RESEARCH LETTER

Evaluation of reduced bone mineral density among patients with Crohn disease depending on blood levels of 25-hydroxyvitamin D and calcium

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Introduction Crohn disease (CD) is a type of inflammatory bowel disease (IBD), the exact causes of which are not well understood. Its clinical presentation involves not only the gastrointestinal tract but also extraintestinal symptoms, including reduced bone mineral density (BMD). The diagnosis of IBD is based on clinical, endoscopic, radiologic, and histologic criteria as well as additional laboratory markers such as calprotectin. However, recent studies focus on new biomarkers of IBD.[1] The aim of our study was to assess the reduced BMD and its risk factors in patients with CD.

Patients and methods A total of 41 patients with CD (21 women and 20 men; age range, 18–45 years) hospitalized in the Department of Gastroenterology and Hepatology, Wroclaw Medical University, Poland, between 2016 and 2019 were included. Selected parameters were compared with a control group including 20 healthy female and male volunteers (age range, 18–45). Patients with renal or hepatic dysfunction, coexisting endocrine disease, pregnancy, or a neoplasm were excluded from the study. Three questionnaires written by the authors for collecting demographic information and a nutritional analysis interview were used; data concerning the course of disease, previous medical treatment of CD, supplementation of vitamin D / calcium, past pathological fractures, past densitometry results, and amount of sun exposure from March to September were also collected. The level of total calcium and 25-hydroxyvitamin D (25[OH]D) was assessed in blood samples collected in both groups. The activity of CD in the group of patients was evaluated using the Crohn Disease Activity Index (CDAI). In the control group and 27 patients, densitometric examination (DXA) of the bones was conducted using a Discovery W (Hologic, Marlborough, Massachusetts, United States) densitometer in the lumbar spine (L1–L4) and in the whole body (TABLE 1).

Statistical analysis Statistical analysis was performed using the Epi Info, ver. 7.2.3.1 software package (Centers for Disease Control and Prevention, Atlanta, Georgia, United States). The results were analyzed using the Mann–Whitney test (in 2 groups). For discrete parameters, the frequency of characteristics in the groups was analyzed with the χ^2 test. For selected pairs of parameters, Spearman correlation analysis was conducted. A P value of 0.05 or less was considered significant.

The study protocol was approved by the Local Bioethics Committee at Wroclaw Medical University (approval ID: KB/298/2016; as of June 2, 2016). All participants gave their written informed consent to be included in the study.

Results Among the patients, the median 25(OH)D level was 20.3 ng/ml. A deficiency of 25(OH)D or insufficient blood level was confirmed in 52% (n = 21) and 38% (n = 15) of CD patients, respectively. Patients with CD had a higher blood 25(OH)D level than the control group (20.3 [13.3–26.2] ng/ml vs 13.5 [9.7–16.6] ng/ml; P = 0.004). A greater proportion of patients with CD (43.9%; n = 18) took vitamin D supplements (P = 0.003) compared with controls. The median concentration of total calcium among the patients was 9.4 mg/dl; the serum total calcium level was lower than that of the control group (9.5 [9.7–9.8] mg/dl vs 10.0 [9.65–10.15] mg/dl; P <0.001). In our study, only 8% (n = 3) of patients

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TABLE 1 Characteristics of the study and control groups (Mann–Whitney test)

Parameter	Study group (n = 41)	Control group (n = 20)	*P* value[a]	Subgroups					
				No vitamin D supplementation (n = 14)	Vitamin D supplementation (n = 13)	*P* value	No immunosuppressive treatment (n = 14)	Immunosuppressive treatment (n = 13)	*P* value
25(OH)D, ng/ml	20.3 (13.3–26.2); n = 41	13.5 (9.7–16.6)	0.004	–	–	–	–	–	–
Total calcium, mg/dl	9.5 (9.7–9.8); n = 38	10 (9.65–10.15)	<0.001	–	–	–	–	–	–
Z score, L1–L4	–1.200 (–1.600 to –1.100); n = 17	–0.150 (–1.200 to 0.400)	0.11	–0.800 (–1.400 to 0.900)	–1.500 (–1.700 to –0.800)	0.04	–0.650 (–1.500 to 0.900)	–1.400 (–1.700 to 0.900)	0.11
T score, L1–L4	–1.200 (–1.700 to –0.100); n = 27	–0.150 (–1.200 to 0.350)	0.09	–0.800 (–1.500 to –0.750)	–1.500 (–1.800 to –0.800)	0.048	–0.700 (–1.500 to 0.700)	–1.400 (–1.700 to 0.900)	0.12
Z score, total body	–0.800 (–1.400 to 0.300); n = 27	–0.300 (–0.800 to 0.450)	0.21	0.350 (–0.900 to 1.400)	–1.300 (–1.700 to –0.800)	0.03	–0.100 (–1.000 to 1.800)	–1.200 (–1.700 to –0.600)	0.03
T-score, total body	–0.800 (–1.400 to 0.400); n = 27	–0.250 (–0.700 to 0.650)	0.13	0.300 (–0.900 to 1.800)	–1.300 (–1.700 to –0.700)	0.02	0.000 (–1.000 to 1.400)	–1.300 (–1.600 to –0.700)	0.03

Data are presented as median (interquartile range).

SI conversion factors: to convert total calcium to mmol/l, multiply by 0.25.

Abbreviations: 25(OH)D, 25-hydroxyvitamin D; IQR, interquartile range; n, number

with CD had a decreased concentration of total calcium in the blood. In CD patients, 12.2% (n = 5) confirmed that they use calcium supplements. A negative correlation was observed between the total calcium level and the CDAI in the group of patients with CD ($R = -0.47$; $P = 0.004$). No statistically relevant differences between the 2 groups were confirmed regarding the intake of food products rich in calcium and vitamin D or exposure to sunlight. Most respondents (60.98%; n = 27) indicated that they spend more than 30 minutes a day in the sun. Only 4.88% (n = 2) of patients indicated a duration of less than 5 minutes a day. None of the participants in either group met the criteria for a diagnosis of osteoporosis. The study group had slightly lower T scores at the lumbar spine, but this finding was not significant ($P = 0.09$). In patients with CD taking vitamin D supplements, lower T scores and Z scores were observed in both the lumbar spine and the whole body compared with patients with CD without vitamin D supplementation ($P = 0.048$; $P = 0.04$; $P = 0.03$; and $P = 0.02$, respectively) (TABLE 1). Data were analyzed for relationships between CDAI, 25(OH)D level, total serum calcium levels, disease duration, location of inflammatory lesions, and T score and Z score of the lumbar spine and whole body. There was a tendency for a positive correlation between the level of total calcium and the T scores and Z scores in the lumbar spine, but it did not reach statistical significance ($P = 0.09$; $P = 0.83$, respectively). Patients using glucocorticoids in the previous 12 months had a tendency for slightly lower T scores and Z scores in the lumbar spine ($P = 0.08$). In patients with CD taking immunosuppressive medication, lower T scores and Z scores were calculated for whole-body measurements ($P = 0.03$ and $P = 0.03$, respectively) (TABLE 1).

Discussion Vitamin D, due to its immunomodulatory properties, is of interest to researchers in the context of its influence on possible complications of CD, including reduced BMD.[2]

Surprisingly, in our study, higher values of 25(OH)D were observed among patients with CD than in the control group ($P = 0.004$). However, it is important that a greater proportion of patients with CD took vitamin D supplements ($P = 0.003$).

In the available studies, data relating to vitamin D deficiency in patients with CD are contradictory. Kabbani et al[3] observed more frequent vitamin D deficiency in patients with CD, while De Buryn et al[4] did not find lower values of 25(OH)D in patients with CD.

Based on data from other publications, vitamin D deficiency affected 17% to 68% of patients with CD in previous studies.[5] In our control group, 90% of participants were found to be 25(OH)D deficient, and the remaining 10% had insufficient 25(OH)D levels. Our results may reflect the prevalence of vitamin D deficiency in this population. At the same time, the question

arises of whether—due to the prevalence of vitamin D deficiency—the applicable norms should be modified.

The relationship between serum 25(OH)D concentrations and CDAI was investigated, but no correlation was found ($R = -0.07$; $P = 0.69$). Tajika et al[6] investigated the risk factors of 25(OH)D deficiency in patients with CD. Out of 33 participants, 27.3% were found to be deficient, but no relationship between serum 25(OH)D concentrations and CDAI was confirmed. Conflicting observations were made by Jørgensen et al[7] who reported that low values of 25(OH)D were associated with higher CD activity as assessed by CDAI.

Due to the fact that vitamin D is synthesized by the skin, exposure to sun from March to September was analyzed. No statistically significant difference was found in the duration of exposure to sun between the study groups ($P = 0.21$). Vernia et al[8] reported that patients with CD had less sun exposure than patients with ulcerative colitis or healthy volunteers ($P < 0.001$).

In a prospective study conducted in Romania, the incidence of low BMD in patients with IBD (mean age, 44 years) was assessed. DXA was performed in the lumbar spine and the femoral neck. Osteoporosis was diagnosed in 15.38% of CD patients.[9] Shoon et al[10] assessed the risk of osteoporosis in 56 CD patients aged 18 to 54 years; DXA was performed in the same location, and osteoporosis was diagnosed in 35.7% of the patients.

Interestingly, in patients with CD taking supplemental vitamin D, lower T scores and Z scores were found in the lumbar spine and in the whole body ($P = 0.048$; $P = 0.04$; P = 0.03; $P = 0.02$). This raises the question of proper vitamin D supplementation in this group of patients and whether lower values of BMD indices occurred even before starting vitamin D supplementation. It is worth noting that among those who received DXA, 92.6% had never been assessed by DXA before.

Over the past few years, numerous studies have been published that investigated the possible factors that influence BMD in patients with CD. However, the results of these studies have not been consistent. It should also be emphasized that the currently available literature lacks data on the risk of reduced BMD in young patients with CD.

In this study, among patients with CD treated with immunosuppressants, significantly lower T scores and Z scores were noted in the whole body assessment ($P = 0.03$). The abnormalities occurring in patients with CD receiving immunosuppressive therapy may be explained by the need to reduce sun exposure due to the increased risk of nonmelanoma skin cancer with this type of treatment.[11]

The results obtained among patients with CD (more frequent supplementation of vitamin D and higher concentrations of its vitamin D metabolites in the blood) indirectly show that the care of patients with IBD has improved. The awareness among this group of patients and among physicians of the risk of reduced BMD is clearly greater. However, there is still a need to improve the situation of patients with CD with regard to diagnosis, prevention, and treatment of osteoporosis. A significant limitation of our study was the small sample population; it would be advisable to conduct a similar study on a larger group of patients.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

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