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Coeliac disease, diet adherence and depressive symptoms

Nathalie J.M. van Hees [a,*], Willem Van der Does [a,b], Erik J. Giltay [b]

[a] Institute of Psychology, Leiden University, Leiden, The Netherlands
[b] Department of Psychiatry, Leiden University Medical Center, Leiden, The Netherlands

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ABSTRACT

Objectives: We aimed to investigate whether long-term adherence to a gluten-free diet is related to depressive symptoms in coeliac disease (CD) patients.
Methods: A cross-sectional survey was performed in 2265 adult CD patients recruited through the Dutch Coeliac Association. Self-reported diet adherence was compared among groups based on self-reported depressive symptoms (categorized into current [1-month], remitted, and never).
Results: The life-time prevalence rate of self-reported depressive symptoms was 39.0% (n = 883), of whom 270 (11.9%) suffered from current depressive symptoms. Adherence to gluten-free diet was strict in 50.2% of patients, sufficient in 46.3%, and insufficient in 3.6%. Insufficient adherence was not associated with current depressive symptoms (odds ratio [OR] 0.95; 95% confidence interval [CI]: 0.48–1.92). Keeping a gluten-free diet for longer than five years was associated with lower OR of current depressive symptoms compared to being on a diet for less than two years (OR 0.69; 95% CI: 0.50–0.95).
Conclusions: Lifetime depressive symptoms may be present in one third of the CD patients who adhere to gluten-free diet. Long-term adherence to the gluten-free diet may reduce the risk of current depressive symptoms.

Introduction

Coeliac disease (CD) is an immune-mediated intolerance for gluten in genetically predisposed individuals and is characterized by an inappropriate immune response of the T-lymphocytes of the small intestines to gluten peptides. This results in intestinal malabsorption, atrophy of the intestinal villi and chronic inflammation of the jejunal mucosa of the small intestine. The clinical presentation varies widely, as CD is now considered a multisystem disorder affecting multiple organs, such as the skin, thyroid, heart, nervous system, pancreas, spleen, liver [1], as well as the brain. CD has a prevalence rate in Europe and the USA of about 1:100 [2] and is associated with an increased prevalence of psychopathology [3,4]. The only available treatment is a strict gluten-free diet (GFD), which leads to restoration of the atrophied intestinal villi. It may, however, take years to achieve complete recovery of the intestinal villi [5], and the effects of the diet on mood and psychiatric symptoms are largely unknown.

Common psychiatric symptoms in untreated CD are depressive symptoms, apathy, anxiety, and irritability [6–9]. A cross-sectional, case–control study in 36 CD patients and 144 controls used the Composite International Diagnostic Interview (CIDI) to assess life-time psychopathology [7]. They found that the risks of major depression (MD; 41.7%), dysthymic disorder (8.3%), adjustment disorders (30.5%), and panic disorder (13.9%) were increased in CD. Increased rates of depressive and anxiety symptoms were also found in CD patients on a GFD [4,10,11]. The reported prevalence of depressive symptoms in CD patients varies widely across studies, ranging from 6 to 69% [8,12–17]. Differences in patient characteristics, cultural background, and study design may account for the large variability [3,18,19]. In a large longitudinal population-based cohort study, CD patients were at an 80% increased risk of depression compared to controls [19]. Only one case–control study found equal prevalence rates of depression (17.2% versus 16%) [20]. However, diagnoses for depression in this study were solely based on notes from primary care providers or gastroenterologists and reliability may be questioned.

The increased risk of depressive symptoms in CD patients could be explained by several mechanisms. Firstly, dietary non-compliance and sustained malabsorption may play a role [18], which could lead to sustained nutritional deficiencies (e.g. of vitamin B6, vitamin B12, and folic acid) which in turn may have increased the risk of depression [21]. Secondly, nutritional deficiencies may be a consequence of the strict restrictive GFD. Many of the gluten-free grains do not inherently contain thiamin, riboflavin, niacin, folate, and iron, nor are gluten-free food products in general required to be enriched with these micronutrients by food authorities [22–24]. Whether nutritional deficiencies caused by the daily diet in general contribute to the risk of depression is unknown at this time. There might also be reductions in brain monoamine availability and metabolism [27] and regional cerebral hypoperfusion [28] in patients with CD that may subsequently have induced depression. Thirdly, psychosocial

* Corresponding author at: Institute of Psychology, Leiden University, Wassenaarseweg 52, 2333 AK Leiden, The Netherlands. Tel.: +31 71 527 6751; fax: +31 71 527 3932.
E-mail address: heesnjmvan@fsw.leidenuniv.nl (N.J.M. van Hees).

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mechanisms may be involved. Due to the strict dietary regimen CD patients may avoid social situations which involve eating and also may experience more psychological distress due to daily hassles, negative responses to the diet by their social surroundings, and continued worrying about dietary mistakes and negative health outcomes [25–28]. Distress, social isolation and loneliness may subsequently lead to depression [29]. Fourthly, depression in CD may be secondary to an association between CD and other auto-immune diseases that carry a high risk of depression, such as thyroid disease and diabetes mellitus [7,20].

It is often assumed that dietary non-compliance increases the risk of depressive symptoms. It is common practice to refer CD patients to a dietician for a diet review. The literature on the relationship between adherence to gluten-free diet and depression however is inconclusive and long term dietary compliance in relation to depression has not been studied in depth. Two case series found that psychiatric disturbances and depressive symptoms improved rapidly after the introduction of a gluten-free diet [30,31], but several other studies found no improvement [7,25,32]. One study even reported more depressive symptoms for GFD-treated versus untreated CD patients [33]. In addition, one study found a small significant correlation between non-compliance and depressive symptoms [34], one study found diet adherence not to be a predictor of depressive symptoms [35], and one study found that strict diet adherence was related to an increase in depressive symptoms independent from duration of diet [12]. Most studies included recently diagnosed CD patients and did not study patients who were on a diet for more than one year, while the restoration of the absorption function may take two [36] to five years [5].

In the present study, we investigated the association of duration and stringency of the GFD with the prevalence of depressive symptoms. We performed a cross-sectional survey on a representative sample, comparing groups of adult CD patients who report never having had depressive symptoms, who are remitted from depressive symptoms or who currently experience depressive symptoms. We hypothesized that CD patients who adhere badly to the GFD have an increased risk of currently having depressive symptoms compared to CD patients who strictly adhere to the GFD. We also expected that increased length of the GFD is associated with a lower risk of depressive symptoms.

Methods

Patients

Participants were recruited from the 7119 adult members of the Dutch Coeliac Association (NCV). The NCV comprises CD patients with varying treatment history and severity of illness. According to self-report, 87% of this population had the diagnosis of coeliac disease confirmed by a biopsy of the intestinal lining. In 7% the diagnosis was made by other means and 5% was on GFD for other medical reasons [37].

Instruments

Adherence to gluten-free diet

Diet adherence of the GFD was assessed by one self-report reply to the question: “I keep my diet: very stringent/simply right/moderately well/not well”. Similar questions and methodology have been used in other studies [8,28,35,38–41].

Self-reported depressive symptoms

Self-reported current and past depressive symptoms were assessed with the Major Depression Questionnaire (MDQ) [42], an 18 item self-reported questionnaire which assesses the diagnostic criteria for MD according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV-TR) [43] criteria for MD. A previous validation study in a small sample ($n = 39$) showed excellent sensitivity (100%) and negative predictive value (100%), good positive predictive value (79%), specificity (75%) and overall kappa (0.75), compared with interview-based diagnoses [44]. The MDQ consists of a series of questions that cover all DSM-IV diagnostic criteria for current and past major depression [43], including impact on functioning and exclusion criteria (e.g., mourning). The scoring criteria and the cut-off for caseness versus noncaseness also follow DSM-IV, in other words no case of depression is assumed when both core symptoms of depression are absent or self-reported impact on functioning is low. This leads to self-reported depressive symptoms which can be categorized as MDQ cases and MDQ noncases. MDQ caseness can be further subdivided in never, remitted and current cases. The items that make up a positive caseness score in the MDQ include an item on changes in quality of sleep and an item on changes in body weight. As these symptoms may overlap with those of CD, we made an attempt to exclude the most profound physical consequences of CD through additional instructions and item-wording. Although participants were instructed to disregard the cause of physical symptoms and just report whether the symptom was present or not, they were asked to only report weight change achieved without intent and caused by increased or decreased appetite and only to report sleep disturbance leading to at least a 2 hour change from usual for most of the time during a 2 week period.

Symptoms of anxiety and depression

The Hospital Anxiety and Depression Scale (HADS) [45] is a 14 item self-reported questionnaire for the assessment of symptoms of anxiety and depression with good case-finding ability. Cronbach's alpha is .83 for the HADS anxiety scale (HADS-A) and .82 for the HADS depression scale (HADS-D). The optimal cut-off score is 8 and the concurrent validity of the HADS was found to be good to very high [46]. The Dutch version has good internal consistency in medical outpatients (HADS total score, $\alpha = .90$). The sensitivity and specificity to detect MD with a cut-off point of 8 on the depression subscale are 56% and 82%, respectively [47]. The HADS is designed to screen non-psychiatric hospital outpatients for possible anxiety or depressive disorder and items referring to eating and sleep disturbances are not included in the scale making it a fitting tool for populations with somatic illness such as CD. It has been suggested in a recent review that the results of the HADS should be interpreted as a unidimensional measure of “emotional distress” [48] and therefore we reported both the HADS subscale scores as well as total scores.

Vulnerability to depression

Cognitive vulnerability to depression was measured with the short (6-item) version of the self-report Leiden Index of Depression Sensitivity (Leids-R-SF), derived from the 34 item Leids-R [49]. The Leids-R consists of questions like “When I am feeling down, I more often think about how I am unable to make anyone happy” and “I can only think positive when I feel well” followed by a five point Likert scale. The Leids-R-SF in our sample had good internal consistency ($\alpha = 0.87$).

Procedure

The questionnaires were bundled in a questionnaire-booklet, which was sent out as unsolicited mail accompanying a 2007 issue of the NCV quarterly magazine. The questionnaires were also handed out during five NCV events, were made available online, and were announced on various Dutch CD websites, forums and mailing lists. Articles about the questionnaire and the study were published in four issues of the quarterly magazine and these articles were also made available through the online questionnaire website. This study was approved by the ethics committee of the institute of psychology of