

Differences in dietary habits between patients with inflammatory bowel disease in clinical remission and a healthy population

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Abstract

Background Although patients with active inflammatory bowel disease (IBD) change their dietary habits according to suggestions from their healthcare team, no restriction is required in the remission phase. Accordingly, we compared eating patterns in IBD patients with drug-induced clinical remission with those in healthy subjects.

Methods A total of 150 IBD patients, 84 with Crohn's disease (CD) and 66 with ulcerative colitis (UC), in clinical remission, receiving immunomodulator/biologic therapy, and 100 healthy volunteers (controls) were enrolled. The IBD diagnosis had previously been established by a combined assessment of symptoms, endoscopy, histology and abdominal imaging. Clinical remission was defined as a Harvey Bradshaw index <5 for CD and a partial Mayo score <2 for UC. An experienced nutritionist guided the compilation of a food diary for 7 days according to current guidelines. Macronutrient and fiber intake was evaluated using dedicated software. Comparison between continuous variables was performed using Student's *t*-test or analysis of variance plus Bonferroni *post-hoc* analysis. Categorical variables were tested with the χ^2 test.

Results No difference in protein and carbohydrate intake was observed. IBD patients ate more calories (1970.7 ± 348.4 vs. 1882.1 ± 280.2 kcal/day, $P=0.03$), more lipids (68.9 ± 15.2 vs. 59.4 ± 19.0 g/day, $P<0.001$) and less fibers (11.9 ± 4.7 vs. 15.5 ± 8.3 g/day, $P<0.001$) than controls. No significant difference in total calories, proteins, lipids, carbohydrates or fibers was seen between CD and UC patients.

Conclusion IBD patients have a different macronutrient and fiber intake compared to healthy subjects, even when clinical remission and no symptoms do not dictate dietary restrictions. Therefore, psychological issues may be involved.

Keywords Inflammatory bowel disease, carbohydrates, fibers, lipids, nutrition, disease activity

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Introduction

Inflammatory bowel disease (IBD) comprises a distinct group of chronic inflammatory disorders of the alimentary tract with a remitting clinical behavior. Ulcerative colitis (UC) and Crohn's disease (CD) are the most common conditions in this spectrum [1]. The IBD pathogenesis and activity include

multiple interactions among predisposing factors, such as genetics, infections, composition of the intestinal microbiota, and diet [2]. The dietary pattern has been mentioned as a possible environmental trigger for IBD. A Japanese study has demonstrated that the incidence of IBD paralleled the socio-cultural dietetic transition from the traditional to a Western diet [3]. In fact, a high-calorie, high-fat, and high-sugar diet could be a risk factor for IBD development [4]. Moreover, an unhealthy diet could alter the composition of the human microbiome. Indeed, a diet rich in milk fats may promote the growth of *Bifidobacterium wadsworthia*, a sulfite-reducing organism reported to induce an enhanced inflammatory immune response of the colon in a murine model, resulting in increased levels of interleukin-10 and other proinflammatory cytokines [5,6].

On the other hand, IBD activity may affect dietary restrictions in patients with severe disease. Indeed, it has been shown that these subjects are likely to avoid consuming processed meats, alcohol and salad [7]. In a previous evaluation of UC patients in both the mild and the severe

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Conflict of Interest: None

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activity phase, Walton *et al* [8] found that these subjects had a reduced intake of fibers and an increased intake of lipids. Moreover, an appropriate diet is recommended in patients with active IBD, since it could be an adjunctive strategy in disease management. For instance, a diet poor in red meat and polyunsaturated fatty acids was associated with a high rate of maintenance of remission, according to Chiba *et al* [9]. Likewise, a specific carbohydrate diet, i.e., the restriction of grains and refined sugars, may improve clinical and laboratory parameters [10].

Dietary changes in IBD patients are usually suggested by the healthcare team, though self-limitations based on personal experiences and/or information drawn from the media are frequently observed. Taking into account that dietary habits and intake in patients with IBD may often be the result of a combination of information drawn from different sources, we believed that in the present study it could be of interest to investigate a singular aspect, i.e. the dietary habits of asymptomatic IBD patients in pharmacologically-induced clinical remission. These subjects do not require any dietary restriction and should eat like the healthy population.

Patients and methods

Patients and controls

We designed the present study as a cohort study according to the STROBE statement (Supplementary Table 1) [11], enrolling asymptomatic outpatients with IBD in clinical remission referred to our Unit and healthy volunteers as a control group. The study was reviewed and approved after a meeting of all authors in the Gastroenterology Unit of Bari University Hospital Policlinico (Italy). It included only routine checks in subjects seen regularly in the IBD outpatients service of our Unit. As required by Italian law, each patient gave written informed consent for each investigation performed. The control group consisted of 100 healthy volunteers, shown to be healthy on the basis of medical screening, clinical history, physical examination, routine laboratory testing and 12-lead electrocardiogram, and were taking no drugs or observing any self-prescribed dietary restrictions, selected from among the population referred to the gastroenterology general outpatients service. Written informed consent was obtained from each subject.

One hundred fifty IBD patients (84 CD and 66 UC) were enrolled. The IBD diagnosis had been established by a combined assessment of symptoms, endoscopy, histology, and abdominal imaging. Additionally, for each patient we collected data about age, sex, disease clinical activity—partial Mayo and Harvey Bradshaw index (HBI) scores for UC and CD, respectively—current medications and smoking habit. Clinical remission was defined as HBI <5 for CD and partial Mayo score <2 for UC. The exclusion criteria were pregnancy or lactation, a history of alcohol or drug abuse and previous bowel surgery. A further inclusion criterion for both IBD patients and controls was a body mass index between 18 and 30 kg/m².

Dietary survey

An experienced nutritionist guided the compilation of a food diary for 7 days according to current guidelines [12]. The dietary analysis was carried out using Winfood™ software (Medimatica Srl Unipersonale, C.da S. Giovanni, 75 - 64010 Colonnella (TE), Italy), as described elsewhere [13]. According to Italian law, “within the 4-5 years of their training, nutritionists acquire highly qualified knowledge and skills in the field of basic sciences, prevention and nutrition in general, with different competences for doctors and non-physicians”, as defined by the legislator in 2005 [14].

Statistical analysis

Comparison between continuous variables was performed using Student's *t*-test or analysis of variance plus Bonferroni *post-hoc* analysis for multiple comparisons. Categorical variables (proportions) were tested using the χ^2 test. The statistical analysis was performed using statistical software SPSS version 21 for Windows (IBM Corp., Armonk, NY).

Results

All 150 IBD patients were in clinical remission; the mean Partial Mayo score was 1.1±0.6 (median 1, range 0-2) and mean HBI was 2.5±1.0 (median 2, range 0-4). Fifty patients were receiving immunomodulator drugs (thiopurines), while the remaining 100 subjects were given biologic treatment (50 infliximab and 50 adalimumab). All IBD patients were taking mesalazine.

In Table 1 we summarize the main demographic and clinical features of the enrolled patients and controls. The mean age of the 100 age- and sex-matched controls was 43.5±15.8 years, comparable to that of the IBD patients (42.8±12.9, *P*=0.71). The male/female ratio was 1:1.08 in the control group and 1:1.11 in the IBD group (*P*=0.97), and 7% of controls were smokers, similar to the percentage in the study group (7.3%, *P*=0.92).

As reported in Table 2, IBD patients showed a higher daily caloric intake than controls and they ate more total lipids and less fibers. The subanalysis according to the type of immunomodulator therapy demonstrated that the intake of macronutrients and fibers was comparable in the two groups (Table 3). In the comparison CD vs. UC, no statistically significant difference was recorded in total calories, proteins, lipids, carbohydrates or fibers (Table 4). IBD patients who were smokers consumed less fibers (9.1±4.0 vs. 12.0±4.6 g/day, *P*=0.046).

Discussion

The role of diet in both the pathogenesis and the clinical course of IBD has been amply discussed [4]. A western diet, characterized by a very high intake of fats and calories,

Table 1 Main demographic characteristics of the control group vs. the inflammatory bowel disease (IBD) group

Variable	IBD (n=150)	Controls (n=100)	P
Age (years)	42.8±12.9	43.5±15.8	0.71
Smoking habits	11 (7.3%)	7 (7%)	0.92
Male sex	72 (48%)	47 (47%)	0.97
Low education level*	39 (26%)	28 (28%)	0.77
Body mass index (kg/m ²)	26.2±3.6	25.6±3.8	0.21

*Low education level was defined as less than 8 years of school attendance

Table 2 Comparison of dietary intake between the controls and the inflammatory bowel disease (IBD) group, using Student's *t*-test. Calories are expressed as kcal/day, macronutrients and fibers as g/day

Dietary intake	Controls (n=100)	IBD (n=150)	P
Total calories	1882.1±280.2	1970.7±348.4	0.03
Proteins	86.9±25.2	87.6±21.4	0.8
Carbohydrates	257.3±53.6	253.4±67.9	0.62
Lipids	59.4±19.0	68.9±15.2	<0.001
Fibers	15.5±8.3	11.9±4.7	<0.001

Table 3 Comparison of dietary intake and body mass index (BMI) between patients with inflammatory bowel disease receiving thiopurines or biologics, using Student's *t*-test. Calories are expressed as kcal/day, macronutrients and fibers as g/day

Dietary intake and BMI	Thiopurine (n=50)	Biologics (n=100)	P
Total calories	1970.2±333.1	1970.4±357.3	0.97
Proteins	83.5±16.5	89.7±23.3	0.09
Carbohydrates	255.6±70.1	252.3±67.1	0.77
Lipids	69.7±11.6	68.6±16.8	0.69
Fibers	10.8±4.7	12.4±4.7	0.06
BMI	26.7±3.9	25.9±4.1	0.25

Table 4 Analysis of dietary intake according to inflammatory bowel disease subtype—ulcerative colitis (UC) vs. Crohn's disease (CD)—and body mass index (BMI), using Student's *t*-test. Calories are expressed as kcal/day, macronutrients and fibers as g/day

Dietary intake and BMI	CD (n=84)	UC (n=66)	P value
Total calories	1957.0±378.4	1985.4±306.3	0.62
Proteins	86.2±20.9	89.4±22.1	0.38
Carbohydrates	253±72	252±21	0.48
Lipids	68.2±14.3	69.9±16.4	0.53
Fibers	11.9±4.7	11.6±4.6	0.65
BMI	25.4±4.5	26.7±3.8	0.06

has been implicated as an environmental factor triggering IBD [15], as demonstrated in second-generation immigrants in Sweden, who developed a comparable IBD incidence to that of the native Swedish population, possibly as a result of dietary changes [15]. In this regard, it has been proposed that a high dietary intake of omega-6 and polyunsaturated fatty acids may increase susceptibility to IBD [16]. The potentially dangerous effect of a high-calorie, fatty diet has been reported even in mouse models [17]. Moreover, an increased lipid intake may represent not only a potential risk factor for intestinal inflammation, but also an atherogenic factor in a condition featuring a well-known increased risk of cardiovascular and endothelial dysfunction [18,19]. Despite such evidence, in the present study we found a high lipid and total calorie intake in the IBD population even if the patients were asymptomatic and in clinical remission. A similar dietary pattern was observed by Walton *et al* [8] in the active disease phase. Finally, we could not assess the possible consequences of the different macronutrient and fiber intake in IBD patients compared to healthy subjects [20], since we selected only subjects with a satisfactory nutritional condition, and body composition was not considered helpful for our purpose. Two further limitations of the present study should be mentioned. We did not have any data about the dietary pattern before the diagnosis of IBD, since this was a prospective study, therefore we could not ascertain whether the disease onset could have induced a change in dietary habits and macronutrient intake. Additionally, the interview was aimed to estimate macronutrient intake in IBD patients and we did not ask why most patients were observing self-prescribed dietary restrictions. An excess of carbohydrates in the diet has been observed in IBD patients [21]; thus, some authors have hypothesized a possible direct correlation with the onset and activity of the disease [22]. More specifically, refined sugars have been proven to upregulate oxidative stress in mice [23]. Additionally, diets that specify a low content of industrial sugars may improve the IBD course [24]. However, large epidemiologic studies failed to confirm a conceivable link between carbohydrate intake and the risk of IBD onset [25]. In our study, we did not find any difference in carbohydrate consumption between IBD patients and controls. However, an important point for future investigations should be the analysis of carbohydrate subtypes, since short-chain types have been proven to worsen the clinical picture of IBD in several trials [26], while others, such as starch, may have a beneficial effect on mucosal inflammation [27].

A final remark about fiber assumption in IBD is justified. We observed that even IBD patients without clinical manifestations ate less fibers than controls. This finding is in complete agreement with several reports indicating that such patients are likely to avoid fibers, presumably because of worries about a disease complication, despite the fact that these dietary elements have been shown to have a beneficial effect in maintaining the remission [28-30].

In conclusion, the design of our study allows us to depict an interesting scenario of macronutrient and fiber intake in subjects with IBD, even when clinical symptoms are absent and no dietary restrictions are imposed. The most likely explanation

for our findings is that their knowledge of the disease induces IBD patients to modify their dietary habits, reducing the intake of fibers and increasing lipids and overall calories. Therefore, the achievement of clinical remission did not parallel a modification of dietary habits; psychological issues [31], such as the fear of sub-occlusive complications or diarrhea, may be involved [32]. Consequently, our results suggest that a dietary imbalance should be taken into account by the healthcare team and adequately corrected, even in IBD subjects who are well. Therefore, we recommend nutritional counseling for IBD patients, aimed at correcting inappropriate dietary patterns and endorsing the importance of fibers (if not contraindicated), since this aspect has not yet been adequately highlighted and could be an interesting topic to explore in the near future.

Acknowledgment

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Summary Box

What is already known:

- Dietary changes in inflammatory bowel disease (IBD) patients are suggested by the healthcare team, unless the patient is in the remission phase
- Self-limitations based on personal experience and/or information drawn from the media are frequently observed

What the new findings are:

- IBD patients have a different macronutrient and fiber intake from healthy subjects, despite being in clinical remission with no symptoms
- Unnecessary dietetic restrictions are observed; therefore, psychological issues and nutritional counseling are advisable in IBD subjects

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Supplementary Table 1 STROBE Statement—Checklist of items that should be included in reports of cohort studies

Checklist of items	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract – page 2 (b) Provide in the abstract an informative and balanced summary of what was done and what was found – page 2
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported – page 3
Objectives	3	State specific objectives, including any pre-specified hypotheses – page 3
Methods		
Study design	4	Present key elements of study design early in the paper – page 4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow up, and data collection – pages 4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow up – pages 4 (b) For matched studies, give matching criteria and number of exposed and unexposed – pages 4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable – pages 4
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group – pages 4
Bias	9	Describe any efforts to address potential sources of bias – page 4
Study size	10	Explain how the study size was arrived at – page 4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why – pages 4
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding page 4 (b) Describe any methods used to examine subgroups and interactions - pages 4 (c) Explain how missing data were addressed - pages 4 (d) If applicable, explain how loss to follow up was addressed – not applicable (e) Describe any sensitivity analyses – not applicable

(Contd...)

Supplementary Table 1 (*continued*)

Checklist of items	Item No	Recommendation
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow up, and analyzed – page 5 (b) Give reasons for non-participation at each stage– page 5
Descriptive data	14*	(a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders – page 5 (b) Indicate number of participants with missing data for each variable of interest -- not applicable (c) Summarize follow-up time (e.g., average and total amount) – not applicable
Outcome data	15*	Report numbers of outcome events or summary measures over time – 5
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included – not performed (b) Report category boundaries when continuous variables were categorized – not applicable (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period – not performed
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses – not applicable
Discussion		
Key results	18	Summarize key results with reference to study objectives – page 6,7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias – page 6,7
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence –pages 6, 7
Generalizability	21	Discuss the generalizability (external validity) of the study results – page 7
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based – page 7

*Give information separately for exposed and unexposed groups.

An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>