Dietary calcium intake in patients with inflammatory bowel disease

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Abstract

Background & aims: Osteopenia and increased risk for fractures in IBD result from several factors.
Aim of the study: To investigate the dietary intake of calcium in IBD patients.
Methods: A 22-item quantitative validated frequency food questionnaire was used for quantifying dietary calcium in relation to gender and age, in 187 IBD patients, 420 normal- and 276 diseased controls.
Statistical analysis: Mann–Whitney, chi-square- and T-tests.

Results: The mean calcium intake was 991.0 ± 536.0 (105.8% Recommended Daily Allowances) and 867.6 ± 562.7 SD mg/day (93.8% RDA) in healthy and diseased controls, and 837.8 ± 482.0 SD mg/day (92.7% RDA) in IBD, P < 0.001. Calcium intake was high in celiac disease (1165.7 ± 798.8 SD mg/day, 120% RDA), and non-significantly lower in ulcerative colitis than in Crohn's disease (798.7 ± 544.1 SD mg/day vs 881.9 ± 433.0). CD and UC females, but not males, had a mean calcium intake well under RDA. In all study groups the intake was lower in patients believing that consumption of lactose-containing food induced symptoms, versus those who did not (105.8% vs 114.3% RDA in normal controls; 100.4% vs 87.6% RDA in IBD).

Conclusions: Diet in IBD patients contained significantly less calcium than in healthy controls. Gender and age, more than diagnosis, are central in determining inadequate calcium intake, more so in IBD. Self-reported lactose intolerance, leading to dietary restrictions, is the single major determinant of low calcium intake. Inadequate calcium intake is present in one third of IBD patients and represents a reversible risk factor for osteoporosis, suggesting the need for tailored nutritional advice in IBD.

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KEYWORDS
IBD;
Osteoporosis;
Dietary calcium;
Lactose intolerance;
Ulcerative colitis;
Crohn's disease

Abbreviations: BMD, bone mass density; Ca, calcium; CD, Crohn's disease; FFQ, food frequency questionnaire; IBD, inflammatory bowel diseases; RANKL–OPG, receptor activator of nuclear factor kappa-B ligand–osteoprotegerin; RDA, recommended dietary allowance; UC, ulcerative colitis.

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1. Introduction

Inflammatory bowel diseases (IBD) are associated with increased incidence of osteopenia and osteoporosis, with reported frequencies 28–77% and 18–42%, respectively.1–6 The risk of low-trauma fractures in patients with Crohn’s disease (CD) is correspondingly increased by 30%, and 20% in ulcerative colitis (UC), compared to normal controls.7,8

The pathogenesis of IBD associated bone loss is not fully understood, but several factors are involved in the process, mainly through their effect on the RANKL–OPG system.9 Pro-inflammatory cytokines, malnutrition associated with low body mass index and prolonged/high-dose administration of corticosteroids are considered to be of prime importance. The inflammatory component is relevant in both diseases, while malnutrition/absorption is more important in CD and corticosteroid treatment in UC.10–15 Although glucocorticoid use, beside age, is the most well-recognized risk factor for osteoporosis in IBD, reduced bone mineral density (BMD) is also observed in the absence of steroid use.16 Vitamin D deficiency is common in adults and children with IBD, especially CD,17–20 and a graded relative risk in CD, but not in UC, has been reported to correlate with areas of low sunlight exposure.21

Irrespective of other factors influencing bone metabolism, the minimum daily calcium dose necessary to prevent a negative balance is 1000 mg of elemental calcium for men and premenopausal women, and 1200–1500 mg for postmenopausal women and men older than 60 years.22 IBD patient diet has been reported to contain less than the recommended daily intake of calcium and vitamin D,23 but this issue has been less frequently addressed at than other possible mechanisms of osteoporosis and osteopenia. Aim of the present study has been that of investigating the dietary intake of calcium in a large series of patients regularly followed in our tertiary referral Center for IBD.

2. Materials and methods

Our study included 187 IBD outpatients, 95 female and 92 male, mean age 47.1 ± 16.3 SD (96 UC and 91 CD) in our Institution, who accepted to take part in the survey. Diagnosis of UC and CD was based on the usual clinical, endoscopical, histological and imaging criteria. Type and activity of the diseases and site/extent of lesion were classified according the Montreal classification.24

Information on the diet during the week prior to observation was acquired using a 22-item quantitative validated FFQ, administered by a dietician.25 The questionnaire provides detailed information on all the high calcium containing aliments most frequently used in the Italian diet (milk and milk derivatives, pasta and rice, meat and fish, eggs, legumes, fruit, vegetables, ice cream/chocolate, mineral and tap water). The frequency of consumption for each food item in the previous week was assessed and the “usual” serving size was evaluated for each patient using a photographic atlas of food portions.26 To estimate daily calcium intake from diet, frequency and serving size for each food consumed were multiplied by the nutrient content of that food.27 The participants were also asked about dietary supplements of calcium, allowing quantification of the total intake of the nutrient. Data were compared to the Recommended Daily Allowances (RDA) calculated for the Italian population28 in relation to age and gender, and expressed as percent of RDA. These values are in the same order as those indicated in the American RDA.29 The only major difference is an increased need for higher calcium intake versus younger age groups suggested for males >60 and females >50 years, in the Italian RDA.

The same FFQ was administered to 695 controls, subdivided into 2 groups: 420 normal controls, 270 female and 150 male, mean age 39.7 ± 16.1 SD (medical staff, family members of patients visited for non-gastroenterological problems) and 276 patients with differing diseases, 219 female and 57 male, mean age 43.6 ± 15.8 SD. This group was further classified as follows: 147 outpatients with non-gastroenterological diseases (105 female, 42 male), 36 patients with celiac disease (29 female and 7 male), 93 patients with lactose malabsorption/intolerance (82 female, 11 male). Celiac disease was diagnosed on the base of serology (anti-transglutaminase antibodies) and histological findings in duodenal biopsies. Lactose malabsorption/intolerance was diagnosed on the basis of a positive hydrogen breath test after an oral load of 25 g lactose, in the presence or absence of clinical symptoms during or in the 6 h following the test.30

The prevalence of lactose malabsorption in the background Italian population is high, ranging from 45 to 71%.31,32 Thus, all IBD patients and controls were specifically requested to state whether they had abdominal symptoms following the intake of milk and lactose-containing milk derivatives and, if so, whether this had implications on their usual diet.

Statistical analysis was performed using the 2010 SPSS statistical package (SPSS Inc. Chicago, IL, USA). Data were compared using the T-Test for normally distributed parameters, the Mann–Whitney Test for skewed data and the chi-square test for proportional data.

3. Results

3.1. Demographics

The group of 420 healthy controls was composed as follows: 270 female and 150 male, mean age 39.7 ± 16.1 SD years, mean weight 65.8 ± 12.8 SD kg and mean height 166.8 ± 14.6 SD cm. The diseased control group was composed by 276 patients, 219 female 57 male, mean age 43.6 ± 15.8 SD years, mean weight 62.6 ± 11.8 SD kg and mean height 163.5 ± 12.9 SD cm. Demographics and physical characteristics of the 187 IBD patients (95 female and 92 male, mean age 47.13 ± 16.3 SD years, mean body weight 68.7 ± 13.8 SD kg, mean height 167.9 ± 9.5 SD cm) are similar, and non-significantly different, from those of control patients, with the exception of gender. The proportion of females was significantly higher in both control groups (P < 0.001) versus IBD patients.

3.2. Calcium intake in inflammatory bowel disease and controls

The mean calcium intake in inflammatory bowel disease was 837.8 ± 482.0 SD mg/day corresponding to 92.7% of RDA. In healthy controls mean calcium intake was 991.0 ± 536.0 SD mg/day corresponding to 105.8% of RDA. Considering together all diseased controls, the mean calcium intake

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was 867.6 ± 562.7 SD mg/day corresponding to 93.8% of RDA. The difference between healthy controls and IBD patients was statistically significant (P < 0.001). The same proved true between healthy and diseased controls (P < 0.001). No difference was found between IBD patients and diseased controls.

Subdividing IBD patients in UC and CD it appeared that total daily calcium intake was non-significantly lower in UC (798.7 ± 544.1 SD mg/day, 88.1% RDA) than in CD (881.9 ± 433.0 SD mg/day, 96.8% RDA). The difference versus healthy controls was significant both for CD (P < 0.01) and UC (P < 0.001). The difference versus diseased controls was non-significant both for CD and UC.

### 3.3. Calcium intake in relation to gender

The mean daily calcium intake in IBD patients and controls is reported in Table 1. The present data also indicate that male IBD patients had a mean daily calcium intake within the range of RDA, and the difference versus healthy and diseased controls was minimal and non-significant. Female had a calcium intake identical to RDA in healthy controls and slightly reduced in diseased controls (90.8% RDA). Both CD and UC female patients had a mean daily calcium intake well under RDA, 82.8% and 79.0%, respectively (P < 0.05). Data from diseased controls, subdivided according to diagnosis are reported in Table 2. It clearly appears that patients with celiac disease had a mean calcium intake well above RDA both for male and female. Patients with lactose malabsorption/intolerance were markedly different according to gender, females having a very low daily calcium intake, as compared to RDA (71.3%). The difference was highly significant (P < 0.001) versus all other groups and versus normal controls. Patients with no gastrointestinal pathologies showed a mean daily calcium intake which was non-significantly lower than RDA, in both genders. These values did not significantly differ from healthy controls.

### 3.4. Calcium intake in different age groups

The mean calcium intake in IBD patients and controls subdivided according to age is reported in Table 3. The group 9–17 years was represented only by a small number of subjects in all study groups and data do not necessarily reflect those of the general population. Thus, they are not reported in detail. The observed daily calcium intake, however was lower than recommended (between 68 and 86% RDA).

Considering older subjects, it should be noted that the age groups were differently divided in relation to gender. As previously stated, RDA values are higher in males over 60 years and in females over 50 years, versus those of younger subjects. Only in IBD females between 30 and 49 years and in females over 50 years the difference was significant (P < 0.01) versus healthy- but not versus diseased controls. Significantly lower calcium intake was also observed between healthy females over 50 years and the corresponding group of diseased controls (P < 0.01). A slight but not significant trend toward lower calcium intake was observed in IBD and diseased controls versus healthy controls, in most age groups with the exception of males in the 30–59 year group.

### 3.5. Calcium intake and self-reported milk intolerance

The daily calcium intake was analyzed in all study groups according to the patients' belief that milk and dairy products induced/exacerbated abdominal symptoms (Table 4). As expected, in all study groups the daily calcium intake was lower in those that held the belief that consumption of lactose-containing food was related to abdominal symptoms, but the significance level was not attained.

### 4. Discussion

IBD patients often present with low bone mineral density, due to differing factors. The relative contribution to the imbalance of the RANKL–OPG system is difficult to assess, as therapy, duration and severity of the disease have a significant impact on bone metabolism, and differ in individual patients. Increased levels of pro-inflammatory cytokines are

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**Table 1** Mean daily calcium intake expressed in mg/day ± SD in Crohn’s disease, ulcerative colitis and control groups in relation to gender.* Significant versus healthy controls (P < 0.05).

<table>
<thead>
<tr>
<th></th>
<th>Overall series</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crohn’s disease</td>
<td>881.9 +/- 433.0 (96.8%)</td>
<td>805.9 +/- 363.5 (88.2%)*</td>
<td>941.7 +/- 475.1 (107.8%)</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>798.8 +/- 544.1 (88.1%)</td>
<td>768.7 +/- 385.8 (79.0%)*</td>
<td>832.3 +/- 553.6 (98.3%)</td>
</tr>
<tr>
<td>Healthy controls</td>
<td>991.0 +/- 536.0 (105.8%)</td>
<td>983.8 +/- 563.6 (101.8%)</td>
<td>1003.8 +/- 484.0 (112.9%)</td>
</tr>
<tr>
<td>Diseased controls</td>
<td>867.6 +/- 562.8 (93.8%)</td>
<td>852.6 +/- 590.0 (90.8%)</td>
<td>925.0 +/- 442.5 (105.3%)</td>
</tr>
</tbody>
</table>

**Table 2** Mean daily calcium intake expressed in mg/day ± SD in diseased controls, subdividing data according to disease and gender.*significant versus healthy controls(P < 0.001), § significant versus IBD patients (P < 0.001).

<table>
<thead>
<tr>
<th></th>
<th>Overall series</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celiac disease</td>
<td>1165.7 +/- 398.8 (129.4%)*§</td>
<td>1201.7 +/- 976.6 (129.9%)*§</td>
<td>1016.3 +/- 322.6 (127.1%)</td>
</tr>
<tr>
<td>Lactose intolerant</td>
<td>699.7 +/- 356.0 (73.9%)*</td>
<td>675.9 +/- 327.2 (71.3%)*</td>
<td>952.7 +/- 548.7 (101.9%)</td>
</tr>
<tr>
<td>Non GI tract diseases</td>
<td>905.3 +/- 572.2 (97.3%)</td>
<td>907.4 +/- 608.2 (95.3%)</td>
<td>906.7 +/- 444.5 (100.9%)</td>
</tr>
</tbody>
</table>
considered to represent an independent risk factor, but in clinical practice patients with severe disease and/or frequent relapses are more likely treated with steroids. As a consequence preventive strategies or effective treatment regimens are difficult to assess. Unlike bisphosphonates, long term calcium and vitamin D supplements do not consistently improve BMD in normal subjects and patients with IBD on corticosteroid therapy. Nonetheless, it is widely accepted that adequate intake of calcium and Vit D may prevent or counteract negative calcium balance and altered bone metabolism, both in children and in adults. Most important, unlike other factors favoring osteoporosis and osteopenia in IBD, inadequate intake of calcium is easily reversible with dietary modification and/or supplementation, is inexpensive and does not require the use of drugs. These favorable characteristics are shared only by the cessation of smoking in CD. The identification of inadequate calcium intake is thus relevant.

Dietary association studies are susceptible to methodological limitations, in particular when diet is ascertained retrospectively. In the present study we attempted to overcome some limitations, assessing the diet of the previous week by means of a validated 22-item FFQ, in a large series of patients and controls. Besides considering the frequency of consumption for each food item, the usual serving size in individual patients was assessed using a photographic atlas of food portions. The good reproducibility of this approach was double-checked in a proportion of patients, asking them to fill again the questionnaire 6–12 months later, provided that they were in the same phase of the disease, remission or activity (data not reported).

The present study indicates that normal controls, as well as patients with non-gastroenterological diseases, have a calcium intake well within RDA. IBD patients had a non-significantly lower calcium intake as compared to normal controls. The trend was observed both in UC and CD (88.1% and 96.8% RDA, respectively, versus 105.8% in normal controls). It could have been anticipated that patients with CD have more problems with their diet than those affected by UC. However, this was not the case in the present series.

On the contrary, the calcium intake was high (120% RDA) in patients with celiac disease. This may be explained considering that over two thirds of patients already were on a gluten-free diet, and underwent regular dietary counseling. Thus, they were well aware of the increased risk of low mineral density related to gluten enteropathy and had correspondingly modified their diet. Conversely females, but not males, with lactose malabsorption/intolerance show a marked reduction in calcium intake.

Besides the underlying disease, large variations were observed in all study groups in relation to gender, age and the self-reported belief of lactose intolerance. Gender is a well-known determinant of calcium intake. Postmenopausal women are at high risk group for osteoporosis and osteopenia, nonetheless the consumption of calcium containing food has often been reported to be particularly low in this group of subjects. The same was documented in the present series in females with IBD and diseased controls, with calculated values ranging from 79% to 90.8% RDA. The lowest intake was observed in UC females. On the contrary, values were within or over RDA in males, irrespective of diagnosis, the calcium intake ranging from 98.3% to 112.9% RDA. Female, but not male patients with lactose malabsorption/intolerance showed values well below RDA (71.3%). The reason for this finding is unclear, but a large proportion of female undergoing the lactose hydrogen breath test present with gaseousness and bloating, which is often attributed to lactose and dairy products. This belief likely leads to dietary restrictions, also in the absence of documented lactose malabsorption.

Dietary habits indeed are influenced by age. In our series, age-related variations were relatively minor in normal subjects, whereas a significant reduction in calcium intake was documented in the older age groups, in IBD and diseased controls. This proved true for females over 50 years (63.4% and 61.5% RDA, respectively), as well as in males over 60 (IBD 79.0% RDA and diseased controls 79.5%). This seems to imply that the presence of "any" disease favors a modification of dietary habits, in addition to that related to age. In this respect IBD patients in the older age groups behave similarly to patients affected by other diseases, the only difference being a non-significant trend toward lower calcium intake.

### Table 3
Mean daily calcium intake in relation to age and gender. Data expressed in mg/day ± SD. Data between brackets report the percent value versus RDA. *P < 0.05 versus healthy controls. Data from subjects less than 18 years old are not included due to the small sample size. Age groups are subdivided in relation to gender, thus the cut-off values are 50 years for females and 60 for males.

<table>
<thead>
<tr>
<th>Age group/gender</th>
<th>Healthy controls</th>
<th>Diseased controls</th>
<th>IBD</th>
</tr>
</thead>
<tbody>
<tr>
<td>18–29 Female</td>
<td>1088.0 +/- 734.0 (108.9%)</td>
<td>934.7 +/- 667.7 (93.5%)</td>
<td>1027.0 +/- 768.4 (102.0%)</td>
</tr>
<tr>
<td>18–29 Male</td>
<td>1100.4 +/- 555.1 (110.3%)</td>
<td>920.0 +/- 521.8 (92%)</td>
<td>962.9 +/- 266.7 (96.3%)</td>
</tr>
<tr>
<td>30–49 Female</td>
<td>943.9 +/- 465.9 (117.5%)</td>
<td>912.8 +/- 640.9 (114.1%)</td>
<td>783.7 +/- 392.8 (93.7%) *</td>
</tr>
<tr>
<td>30–59 Male</td>
<td>963.2 +/- 447.6 (120.4%)</td>
<td>954.0 +/- 436.5 (119.2%)</td>
<td>956.1 +/- 579.0 (118.1%)</td>
</tr>
<tr>
<td>&gt;50 Female</td>
<td>941.2 +/- 447.7 (94.1%)</td>
<td>738.2 +/- 456.7 (61.5%)</td>
<td>713.9 +/- 356.9 (63.4%) *</td>
</tr>
<tr>
<td>&gt;60 Male</td>
<td>904.7 +/- 292.8 (90.5%)</td>
<td>795.5 +/- 324.7 (79.5%)</td>
<td>754.6 +/- 360.2 (79.0%)</td>
</tr>
</tbody>
</table>

### Table 4
Calcium intake in relation to "self-reported lactose intolerance", defined as the patients’ belief that milk and dairy products induce/exacerbate abdominal symptoms. Data expressed in mg/day ± SD. *P < 0.03, **P < 0.005.

<table>
<thead>
<tr>
<th></th>
<th>Self-reported lactose intolerance</th>
<th>Self-reported lactose tolerance</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBD</td>
<td>772.4 +/- 438.3 (96 pt– 87.6%)</td>
<td>919.51 +/- 510.0 (91 pt– 100.4%) *</td>
</tr>
<tr>
<td>Healthy controls</td>
<td>895.3 +/- 490.6 (205 pt– 105.8%)</td>
<td>1083.0 +/- 562.8 (215 pt– 114.3%) **</td>
</tr>
<tr>
<td>Diseased controls</td>
<td>814.7 +/- 470.1 (204 pt– 88%)</td>
<td>1029 +/- 535.2 (72 pt– 109.2%) **</td>
</tr>
</tbody>
</table>
The present data show that calcium intake is only slightly reduced in the overall series of IBD patients, the significance threshold being attained only in the oldest age groups, more so in females. Nonetheless, the daily calcium intake in IBD showed wide variations in the present and other series, suggesting that a proportion of patients believe that milk and dairy products exacerbate the disease, so that the intake of calcium is less than recommended for primary prevention. This belief is shared by a proportion of physicians, supporting the widespread opinion that milk and dairy products should be avoided in diarrheal diseases. Conversely little attention is paid to the fact that many dairy products have minimal lactose content, and are a good source of dietary calcium.

Similar dietary habits have been reported in a series of pediatric UC patients. Seventy-one of them altered their diet to avoid aliments, usually milk, that they felt worsened their condition, and symptoms were reported to improve as a result in 73% of them. The primary role of subjective beliefs in modulating abdominal symptoms has been documented in other conditions, including self-reported lactose intolerance. Subjective reports of how IBD patients experience their relation to food and dairy products, indicate this is part of the process leading to inadequate calcium intake. This is true also in the present series, as the subjective belief of milk intolerance implied significant modification of diet, leading to 20% reduction of calcium intake, in all study groups.

Less than optimal calcium and Vit D intake may be easily reversed by supplementation of these nutrients, but this approach seems to be burdened by a small increase in kidney stones, in postmenopausal women. This is not the case when adequate calcium intake is granted by optimal dietary habits, including milk and dairy products which are the best source of these nutrients. The observation that celiac patients on low gluten diet have a calcium intake well over RDA further supports the need for tailored nutrition advice in patients with IBD, using diet as a key preventative measure to reduce the risk of osteoporosis. This seems to be of prime importance in about one third of IBD patients, whose diet is particularly poor in calcium containing food, more so in those believing that milk and dairy products may worsen abdominal symptoms, irrespective of documented lactose malabsorption.

**Conflict of interest statement**

P Vernia has been lecturing for Otsuka Pharmaceutical SA, Spain and Otsuka Pharma Scandinavia AB. All other authors declare that there are no potential financial, professional or personal conflicts of interest.

**Contributors**

Piero Vernia: study concept and design, drafting of the manuscript, study supervision.

Panagiotis Loizos, Irene Di Giuseppantonio, Barbara Amore, Ambra Chiappini: acquisition of data, material support, analysis and interpretation of data. Santi Cannizzaro: acquisition of data, analysis and interpretation of data, drafting of the manuscript.

**References**
