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CHAPTER 6

Dietary compliance and health-related quality of life in patients with celiac disease

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ABSTRACT

Objective: Celiac disease is treated with a lifelong gluten-free diet. The aim of our study was to investigate whether dietary (non-) compliance is associated with health-related quality of life (HRQoL) of celiac patients.

Patients and methods: Patients from our hospital, known with celiac disease for more than 10 years, were invited to participate in a study on possible gluten tolerance. HRQoL was assessed by the SF-36, symptoms by the Gastrointestinal Symptom Rating Scale and dietary compliance by a food frequency questionnaire. HRQoL of celiac patients was compared with that of the general population.

Results: Fifty-three biopsy-confirmed celiac patients were divided into three groups according to gluten consumption: gluten-free diet (n=33), gluten transgression (<10 g gluten/day; n=8), and normal gluten-containing diet (>10 g gluten/day; n=12). Compared with the general population, celiac patients scored significantly worse on general health perception but significantly better on bodily pain and limitations due to physical problems. The results of the Gastrointestinal Symptom Rating Scale and the SF-36 were similar in all three dietary groups.

Conclusions: Although adhering to the gluten-free diet strictly is important to prevent future complications, patients with partial or non-adherence report similar HRQoL compared with patients with strict adherence in this group of adult celiac patients.

INTRODUCTION

Gluten in the diet of celiac disease (CD) patients causes histological alterations in their small bowel that may lead to disturbances in nutrient absorption, to symptoms such as diarrhea and abdominal pain, or to extra-intestinal complications such as osteoporosis, infertility, and cancer (1). The treatment of CD consists of a lifelong gluten-free diet (GFD) to heal the duodenal mucosa, improve symptoms, and protect from development of complications (2,3), although in some cases histological remission is incomplete (4). Treatment with a GFD has in general a positive effect on the patients' medical condition (1), but results from studies on the impact of treatment on their emotional and psychological well-being differ in outcome. The psychological well-being and health-related quality of life (HRQoL) of treated CD patients have been reported to be similar to healthy controls, both in children (5) and in adults (6,7). On the other hand, a negative impact of CD on social life and a lower HRQoL in CD patients have also been described (8-11). Furthermore, gender differences seem to play a role in the HRQoL of CD patients, in particular being a disadvantage for women (6,7,12).

The dietary compliance of CD patients has frequently been studied (13,14) and compliance with the GFD may be one of the factors associated with HRQoL (7,9). It is known that HRQoL improves once newly diagnosed CD patients are treated with a GFD (15,16). Some patients, however, stop following the GFD and remain consuming gluten for a long time with good clinical tolerance to the challenge (17,18). In our study on possible development of tolerance to gluten among adult CD patients, we found that 23% of them did not adhere to the GFD (18). The aim of the present study was to investigate whether the HRQoL was associated with dietary (non-) compliance in the group of CD patients recruited for that study.

METHODS

Adult CD patients known to have CD for at least 10 years and diagnosed at the Leiden University Medical Center (LUMC) were invited to participate.

Dietary compliance

Dietary information was obtained by a questionnaire in which the patients were asked to register their degree of compliance with the diet as strict, partial, or none. The consumption of gluten-containing products was checked by a food frequency questionnaire. The food frequency questionnaire for this study was developed according to the database of the Dutch Food consumption study, held in 1998 (19), and according to the Dutch Food composition table (20). Gluten intake was estimated by multiplying the grams of vegetable protein from gluten-containing cereals by 0.8 (21). Based on

gluten intake, three groups were distinguished: 1) gluten-free diet (GFD); 2) gluten transgression (GT: < 10 g gluten/day), and 3) normal gluten-containing diet (GCD: >10 g gluten/day) (22).

Assessment of the health-related quality of life

The SF-36 health survey was used to assess the general HRQoL (23). It is composed of 36 questions and standardized response choices, organized into eight multi-item scales: physical functioning, role limitations due to physical health problems, bodily pain, general health perception, vitality, social functioning, role limitations due to emotional problems, and general mental health.

Comparison with the general population

Data from a random, nationwide sample in the Netherlands (1742 respondents, 56% male, age 16-94 years), were used as a reference to compare the results of the SF-36 (23).

Assessment of symptoms

Specific gastrointestinal symptoms were evaluated according to the Gastrointestinal Symptom Rating Scale (GSRS), which rates gastrointestinal symptoms from 1 'no discomfort at all' to 7 'very severe discomfort' (24).

Statistics

Statistics were performed by means of SPSS for Windows version 14.0 (SPSS Inc., Chicago, Ill., USA). To compare patient characteristics and results, the Kruskal Wallis and Mann-Whitney U tests were used for skewed distribution and the ANOVA and Student T-test for normal distribution. Numbers of patients were compared using the Fisher's Exact test. P-values <0.05 were considered significant. The internal consistency of the SF-36 and the GSRS was evaluated using Cronbach's alpha, and 0.7 or higher was considered to represent adequate reliability. For better comparison, the results of all the items of the SF-36 were recoded in the same direction and transformed into a scale of 0 to 100. Results of the SF-36 and the GSRS are presented as means (standard deviation). By using the data from the general population (23), we calculated expected values of the items of the SF-36, based on the distribution of age, gender and the total number of chronic health conditions of our sample. Mean scale scores of the SF-36 and the GSRS were corrected for group differences in age, gender and presence of chronic health conditions by multivariate regression analyses. Selective IgA deficiency was not considered to play a role in the HRQoL and thus was not corrected for. 95% Confidence intervals were used to compare the results of the SF-36 with the general population.

ETHICS

The study protocol was approved by the Medical Ethics Committee of the LUMC.

RESULTS

Of the 77 CD patients eligible to be invited for participation in the original study on possible development of tolerance to gluten (18), 66 gave informed consent. In 13 of them CD could not be confirmed by revision of the diagnostic biopsy, and only the remaining 53 patients with biopsy-confirmed CD participated in the study. Their characteristics, grouped according to their dietary habits, are presented in Table 1.

Table 1. Clinical characteristics of 53 patients with biopsy-confirmed celiac disease according to their dietary habits.

Median (range)	Gluten-free diet (GFD) (n=33)	Diet with gluten transgression (GT) (n=8)	Gluten-containing diet (GCD) (n=12)	Overall p-value
Sex (m)	7	5	4	0.07*
Age (y)	57 (21-77)	26 (22-66)	30 (25-53)	0.001**
Age at diagnosis (y)	24 (1-65)	4 (0.9-32)	2 (0.7-15)	0.001**
Duration of diagnosis (y)	25 (12-52)	24 (17-34)	28 (16-44)	0.48
Duration of actual gluten consumption (y)	0	8 (2-34)	18 (1-32)	0.001**
Gluten intake (g/day)	0	0.9 (0.004-3)	15 (10-24)	0.001**§
Associated chronic health condition n (%)	10 (30%)	2 (25%)	5 (42%)	0.70
BMI, kg/m ² (mean ± SD)	24.6 ± 3.6	22.8 ± 2.5	22.4 ± 3.3	0.20

Gluten-free diet = no gluten/day; gluten transgression = < 10 g gluten/day; gluten-containing diet = >10 g gluten/day; *= significance between GFD and GT; **= significance between GFD and GCD; §=significance between GT and GCD.

An associated chronic health condition was reported 27 times (by 32% of the patients). Some patients had more than one associated disease. Divided over the three diet groups, there were patients with selective IgA deficiency (n=5), hypothyroidism (n=4), dermatitis herpetiformis (n=3), diabetes mellitus type 1 (n=2), rheumatoid arthritis (n=2), Sjögren syndrome (n=2), cancer (n=2), secondary hyperparathyroidism (n=1), ulcerative colitis (n=1), multiple sclerosis (n=1), systemic lupus erythematosus (n=1), scleroderma (n=1), fertility problems (n=1) and miscarriages (n=1). There were no significant differences in

the distribution of patients with an associated chronic health condition between the three groups (Table 1).

Dietary compliance

The self-reported strict compliance with the GFD was 62% (33/53). Twelve patients (23%) reported to consume a normal GCD, and eight reported to consume low amounts of gluten (GT). The duration of CD was comparable in all three groups. However, the patients consuming gluten (GCD or GT) were diagnosed with CD at a significant younger age and are presently significantly younger than the ones strictly adhering to a GFD (Table 1).

SF-36

The internal consistency of the SF-36 subscales ranged from 0.77 to 0.95. Results of the SF-36 are presented in Table 2 and 3.

Comparing the HRQoL of the three groups of CD patients with different dietary compliance, significantly better scores were found in the patients consuming gluten: better general mental health in patients with GT and less bodily pain in patients with a GCD. These differences, however, disappeared when the comparisons were corrected for age, gender and presence of associated chronic health conditions (Table 2).

Table 2. Mean $\pm$ standard deviation scores of the SF-36 in 53 patients with biopsy-confirmed celiac disease according to their dietary regimen.

	Gluten-free diet (n=33)	Diet with gluten transgression (n=8)	Gluten-containing diet (n=12)	Overall p-value*
General health perception	59.9 $\pm$ 24.3	60.6 $\pm$ 21.5	70.8 $\pm$ 24.9	0.21
General mental health	75.4 $\pm$ 18.5	90.5 $\pm$ 9.8	75.0 $\pm$ 17.0	0.41
Vitality	61.7 $\pm$ 20.3	74.4 $\pm$ 18.6	71.3 $\pm$ 16.7	0.96
Social functioning	80.7 $\pm$ 26.3	92.2 $\pm$ 22.1	87.5 $\pm$ 22.6	0.92
Physical functioning	85.3 $\pm$ 23.3	85.0 $\pm$ 34.6	94.6 $\pm$ 6.9	0.11
Bodily pain	80.7 $\pm$ 20.4	93.8 $\pm$ 7.4	94.6 $\pm$ 12.5	0.72
Limitations due to physical problems	85.8 $\pm$ 33.3	87.5 $\pm$ 35.4	93.8 $\pm$ 11.3	0.21
Limitations due to emotional problems	83.3 $\pm$ 32.5	100.0 $\pm$ 0	88.9 $\pm$ 21.7	0.67

*p-value when corrected for group differences in age, gender and associated chronic health conditions.

Overall, corrected for age and gender (Table 3), CD patients reported significantly worse general health perception but significantly better HRQoL for the domains bodily pain and limitations due to physical problems compared with the general population. Upon that, when corrected for the presence or absence of chronic health conditions CD patients showed significantly higher scores for the domains physical functioning and limitations due to emotional problems (Table 3).

Table 3. Mean (95% CI) scores of the SF-36 in 53 patients with biopsy-confirmed celiac disease (CD) compared with results from the general population (GP; n=1742), corrected for the distribution of age, gender and chronic health conditions of our sample.

	CD patients	GP-age	GP-gender	GP-chronic health conditions
General health perception	62.5 (55.8-69.1)	71.3*	70.4*	65.0
General mental health	77.6 (72.7-82.6)	77.2	75.3	73.7
Vitality	65.8 (60.3-71.2)	68.8	66.7	64.4
Social functioning	84.0 (77.1-90.8)	84.6	83.2	80.0
Physical functioning	87.5 (81.0-94.0)	84.8	82.0	77.6*
Bodily pain	86.1 (80.9-91.3)	75.9*	73.5*	69.0*
Limitations due to physical problems	88.0 (79.6-96.4)	78.5*	75.3*	68.0*
Limitatons due to emotional problems	87.3 (79.5-95.2)	83.2	80.6	78.0*

GP; Aaronson *et al.*²³ ; *=significant different from the corrected general population.

GSRS

The internal consistency of the GSRS subdimensions ranged from 0.64 to 0.92. Results of the GSRS are presented in Table 4. No significant differences were found in the mean scores of the GSRS between the different dietary groups, corrected for age, gender or associated chronic health conditions.

Table 4. Means $\pm$ standard deviation scores of the Gastrointestinal Symptom Rating Scale (GSRS) in the 53 patients with biopsy-confirmed celiac disease according to their dietary regimen.

	Gluten-free diet (n=33)	Diet with gluten transgression (n=8)	Gluten-containing diet (n=12)	Overall p-value*
Abdominal pain	1.6 $\pm$ 0.8	1.6 $\pm$ 0.7	1.8 $\pm$ 1.5	0.92
Indigestion	2.1 $\pm$ 0.9	2.5 $\pm$ 1.1	2.0 $\pm$ 1.2	0.47
Diarrhea	2.0 $\pm$ 1.7	2.1 $\pm$ 1.5	1.5 $\pm$ 0.7	0.23
Constipation	2.6 $\pm$ 1.5	1.9 $\pm$ 1.3	1.9 $\pm$ 1.6	0.38

*p-value when corrected for group differences in age, gender and associated chronic health conditions.

DISCUSSION

In this study among CD patients with and without adherence to the GFD, we have found a similar HRQoL in patients with different dietary compliance. Our findings are in agreement with earlier reporting in Swedish patients (12), but are in contrast with the better HRQoL found in Italian patients with a better dietary compliance (9). In the latter study, however, patients had a shorter duration of CD (e.g. 2 years) possibly explaining their better HRQoL.

One of the factors associated with HRQoL in CD patients may be the presence of symptoms (16). Considering the gastrointestinal symptoms scored by GSRS, we did not find differences between the three groups of patients with different dietary compliance. This similarity of the GSRS scores may partly explain the similarity in HRQoL between the three dietary groups. On the other hand it is possible that the GSRS is not sensitive enough since it was not specifically designed to study symptoms in CD patients, although in earlier studies, the instrument discriminated symptom scores between male and female CD patients (12,25). Another possibility is that the presence of symptoms in CD patients is not associated with dietary compliance and that patients adhering to a strict GFD for several years may continue to have gastrointestinal symptoms (12,25,26).

The risk of CD related co-morbidity or potential complications are other factors associated with HRQoL (16) and can be measured with the item 'I expect my health to deteriorate' as part of the general health perception domain of the SF-36. In our study, we did not find significant differences in this domain between the three dietary groups. Furthermore, we were able to compare CD patients with associated chronic health conditions already present with CD patients without these and found comparable SF-36 scores (data not shown).

The HRQoL might also be associated with factors not related to CD. It is known that, concerning the results of the SF-36, in general older respondents score significantly lower than younger respondents and women have lower scores than men (23). In our study, the patients adhering to the GFD tended to have lower HRQoL scores than the other groups, but this apparent difference can be explained because the group was older and contained a higher percentage of females.

When comparing HRQoL of the CD patients in general with the reference population, celiac patients showed worse general health perception, confirming earlier studies (9,10,12), but they had better scores concerning the physical domains. Presumably, CD patients, once diagnosed and treated, experience their new-found vitality and health as a relief, as has been reported by patients 10 years after diagnosis (27), which may positively influence the interpretation of the questions of the SF-36.

The interest within the medical community in measuring QoL is increasing (7-12,28-30). It has been argued that what matters in HRQoL is the way patients feel about their functioning, not their functioning itself (31). The subjective assessment of physical, mental, and social dimensions of well-being and social functioning can be performed by generic or disease-specific instruments. In this study, we have used the SF-36. Being a generic instrument for QoL measurement, the SF-36 can be used to measure the impact of treatment on HRQoL but not to measure the disease-specific QoL aspects such as, in the case of CD, the possible social and financial restrictions due to the GFD. Therefore, the use of both generic- and disease-specific instruments is recommended to assess the HRQoL (32). Recently, disease-specific instruments to assess HRQoL in celiac patients have been developed and validated, both for adults (CDQ; 33) and for children (CDDUX; 11).

In light of upcoming developments for new treatment strategies for CD (34-37), the comparison of HRQoL of celiac patients with current and alternative treatment will be necessary in the future to get information on which treatment under which circumstances will be most appreciated. The disease-specific instruments to assess HRQoL in CD, may be valuable tools for the caregivers to get information on the HRQoL of adult and pediatric CD patients aiming to ameliorate their treatment.

Limitations of our study were that the CD patients were originally invited to participate in a study on the possible development of tolerance to gluten (18), and that it was performed among a limited number of patients all diagnosed at the same university hospital. Therefore, further studies are needed to confirm our results in larger samples and in a more general group of CD patients.

In conclusion, the HRQoL of the chronic ill patient is an important factor in his treatment. Equally important is the prevention of co-morbidity and complications of CD patients. We and others have found that strict adherence to the GFD does not have negative consequences for the HRQoL, hence, considering the importance of prevention

of co-morbidity and complications of CD patients, achieved by strict adherence to the GFD, the GFD should be advised to all the CD patients.

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