Are Patients with Coeliac Disease Seeking Alternative Therapies to a Gluten-free Diet?

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Abstract

Background & Aims: The cornerstone of treatment for coeliac disease is a gluten-free diet (GFD). However, adherence to a GFD is variable. Recently investigators have been reporting their preliminary findings using novel therapies. In addition, there is a growing interest in the use of complementary or alternative medicine (CAM) in gastrointestinal illnesses. These observations suggest that patients with coeliac disease may be dissatisfied with a GFD and possibly are seeking/using alternative therapies for their disease. Our aim was to assess the satisfaction levels of adults with coeliac disease towards a GFD, their use of oral CAM and views regarding novel therapies. **Methods**: 310 patients with coeliac disease completed a questionnaire survey while attending their out-patient appointment. The control group comprised 477 individuals. **Results**: Over 40% of patients with coeliac disease were dissatisfied with a GFD. The frequency of CAM use in patients with coeliac disease was 21.6% (67/310) vs 27% in the control group (129/477), p=0.09. All patients expressed an interest in novel therapies, with a vaccine being the first choice in 42% of patients, 35% and 23% for anti- zonulin and peptidases, respectively. Universally, patients placed genetically modified wheat as the lowest preference. **Conclusions**: A large proportion of patients with coeliac disease are dissatisfied with a GFD. Coeliac patients are not taking CAM any more than controls, suggesting they do not view CAM as an alternative to a GFD. However, all the patients in this survey were keen to consider novel therapies, with a vaccine being the most preferred option.

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Key words

Complementary medicine – alternative medicine – coeliac disease – gluten free diet.

Introduction

Coeliac disease is defined as a state of heightened immunological responsiveness to ingested gluten (from wheat, barley, or rye) in genetically susceptible individuals [1]. Historically, it has been considered as an uncommon condition but recent studies have shown that coeliac disease affects around 1% of the general population [2-5].

The cornerstone of treatment for coeliac disease is lifelong adherence to a strict gluten-free diet (GFD). For the majority of patients, a GFD leads to clinical and histological remission, normalisation of standardised mortality rates [6, 7], a reduction in long term health complications (i.e. osteoporosis) [8-10] and in some studies, an improvement in psychological well-being and quality of life [11, 12].

Despite the high rate of adherence to treatment in chronic gastrointestinal illnesses (mean 80.4%) [13], adherence to a GFD has been shown to be variable, ranging from 36 to 96% [14-17]. In general, adherence to dietary advice is the lowest of all the treatment modalities [13]. Furthermore, studies have examined a range of additional factors that may influence adherence specifically to a GFD, including sociodemographic status, patient symptoms, treatment availability/palatability, psychosocial and cultural status. A large systematic review of these studies identified adherence to a GFD to be lowest amongst ethnic minorities and those diagnosed in childhood, and greatest amongst those with cognitive, emotional and sociocultural influences. Membership of an advocacy group and regular dietetic follow-up also had a positive effect on adherence rates [17].

With recent advances in our understanding of the molecular basis of coeliac disease, targeted non-dietary therapies have been devised [18-20], some of which are currently at the clinical trials stage in their development. These alternative treatment modalities focus on modification of dietary gluten, enzymatic degradation of gluten (i.e.

peptidases) [21], inhibition of intestinal permeability (i.e. anti-zonulin) [22] and modulation of the immune response (i.e. vaccine). The views of patients with coeliac disease towards novel therapies and their preferences have not previously been assessed.

In addition, over recent years there has been a growing interest in the use of complementary and alternative medicine (CAM) by the general public. Complementary and alternative medicine is defined as medical practices that are not currently considered to be a part of conventional medicine [23]. The use of CAM has increased in the western world, with the United Kingdom (UK) public spending more than £40m a year on herbal products [24]. Factors influencing the use of CAM include longer consultation times (with the CAM practitioner), the perception of fewer side effects, dissatisfaction with conventional medicine, chronic disease, and poorer health status (e.g. hospitalization) [25-30]. In gastroenterological practise, CAM usage has historically been described in patients with functional bowel disorders and inflammatory bowel disease [25, 29, 31, 32]. One small, uncontrolled historical study (n=145) assessed whether patients with coeliac disease had seen alternative practitioners (for example, osteopaths, reflexologists, or herbalists) [29]. However, this study did not comment on whether patients were purchasing oral CAM. To our knowledge, there has been no data assessing the use of oral CAM in patients with coeliac disease.

Based on poor adherence rates to a GFD, we hypothesised that patients with coeliac disease may be using oral CAM more frequently than the general public. We also sought to assess whether patients with adult coeliac disease were satisfied with their GFD and were willing to consider novel therapies.

Methods

Patients with coeliac disease were prospectively recruited whilst attending their specialist outpatient follow-up appointment at the Royal Hallamshire Hospital in Sheffield, UK, between 2008-2009. Ethical approval was obtained from the South Sheffield Research and Ethics Committee.

All patients were directly questioned using a short structured questionnaire comprising three sections. The first section of the questionnaire involved asking patients about their satisfaction with a GFD using a five-point Likert scale (Appendix, Table I).

The second section questioned patients on their use of oral CAM. The CAM listed in the questionnaire was based on those products commonly available in the UK shopping malls. To allow individuals to inform the investigator of any other CAM products they were taking, we also provided a free text section ("others", Appendix Table II). The control group were customers at four local supermarkets in the same geographical area as the hospital.

The final section of the questionnaire asked coeliac patients whether they would be interested in novel therapies and if so, the type of novel therapy they would prefer (Appendix, Table III). Patients were asked to arrange in order of preference 1 to 4 whether they would like a vaccine, genetically modified wheat, peptidases or anti-zonulin. We provided a basic written/verbal explanation as to what the novel therapies were. In addition, in our discussion with patients we explained that treatments differed in a number of significant ways. Treatments ranged from being hypothetical, to proof of concept or were at the clinical trial stage. For example, the vaccine therapy is still in preclinical development and no proof of concept had been presented whilst non-toxic genetically modified wheat is a hypothetical concept. For peptidase supplements and zonulin antagonists we explained that these would be supplements to a GFD and would not result in the healing of the small bowel mucosa but could be taken as an adjuvant, or for an occasional GFD 'holiday' when the patient could take a meal containing gluten. We also discussed the different ways in which these treatments were taken by the patient. We specified that peptidase supplements and zonulin antagonists are being developed as oral medications, while others such as the "vaccine" are being developed as an injection.

Patients with coeliac disease were divided into two sub-groups, "typical" or "atypical", according to their presenting symptoms. "Typical" patients presented with gastrointestinal symptoms, anaemia or a combination of both. "Atypical" patients had neither of these symptoms but may have presented with, for example, osteoporosis or a family history.

Statistical analyses of data were performed using SPSS. Differences between the groups were assessed using the Fisher's Exact Test.

Results

Three hundred and ten patients with coeliac disease completed the survey (83 male, age range 19-97, mean age 56). Patients were classified according to their presenting symptoms, with 258 having "typical" symptoms and 52 "atypical". The control group comprised 477 individuals (228 male, age range 17-88, mean age 45.9).

Using a Likert scale, 42% of patients with coeliac disease expressed dissatisfaction with a GFD (Fig. 1). Just over 20% reported a GFD as being a good or an excellent way of treating their disease.

The frequency of CAM usage (Table I) in patients with coeliac disease was 21.6 % (67/310) and in the control group the frequency was 27% (129/477). Comparisons between these two groups showed no statistically significant difference in CAM use ($p = 0.09$). There was a female preponderance amongst those taking oral CAM, similar in both the coeliac (51/67) and control group (86/129), $p = 0.19$. Multi-vitamins were highly popular in those taking oral CAM products – 46% (31/67) coeliac versus 52.7% (68/129) controls, $p = 0.45$. Furthermore, there was no statistically significant difference in CAM usage when comparing the two sub-groups of coeliac disease, with 21.3% (55/258) of patients with "typical" symptoms using CAM, compared to

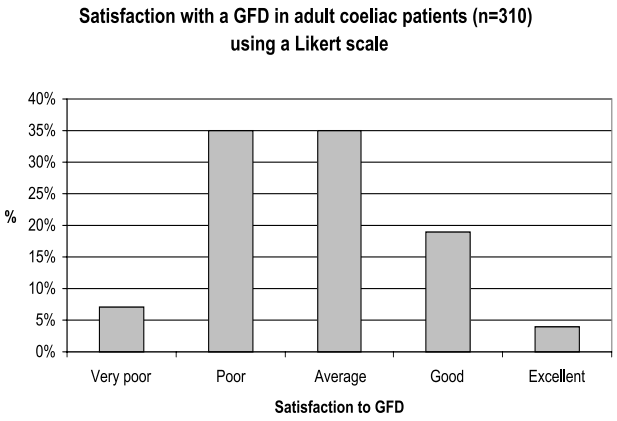

Fig 1. Satisfaction with a gluten-free diet (GFD) in adult coeliac patients using a Likert scale.

23.1% (12/52) of patients with "atypical" symptoms (p = 0.85). There were differences between the control group and coeliac patients for age and for sex (p<0.0001). The coeliac population were older and had a higher prevalence of women – which is reflective of this population of patients.

Table I. The use of oral Complementary or Alternative Medicine (CAM).

	Coeliac - all	Subgroup of coeliac patients		Control group
		Typical	Atypical	
No of pts (%)	310	258 (83.2%)	52 (16.8%)	477
CAM use (%)	67 (21.6%)	55 (21.3%)	12 (23.1%)	129 (27%)

All patients in this survey were keen to consider novel therapies. The first choice novel therapy was vaccine in 42% of patients, anti-zonulin in 35% and peptidases in 23%. Universally patients placed genetically modified wheat as the lowest preference.

Discussion

This is the first study to our knowledge that has assessed the use of oral CAM in patients with coeliac disease and made comparisons against a control group. In addition, we compared the use of CAM between different subgroups of coeliac patients, as well as demonstrating their views towards novel therapies.

The main limitation to our study is that the coeliac and control group were not age or sex matched (p <0.0001). With regards to age, the use of CAM has recently been shown to be similar between the ages 30-69 (CAM usage range 39.6-41%) [33]. In addition, there is also evidence of greater usage of CAM amongst women compared to men in the general population [33]. Given that there was a higher prevalence of women in the coeliac group, this would have affected our results by giving a higher prevalence of CAM usage in the coeliac group (positive ascertainment bias). Despite this, the overall CAM usage in coeliac patients was still less than that of controls. Thus the clinical message is that patients with coeliac disease do not view CAM as an alternative to their GFD.

Another possible weakness was that the control group were not questioned about any GI symptoms or diagnoses. We have previously shown that roughly 10% of a randomly selected population from Sheffield have GI symptoms [3]. In addition, this particular study also found the prevalence of coeliac disease amongst the general population to be 1% [3]. Therefore, it could be possible that amongst the control group there may have been individuals with GI symptoms, and even a possible gastrointestinal diagnosis such as coeliac disease, thus actually falling into the study group. However, these patients were not questioned about this issue for two reasons – firstly, the impracticalities of being able to validate their possible diagnosis without consent or access to their medical records. Secondly, using the blind approach provides a true reflection of CAM usage in the local population.

In **conclusion**, we found that more than 40% of patients with coeliac disease are dissatisfied with their GFD. However, these patients were not taking oral CAM any more than individuals without coeliac disease. This suggests that they do not view CAM as an alternative to a GFD. All the patients with coeliac disease were keen to consider novel therapies, with a vaccine being the most preferred option.

Disclosures / Conflicts of interest

DSS has acted as an advisory consultant to Oxford Outcomes and Shire. Both Oxford Outcomes and Shire have considered undertaking trials in the use of novel therapies in coeliac disease. Neither Oxford Outcomes nor Shire had any involvement in this study nor have they seen the data.

Contributors

VP helped recruit patients; collect, analyse and interpret data. IA helped design the study; collect, analyse and interpret data; and draft the article. KEE helped collect, analyse, interpret data; and review the final version of the manuscript. DSS conceived and designed the study; helped recruit patients; collect, analyse and interpret data; and review the final version of the manuscript. Guarantor of the article: Dr Imran Aziz.

Appendix

Table I: Satisfaction with a GFD

How satisfied are you with having to take a gluten-free diet to treat your coeliac disease?

(Please tick one box only)

Very poor	Poor	Average	Good	Excellent
				

Table II: Complementary or Alternative Medicine Survey
Are you currently taking any of these medications?

Multi-vitamins □	Multi-minerals □	Vitamin C □
Magnesium □	Zinc □	Iron □
Glutamine □	Creatine □	Glucosamine □
Fish/Cod liver Oil □	Selenium □	Vitamin E □
Vitamin B □	Co-enzyme Q10 □	Calcium □

Others: _____

Do you take:

St. John's Wort □	Kava □	Ginkgo Biloba □
Ginseng□	Evening Primrose Oil □	Milk Thistle □
Echinacea □	Aloe Vera □	Garlic □
Imedeen □	Cimicifuga Racemosa □	Isoflavones □
Homeopathy Medication □	Artichoke (Cynara Scolymus) □	Sea Kelp □

Others: _____

Table III: Novel therapies

Would you be interested in alternatives options (to a gluten free diet) to treat your coeliac disease

Yes No

If yes, please number the options below 1 to 4 for your preferred choices (1 = most preferable, 4 = least preferable)

Please ask staff members for further explanation if any queries

Vaccine (to develop an immune protection against gluten)	
Genetically modified wheat	
Peptidases (enzyme to break down gluten)	
Anti-zonulin (prevents absorption of gluten)	

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