse correlation between the risk of developing MS and the concentration of 25 (OH)D, but only in reference to the white race patients, particularly younger than 20 years of age [37]. There are also reports indicating a relationship between the date of birth (month), and the risk of developing MS. They point to May as the month connected with the highest risk of developing MS in the future, whereas November and December as months with the lowest risk [38,39]. One can attempt to explain it as the effect of low concentration of vitamin D in a mother on the fetus in the period of late pregnancy; when there is the slightest sunlight — winter, early spring. Studies on the application of vitamin D in MS are rare and limited in scope [40]. In the study published in 1986 by Goldberg, in 10 MS patients there was identified a 60% reduction of the estimated number of relapses after they had been subject to two years' treatment with vitamin D (5000 IU/per day in form of cod liver oil) [41]. This study does not contain any control group. In another study 15 patients who ultimately were receiving 2.5 micrograms of calcitriol/per day (100 IU) for 48 weeks (the dose was gradually increased) experienced a 50% reduction in recurrence [42]. In the literature it is also possible to encounter the latest reports from Finnish studies on the effects of vitamin D on the course of MS in patients treated with interferon β -1b [43]. The tested group consisted of 66 patients suffering from MS: 34 patients received additionally vitamin D (Dekristol capsules 20.000 IU/week), whereas the other 32 persons were in the control group. They were randomized, double-blind, lasting a year, in which the authors measured the burden of disease (BOD) calculated as the volume of pathological changes in MRI T2 images. While the median of the BOD increase within one year in patients from the control group was 287 mm³, for patients supplementing vitamin D it was lower, reaching 83 mm³ ($p=0.105$). In the case of the patients receiving vitamin D the researchers found significantly fewer hyperintense changes in T1 images ($p=0.004$). In the group receiving supplementation there was also noted a trend towards smaller disability ($p=0.071$). No effect of the intervention on the height of the annual rate of relapses was stated. The authors sum up the data obtained by writing that the addition of vitamin D₃ to treatment with interferon β -1b reduces disease activity in MR images in patients with multiple sclerosis.

Conclusions

The increased interest in vitamin D in the scientific world as well as drawing attention to its ectopic activity proves the issue to be both important as well as interesting. Particularly, that there are more and more reports on the possibility of positive effects of this vitamin on many diseases that are chronic, progressive and often leading to significant deterioration of health condition. It should be clearly emphasised that many effects of vitamin D probably have not been discovered yet, and even those identified require a deeper knowledge. Perhaps the conclusions from research on this vitamin will expand the indications for its use in the prevention and treatment of many diseases. Taking into account beneficial effects of vitamin D it is worth remembering that the vitamin can be easily acquired in the summer, by means of safe sunbathing. Whereas in the autumn-winter period one can consider the possibility of enriching the diet with products rich in this vitamin. When supplementing vitamin D the latest recommendations from the specialists in this field should be taken into account — age, the medications currently taken, health condition and lifestyle.

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Corresponding Author:

Monika Biercewicz
Klinika i Katedra Geriatrii
ul. M. Skłodowskiej-Curie 9, 85-094 Bydgoszcz, Poland
e-mail: kamamb@cm.umk.pl

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Author Contributions: Monika Biercewicz^{A, C, E, F}, Łukasz Pietrzykowski^{C, F}, Kornelia Kędziora-Kornatowska^{G, H}

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