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ORIGINAL ARTICLE

The utility of food antigen test in the diagnosis of Crohn's disease and remission maintenance after exclusive enteral nutrition

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KEYWORDS
Crohn disease;
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Summary
Background: Crohn's disease (CD) involves intensive immunologic responses to food antigens. Exclusive enteral nutrition (EEN) showed efficacy in inducing disease remission. However, relapse commonly occurred when normal diet was reintroduced. We aimed to investigate the food-specific IgG antibodies of CD, and clarify the effects of exclusion diet guided by food-specific antibodies on remission maintenance after EEN.
Methods: All available data of food-specific antibodies were retrieved from the database and analyzed for the diagnostic value. Thereafter, we retrospectively recruited qualified patients who reintroduced their diet excluding the moderately and strongly immunoreactive foods with prospective follow-up data. Matched patients without diet intervention after EEN served as control. CD activity index (CDAI), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and endoscopic score were compared.
Results: A significantly enhanced immune response to rice, tomato, egg white/egg yolk and maize was observed in CD patients. The number of IgG-positive items had the greatest power to discriminate CD from ulcerative colitis and the control group with area under the curve of 0.819 and 0.828. Each diet group included 32 patients, and disease relapsed in 12.5% of the exclusion group compared with 25% of the control. The increase of CDAI and ESR was more remarkable in the control group than in the exclusion diet group ($P < 0.05$).

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Conclusions: CD patients presented intensive immune responses to food antigens. The number of IgG-positive food items had potential to be a diagnostic marker of CD. Diet guided by food antibody test might help maintain disease remission.

Introduction

Crohn's disease (CD) is one of two major forms of inflammatory bowel diseases (IBD) with chronic relapsing-remitting characteristics involving the whole digestive tract, whose etiology remains unclear. Copious amounts of epidemiological studies suggested that diet might affect both the initiation and progression of CD [1,2], and contributed to the increasing incidence of CD in the developing countries [3,4], supporting the notion that dietary adjustment might help control disease activity.

The most effective and restrictive dietary intervention for CD patients is exclusive enteral nutrition (EEN), which critically forbids the intake of normal food. A growing body of evidence demonstrated the favorable effects of EEN in the adult patients in terms of disease activity and quality of life [5], inflammatory bowel stricture [6], and postoperative outcomes [7]. Thus far the exact mechanism underlying the benefits of enteral nutrition remains unclear, likely involving anti-inflammatory effects, inducing mucosal healing, modifying intestinal microbiota and helping bowel rest [8]. Though EEN offers a promising alternative in the management of CD that not only induces disease remission but also has nourishing effects on the malnourished patients, a large proportion of patients in remission suffered relapse when normal foods were reintroduced after EEN [9—11]. Therefore it poses a challenge to the clinicians how to manage the patients after they achieve remission on elemental diet.

Dietary reintroduction that excluded the foods provoking symptoms such as diarrhea and pain was shown to help maintain remission after element diet was withdrawn [12]. In consideration of the delay onset of symptoms, the possibility of asymptomatic enteritis and the differences of subjective tolerance among patients, an objective serological indicator might therefore be valuable. Immunologic responses to foreign intestinal antigens such as food antigens have been considered to be implicated in the etiology of CD, and the abnormal elevation of food-specific serum antibodies has long been observed [13]. Dietary interventions based on plasma antibodies against food antigens proved to be effective to improve the symptoms [14,15].

Given IgG food antibodies might differ due to specific diet habits in China, we first investigated the IgG antibodies towards common foods in patients with CD, ulcerative colitis (UC) and the controls without intestinal disorders and food intolerance, and evaluated the value of serum IgG profiles in differentiating CD from UC and the controls. Next, we assessed the efficacy of the diet that excluded the moderately and strongly immunoreactive foods in maintaining disease remission after EEN.

Methods

Part I food-specific antibody profiles

To assess the antibody profiles against food items in patients with IBD, the database of clinical laboratory in Jinling hospital was used. Serum antibodies toward 14 common foodstuffs have been tested in our hospital since January 2013, hence all available data regarding the results of food-specific antibody tests from January 2013 to June 2015 was retrieved. To evaluate the overall diagnostic value of food antibodies, IBD patients with different disease status were unselectively included, encompassing 182 CD patients and 103 UC patients. For comparison, the control group was set consisting of those undergoing health examination or admitted without digestive and allergic symptoms. Seventy-eight controls that underwent food antibody tests were therefore included as well.

Part II diet intervention in remission

In our center, EEN was used for 1 to 3 months to induce remission among active adult patients and to prevent disease relapse after definitive bowel resections. EEN administered in this study was a product of Nutricia Company called Peptison Liquid and was given through nasogastric tubes routinely. After EEN, patients who were in remission (defined as a Crohn's disease activity index [CDAI] score less than 150) and had no existing surgical complications would resume oral diet and were commonly maintained with oral mesalazine. To clarify the effect of the exclusion diet guided by serum food antibodies, we retrospectively recruited qualified patients with prospective follow-up data. As illustrated in Fig. 1, 32 outpatients who tested the food antibodies and excluded the moderately and strongly immunoreactive foods when reintroducing diet were retrospectively enrolled (exclusion diet group). The patients in the exclusion group were asked to record the dishes that contained the moderately and strongly immunoreactive foods and to exclude them in the diet. Another 32 outpatients who resumed normal diet after EEN were matched with the ratio of 1:1 (normal diet group). Data used for analysis including CDAI, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were extracted from our maintained CD database. Seventeen patients in the exclusion diet group and 21 patients in the normal diet group underwent endoscopy examination before and after the diet, hence the Simple Endoscopic Score for Crohn's Disease (SES-CD) [16] was also compared. The follow-up period was 3 months. Disease relapse was defined as a CDAI > 150. The present study was approved by the Ethics Committee of Jinling hospital, and was done in

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