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Low bone mineral density in adult patients with coeliac disease

Niska gęstość mineralna kości u dorosłych chorych na celiakię

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Abstract

Introduction: Calcium and vitamin D malabsorption in coeliac disease (CD) predispose to skeletal demineralisation. The aim of this study was to evaluate the prevalence of bone mineral density (BMD) and calcium deficiencies in adult patients with CD and assess whether a gluten-free diet is sufficiently effective for BMD restoration.

Material and methods: BMD and biochemical parameters of bone and mineral metabolism were measured in 35 adult CD patients receiving (19) or not receiving (16) a gluten-free diet (GFD) and in 36 controls. Then the CD patients were treated with a GFD and calcium (1.0 g/day) plus alfacalcidol (0.25–1 μg/day) for one year.

Results: Reduced BMD was diagnosed in 57–77% of the patients. Mean calcaemia, calciuria, and 25(OH) vitamin D were lower, but serum PTH and bone-turnover markers (ALP, osteocalcin, ICTP) were significantly higher in the CD patients than in the controls. In the patients on the diet (GFD(+)), BMD was higher than in the GFD(–) patients, but lower than in the controls. The biochemical parameters were normal in the GFD(+) patients except for diminished calciuria. Mean BMD after one year of treatment significantly increased ($p < 0.05$), mostly in the lumbar spine (mean: 7.3%), but decreased in five patients who did not strictly adhere to the GFD.

Conclusions: Deficiencies in calcium, vitamin D, and BMD are very common in adult CD patients. Gluten avoidance increased BMD, although the values remained markedly lower in several patients. Because of chronic calcium deficiency despite GFD, calcium and vitamin D supplementation in most adult CD patients is proposed. **(Endokrynol Pol 2012; 63 (4): 270–276)**

Key words: *bone mineral density, bone turnover markers, coeliac disease, gluten-free diet, hypocalcaemia*

Streszczenie

Wstęp: Upośledzone wchłanianie wapnia i witaminy D w przebiegu celiakii (CD) sprzyja demineralizacji szkieletu. Celem niniejszej pracy było zbadanie gęstości mineralnej kości (BMD) i niedoborów wapnia u dorosłych chorych na CD oraz ocena skuteczności stosowania diety bezglutenowej w odbudowie BMD.

Materiał i metody: Gęstość mineralną kości oraz biochemiczne wykładniki metabolizmu kostnego zmierzono u 35 dorosłych chorych na CD, wśród których 19 stosowało, a 16 nie stosowało diety bezglutenowej, oraz u 36 osób z grupy kontrolnej. Następnie wszystkim chorym na CD zalecono stosowanie diety bezglutenowej, wapnia (1 g/d.) i alfakalcydolu (0,25–1 μg/d.) przez rok.

Wyniki: Obniżoną BMD stwierdzono u 57–77% chorych na CD. Średnie kalcemia, kalciuria i stężenie witaminy 25(OH)D były u nich niższe, natomiast stężenia PTH i markerów obrotu kostnego (fosfatazy alkalicznej, osteokalcyny, ICTP) były wyższe niż w grupie kontrolnej. U chorych na CD stosujących dietę bezglutenową (GFD(+)) BMD była wyższa niż u chorych niestosujących tej diety (GFD(–)), ale niższa niż u zdrowych osób. Wyniki badań biochemicznych w grupie GFD(+) były prawidłowe, pominąwszy kalciurię, która utrzymywała się na zmniejszonym poziomie. Po roku leczenia dietą z suplementacją wapnia i witaminy D obserwowano istotny wzrost BMD ($p < 0,05$), zwłaszcza w obrębie kręgosłupa lędźwiowego (średnio o 7,3%). U 5 chorych, którzy nie przestrzegali ściśle diety, BMD obniżyła się.

Wnioski: W przebiegu CD niedobory wapnia, witaminy D i BMD są bardzo częste. Stosowanie diety bezglutenowej poprawia BMD, jednak u wielu chorych pozostaje ona obniżona. Według autorów, ze względu na przewlekły niedobór wapnia, u dorosłych chorych na CD, oprócz diety bezglutenowej, należy stosować suplementację wapnia i witaminy D. **(Endokrynol Pol 2012; 63 (4): 270–276)**

Słowa kluczowe: *gęstość mineralna kości, markery obrotu kostnego, celiakia, dieta bezglutenowa, hipokalcemia*

Introduction

Coeliac disease (CD) is a disorder resulting from the exposure of predisposed individuals to some cereal grain proteins (gluten) and is associated histologically with villous atrophy of the mucosa of the small intestine. The diagnosis of CD is made most frequently during childhood, with another peak during the fourth and fifth decades of life. According to recent screening studies, coeliac disease affects about 1% of the adult population [1], but the prevalence of coeliac disease among osteoporotic individuals is much higher, from 1.7% [2, 3] to 3.4% [4].

The diagnosis of CD may be very difficult because the clinical picture is highly variable and characteristic intestinal symptoms may be absent. Patients with

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coeliac disease often have osteopenia, osteomalacia, or osteoporosis because of calcium and vitamin D malabsorption and secondary hyperparathyroidism. Impaired absorption of calcium results principally from the loss of villous cells in the proximal intestine, where calcium is most actively absorbed, and also from unabsorbed fatty acids which bind calcium in the intestinal lumen and may reduce dietary vitamin D absorption. A gluten-free diet (GFD) is suspected to reverse the metabolic bone disease.

The aim of our study was to evaluate the prevalence of bone mineral density (BMD) and calcium deficiencies in adult patients with coeliac disease and to assess whether a gluten-free diet is sufficiently effective for BMD restoration or whether calcium and vitamin D supplementation should be additionally applied.

Materials and methods

The study group consisted of 35 adults with CD (six men and 29 premenopausal women), 41.5 ± 13.6 years old, with a mean BMI (body mass index) of 20.07 ± 2.53 kg/m^2. The patients were selected from a group of about 6,000 persons hospitalised during two consecutive years in the Departments of Endocrinology and Gastroenterology at Wroclaw Medical University. Nine patients were referred to our Endocrinology Department for evaluation of hypocalcaemia or low BMD without prior CD diagnosis, and 26 patients were recruited to the study from the Gastroenterology Department with already established coeliac disease and were on a gluten-free diet or were newly diagnosed.

The diagnosis of coeliac disease was based on clinical presentation, small-intestinal biopsy prior to treatment with a gluten-free diet, and clinical improvement on gluten withdrawal. All patients had villous atrophy in the proximal small bowel of grade III or IV on the basis of Marsh's classification [5]. In all patients, IgA-class antiendomysial antibody (EMA) and tissue transglutaminase antibody (tTGA) were positive before treatment [6]. It is very difficult to establish the mean illness duration because the clinical picture of CD in adults is highly variable and the intestinal signs may not be characteristic, or even completely absent. According to the illness history, we assumed that the mean duration of illness in our patients was about 16.8 ± 11.7 years (range: 1–44 years).

Exclusion criteria were other diseases and medications known to affect bone mineral density, especially vitamin D or mineral supplementation during the year before examination, as well as impaired renal function. Four patients had a history of previous bone fracture. In two cases, the fractures were posttraumatic (hand and lower leg), one patient had a low-energy fracture of the arm and another had compression of the thoracic spine. Most of the patients (65.7%) had anaemia, usually multideficiency anaemia. A transitory clinical manifestation of hypocalcaemia in the form of tetany was observed in 14 of the patients. The coeliac disease patients also suffered from other autoimmune diseases, such as Hashimoto's disease (six persons with proper L-thyroxin supplementation), vitiligo (2), and dermatitis herpetiformis (1). At the start of the study, 19 patients had been receiving a gluten-free diet for at least one year, while 16 persons did not apply it, or applied it inconsistently.

The control group consisted of 36 healthy volunteers (ten men and 26 premenopausal women), 39.1 ± 12.7 years old, with normal BMIs (23.9 ± 3.3 kg/m^2). There was no significant difference in age between the study and control groups, but the mean body mass index was lower in the CD patients ($p < 0.001$), which is typical of this illness.

Study protocol

Bone mineral density at the lumbar spine (L2–L4), femoral neck, distal third and ultradistal sites of the forearm, and of the total body, was measured by dual-energy X-ray absorptiometry (DPX-L, Lunar, USA). T-scores (the number of SDs above or below the young adult mean BMD) and Z-scores (age-adjusted BMD) were calculated with reference to a local normative population BMD database. Osteoporosis was recognized when the BMD value was lower than 2.5 SD below that of a young adult person (T-score) according to the WHO definition. The in vivo precision (CV-coefficient of variation) of the BMD measurements were 1.48% for the lumbar spine, 2.68% for femoral neck, 2.6% for the distal part of the forearm, 4.49% for the ultradistal part of the forearm and 0.76% for the total body. LSCs (least significant changes) were calculated using the advanced calculator on the www.pfo.pl recommended by The Polish Foundation of Osteoporosis, according to the following formula: LSC = 2.77 × RMS SD (root mean square standard deviation) which would represent a statistical difference at the 95% confidence level.

Laboratory analyses

Serum and urinary solutes and alkaline phosphatase (ALP) were measured using standard laboratory methods. Osteocalcin (a bone formation indicator) was estimated by IRMA using a kit (OSTEO-RIACT, France). Serum intact parathormone was analysed using an IRMA kit (Bio-Source, Europe S.A.). The bone resorption marker ICTP (C-terminal telopeptide of type I collagen) was exstimated using a RIA kit (Orion Diagnostica). 1,25-dihydroxy vitamin D (1,25-$(OH)_2D_3$) and 25-hydroxy vitamin D (25-OH D_3) plasma concentrations were measured using a RIA kit (BioSource, Europe S.A).

Table I. *Mean bone mineral density in patients with coeliac disease (n = 35) and in the control group (n = 36). Results are presented as the T-score and Z-score (mean ± SD)*

Tabela I. *Gęstość mineralna kości u chorych z celiakią (n = 35) i w grupie kontrolnej (n = 36). Wyniki przedstawiono jako* **T-score** *i* **Z-score** *(średnia ± SD)*

	T-score			Z-score		
	Coeliac disease	p value	Control group	Coeliac disease	p value	Control group
Femoral neck	–1.27 ± 1.27	***	0.12 ± 0.87	–0.6 ± 1.0	**	0.09 ± 0.65
Lumbar spine	–1.47 ± 1.72	***	0.64 ± 1.15	–0.91 ± 1.43	***	0.73 ± 0.85
Forearm, distal	–1.53 ± 1.44	*	–0.55 ± 0.79	–1.37 ± 1.24	*	–0.3 ± 0.83
Forearm, ultradistal	–2.22 ± 1.44	**	–0.68 ± 1.8	–2.11 ± 1.36	*	–0.42 ± 2.08
Total body	–1.99 ± 1.41	***	–0.17 ± 0.86	–1.27 ± 1.18	***	0.18 ± 0.7

*p < 0.05, **p < 0.01, ***p < 0.001; SD — standard deviation

After the initial examination, all the CD patients were obliged to follow a gluten-free diet with vitamin D analogue and calcium supplementation in individual doses that normalised serum calcium levels, removed tetany, and usually lowered increased PTH level. We usually used 0.25–1 μg of alfacalcidol (Alfadiol, GlaxoSmithKline Pharmaceuticals) and 1,000 mg of elementary calcium daily. One year later, all the biochemical analyses and bone mineral density measurements were repeated.

Statistical analysis

The statistical significance of differences between paired data was calculated using Wilcoxon's signed rank test and the Mann-Whitney U test was used to compare values between different sample groups. Correlation coefficients were determined using Spearman's rank correlation. The results are presented as the mean ± SD. Statistical significance was defined as $p < 0.05$.

The study was approved by the Wroclaw Medical University Local Ethics Committee.

Results

Bone mineral densities in the patients with coeliac disease were significantly lower than in the controls (Table I). The lumbar spine appeared to be particularly affected ($p < 0.001$). Reduced BMDs were found in most patients with coeliac disease, as shown in Table II.

As a result of calcium deficiency in the CD patients, we observed slightly lower serum calcium concentrations and much lower 24-hour urine calcium excretion compared to the control group. The 25-OH vitamin D serum concentration was also diminished. The mean PTH level was higher in the patients with CD than in the controls. At the time of the study, we observed PTH concentrations above the normal value (6.5–29.0 pg/mL) in eight patients, but 21 patients had a history of elevated PTH in tests performed previously. The serum concentrations of biochemical markers of bone turnover, such as ALP, osteocalcin, and ICTP, were also significantly higher, as presented in Table III.

Table II. *Frequency of decreased bone mineral density (BMD) in patients with coeliac disease expressed as a percentage of the patients (n = 35)*

Tabela II. *Częstość zmniejszonej gęstości mineralnej kości (BMD) u chorych z celiakią wyrażona jako odsetek chorych (n = 35)*

	Total patients with BMD deficiency	Osteoporosis
	(T-score < –1.0) [%]	(T-score ≤ –2.5) [%]
Femoral neck	62.8	20
Lumbar spine	57.2	28.6
Forearm, distal	57	22.8
Forearm, ultradistal	77	42.8
Total body	77.1	31.4

Bone mineral density negatively correlated with patient age ($p < 0.05$). Age-adjusted BMD (Z-score) at all sites positively correlated with calcium serum concentration, and BMD in the lumbar spine and total body positively correlated with 25-OH D_3 concentration ($p < 0.05$) but negatively with osteocalcin ($p < 0.01$). Negative correlations with BMD at all sites were also observed for parathormone and alkaline phosphatase ($p < 0.05$). Apart from BMD, parathormone negatively correlated with calcium and 25-OH D_3 serum concentration ($p < 0.05$) and positively correlated with such bone-turnover markers as osteocalcin ($p < 0.001$), alkaline phosphatase, and ICTP ($p < 0.05$). Bone mineral density and biochemical parameters in the patients

Table III. *Serum and urine biochemistry in patients with coeliac disease and controls*
Tabela III. *Wyniki badań biochemicznych surowicy krwi i moczu u chorych z celiakią i w grupie kontrolnej*

Parameter	Coeliac disease N = 35	p value	Control group N = 36
Calcaemia [mmol/L]	2.17 ± 0.22	*	2.29 ± 0.14
Calciuria [mmol/24-h]	1.80 ± 1.35	***	4.49 ± 0.87
Phosphataemia [mmol/L]	0.98 ± 0.28	ns	1.08 ± 0.17
ALP [U/L]	260.7 ± 149.6	*	174.3 ± 47.0
PTH [pg/mL]	20.17 ± 15.0	*	12.2 ± 6.9
25-OH D_3 [ng/mL]	29.9 ± 18.3	*	39.5 ± 19.0
1,25-$(OH)_2D_3$ [pg/mL]	40.08 ± 15.5	ns	36.6 ± 14.5
Osteocalcin [ng/mL]	35.31 ± 18.84	**	23.6 ± 8.6
ICTP [μg/mL]	5.9 ± 5.06	**	3.3 ± 1.8

*p < 0.05, **p < 0.01, ***p < 0.001; ns — not significant; ALP — alkaline phosphatase; PTH — intact parathormone; ICTP — C-terminal telopeptide of type I collagen; 1,25-$(OH)_2D_3$ — 1,25-dihydroxyvitamin D; 25-OH D_3 — 25-hydroxyvitamin D

Table IV. *Serum and urine biochemistry in patients with coeliac disease receiving or not receiving a gluten-free diet*
Tabela IV. *Wyniki badań biochemicznych surowicy krwi i moczu u chorych z celiakią stosujących dietę bezglutenową lub niestosujących tej diety*

	Coeliac disease GFD (–) N = 16	p value	Coeliac disease GFD (+) N = 19	p value	Control group N = 36
Calcaemia [mmol/L]	2.07 ± 0.28	*	2.26 ± 0.11	ns	2.29 ± 0.14
Calciuria [mmoL/24-h]	1.13 ± 0.58	*	2.39 ± 1.5	***	4.49 ±.0.87
ALP [U/L]	309.9 ± 137.1	*	210.5 ± 146.2	ns	174.3 ± 47.0
PTH [pg/mL]	27.3 ± 18.4	*	15.1 ± 8.5	ns	12.2 ± 6.9
25-OH D_3 [ng/mL]	19.9 ± 18.8	*	37.8 ± 13.8	ns	39.5 ± 19.0
1,25-$(OH)_2D_3$ [ng/mL]	45.2 ± 17.5	ns	35.8 ± 12.7	ns	36.6 ± 14.5
Osteocalcin [ng/mL]	46.0 ± 23.6	*	26.9 ± 6.7	ns	23.6 ± 8.6
ICTP [μg/mL]	8.0 ± 6.4	*	4.3 ± 2.9	ns	3.3 ± 1.8

*p < 0.05, ***p < 0.001; ns — not significant; ALP — alkaline phosphatase; PTH — intact parathormone; ICTP — C-terminal telopeptide of type I collagen; 1,25-$(OH)_2D_3$ — 1,25-dihydroxyvitamin D; 25-OH D_3 — 25-hydroxyvitamin D; GFD (+) — patients receiving a gluten-free diet; GFD (–) — patients not receiving a gluten-free diet or applying it inconsistently

who strictly followed the gluten-free diet were generally better than in the newly diagnosed patients and patients who did not apply the diet consistently, but their results were different from those of the control group (*see* Tables IV and V).

During the ensuing year, all the CD patients received a gluten-free diet and vitamin D and calcium supplementation in individual doses that normalised serum calcium levels, removed tetany, and usually lowered increased PTH level.

After one year of the treatment, we repeated the BMD and serum and urine parameter measurements. The mean BMD in the whole CD patient group after one year of treatment was significantly higher at all sites ($p < 0.05$) except for the ultradistal forearm. The highest increase in BMD was in the lumbar spine, as shown in Table VI. Unfortunately, in five patients we observed decreases in BMD (Figure 1). The control tests for tTGA were positive, indicating lax adherence to the gluten-free diet. There were no new fractures during the study.

The increases in femoral, lumbar, and total body BMD positively correlated with initial ICTP concentration ($p < 0.01$). The biochemical abnormalities were considerably reduced after one year. We observed increases in serum calcium ($p < 0.05$) and 25-OH D_3 ($p < 0.01$) concentrations. The 24-h calciuria level increased significantly ($p < 0.01$) and reached 3.2 ± 1.6 mmol/24-h

Table V. *Bone mineral density (BMD) in patients with coeliac disease receiving or not receiving a gluten-free diet, and in the control group. The results of BMD measurement are given as the Z-score (mean ± SD)*

Tabela V. *Gęstość mineralna kości (BMD) u chorych z celiakią stosujących dietę bezglutenową lub niestosujących tej diety oraz w grupie kontrolnej. Wyniki przedstawiono jako* **Z-score** *(średnia ± SD)*

	Coeliac disease GFD (–) N = 16	p value	Coeliac disease GFD (+) N = 19	p value	Control group N = 36
Femoral neck	–1.12 ± 0.87	*	–0.23 ± 0.98	ns	0.09 ± 0.65
Lumbar spine	–1.96 ± 1.1	**	–0.14 ± 1.11	**	0.73 ± 0.85
Forearm, distal	–1.56 ± 1.32	ns	–1.23 ± 1.24	*	–0.3 ± 0.83
Forearm, ultradistal	–3.11 ± 0.98	***	–1.39 ± 1.21	ns	–0.42 ± 2.08
Total body	–1.96 ± 1.82	ns	–0.83 ± 0.92	**	0.18 ± 0.7

*p < 0.05, **p < 0.01, ***p < 0.001; ns — not significant; GFD (+) — patients receiving a gluten-free diet; GFD (–) — patients not receiving a gluten-free diet or applying it inconsistently

Table VI. *Change in bone mineral density (BMD) after one-year treatment with gluten free diet, calcium, and alfacalcidol in coeliac disease patients (n = 35). Results are given as the percentage of the initial BMD value*

Tabela VI. *Zmiany gęstości mineralnej kości (BMD) po roku leczenia dietą bezglutenową, wapniem i alfakalcydolem u chorych z celiakią (n = 35). Wyniki przedstawiono jako odsetek wyjściowej wartości BMD*

	Initial BMD [g/cm²]	Change in BMD [%]		
	Mean ± SD	Mean ± SD	Minimum	Maximum
Femoral neck	0.84 ± 0.15	2.5 ± 6.9	–13.2	15.9
Lumbar spine	0.87 ± 0.46	7.3 ± 13.2	–11.0	35.8
Forearm, distal	0.62 ± 0.10	3.0 ± 4.3	–3.8	12.8
Forearm, ultradistal	0.30 ± 0.06	0.43 ± 12.0	–25.8	28.6
Total body	0.97 ± 0.10	1.4 ± 4.4	–6.8	9.0

but, unlike other parameters, it was still lower than in the control group ($p < 0.05$). The osteocalcin and PTH concentrations were significantly diminished after treatment ($p < 0.01$ and $p < 0.05$, respectively).

Discussion

Reduced BMD was found in 57–77% of our patients, depending on the site examined. This confirms opinions that coeliac disease affects bone mineral density in most cases [7–13]. Based on the histories of 13,000 patients with coeliac disease, Ludvigsson et al. stated that individuals with coeliac disease, including children, may be at increased risk of hip fracture and fracture of any type [14]. The most important mechanism of BMD decline is probably initial calcium malabsorption [15, 16] caused by villous atrophy and, secondarily, by coexisting vitamin D deficiency [16–19]. This leads to secondary hyperparathyroidism [11, 17–22], increased bone resorption, and increased but inadequate bone formation. Increased levels of bone-turnover markers can be detected as evidence of enhanced bone remodelling [18, 20, 23]. We observed all the above pathologies in most of our patients with coeliac disease. The mean calcaemia, calciuria, and vitamin 25-OH D_3 levels in the CD patients were lower than in the control group, but parathormone, bone formation markers (alkaline phosphatase, osteocalcin), and bone resorption marker (C-terminal telopeptide of type I collagen) serum concentrations were significantly higher. The 1,25-$(OH)_2$ D_3 level was normal or elevated in most of CD patients, presumably because of stimulation of renal 25OHD-1-alpha-hydroxylase by PTH.

A gluten-free diet is essential for the treatment of coeliac disease and, if strictly followed, should remove the nutritional deficiency and reverse bone metabolic disease. At the start of our study, the patients receiving a gluten-free diet over a longer period (at least one year) had normal values of bone-turnover markers and other biochemical parameters, except for calciuria, which was lower than in the control group ($p < 0.001$). Bone mineral density values were significantly higher in the patients receiving than in those not receiving a GFD, but worse than in the control group. After one year of treatment with a gluten-free diet,

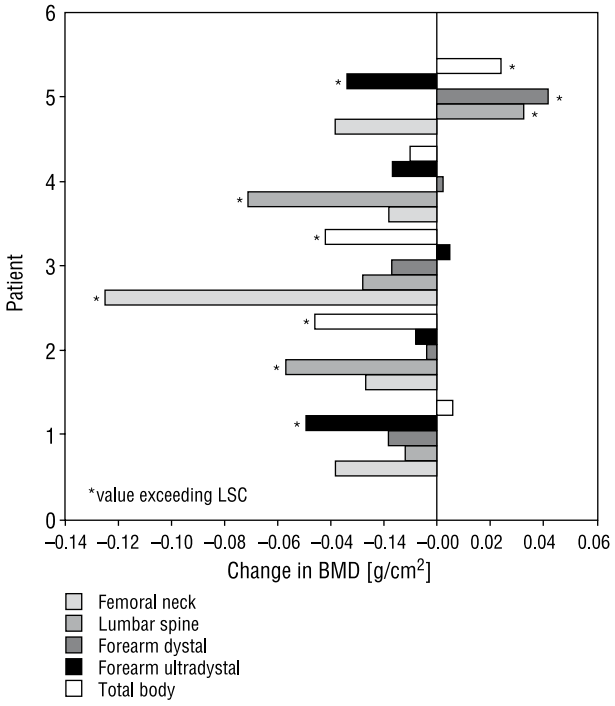

Figure 1. *Individual changes in bone mineral density (BMD) values after one-year treatment in 5 patients with lax adherence to the gluten-free diet; LSC — least significant change*

Rycina 1. *Indywidualne zmiany gęstości mineralnej kości (BMD) po roku leczenia u 5 chorych, którzy nie przestrzegali ściśle diety bezglutenowej; LSC — najmniejsza istotna zmiana*

calcium, and alfacalcidol, the coeliac patients, as a group, increased their BMD. The individual changes were different and the greatest improvement was by as much as 35% of the initial BMD value, occurring in the lumbar spine. However, in five patients there was a decrease in BMD, and the control tests for anti-tissue transglutaminase antibody were positive in these persons, indicating mistakes, probably unintentional, in adherence to the gluten-free diet [24, 25].

Studies performed in children with coeliac disease showed a marked improvement in bone density values after short-term treatment and the maintenance of normal BMD values after long-term treatment [26–28]. In adults, the frequent lack of gastrointestinal symptoms in some patients delays diagnosis of and specific therapy for coeliac disease. Patients are mostly diagnosed in adulthood, after the age at which the maximum rate of gain in bone mass occurs, and a possible explanation for the observed low BMD is that they failed to reach an optimal peak bone mass in early adulthood. This is perhaps the main reason for the different degrees of BMD deficiency and different levels of effectiveness of a gluten-free diet observed in adults. Many authors confess that although there is improvement in clinical symptoms and BMD with a gluten-free diet in adults, attainment of normal bone density may take several years, and in some individuals may not occur at all [8, 22, 29–31]. There are also suggestions that the inflammatory process in active CD, which is associated with inflammatory cytokines release, might have a role in BMD deficiency [32, 33].

The 24-h calciuria level after one year of treatment in our CD patients increased significantly ($p < 0.01$), but, unlike other parameters, it was still lower than in the control group ($p < 0.05$), suggesting a chronic calcium deficiency. We propose the addition of calcium and vitamin D to a gluten-free diet in coeliac patients, especially as a gluten-free diet may not provide adequate dietary calcium due to the lack of bread and cereals. In addition, some CD patients are deficient in lactase and may avoid dairy products high in calcium to prevent symptoms of lactose intolerance. Adequate provision with calcium and vitamin D is particularly important in patients with an elevated PTH serum concentration [34], because this can stop enhanced bone resorption faster that diet alone. In some of our patients with high PTH levels at the start of the study, we were not able to normalise it quickly using GFD and average doses of calcium and vitamin D, although the parathyroid gland showed proper reaction on intravenous calcium infusion.

Conclusions

We would like to state that calcium and vitamin D deficiency is very common in adult patients with coeliac disease. This leads to secondary hyperparathyroidism and low bone mineral density. A gluten-free diet improves calcium and vitamin D absorption, diminishes secondary hyperparathyroidism, and increases BMD, but does not guarantee full recovery, as we observed in our group receiving GFD before the study. We recommend calcium and vitamin D supplementation in adult coeliac patients, especially at the beginning of treatment. We suggest that bone mineral density, serum calcium, ALP, PTH, and daily calciuria be routinely measured in all coeliac disease patients. Patients with unexplained low BMD, hypocalcaemia, hypocalciuria, and secondary hyperparathyroidism should be examined for malabsorption and CD, even in the absence of gastrointestinal symptoms.

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