Regional variations in the use of complementary and alternative medicines (CAM) for inflammatory bowel disease patients in Italy: An IG-IBD study

Perla Bertomoro [a], Sara Renna [b], Mario Cottone [b], Gabriele Riegler [c], Fabrizio Bossa [d], Licio Giglio [e], Luca Pastorelli [f], Claudio Papi [g], Fabiana Castiglione [h], Erika Angelucci [i], Roberta Pica [j], Maria Carla Di Paolo [k], Renata D'Incà [a],*

[a] Department of Surgical and Gastroenterological Sciences, Gastroenterology Section, University of Padua, Italy
[b] Department of General Medicine, Pneumology and Nutrition Clinic, Palermo University, V. Cervello Hospital, Italy
[c] Gastroenterology and Digestive Endoscopy Unit, University II of Naples, Italy
[d] Gastroenterology Unit, CSS-IRCCS Hospital, San Giovanni Rotondo, Italy
[e] San Camillo Forlanini Hospital, Rome, Italy
[f] Mangiagalli e Regina Elena Policlinic; Department of Medical Sciences, University of Milan, Italy
[g] Gastroenterology Unit, S. Filippo Neri Hospital, Rome, Italy
[h] Gastroenterology Unit "Federico II", Naples, Italy
[i] University of Rome, "La Sapienza", Rome, Italy
[j] Department of Clinical Sciences, Gastroenterology Unit, University of Rome "La Sapienza", Italy
[k] UOSD Gastroenterology and Digestive Endoscopy, San Giovanni Addolorata Hospital, Rome, Italy

Abstract

Background and aim: Complementary and alternative medicines (CAM) are being used increasingly by patients with Crohn's disease (CD) and ulcerative colitis (UC). We aimed to assess the prevalence and usage of CAM in different geographical areas of Italy and possible predictors of their use.
Methods and materials: A structured questionnaire, administered to outpatients, attending 8 general hospitals and 9 tertiary referral centres, was completed by 2011 patients (909 CD, 1087 UC and 15 indeterminate colitis). 583 patients lived in the North, 659 in Central Italy and 769 in the South.
Results: CAM users were 475 (23.6%) with no regional differences in their distribution. Usage correlated significantly with female gender (*p*=0.030), higher education (*p*=0.021), hospitali-

* Corresponding author. Dipartimento di Scienze Chirurgiche e Gastroenterologiche, Sezione di Gastroenterologia, Azienda Ospedaliera, Via Giustiniani 2, 35127 Padova, Italy. Tel.: +39 049 821 2893; fax: +39 049 876 0820.
E-mail address: dinca@unipd.it (R. D'Incà).

zation rates ($p=0.000$), extra-intestinal complications ($p=0.000$), non-adherence to conventional treatments ($p=0.054$), adverse reactions to conventional treatments ($p=0.000$), and active disease ($p=0.007$); 5-ASA usage was associated with a more limited use of CAM ($p=0.005$). Dietary changes or supplements and prayer were significantly more frequently reported in South, while Northern Italian patients more frequently used homeopathy, herbal medicines and physical exercises. Patients in Central Italy adopted an intermediate behavior. CAM use ameliorated the patient's general well-being according to two thirds of the users. Costs were higher for Northern patients than in Central or Southern Italy.

Conclusion: One in four IBD patients in Italy use CAM. More money is spent on CAM in Northern Italy. Regional differences emerged as regards the type of CAM but not in terms of disease features, frequency of and reasons for CAM use, or perceived effects.

1. Introduction

The general population has shown an increasing interest in complementary and alternative medicine (CAM) and has made more use of them in recent years, mainly because they are considered "healthy" and "natural". The most frequent users are patients with chronic conditions. Chronic and incurable diseases, and the need for long-life therapy affect the quality of life, influencing a patient's social and occupational sphere. Major CAM users are patients with asthma, arthritis, psoriasis, cancer, chronic liver disease, irritable bowel disease, gastroesophageal reflux disease, dyspepsia and constipation.[1–8] An Italian survey conducted by the ISTAT (Italian Statistics Institute) in 2004 revealed that 15.6% of the general population have used CAM. Alternative remedies are associated with a more naturalistic, healthier life-style, adherence to screening tests, regular outpatient visits, physical exercise and not smoking.[9]

The percentage of CAM users among IBD patients fluctuates from 20% to 68% depending on the series considered. The lowest levels have been reported in the Mediterranean area, with France reaching 21% and Spain 26% as opposed to 52% of users in Germany, 39% in Austria, 47% in Switzerland, 49% in the UK, and 36% in Sweden. The diffusion of CAM in northern Europe is much the same as in North America.[8,10–16] A previous study on 552 Italian IBD outpatients revealed that about 28% of them used CAM.

The type of CAM used seems to vary in different geographical areas: herbal remedies and dietary changes are preferred in the USA, acupuncture in Asia, and homeopathy in Europe. Given these differences, the Italian Group for the study of IBD analyzed the use of CAM by these patients in various parts of Italy.

2. Methods

The survey was conducted from June 2006 to September 2007 using a structured anonymous questionnaire based on previously published surveys conducted by our group. The questionnaire was tested for ambiguity and ease of completion on a small group of 10 patients living nearby. We balanced gender, age, education and employment status to obtain a heterogeneous sample. Content validity was assessed by asking patients if the items in the questionnaire were easy to understand and relevant to their disease and general attitude to their health. Only items rated as readily comprehensible and relevant by more than 80% of the patients were retained in the final version, which included 37 items regarding diagnosis, disease duration, disease-related concerns, past and present medical treatments, general health attitudes and behavior, demographic characteristics, type of therapy, personal details, any use of CAM, the types of CAM used, reasons for their use and satisfaction. Patients were recruited at 8 general hospitals and 9 tertiary referral centres Italy. At each centre, the questionnaire was administered to outpatients attending scheduled check-ups while they were in the waiting room. All patients gave their informed consent to participation in the study. Each centre involved in the study created a database and the data were subsequently pooled into a single database. The reliability across different Italian regions was estimated using Cronbach's alpha. A reliability coefficient of 0.70 was considered acceptable.[17,18] Cronbach's alpha for the whole sample was 0.76, ranging from 0.74 for patients in the South to 0.78 for those in the North. The data were analyzed using a two-step procedure, with univariate regression analysis to select significant variables and the χ^2-test and Fisher's exact test to assess differences between groups. Variables with a p-value <0.005 were entered in a binary logistic regression model to pinpoint the predictors of CAM usage and to assess any differences between the three Italian regions. The odds ratio (OR) was used to measure the risk of CAM use, calculated with a 95% confidence interval. The statistical analysis was completed using the SPSS for Windows (Statistical Package for the Social Sciences) rel. 13.0.

3. Results

3.1. Patients' characteristics

The survey included 1099 males (54.4%) and 912 females (45.2%): 909 (45.2%) were patients with Crohn's disease (CD), 1087 (54.1%) had ulcerative colitis (UC) and 15 (0.7%) patients with indeterminate colitis. The patients' socio-demographic and disease-related characteristics are given in Table 1. Female gender (49.5% vs 43.8%, $p=0.030$) and a higher education (63.2% vs 57.2%, $p=0.021$) were significantly associated with CAM use. Other factors were hospitalization rates (71.8% vs 62.4%, $p=0.000$), extra-intestinal complications (44.2% vs 33.7%, $p=0.000$) and drug side-effects (27.4% vs 16.1%, $p=0.000$). Analyzing

Table 1 Socio-demographic and disease-related characteristics of IBD patients under study.

	CAM %	CT %	p	OR	C.I
	n = 475	n = 1496			
Socio-demographics					
Age (mean ± SD)	44 ± 12.88	46 ± 15.20			
Gender					
Male	50.5	56.2			
Female	49.5	43.8	0.030	1.26	1.02–1.54
Education					
Primary	36.8	42.8			
Academic	63.2	57.2	0.021	1.27	1.04–1.59
Diagnosis					
Crohn's disease	44.9	45.7			
Ulcerative colitis	55.1	54.3	0.753	1.03	0.84–1.27
Disease-related characteristics					
Hospitalizations	71.8	62.4	0.000	1.53	1.22–1.92
Surgery	29.1	27.1	0.417	1.10	0.88–1.38
Gastroenterological visits >3	40.4	40.2	0.942	1.01	0.82–1.24
Extra-intestinal complications	44.2	33.7	0.000	1.56	1.27–1.93
Adverse reactions to drugs	27.4	16.1	0.000	1.97	1.55–2.52
Non-adherence	45.7	40.7	0.054	1.23	1.00–1.51
Disease duration >5 years	83.2	74.2	0.000	0.58	0.45–0.76
Types of therapy					
Steroids	42.5	35.7	0.007	1.33	1.08–1.65
Mesalazine	71.6	77.9	0.005	0.72	0.57–0.90
Sulphasalizine	11.6	8.6	0.050	1.39	0.99–1.94
Infliximab	7.2	3.5	0.001	2.16	1.38–3.36
Antimicrobial	21.3	15.8	0.005	1.44	1.11–1.87

CAM = users of complementary and alternative therapies, CT = conventional therapy.

disease duration revealed that CAM use was significantly associated with a longer history of the condition (83.2% in patients with disease of more than 5 year duration vs 74.2% in patients with a shorter history of disease, p = 0.000).

Non-adherence to conventional therapy was associated with CAM use in 45.7% of users. Previous recourse to steroids (42.5% vs 32.7%, p = 0.007), antimicrobial agents (21.3% vs 15.8%, p = 0.005) and anti TNF biologics (7.2% vs 3.5%, p = 0.001) were significantly associated with CAM use, while mesalazine therapy (71.6% vs 77.9%, p = 0.005) correlated inversely with CAM use (Table 1).

3.1.1. CAM users

In all, 475 patients (23.6%) reported using or having used CAM. Their use was mainly as a complementary medicine (about 76% of patients said they used CAM concomitantly with conventional treatments), as an adjunct rather than an alternative to conventional therapy. The most frequent CAM used were: dietary restrictions or dietary supplements (45.1%), homeopathy (37.7%), herbal remedies (23.4%), prayer (22.3%), exercise (20.6%), massage (11.2%), and relaxation (11.2%). Acupuncture, pranotherapy, osteopathy, meditation, iridology, chiropractic, reflexology or hypnosis was used by less than 10% of these patients.

CAM users were characterized by ups and downs in the course of their disease, with significantly more frequent relapses than among non-users (58.3% vs 53.4%, p = 0.001).

The main reasons prompting CAM use were: to ameliorate intestinal symptoms (48.6%), in the hope of a cure (43.4%), to reduce the number of drugs used (35.4%), because they were perceived as more natural (31.6%), or failure to respond to conventional therapy (25.1%).

One third of the patients reported an improvement in their general well-being, 17.5% a partial benefit, 16.6% fewer relapses, and 39.2% reported a worsening of their symptoms.

As for the economic outlay, 16.4% of the patients spent less than €150 on CAM, 12.4% spent €150–600, and 13.5% spent more than €600 altogether; 11.4% of patients were unable to quantify the total cost of their CAM use; 46.3% of CAM users did not keep track of their CAM expenses or they used cost-free remedies.

CAM were used for less than 6 months in 38% of cases, for more than 6 months and less than 3 years in 24%, and for more than three years by 18% of patients; the remaining 20% did not answer this question.

Users and non-users were equally keen to know more about CAM (84% of the patients interviewed).

3.1.2. Patient−doctor relationship

Among the CAM users, 82% of the patients said they were satisfied with their relationship with their doctor and the time spent on them during their outpatient check-ups. However, only about half of these patients (46.7%) told their

doctors about their decision to use a CAM, while 38.7% did not (and 14.6% did not answer this question).

3.1.3. Predictors of CAM use

Logistic regression analysis identified the need for frequent check-ups (p=0.003, OR=1.566, CI=1.16–2.12) as the only predictor of CAM use. On the other hand, the predictors of non-use were the use of topical 5-ASA (0.036, OR=0.182, CI=0.04–0.89) and an interest in knowing more about such remedies from their general practitioner (p=0.042, OR=0.086, CI=0.01–0.92).

3.2. Regional differences in Italy

The questionnaires were then analyzed according to their provenance. A total of 657 questionnaires came from the North, 609 from Central Italy and 800 from the South. Of the 475 patients reportedly using or having used CAM, 160 were in the North (27.6%), 132 in Central Italy (20%), and 183 in the South (23.8%). In all three areas, CAM use was seen more as a complement than as an alternative to conventional therapies, according to 83.8%, 75% and 72.1% of patients, respectively, in each of the three areas. The socio-demographic characteristics of the CAM users are given in Table 2. We also analyzed potential gender-related differences in the frequency and type of CAM chosen (Table 3). Differences in the choice of CAM emerged when we analyzed the three geographical groups separately: Northern Italian

patients tended to prefer homeopathy, herbal remedies, relaxation, pranotherapy, iridology, reflexology and hypnosis; Central Italians opted more for relaxation; in the South, dietary measures and prayer were more popular. The frequency of use of each type of CAM by the three regional groups is given in Table 4.

The reasons for using CAM were similar all over Italy (Table 5), though in the North and Central regions their use correlated significantly more with failure to respond to conventional therapy and with the general conviction that CAM are healthy. The hope of finding a cure was recorded in all areas, but its influence on the frequency of CAM use was stronger in the South.

No differences emerged in the reported effects of CAM use in terms of the frequency of relapses or improvements in IBD symptoms and general well-being, but a worsening of symptoms after using CAM was reported significantly more frequently in the South (14.2%) than in the North (5.6%) or Central Italy (5.2), (p=0.005).

Countrywide, about 38% of patients used CAM only for a short period of time (less than 6 months), with more Northern patients (24.4%) using CAM for longer periods than in Central Italy (14.4%) or the South (15.8%), (p=0.000).

CAM were apparently more costly in the North, since 23.8% of the Northern patients reported spending more than €600, as opposed to 9.1% in Central Italy and 7.7% in Southern Italy (p=0.000). On the other hand, 66% of patients from the South and 51.5% of those in Central Italy

Table 2 Demographic and clinical characteristics of CAM users by geographical area.

	North % n=160 27.6%	Centre % n=132 20%	South % n=183 23.8%	p
Socio-demographics				
Age (mean±SD)	44±12.20	46±13.95	44±12.64	
Gender				
Male (239)	48.1 (77)	47 (62)	54.6 (100)	0.321
Female (236)	51.9 (83)	53 (70)	45.4 (83)	0.321
Education				
Primary	40.6	29.5	41.0	0.076
Academic	59.4	70.5	59.0	0.076
Diagnosis				
Crohn's disease	36.9	53.8	44.8	0.016
Ulcerative colitis	63.1	46.2	55.2	0.016
Disease-related characteristics				
Hospitalizations	68.8	74.2	72.7	0.551
Surgery	22.5	40.2	26.2	0.003
Gastrointestinal visits >3	35.0	45.5	41.5	0.180
Extra-intestinal complications	45.0	44.7	43.2	0.935
Side-effects of drugs	24.4	31.1	27.9	0.442
Non-adherence	45.6	53.8	39.9	0.051
Types of therapy				
Steroids	34.4	40.2	51.4	0.005
5-ASA products	76.9	68.2	69.4	0.184
Immunosuppressants	20.6	28.8	19.1	0.104
Infliximab	5.0	12.9	4.9	0.011
Antimicrobial	16.3	21.2	25.7	0.103

Table 3   Frequency of disease-related characteristics of CAM users by gender and geographical area.

	Male				Female			
	N%	C%	S%	p	N%	C%	S%	p
	77/32.2%	62/25.9%	100/41.8%		83/35.3%	69/29.4%	83/35.3%	
Diagnosis								
Crohn's disease	28.6	69.9	45.0	0.000	44.6	46.4	44.6	0.990
Ulcerative colitis	70.1	50.1	55.0	0.000	54.2	53.6	55.4	0.990
Disease characteristics								
Hospitalizations	63.6	74.2	75.0	0.210	73.5	73.9	69.9	0.899
Surgery	20.8	50.0	30.0	0.001	24.1	30.4	22.9	0.531
Gastrointestinal visits >3	33.8	41.9	40.0	0.568	36.1	47.8	43.4	0.334
Extra-intestinal complications	41.6	48.4	41.0	0.618	48.2	42.0	45.8	0.748
Side-effects of drugs	23.4	24.2	26.0	0.168	25.3	37.7	28.9	0.426
Non-adherence	45.5	36.8	37.0	0.478	45.8	60.9	43.4	0.072
Types of therapy								
Steroids	32.5	33.9	55.0	0.003	36.1	44.9	47.1	0.329
5-ASA products	72.7	67.7	70.0	0.812	80.7	68.1	68.7	0.128
Immunosuppressants	15.6	35.5	22.0	0.020	25.3	21.7	15.7	0.304
Infliximab	3.9	12.9	6.0	0.128	6.0	13.0	3.6	0.096
Antibiotics	13.0	25.8	25.0	0.096	19.3	17.4	26.5	0.337
Types of CAM								
Homeopathy	49.4	35.5	25.0	0.004	48.2	42.0	30.1	0.055
Dietary measures	36.4	41.9	47.0	0.364	43.4	37.7	61.4	0.008
Herbal medicine	26.0	19.4	19.0	0.483	44.6	18.8	12.0	0.000
Exercise	24.7	33.9	15.0	0.020	21.7	15.9	16.9	0.604
Relaxation	16.9	9.7	4.0	0.016	16.9	18.8	3.6	0.008
Prayer	13.0	21.0	27.0	0.076	14.5	18.8	36.1	0.002
Massage	3.9	11.3	11.0	0.183	16.9	10.1	13.3	0.481
Pranotherapy	6.5	6.5	3.3	0.489	13.3	0.0	3.6	0.001
Acupuncture	9.1	12.9	7.0	0.450	7.2	8.7	7.2	0.929
Osteopathy	6.5	3.2	2.2	0.289	8.4	7.2	3.6	0.495
Iridology	5.2	1.6	0.0	0.046	9.6	0.0	1.2	0.003
Meditation	1.3	8.1	3.2	0.080	9.6	2.9	6.0	0.229
Reflexology	3.9	0.0	0.0	0.049	4.8	2.9	1.2	0.398
Chiropractic	2.6	0.0	0.1	0.481	4.8	4.3	0.0	0.109
Hypnotherapy	5.2	0.0	0.0	0.014	1.2	0.0	0.0	1.000

failed to mention their expenses, while this was true of only 19.4% of Northern Italian patients (Table 5).

More patients in Northern Italy were satisfied with their relationship with their specialist: this was true of 54.4% of cases in the North vs 44.7% of patients in Central Italy and 40.7% in the South (p=0.018); a good level of satisfaction was recorded in all three areas, however, as regards the information provided by physicians and the time dedicated to patients during check-ups (81%). The majority of patients (75%) were interested in knowing what the specialists thought about these alternative therapies (Table 6).

3.3. CAM use

There were 393 patients who used CAM as a complementary resource, the greater proportion of them living in the North (83.8% vs 75% in Central Italy and 72.1% in the South, p=0.000). In Central Italy such a complementary use was

significantly more associated with Crohn's disease than with ulcerative colitis (37.7% in the North vs 52.2% vs 45.5% in the South, p=0.023), surgery (21.9% in the North vs 38.9% vs 26.1% in the South, p=0.008) and poor adherence to conventional therapy (41.8% in the North vs 55.8% vs 39.6% in the South, p=0.024), while it was significantly more associated with ulcerative colitis in the North (61.6% vs 45.1% in Central Italy vs 54.5% in the South, p=0.023), and with the use of steroids in the South (39% in the North vs 39.8% in Central Italy vs 53%, p=0.036).

As for the types of remedy used, CAM users in the North tended to prefer homeopathic medicines (45.9% vs 32.7% of Central Italian users and 20.9% of Southerners, p=0.000), herbal medicines (32.2% vs 19.5% and 13.4%, p=0.001), relaxation (17.1% vs 15.9% and 3.7%, p=0.001), hypnosis (3.4% vs 0% and 0%, p=0.014) and iridology (6.2% vs 0.9% and 0.7%, p=0.0012), while the favorite types of CAM among Southern Italians were dietary changes (40.4% in the North,

Table 4   Types of CAM preferred by users in Northern, Central and Southern Italy.

Type of CAM	North %	Centre %	South %	p
Homeopathy	48.8	38.6	27.3	0.000
Dietary measures	40.0	39.4	53.6	0.013
Herbal medicine	35.6	18.9	15.8	0.000
Exercise	23.1	24.2	15.8	0.021
Relaxation	16.9	14.4	3.8	0.000
Prayer	13.8	20.1	31.1	0.000
Massage	10.6	10.6	12.0	0.894
Pranotherapy	10.0	3.0	3.3	0.008
Acupuncture	8.1	10.6	7.1	0.536
Osteopathy	7.5	5.3	2.7	0.131
Iridology	7.5	0.8	0.5	0.000
Meditation	5.6	5.3	3.8	0.710
Reflexology	4.4	1.5	0.5	0.045
Chiropractic	3.8	2.3	0.5	0.114
Hypnotherapy	3.1	0.0	0.0	0.006

42.5% in Central Italy and 58.2 in the South, $p=0.006$) and prayer (19.2% vs 23% vs 32.8%, $p=0.026$).

Seventy-two patients used alternative therapies, mainly involving pranotherapy in the North (13% vs 0% vs 0%, $p=0.052$) and prayer in the South (0% vs 14.3% vs 25%, $p=0.025$).

4. Discussion

This survey identified regional variations in CAM use among Italian IBD patients: their reported use by a median 24% of patients was slightly higher in the North (27%) than in Central (20%) or Southern Italy (24%).

Different surveys have already shown that women are more likely to adopt CAM than men, especially when well educated. CAM use is also common among children, especially if there is another user in the family.[19,20] These data are confirmed in Italy too, both among the general population (ISTAT survey, 1999–2000) and in the IBD subpopulation.[10,21] We confirm here that higher levels of education are significantly associated with recourse to CAM.

Table 5   Details of CAM use.

	North %	Centre %	South %	p
Reasons				
To ameliorate intestinal symptoms	51.9	43.2	49.7	0.312
To reduce number of drugs	41.3	34.1	31.1	0.139
Hope of cure	40.6	32.6	53.6	0.001
More natural therapy	36.3	33.3	26.2	0.121
Lack of response to conventional therapy	31.9	15.2	26.2	0.004
Because they are healthy	29.4	27.3	17.5	0.023
Recommended by friends	26.3	23.5	18.6	0.226
Tired of long-standing disease/therapy	25.0	18.2	19.7	0.307
Less drug-related toxicity	12.5	6.8	13.1	0.173
Curiosity	23.8	18.2	15.8	0.169
In hope of ameliorating joint symptoms	22.5	26.5	18.6	0.243
Side-effects of conventional drugs	20.6	12.9	13.1	0.097
To avoid using pain killers	21.3	20.5	14.8	0.242
Last resort	16.9	18.9	14.2	0.525
Outcomes				
Less frequency of relapses	18.1	16.7	15.3	0.782
Improvement of IBD symptoms	38.1	31.1	30.6	0.272
Partial benefit	14.4	15.2	21.9	0.135
No benefit	39.4	33.3	36.1	0.601
Only general well-being	41.3	41.5	35.5	0.436
Worsening of IBD symptoms	5.6	5.3	14.2	0.005
Duration of use				
1–6 month	38.8	38.6	37.2	
6 month–3 years	28.1	24.2	18.6	0.000
>3 years	24.4	14.4	15.8	0.000
Costs				
Less than 150€	21.3	17.4	11.5	0.000
150€–600€	16.3	8.3	12.0	0.000
More than 600€	23.8	9.1	7.7	0.000
No quantified	19.4	13.6	2.7	0.000

Table 6   Aspects of CAM users' relationship with their specialists.

	North %	Centre %	South %	*p*
They know the specialist's opinions of CAM	76.3	73.5	77.0	0.014
Satisfied with the specialist's explanations	75.6	69.7	79.2	0.065
Adequate time dedicated during visits	81.3	78.8	81.4	0.738
Consideration of patient's point of view	75.0	66.7	71.0	0.060
Satisfaction with medical care:				
− Excellent	41.3	49.2	53.0	0.018
− Fairly good	54.4	44.7	40.4	0.018
Benefit of specialist's advice	77.5	75.8	71.6	0.032

The variance showed the same trend in the three areas (*p* = 0.038). UC patients use CAM more often than CD patients in Spain and Germany,[11] while the opposite applies in Canada.[22] We found no significant differences between UC and CD users in our population as a whole but some regional differences emerged.

An important feature influencing a patient's use of CAM lies in the course of his/her disease. Cases of extensive and severe disease characterized by frequent relapses, repeatedly needing steroids, hospitalization and surgery, extra-intestinal complications, comorbidities and the need for psychotherapy are all predictors of CAM use, especially if associated with longer disease duration.[3,21,23,24]

Non-adherence is often a key factor, influencing the course of IBD with more relapses, worse symptoms and extra-intestinal manifestations[25]: in this study, CAM users in Central Italy frequently failed to adhere to conventional therapies.

The diffusion of CAM has been analyzed in various countries, showing that the types of remedy chosen vary, correlating with traditional and cultural aspects, while the reasons for using CAM are much the same. The Italian patients considered here also hoped to ameliorate their symptoms and possibly even find a cure, and to reduce the number of drugs they had to take. In addition to being dissatisfied with the effects of conventional medication, they associated CAM with advertising that promotes these remedies as being healthy and effective. On the other hand, patients responding well to conventional therapy and those who had tried CAM for other medical reasons and found them ineffective usually tended to avoid these remedies. Among the reasons influencing the choice of a CAM, the patients' relationship with their physician and their desire to share therapeutic decisions with their doctor appear to be important issues.[10,12,15,19,21,24,26]

CAM seem to be effective in quite a high proportion of patients, with 39.2% claiming a good general benefit, 33.3% reporting fewer IBD symptoms and 16.6% fewer relapses. On the other hand, 17.5% of patients found only an initial benefit and 8.8% even reported worsening symptoms, as already mentioned in other studies.[10,12]

Differences in culture and traditions can probably explain the variation in the choice of CAM in different countries. In Germany, the national health system now covers the cost of probiotics and their use is becoming common because they have proved effective in preventing IBD relapses and maintaining remission in UC.[27,28] This is the case of an *alternative* treatment that has come to be accepted as a *conventional* therapy.

We recorded different preferences regarding the type of CAM in the three geographical areas of Italy. In the North, patients preferred natural-biological substances or intervention on the body, while in the South patients preferred dietary changes and intervention on the mind, with Central Italians coming somewhere between the two. Moreover, Northern patients used more expensive remedies and for longer periods of time than in Central or Southern Italy.

A favorite choice was to introduce dietary changes, as reported by 45% of patients (though the questionnaire did not ask them to specify what type of changes they had made). From the literature, we know that many people with IBD avoid certain foods (mainly dairy products) or integrate their diet with probiotics.[29] Numerous studies have demonstrated that a diet rich in probiotics, fiber and glutamine modifies the intestinal microbiota and the availability of long/short fatty acids and fish oil (omega-3), which have a known anti-inflammatory effect.[30–34] Oral oligofructose-enriched inulin supplementation may reduce intestinal inflammation in acute UC by lowering fecal calprotectin.[35] A Japanese study demonstrated the preventive effect of a moderate dietary temperance on CD relapses.[36] The Mediterranean diet is considered a healthy way of eating, because it includes large amounts of fruit, vegetables, fiber, fish and olive oil. The antioxidant properties of this diet (due to vitamins, lycopene and phenolic substances) have a protective effect on the cardiovascular system and against chronic degenerative and inflammatory diseases involving the production of large amounts of reactive oxygen species.[37–40] This Mediterranean diet also seems to have chemoprotective effects against breast and colon cancer.[41] This probably explains why about 53% of Southern Italian patients believed that diet is important.

Homeopathy appears to be the favorite choice of CAM in Northern Italy. In a meta-analysis comparing homeopathy vs placebo and conventional therapies, Shang et al identified no superiority of homeopathy, though its use is widespread among IBD patients in Europe.[10,23]

Herbal medicines were used by 23% of the IBD patients in our survey. Some of these remedies have already demonstrated their therapeutic effect (especially plants with antioxidant and anti-inflammatory properties) by preventing oxidative damage,[42] which is one of the crucial steps in triggering the inflammatory process that activates NF-kB.[43]

Although it is not a CAM in the true sense of the word, 22.3% of our patients used prayer as an "alternative" to conventional therapy. The widespread resort to this practice probably derives from the patients' background and their cultural roots and traditions. Prayer represents a form of

inquiry on the meaning of life, illness and death,[44] finding a new balance and the conviction that "God" or a supreme being can provide support, encouragement and peace, however severe the patient's disease may be. It may help patients to cope with their psychological and physical stress, and self-love seems to be a predictor of higher levels of well-being.[45,46] Prayer may be seen as a spiritual need for hope.[47] Nurtured by numerous examples of "miraculous" healing, hope is an important individual quality that gives people energy and a sense of power and a capacity to go beyond their own limitations.[48]

Twenty-one percent of the IBD patients in our sample reported exercising routinely to ameliorate their symptoms. Many studies have demonstrated the utility of exercise in IBD patients in remission or with a moderate disease activity.[49–51] A better control of psycho-physical stress and anxiety may help to explain its apparent efficacy.[52] Stress negatively affects the course of IBD, exacerbating its activity and the frequency of relapses.[53] IBD patients very often suffer from stress and are aware that it negatively influences their illness,[23,54] with low levels of self-control.[55]

Italian CAM-user IBD patients tended not to abandon their conventional therapy. Both users (36%) and non-users (47.3%) were curious about the effects of these remedies but only half of them informed their physician about their decision to use a CAM. Talking about any use of such remedies with the doctor may be important because physicians could then report on their hidden side-effects,[56] or interferences with conventional medicine.[57]

5. Conclusions

CAM use is common among IBD patients, especially in women with severe and extensive disease requiring hospitalization and/or surgery. CAM are used by approximately one in four Italian IBD patients, with regional differences in their choice of CAM: patients in the North prefer homeopathy, herbal medicines and exercise, while Southerners opt for dietary changes and prayer. More money is spent on CAM in Northern Italy. No regional differences emerged in terms of disease features, frequency or reasons for using CAM, or their perceived effects. CAM usage is increasing, prompted by advertising, the general opinion that they are healthy and natural, and the increasing numbers of shops and medical clinics providing them. It is therefore important that physicians improve their understanding of the benefits and risks of these alternative "practices". Some CAM have demonstrated a certain scientific efficacy in IBD therapy, but more clinical trials are needed to establish their therapeutic usefulness. In future, some of these alternative remedies may come to be classified as allopathic.

Acknowledgements

References

1. Markham AW, Wilkinson JM. Complementary and alternative medicines (CAM) in the management of asthma: an examination of the evidence. *J Asthma* 2004;**41**:131–9.

2. Soeken KL. Selected CAM therapies for arthritis-related pain: the evidence from systematic reviews. *Clin J Pain* 2004;**20**: 13–8.

3. Ben Arye E, Ziv M, Frenkel M, Rosenman D. Complementary medicine and psoriasis: linking the patient's outlook with evidence-based medicine. *Dermatology* 2003;**207**:302–7.

4. Molassiotis A, Fernandez-Ortega P, Pud D, Ozden G, Scott JA, Panteli V, et al. Use of complementary and alternative medicine in cancer patients: a European survey. *Ann Oncol* 2005;**16**:655–63.

5. Strader DB, Bacon BR, Lindsay KL, La Brecque DR, Morgan T, Wright EC, et al. Use of complementary and alternative medicine in patients with liver disease. *Am J Gastroenterol* 2002;**97**:2391–7.

6. Carmona-Sánchez R, Tostado-Fernández FA. Prevalence of use of alternative and complementary medicine in patients with irritable bowel syndrome, functional dyspepsia and gastro-esophageal reflux disease. *Rev Gastroenterol Mex* 2005;**70**(4): 393–8.

7. Bub S, Brinckmann J, Cicconetti G, Valentine B. Efficacy of an herbal dietary supplement (Smooth Move) in the management of constipation in nursing home residents: a randomized, double-blind, placebo-controlled study. *J Am Med Dir Assoc* 2006;**7**(9): 556–61.

8. Kong SC, Hurlstone DP, Pocock CY, Walkington LA, Farquharson NR, Bramble MG, et al. The incidence of self-prescribed oral complementary and alternative medicine use by patients with gastrointestinal diseases. *J Clin Gastroenterol* 2005;**39**:138–41.

9. Menniti-Ippolito F, Bologna E, Gargiulo L, Forcella E, Sabbadini LL, Raschetti R. Caratteristiche individuali e familiari degli utilizzatori di terapie non convenzionali in Italia. *Ann Ist Super Sanità* 2004;**40**(4):455–61.

10. Bensoussan M, Jovenin N, Garcia B, Vandromme L, Jolly D, Bouché O, et al. Complementary and alternative medicine use by patients with inflammatory bowel disease. Results from a postal survey. *Gastroenterol Clin Biol* 2006;**30**:14–23.

11. Garcia-Planella E, Marin L, Domenech E, Bernal I, Mañosa M, Zabana Y, et al. Use of complementary and alternative medicine and drug abuse in patients with inflammatory bowel disease. *Med Clin (Barc)* 2007;**128**(2):45–8.

12. D'Incà R, Garribba AT, Vettorato MG, Martin A, Martines D, Di Leo V, et al. Use of alternative and complementary therapies by inflammatory bowel disease patients in an Italian tertiary referral centre. *Dig Liv Dis* 2007;**39**:524–9.

13. Moser G, Tillinger W, Sachs G, Maier-Dobersberger T, Wyatt J, Vogelsang H, et al. Relationship between the use of unconventional therapies and disease-related concerns: a study of patients with inflammatory bowel disease. *J Psychosom Res* 1996;**40**:503−9.

14. Ausfeld-Hafter B, Hoffmann S, Seibold F, Quattropani C, Heer P, Straumann A. A status of alternative medicine in Crohn disease and ulcerative colitis patients: a questionnaire survey. *Forsch Komplementarmed Klass Naturheilkd* 2005;**12**(3):134−8.

15. Joos S, Rosemann T, Szecsenyi J, Hahn EG, Willich SN, Brinkhaus B. Use of complementary and alternative medicine in Germany − a survey of patients with inflammatory bowel disease. *BMC Complement Altern Med* 2006:6−19.

16. Rawsthorne P, Shanahan F, Cronin NC, Anton PA, Löfberg R, Bohman L, et al. An international survey of the use and attitudes regarding alternative medicine by patients with inflammatory bowel disease. *Am J Gastroenterol* 1999;**94**:1298−303.

17. Nunnally JC. Psychometric theory. 2nd edn. New York: McGraw-Hill; 1978.

18. Helmstadter GC. Principles of psychological measurement. New York: Appleton-Century Crofts, New Appleton-Century Crofts; 1964.

19. Wong AP, Clark AL, Garnett EA, Acree M, Cohen SA, Ferry GD, et al. Use of complementary medicine in pediatric patients with inflammatory bowel disease: results from a multicenter survey. *J Pediatr Gatrsoenterol Nutr* 2008;**48**:55−60.

20. Li FX, Verhoef MJ, Best A, Otley A, Hilsden RJ. Why patients with inflammatory bowel disease use or do not use complementary and alternative medicine: a Canadian national survey. *Can J Gastroenterol* 2005;**19**(9):567−73.

21. Scott CM, Verhoef MJ, Hilsden RJ. Inflammatory bowel disease patients' decision to use complementary therapies: links to existing models of care. *Complement Ther Med* 2003;**11**:22−7.

22. Burgmann T, Rawsthorne P, Bernstein CN. Predictors of alternative and complementary medicine use in inflammatory bowel disease: do measures of conventional health care utilization relate to use? *Am J Gastroenterol* 2004;**99**:889−93.

23. McCann LJ, Newell SJ. Survey of paediatric complementary and alternative medicine use in health and chronic illness. *Arch Dis Child* 2006;**91**:173−4.

24. Langhorst J, Anthonisen IB, Steder-Neukamm U, Lüdtke R, Spahn G, Michalsen A, et al. Amount of systemic steroid medication is a strong predictor for the use of complementary and alternative medicine in patients with inflammatory bowel disease: results from a German national survey. *Inflamm Bowel Dis* 2005;**11**(3):287−95.

25. Kane SV. Systematic review: adherence issues in the treatment of ulcerative colitis. *Aliment Pharmacol Ther* 2006;**23**:577−85.

26. Langhorst J, Anthonisen IB, Steder-Neukamm U, Lüedtke R, Spahn G, Michalsen A, et al. Patterns of complementary and alternative medicine (CAM) use in patients with inflammatory bowel disease: perceived stress is a potential indicator for CAM use. *Complemen Ther Med* 2007;**15**:30−7.

27. Rembacken BJ, Snelling AM, Hawkey PM, Chalmers DM, Axon AT. Non-pathogenic *Escherichia coli* versus mesalazine for the treatment of ulcerative colitis: a randomised trial. *Lancet* 1999;**354**:635−9.

28. Kruis W, Fric P, Pokrotnieks J, Lukás M, Fixa B, Kascák M, et al. Maintaining remission of ulcerative colitis with the probiotic *Escherichia coli* Nissle 1917 is as effective as with standard mesalazine. *Gut* 2004;**53**:1617−23.

29. Gerasimidis K, McGrogan P, Hassan K, Edwards CA. Dietary modification, nutritional supplements and alternative medicine in paediatric patients with inflammatory bowel disease. *Aliment Pharmacol Ther* 2007:11−30.

30. Hanai H, Kanauchi O, Mitsuyama K, Andoh A, Takeuchi K, Takayuki I, et al. Germinated barley foodstuff prolongs remission in patients with ulcerative colitis. *Int J Mol Med* 2004;**13**:643−7.

31. Galvez J, Rodriguez-Cabezas ME, Zarzuelo A. Effects of dietary fiber in inflammatory bowel disease. *Mol Nutr Food Res* 2005;**49**:601−8.

32. Shanahan F. Probiotics in inflammatory bowel disease − therapeutic rationale and role. *Adv Drug Deliv Rev* 2004;**56**:809−18.

33. Meister D, Ghosh S. Effect of fish oil enriched enteral diet on inflammatory bowel disease tissues in organ culture: differential effects on ulcerative colitis and Crohn's disease. *World J gastroenterol* 2005;**11**(47):7466−72.

34. Macdonald A. Omega-3 fatty acids as adjunctive therapy in Crohn's disease. *Gastroenterol Nurs* 2006;**29**(4):295−301.

35. Casellas F, Borruel N, Torrejon A, Varela E, Antolin M, Guarner F, et al. Oral oligofructose-enriched inulin supplementation in acute ulcerative colitis is well tolerated and associated with lowered faecal calprotectin. *Aliment Pharmacol Ther* 2007;**25**(9):1061−7.

36. Tanaka M, Iwao Y, Sasaki S, Okamoto S, Ogata H, Hibi T, et al. Moderate dietary temperance effectively prevents relapse of Crohn disease: a prospective study of patients in remission. *Gastroenterol Nurs* 2007;**30**(3):202−10.

37. Keys A, Aravanis C, Van Buchem H, Blackburn H. The diet and all causes death rate in the seven countries study. *Lancet* 1981;**2**:58−61.

38. Willett WC, Sacks F, Trichopoulou A, Drescher G, Ferro-Luzzi A, Helsing E, et al. Mediterranean diet pyramid: a cultural model for healthy eating. *Am J Clin Nutr* 1995;**61**:1402−6.

39. De Lorgeril M, Salen P, Martin JL, Monjaud I, Delaye J, Mamelle N. Mediterranean diet, traditional risk factors and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon diet heart study. *Circulation* 1999;**99**:785−99.

40. Gerber M. Olive oil and cancer. In: Hill MJ, Giacosa A, Caygill CPG, editors. Epidemiology of diet and cancer. Chichester: Ellis Horwood; 1994. p. 263−75.

41. Reifen R, Nur T, Matas Z, Halpern Z. Lycopene supplementation attenuates the inflammatory status of colitis in a rat model. *Int J Vitam Nutr Res* 2001;**71**(6):347−51.

42. Kaplan M, Mutlu EA, Benson M, Fields JZ, Banan A, Keshavarzian A. Use of herbal preparations in the treatment of oxidant-mediated inflammatory disorders. *Complement Ther Med* 2007;**15**:207−16.

43. Siebenlist U, Franzoso G, Brown K. Structure, regulation and function of NF-kappaB. *Annu Rev Cell Biol* 1994;**10**:405−55.

44. Meraviglia MG. The effects of spirituality on well-being of people with lung cancer. *Oncol Nurs Forum* 2004;**31**:89−94.

45. Antonovsky A. Health, stress and coping. London: Jossey Bass; 1979.

46. Kobassa S. Stressful life events, personality and health: an inquiry into hardiness. *J Pers Soc Psychol* 1979;**37**:1−11.

47. Hert K. Fostering hope in terminally ill people. *J Adv Nurs* 1990;**15**:1250−9.

48. Gardner R. Miracles of healing in Anglo-Celtic Northumbria as recorded by Venerable Bede and his contemporaries: a reappraisal in the light of twentieth century experience. *BMJ* 1983;**287**(6409):1927−33.

49. Loudon CP, Corroll V, Butcher J, Rawsthorne P, Bernstein CN. The effects of physical exercise on patients with Crohn's disease. *Am J Gastroenterol* 1999;**94**(3):697−703.

50. Langhorst J, Mueller T, Luedtke R, Franken U, Paul A, Michalsen A, et al. Effects of a comprehensive lifestyle modification program on quality of life in patients with ulcerative colitis: a twelve-month follow up. *Scand J Gastroenterol* 2007;**42**(6):734−45.

51. D'Incà R, Varnier M, Mestriner C, Martines D, D'Odorico A, Sturniolo GC. Effect of moderate exercise on Crohn's disease patients in remission. *Ital J Gastroenterol Hepatol* 1999;**31**:205−10.

52. Kasimay O, Guzel E, Gemici A, Abdyli A, Sulovari A, Ercan F, et al. Colitis-induced oxidative damage of the colon and skeletal muscle is ameliorated by regular exercise in rats: the anxiolytic role of exercise. *Exp Physiol* 2006;**91**(5):897−906.

53. Mawdsley JE, Rampton DS. The role of psychological stress in inflammatory bowel disease. *Neuroimmunomodulation* 2006;**13**(5–6):327–36.

54. Langmead L, Chitnis M, Rampton DS. Use of complementary therapies by patients with IBD may indicate psychosocial distress. *Inflamm Bowel Dis* 2002;**8**:174–9.

55. Kuroki T, Ohta A, Aoki Y, Kawasaki S, Sugimoto N, Ootani H, et al. Stress maladjustment in the pathoetiology of ulcerative colitis. *J Gastroenterol* 2007;**42**(7):522–7.

56. Langmead L, Rampton DS. Review article: complementary and alternative therapies for inflammatory bowel disease. *Aliment Pharmacol Ther* 2006;**23**(3):341–9.

57. Neuman M. Effects metaboliques et interaction medicamenteuses provoquées par certain substances d'origine vegetale: pample-mousse, millepertuis et ail. *Presse Med* 2002;**31**:1416–22.