LETTER TO THE EDITOR

Neurologia i Neurochirurgia Polska
Polish Journal of Neurology and Neurosurgery
2019, Volume 53, no. 5, pages: 388–389
DOI: 10.5603/PJNNS.a2019.0039

ISSN 0028–3843

Is vitamin D deficiency a reliable risk factor for multiple sclerosis development?

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Key words: vitamin 25(0H)D, multiple sclerosis

(*Neurol Neurochir Pol 2019; 53 (5): 388–389*)

We greatly appreciate, and are impressed by, the article written by Halina Bartosik-Psujek and Marek Psujek who reviewed the state of current knowledge regarding vitamin D [25(0H)D] as an immune modulator in multiple sclerosis (MS), especially regarding 25(0H)D's effect on immune cells subsets in relation to experimental and clinical studies [1].

25(0H)D maintains calcium-phosphate homeostasis and modulates an immune response. 25(0H)D inhibits the maturation of antigen-presenting dendritic cells (DCs), the proliferation of T and B cells, the Th1 and Th17 response, the expression of MHC class II, CD40, CD80, CD86, and the production of IgG, IgM and pro-inflammatory IL-1, IL-6, IL-12, TNFα. 25(0H)D increases the differentiation of T regulatory cells (Treg), the proliferation of macrophages, and the Th2 response and production of anti-inflammatory IL-10 [1]. The main route for obtaining 25(0H)D is sunlight exposure, because dietary intake accounts only for 30% of the total amount of 25(0H)D [2].

MS is a chronic inflammatory and neurodegenerative disorder of the central nervous system (CNS) leading to demyelination, axonal loss and damage of oligodendrocytes. 25(0H)D is one of the environmental factors which seem to play an important role in the aetiopathogenesis of MS and influences the course of the disease.

However, the impact of 25(0H)D concentration on MS development and the clinical and radiological activity of the disease is still inconclusive [1]. In many studies, higher concentrations of 25(0H)D have been associated with a reduced risk for MS development and with reduced clinical activity of MS, in terms of a low rate of disease relapse, slow disability progression, and low disease activity measured on brain MRI [3, 4]. 25(0H)D supplementation alone, or as an add-on to a disease-modifying therapy (DMT) in patients with MS, has been shown to significantly reduce new T2-hyperintense and gadolinium-enhanced lesions on brain MRI [5], although other studies have found no influence on disease activity on brain MRI [6, 7].

Referring to the article, we would like to present the results of a study comparing the concentrations of 25(0H)D in serum, assessed using an ELISA Kit (ImmunDiagnostik AG, Bensheim, Austria) with a microplate reader μQuant (Biotek Instruments Inc.,Winooski, Vermont, USA) in patients with relapsing-remitting multiple sclerosis (RRMS) and in healthy subjects from a control group (CG) (Tab. 1). None of the individuals was taking a 25(0H)D supplement, and none had symptoms of acute inflammation (their C reactive protein concentration was within the normal range i.e. < 10 mg/L) (Tab. 1). The study protocol was approved by the Medical University of Bialystok Ethics Committee for Research on Humans and Animals (R-I-002/171/2018). The MS patients (mean time from diagnosis 8 ± 0.5 years) were treated with interferon-β 1b in the Department of Neurology, Medical University of Bialystok. All patients with MS within the last 12 months had had a brain MRI and none had been treated with corticosteroids within the past six months. In patients with MS we assessed correlations between 25(0H)D concentrations and the season of the year in which they were born, the number of disease relapses, and

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Table 1. Clinical characteristics of patients with relapsing-remitting multiple sclerosis (RRMS) and the control group (CG)

Diagnosis	Number of patients (women)	Age (years)	EDSS	CRP (mg/L)
RRMS	57 (40)	43.7 ± 9.5	1.9 ± 1.2	1.0 ± 1.5
CG	19 (17)	41.7 ± 2.5	—	0.9 ± 0.5

CRP — C reactive protein; EDSS — Expanded Disability Status Scale

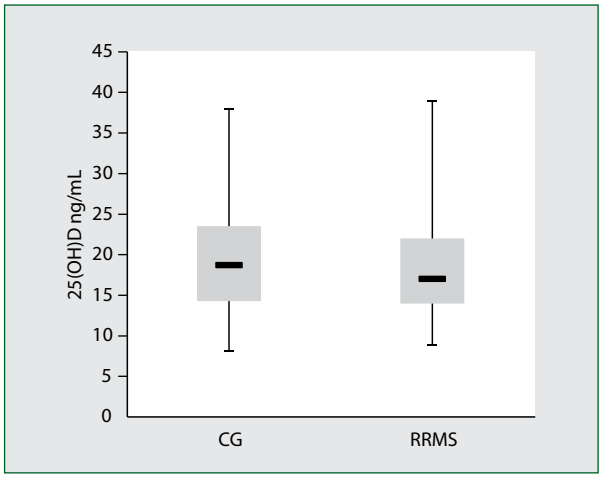

Figure 1. 25(0H)D concentrations in serum of patients with relapsing-remitting multiple sclerosis (RRMS) and in the control group (CG); Kruskal-Wallis test with post hoc Dwass-Steele-Critchlow-Fligner test ($p < 0.897$)

the new T2-hyperintense and gadolinium-enhanced lesions on brain MRI and the EDSS score.

We found no statistically significant differences between the concentrations of 25(0H)D in the serum of patients with RRMS (18.90 ± 6.96 ng/mL) and the control group (19.47 ± 7.78 ng/mL) ($p < 0,897$) (Fig. 1). 25(0H)D concentrations were below laboratory standards (30–40 ng/mL) in 52 patients (91.2%) with RRMS and in 18 subjects in the control group (94.7%). In patients with RRMS we observed a statistically significant relationship between concentrations of 25(0H)D and the number of disease relapses ($p < 0.032$). There was no statistically significant relationship between concentrations of 25(0H)D and the number of new T2-hyperintense lesions and the new gadolinium-enhanced lesions on brain MRI, the season of the year of birth, or the EDSS score.

In relation to the article written by Halina Bartosik-Psujek and Marek Psujek, our results cast doubt as to whether low serum 25(0H)D concentration is a reliable risk factor for developing MS. This is because almost all patients suffering from MS, as well as healthy controls, had low serum levels, which may result from insufficient sun exposure, the use of sun block, limited time spent in outdoor activity, staying indoors, and / or low 25(0H)D dietary intake [8].

Therefore, 25(0H)D should be supplemented in the whole population, especially in MS patients, according to the proven relationship between its concentration and the number of disease relapses.

Conflict of interest. *None declared.*
Acknowledgement of financial support. *None declared.*
Ethics. *The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for Manuscripts submitted to Biomedical Journals.*

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