ELÄMÄNLAATU JA VATSAOIREET PITKÄÄN HOIDETUILLA IHOKELIAKIAPOTILAILLA: POIKKILEIKKAUSTUTKIMUS SUOMESSA.

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REUNALA TIMO, HUHTALA HEINI, SALMI TEEA. QUALITY OF LIFE AND GASTROINTESTINAL

SYMPTOMS IN LONG-TERM TREATED DERMATITIS HERPETIFORMIS PATIENTS: A CROSS-SECTIONAL

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Ihokeliakia on klassisen keliakian ihoilmentymä, jota hoidetaan keliakian tavoin elämän mittaisella, tiukalla, gluteenittomalla ruokavaliolla. Hoidetuilla keliakiapotilailla on enemmän vatsavaivoja ja heidän elämänlaatunsa on huonompi kuin terveellä väestöllä. Vatsavaivojen esiintymistä tai elämänlaatua ei kuitenkaan ole tutkittu ihokeliakiapotilailla. Tutkimuksessa selvitetään, kärsivätkö myös pitkään gluteenittomalla ruokavaliolla hoidetut ihokeliakiapotilaat jatkuvista vatsaoireista ja onko heidän elämänlaatunsa alentunut.

Tässä poikkileikkaustutkimuksessa tutkittiin 78 ihokeliakiapotilasta. Heidän vatsavaivojaan arvioitiin Gastrointestinal Symptom Rating Scale -kyselyn avulla. Elämänlaatua ja hyvinvointia tutkittiin käyttämällä Psychological General Well-Being- ja Short Form 36-kyselyitä. Tuloksia verrattiin 110 terveen verrokin muodostamaan kohorttiin, väestön referenssiarvoihin sekä 371 hoidettuun keliakiakontrolliin.

Ihokeliakia potilaiden mediaani-ikä oli 57 vuotta ja 51 % heistä oli miehiä. Merkitseviä eroja ei löydetty vatsavaivojen tai elämänlaadun suhteen, kun ihokeliakiapotilaita verrattiin kontrolleihin, mutta ihokeliakiapotilaat kärsivät vähemmän vatsavaivoista kuin keliakiakontrollit, ja heidän elämänlaatunsa oli parempi. Naispuolisilla ihokeliakiapotilailla oli kuitenkin vaikeampia vatsavaivoja, ja he olivat vähemmän tarmokkaita kuin miesihokeliakiapotilaat. Iho-oireen esiintyvyys, gluteenittoman ruokavalion kesto tai siinä pysyvyys ei vaikuttanut elämänlaatuun tai vatsavaivojen vaikeuteen.

Pitkään gluteenittomalla ruokavaliolla hoidetut ihokeliakia potilaat eivät siis kärsi gluteenittoman ruokavalion aiheuttamasta tautitaakasta, ja heidän elämänlaatunsa on terveiden verrokkien tasolla.

SISÄLLYSLUETTELO

Quality of life and gastrointestinal symptoms in long-term treated dermatitis herpetiformis patients: a cross-sectional study in Finland

Running head: Quality of life in dermatitis herpetiformis

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Abstract

Background: Dermatitis herpetiformis (DH) is a cutaneous manifestation of coeliac disease. Both conditions are treated with a restrictive life-long gluten-free diet (GFD). Treated coeliac disease patients have been shown to have more gastrointestinal symptoms and inferior quality of life compared to healthy controls, but evidence regarding quality of life in DH is lacking. Objective: The aim was to evaluate whether long-term GFD-treated DH patients suffer from persistent gastrointestinal symptoms and if they experience a drawdown in quality of life. Methods: Gastrointestinal symptoms and quality of life were assessed in 78 long-term GFD-treated DH patients using validated "Gastrointestinal Symptom Rating Scale", "Psychological General Well-Being" and "Short Form 36" questionnaires. The findings were compared to 110 healthy controls, population-based reference values and 371 treated coeliac disease-controls. Results: The median age of the DH patients at the time of the study was 57 years, and 51% were male. Significant differences in gastrointestinal symptoms or quality of life were not detected when treated DH patients were compared to healthy controls, but treated DH patients had less gastrointestinal symptoms and increased quality of life compared to coeliac disease-controls. Female DH patients had more gastrointestinal symptoms and reduced vitality compared to male DH patients. The presence of skin symptoms nor the adherence or duration of GFD did not have any influence on gastrointestinal symptoms or quality of life.
Conclusion: We conclude that long-term GFD-treated DH patients do not suffer from the burden of dietary treatment and have a quality of life comparable to that of controls.

Key points:

- Long-term gluten-free diet treated DH patients did not experience more gastrointestinal symptoms nor had a decline in the quality of life compared to healthy controls.
- Gluten-free diet treated DH women had more gastrointestinal symptoms and decline in vitality compared to DH men

1 Introduction

Dermatitis herpetiformis (DH) is a cutaneous manifestation of coeliac disease, occurring in approximately 12% of coeliac disease patients. [1] DH manifests as an itchy, blistering rash predominantly on the extensor surfaces of elbows and knees, and on the buttocks and scalp. [2] The diagnosis of DH is based on typical clinical manifestation and the demonstration of granular immunoglobulin (Ig) A deposits in the papillary dermis. [3] The majority of DH patients evince small-bowel mucosal villous atrophy characteristic of coeliac disease, and the remainder have coeliac-type inflammation in the gut. Regardless of the mucosal damage, DH patients are thought to suffer only rarely from gastrointestinal symptoms or have signs of malabsorption. [4, 5]

The treatment of choice for coeliac disease and DH is a strict life-long gluten-free diet (GFD). The diet has a positive effect on the small-bowel mucosal villous atrophy and it also alleviates gastrointestinal complaints and malabsorption and the DH rash. [6, 7] A long-lasting strict GFD has also been shown to reduce the risk of malignant diseases such as lymphoma associated with DH and coeliac disease. [8] However, the diet is hard to comply with and it causes drawdown in life quality because of its life-long restrictive nature, which interferes with everyday life. [9-11] Furthermore, the diet is more expensive than the normal gluten-containing diet.

Coeliac disease patients have been found to have a quality of life inferior to that in general population at the time of diagnosis. [12, 13] Even though health-related quality of life (HRQoL) has been shown to improve concomitant with treatment, [12, 14] in most studies the HRQoL of long-term GFD-treated coeliac disease patients does not reach the level of the normal population. [14-17] Furthermore, coeliac disease patients have been shown to suffer from persistent gastrointestinal complaints even after a long-term GFD. [18, 19] DH is a chronic itching skin disease and patients adhere to the same burdensome GFD as coeliac disease patients, but little is known about HRQoL in DH. The aim of this study was to establish whether the burden of restrictive GFD causes a drawdown in DH patients' HRQoL or do the benefits of decreased symptoms overcome the negative effects of GFD. Further, we aimed to find out whether treated DH patients suffer from persistent gastrointestinal symptoms. The results were compared to healthy controls and treated coeliac disease-controls.

2 Materials and Methods

2.1 Patients and controls

This was a cross-sectional study on the Finnish DH population. The cohort was derived from an adult coeliac disease series, including altogether 1111 patients. The series was recruited nationwide between the years 2006 and 2010 by advertising in national and local coeliac disease societies and using newspaper advertisement. Personal or telephone interviews were conducted to the recruited either by a physician or a study nurse specialized in coeliac disease. The interviews included questions about demographic data, the year of DH or coeliac disease diagnosis, skin symptoms, coeliac disease-associated disorders, family history of coeliac disease or DH, duration of the diet and strictness of GFD at the time of the study. The strictness of the diet was assessed based on the interviews and patients were distributed into four groups: 1. strict diet, no dietary lapses, 2. dietary lapses less than once a week, 3. dietary lapses more than once a week and 4. unrestricted gluten-containing diet (Table 1). In addition, validated questionnaires about gastrointestinal symptoms, HRQoL and psychological general well-being were mailed to those enrolled.

Out of the 1111 recruited patients, 569 patients over 18 years answered to the validated questionnaires. Out of these 569, 78 patients had been diagnosed with DH and they were enrolled as cases in the study group. The medical records of the DH patients were reviewed to verify that all had had skin symptoms compatible with DH at the time of diagnosis, and that the presence of skin immunoglobulin A (IgA) deposits in the papillary dermis was confirmed by direct immunofluorescence. [3]

DH patients' gastrointestinal symptoms and quality of life as measured by the Psychological General Well-Being (PGWB) questionnaire were compared to 110 healthy controls, who considered themselves healthy and had no first-degree relatives with coeliac disease. These healthy controls were recruited from the immediate neighbourhood and among friends of the coeliac disease patients. The aim was to obtain a control group from a social and residential environment similar to that of the study patients. The median age of the healthy control group was 48 years (range 23-87) and 19% were male (Table 1). The results of the Short Form SF-36 (SF-36) questionnaire were compared to the age- and gender-adjusted Finnish general population reference values obtained from a nationwide health survey involving 2060 subjects: 45% were male and the mean age was 49 years (standard deviation 17), median not known. [20] Furthermore, 371 GFD-treated coeliac disease patients suffering from abdominal symptoms at the time of the diagnosis, were selected as a

coeliac disease-controls from the same series where DH patients were chosen. The biopsy-proven coeliac disease diagnoses were verified from the medical records. In the coeliac disease control group, 19% of patients were male and the median age at the time of the study was 56 years (range 19-92) (Table 1).

All participants gave their written informed consent. The study protocol was approved by the Regional Ethics Committee of Tampere University Hospital.

2.2 Methods

Gastrointestinal symptoms were assessed using the Gastrointestinal Symptom Rating Scale (GSRS), which is a 15-item questionnaire used to evaluate common gastrointestinal symptoms in five different groups: diarrhoea, indigestion, constipation, abdominal pain and reflux. The questionnaire uses a seven-grade Likert scale for each item, one symbolizing no symptoms and seven indicating the most severe symptoms. A higher score thus indicates more symptoms. The final scores are calculated as a mean for each sub-dimension and the total GSRS score as the mean of all 15 items. [21]

The quality of life was assessed with PGWB and SF-36 questionnaires. The PGWB is a questionnaire used to assess health-related quality of life and well-being. This is a 22-item questionnaire which includes six emotional states: anxiety, depressed mood, self-control, positive well-being, general health and vitality. All of the items use a six-grade Likert scale, where a value of one represents the poorest and value six the best possible well-being. The total score ranges therefore between 22 and 132 points, a higher score indicating better quality of life. [22] The SF-36 is a generic HRQoL questionnaire, which uses eight parameters to quantify the quality of life. These are: general health perceptions, physical functioning, mental health, social functioning, vitality, bodily pain, physical role functioning and emotional role functioning. A scoring algorithm is used to transform the raw scores on each question into a scale ranging from 0-100, higher scores indicating better quality of life. [23] All of the questionnaires have been widely used in coeliac disease research and were chosen in view of their comparability with previous research and their good validity and reproducibility. [14, 24, 25]

2.3 Statistics

The data were analysed with the IBM SPSS Statistics 20 software package (International Business Machines Corp., New York, USA) in cooperation with a statistician. Since the data were not normally distributed, median values and interquartile ranges were calculated for all GSRS and PGWB parameters. Statistical significances were tested by Mann-Whitney U-test. *P* values <0.05 were considered statistically significant. The data with significance were further adjusted by gender and age. In order to make the values comparable with the reference, in SF-36 the means and standard deviations were used to describe the results. Significances between DH patients and the Finnish reference values were evaluated by estimating the confidence intervals for the differences in means.

3 Results

Forty (51%) of the 78 DH patients were male (Table 1). The median age of the DH patients at the time of the diagnosis was 38 years and at the time of the current study 57 years. At the time of the diagnosis all DH patients were shown to have IgA deposits detected by direct immunofluorescence in skin biopsies. Twenty-two out of the 41 (54%) DH patients with available small-bowel biopsy result at the time of the diagnosis had subtotal villous atrophy, 13 (32%) had partial villous atrophy, and 6 (14%) evinced normal villous architecture. At the time of the study, 95% of the DH patients were on a strict GFD, and the median duration of the diet was 18 years. None of the DH patients was consuming a normal gluten-containing diet (Table 1). At the time of the study 73 out of 78 (94%) DH patients had negative endomysial antibodies.

When the GFD-treated DH patients were compared to healthy controls, a non-significant trend emerged in GSRS reflux score, DH patients having more symptoms than healthy controls. However, this significance disappeared when adjusted for gender and age (Table 2). No other differences between DH patients and healthy controls were found in GSRS scores (Table 2). DH patients did not differ from healthy controls in the PGWB total or any sub-dimension scores. Only the unadjusted general health score was inferior in DH patients compared to healthy controls, but again the divergency disappeared when adjusted for gender and age (Table 2). Significant

differences were not detected between DH study patients and healthy controls when the different aspects of quality of life were measured by SF-36 questionnaire (Fig. 1).

At the time of the diagnosis, 191 out of 309 (62%) coeliac disease patients with available data had subtotal villous atrophy in the small bowel mucosa, 109 (35%) had partial villous atrophy and 9 (3%) minor coeliac enteropathy. At the time of the study endomysial antibodies were negative in 350 out of 369 (95%) coeliac disease patients. When the GFD-treated DH patients were compared to treated coeliac disease-controls, DH patients had statistically significantly less symptoms in GSRS total and GSRS sub-dimension scores diarrhoea and pain. When data was adjusted for gender and age, only the difference in GSRS total score remained significant (Table 2). No differences were found in PGWB scores between treated DH patients and coeliac disease-controls. (Table 2) However, in SF-36 questionnaire coeliac disease-controls had significantly lower scores compared to DH patients in physical function, role physical and general health sub-dimension scores. There was also a non-significant trend in bodily pain. When the results were adjusted by gender and age, significance remained in general health and role physical sub-dimensions (Fig. 1).

When DH women were compared to DH men, a statistically significant difference was found in the GSRS parameters ‘total’ and ‘constipation’, DH women having more symptoms than DH men. A similar trend for women to experience more symptoms than men was also seen in other parameters of the GSRS questionnaire (Table 3). In PGWB and SF-36, a significant difference between the genders was found in vitality, which was inferior in DH women in both questionnaires (Table 3). In SF-36, there was also a borderline significant difference (P= 0.061) in mental health, showing poorer mental health in DH women compared to DH men (Table 3). No gender differences were found in coeliac disease-control group (data not shown).

Seventeen per cent of DH patients (13 out of 78) reported having visible skin symptoms compatible with DH or pruritus at the time of the study (Table 1), but the presence or absence of skin symptoms had no influence on GSRS, PGWB or SF-36 scores (data not shown). Similarly, neither adherence to nor duration of GFD had any effect on the presence of persistent skin symptoms or on the questionnaire scores when the results were compared within the DH cohort.

4 Discussion

This is the first large study focusing on gastrointestinal symptoms and quality of life in a long-term GFD-treated cohort of DH patients. We found that long-term GFD-treated DH patients do not suffer from the burden of a GFD nor from the burden of the disease itself, as their quality of life was found to be comparable to that of the general population. Since HRQoL is known to be reduced in other comparable chronic itching skin diseases such as psoriasis and atopic dermatitis [26-28] the fact that our DH patients well-being is comparable to controls could be due to the very specific and curative treatment of GFD.

GFD-treated DH patients did not suffer from gastrointestinal complaints unlike coeliac disease patients who have been shown to suffer from persistent gastrointestinal complaints even when maintaining a strict GFD. [18, 19, 29] In Finland after long-term GFD 96% of coeliac disease patients have shown to evince normal villous architecture in small bowel biopsies. [30] In this study 95% and 98% of DH and coeliac disease patients followed a strict GFD and 94% and 95% of DH and coeliac disease patients were seronegative supporting excellent clinical and histological recovery on GFD in both groups. It has been suggested that the explanation for the persistent gastrointestinal symptoms in GFD-treated coeliac disease patients lies in the low amount of fibre in the diet [29, 31] or in trace amounts of gluten. [32] However, DH patients follow exactly the same strict GFD as coeliac disease patients. Diagnostic delay and severity of gastrointestinal symptoms prior to diagnosis are known to be factors increasing the risk of prolonged gastrointestinal symptoms in coeliac disease. [19] DH patients are thought to suffer from milder gastrointestinal symptoms before the diagnosis but research has been unable to show a difference in the duration of symptoms prior to diagnosis between DH and coeliac disease. [33] Also the composition and diversity of the duodenal microbiota have been shown to vary between untreated classical coeliac disease and DH. [34] Although it has not been studied how GFD-treatment changes the duodenal microbiota, the difference in duodenal microbiota might have a role in explaining the difference in gastrointestinal symptoms between treated DH and coeliac disease patients. Moreover, the prevalence of irritable bowel syndrome-type symptoms has been found to be significantly higher in patients with coeliac disease compared to the normal population, [15, 35] while there is no evidence of this in DH. Thus coexisting undiagnosed gastrointestinal disorders might also influence the incidence of gastrointestinal symptoms in coeliac disease patients.

DH skin symptoms are known to alleviate comparatively slowly with GFD-treatment only, [4] and hence dapsone is a medication that is often used for a few months to a few years in combination with dietary treatment to reduce the skin symptoms more quickly. [4] We did not have data about

the use of dapsone in our study population and therefore in patients with ongoing skin symptoms dapsone usage cannot be excluded even though dapsone is not commonly used in DH patients with a long duration of GFD. Although not scientifically studied in DH, the presence of skin symptoms are known to affect poorly the patients' quality of life. In our data only 13 DH patients were suffering from skin symptoms at the time of the study, and therefore it is possible that we were unable to show the effect of the skin symptoms to the quality of life due to the small cohort size. In addition, instead of using dermatological questionnaires, we used generic quality of life questionnaires, which might have limited accuracy to show the effect of skin symptoms on HRQoL.

In our study cohort we found DH women to have more gastrointestinal complaints, especially constipation, compared to DH men. Coeliac disease women are also known to suffer from increased gastrointestinal symptoms compared to men, [18, 29] although our data showed no gender difference in coeliac-disease control group. In addition, more women than men are known to suffer from irritable bowel syndrome and especially constipation-predominant condition. [36] In this study DH women showed also lower vitality compared to DH men, which would imply that women with DH feel more tired and worn out compared to DH men. A similar distinction between the genders in HRQoL parameters has been widely observed previously in coeliac disease, [24, 25, 29] even though not evident in this current study. Interestingly this gender distinction in HRQoL is not found in all chronic diseases such as type-2 diabetes patients. [37]

In contrast to previous coeliac disease research, we focused here solely on DH patients and our DH cohort size was large. Previous research on HRQoL in DH has been scant; to our knowledge, only Tontini et al. [38] have focused on this aspect. In their coeliac disease study, they assessed the HRQoL of a small subcohort of 10 DH patients with the Italian version of the SF-36 questionnaire. Similarly to ourselves, they found no differences in the HRQoL of treated DH patients when compared to a control group. In addition to cohort size, other strengths of our study were the nationwide approach and the well-verified skin biopsy-proven DH diagnosis. Control patients did not undergo gastroscopy and small bowel biopsy to exclude coeliac disease, but even if there were a few asymptomatic coeliac disease patients among controls this would not have influenced the results. In addition, we used well validated questionnaires, and while they are not coeliac disease- or DH-specific, they are widely used in coeliac disease studies. One limitation in our study is that we used volunteers, which might cause selection bias and possibly mislead the life quality being superior than it actually is. It must also be conceded that since the availability of gluten-free food is

relatively good in Finland and adherence to the GFD is very high, our results may not be directly generalizable to different cultures or to countries with poorer dietary adherence.

5 Conclusions

The aim of this cross-sectional study was to evaluate whether long-term GFD-treated DH patients suffer from persistent gastrointestinal symptoms and if they experience a drawdown in quality of life. The conclusion was that the gastrointestinal symptoms and the quality of life of long-term GFD-treated DH patients are comparable to those in the general population. However, women with DH suffer from more severe gastrointestinal complaints and inferior vitality compared to DH men, which should be recognized during the follow-up.

6 Compliance with Ethical Standards

The study protocol was approved by the Regional Ethics Committee of Tampere University Hospital and has therefore been performed according to the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

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Table 1 Demographic data, associated disorders and gluten-free diet of treated dermatitis herpetiformis (DH) study patients, healthy controls and treated coeliac disease-controls.

	Study patients	Control patients (n=481)	
	DH patients (n=78)	Healthy controls (n=110)	Coeliac disease controls (n=371)
Male, n (%)	40 (51)	21 (19)	69 (19)
Age at diagnosis, median (range), years	38 (10-72)	-	44 (0-79)
Age at time of study, median (range), years	57 (28-81)	48 (23-87)	56 (19-92)
Family history of coeliac disease, n (%)	42 (54)	0	227 (61)
Coeliac disease-associated autoimmune disorders, n (%)			
Thyroid disease	13 (17)	0	67 (18)
Type 1 diabetes mellitus	2 (3)	0	7 (2)
Sjögren's syndrome	2 (3)	0	6 (2)
Duration of gluten-free diet, median (range), years	18 (1-47)	0	9 (0.5-53)
Strictness of gluten-free diet, n (%)			
Strict[a]	74 (95)	0	363 (98)
Dietary lapses 2-3 times/month	3 (4)	0	6 (2)
Dietary lapses more than 1/week	1 (1)	0	0
Normal gluten-containing diet	0	110 (100)	0
Skin symptoms at time of study, n (%)	13 (17)	nd	0

[a]No dietary lapses; nd, no data

Table 2 Unadjusted median values and interquartile ranges for Gastrointestinal Symptoms Rating Scale (GSRS) and Psychological General Well-Being (PGWB) scores for study patients with treated dermatitis herpetiformis (DH), healthy controls and treated coeliac disease-controls. In GSRS higher score indicates more symptoms and in PGWB higher score indicates better quality of life.

		Study patients	Control patients (n=481)			
	Symptom	DH patients (n=78)	Healthy controls (n=110)	Coeliac disease-controls (n=371)	P value[a]	P value[b]
GSRS	Total	1.8 (1.4-2.3)	1.7 (1.4-2.3)	1.9 (1.5-2.6)	0.804	0.014
	Diarrhoea	1.3 (1.0-2.0)	1.0 (1.0-2.0)	1.7 (1.0-2.3)	0.462	0.020*
	Indigestion	2.1 (1.5-3.0)	2.3 (1.5-3.0)	2.3 (1.8-3.3)	0.701	0.142
	Constipation	1.7 (1.0-2.0)	1.3 (1.0-2.3)	1.7 (1.0-2.7)	0.716	0.082
	Pain	1.7 (1.3-2.3)	1.7 (1.0-2.3)	2.0 (1.3-2.7)	0.714	0.012*
	Reflux	1.0 (1.0-2.0)	1.0 (1.0-1.5)	1.5 (1.0-2.0)	0.054*	0.544
PGWB	Total	104 (95-112)	107 (100-114)	105 (92-115)	0.150	0.746
	Anxiety	24 (21-27)	25 (22-27)	24 (21-27)	0.184	0.481
	Depression	17 (15-18)	17 (15-18)	17 (15-18)	0.841	0.836
	Well-being	18 (15-20)	17 (15-19)	17 (14-20)	0.382	0.494
	Self-control	15 (14-17)	16 (14-17)	16 (14-17)	0.582	0.535
	General health	13 (11-15)	15 (13-16)	13 (10-15)	0.001*	0.426
	Vitality	18 (16-20)	19 (17-20)	18 (16-20)	0.095	0.770

[a]Difference between DH patients and healthy controls; [b]Difference between DH patients and coeliac disease-controls;

*Significance disappears when adjusted by gender and age

Table 3 Median scores and interquartile ranges for Gastrointestinal Symptoms Rating Scale (GSRS), Psychological General Well-Being (PGWB), and Short Form 36 Health Survey (SF-36) questionnaires for treated male and female dermatitis herpetiformis (DH) patients. In GSRS higher score indicates more symptoms and in PGWB and SF-36 higher score indicates better quality of life.

	Parameter	DH men (n=40)	DH women (n=38)	P value
GSRS	Total value	1.6 (1.3-2.1)	2.1 (1.5-2.5)	0.006
	Diarrhoea	1.3 (1.0-1.9)	1.3 (1.0-2.1)	0.328
	Indigestion	2.0 (1.5-2.8)	2.4 (1.8-3.3)	0.101
	Constipation	1.3 (1.0-1.7)	1.7 (1.3-2.7)	0.007
	Pain	1.7 (1.0-2.0)	1.8 (1.3-2.3)	0.077
	Reflux	1.0 (1.0-2.0)	1.5 (1.0-2.0)	0.199
PGWB	Total score	107 (96-117)	101 (95-109)	0.135
	Anxiety	24 (21-27)	24 (22-26)	0.717
	Depression	17 (15-18)	16 (14-18)	0.163
	Well-being	18 (15-20)	18 (16-19)	0.771
	Self-control	16 (14-17)	15 (13-17)	0.117
	General health	13 (12-16)	13 (11-15)	0.160
	Vitality	19 (17-21)	17 (15-20)	0.052
SF-36	Physical function	95 (86-100)	93 (75-100)	0.183
	Role physical	100 (75-100)	100 (73-100)	0.940
	Role emotional	100 (41.65-100)	100 (33-100)	0.531
	Vitality	75 (65-85)	70 (49-80)	0.022
	Mental health	86 (73-91)	80 (68-85)	0.061
	Social functioning	88 (75-100)	88 (75-100)	0.588
	Bodily pain	78 (68-90)	78 (54-90)	0.558
	General health	70 (51-84)	65 (55-80)	0.250

Figure 1 Short Form 36 Health Survey (SF-36) mean scores and 95% confidence intervals for long-term gluten-free diet-treated dermatitis herpetiformis (DH) patients (n=78), Finnish general population reference values (n=2060) and treated coeliac disease-controls (n=371). (*Significant difference between DH patients and coeliac disease-controls)