

Complementary and alternative medicine use in Brazilian patients with inflammatory bowel disease

Débora Pereira **HENRIQUES**¹, Rebeca Rodrigues de **OLIVEIRA**¹, Jeslei **VANNI**¹, Henrique Patriota de **LIMA**², Jean Vianney **OTITI**², Fabio Ricardo Monteiro **NEVES**², Marcia Beiral **HAMMERLE**², Lígia Yukie **SASSAKI**¹ and Cyrla **ZALTMAN**²

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ABSTRACT – Background – The conventional treatment of inflammatory bowel disease (IBD) is based on drug therapy, but different studies have shown a progressive increase in the use of complementary and alternative medicine (CAM). The most used CAM comprises of acupuncture, traditional Chinese medicine, Ayurvedic medicine, homeopathy, and herbal medicine, as well as more modern practices, including aromatherapy and reflexology. Data from CAM use in Brazil has previously been scarce and there are no studies among Brazilian patients with IBD. **Objective** – The aim of the study was to evaluate the frequency of, and factors associated with the use of CAM among IBD patients in Brazil, in addition to estimating the satisfaction with CAM use. **Methods** – A cross-sectional study was performed in adult IBD outpatients from two Southeastern Brazilian referral centers, with a total a sample of 227 individuals. A semi-structured questionnaire was used containing CAM products - tea, probiotics, omega 3 or glutamine, homeopathy, and herbal therapy, and factors associated with CAM use and patient satisfaction. We used descriptive statistics, association tests ($P < 0.05$) and logistic regression for statistical analyses. **Results** – In total, 126 patients with Crohn's disease and 101 with ulcerative colitis were included. The mean age was 41.19 ± 14.49 years and 57.27% were female. The time since diagnosis was 10.58 ± 7.5 years, and most patients were in clinical remission. Twenty-nine patients (12.8%) reported having used CAM for IBD treatment, such as tea (5.29%), probiotics (5.29%), omega-3 or glutamine (1.76%), homeopathy (0.88%), and herbal therapies (0.44%). Despite the low frequency, patients were satisfied (>50%). There was no difference between CAM use in Crohn's disease as compared to ulcerative colitis patients ($P = 0.1171$). The factors associated with the use of CAM were regular or poor quality of life (odds ratio 2.084; 95% confidence interval 1.147–3.786, $P = 0.0159$) and a shorter time since diagnosis (odds ratio 0.956; 95% confidence interval 0.918–0.995; $P = 0.0260$). **Conclusion** – The prevalence of CAM use was low, but satisfactory among Brazilian IBD patients. The application of CAM has been associated with poor quality of life and shorter disease duration compared to patients with no use of CAM.

Keywords – Complementary and alternative medicine; Crohn's disease; ulcerative colitis; inflammatory bowel disease.

INTRODUCTION

Inflammatory bowel disease (IBD), mainly consisting of Crohn's disease (CD) and ulcerative colitis (UC), is characterized by chronic inflammation of the gastrointestinal tract, leading to intestinal and extra-intestinal manifestations that compromise quality of life and can be disabling^(1,2). Treatment consists of the use of immunosuppressive drugs such as azathioprine, corticosteroids, JAK inhibitors or biological therapy such as anti-tumor necrosis factor (TNF), anti-integrin, and anti-interleukin agents^(1,2). Surgery is indicated in severe cases refractory to clinical treatment or in the presence of complications^(1,2).

Different studies have shown a progressive increase in the use of complementary and alternative medicine (CAM) by the general population combined with conventional therapy, in order to improve symptoms and reduce the impact of adverse events^(3,4). The use of medicinal plants is considered to be one of the oldest practices in medicine. Even today, mainly in developing countries, this alternative medical treatment may be the only therapeutic

resource accessible to communities and ethnic groups that lack a structured health care system⁽⁵⁾.

The National Center for Complementary and Integrative Health⁽⁶⁾ in the USA states that complementary health approaches include natural products such as herbs, vitamins, minerals, and probiotics; mind-body interventions such as yoga, chiropractic and osteopathic manipulation, meditation, acupuncture, relaxation techniques, tai chi, qi gong, and hypnotherapy. Other complementary health approaches include traditional healers, Ayurvedic medicine, traditional Chinese medicine, homeopathy, naturopathy, and functional medicine.

The popularity of CAM has increased in the recent decades, especially in Western societies and in patients with chronic diseases, such as IBD⁽⁷⁾. It is estimated that up to half of all IBD patients use CAM at some point in the course of the disease. This high prevalence may be related to the high levels of psychological and emotional distress, fatigue, anxiety, and depression in patients with IBD⁽⁸⁾. The motivations for using CAM include the desire for alternative approaches to supplement conventional therapy; use of

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¹ Universidade Estadual Paulista, Faculdade de Medicina, Departamento de Clínica Médica, Botucatu, SP, Brasil. ² Universidade Federal do Rio de Janeiro, Faculdade de Medicina, Departamento de Clínica Médica, Rio de Janeiro, RJ, Brasil.

Corresponding author: Lígia Yukie Sassaki. E-mail: ligiasassaki@gmail.com

more natural medications that are less toxic and with less adverse effects; lack of response from conventional therapy; and greater disease control improving quality of life⁽⁷⁾.

In 2006, Brazil implemented the Complementary and Integrative Practices⁽⁹⁾ as a public health policy program, with the inclusion of the Traditional Chinese medicine/acupuncture, homeopathy, medicinal plants and herbal medicines in the list of treatments offered through the SUS (Brazilian Unified Health System). However, there are no studies of the use of CAM by IBD patients in Brazil. Therefore, the objectives of the study were to identify the frequency and types of CAM most used, in addition to identifying the factors associated with its use, the degree of satisfaction, and the relationship between the use of CAM and adherence to conventional treatment.

METHODS

This cross-sectional study included 227 patients with IBD, of which 143 patients were followed up at the Clinics Hospital of the Botucatu Medical School/UNESP, state of São Paulo, and 84 at the University Hospital Clementino Fraga Filho, UFRJ Medical School, state of Rio de Janeiro, Brazil. Both institutions are public and referral centers for the treatment of IBD in the Southeast region of Brazil. The study was performed from July 2016 to December 2018.

Patients with a confirmed diagnosis of CD or UC and age 18 years or older were included. Pregnant women or nursing mothers, patients with ostomy, human immunodeficiency virus (HIV) or tuberculosis infection, cancer, heart, liver, kidney failure, or mental changes that prevented the understanding of the questionnaires or the consent form were excluded. Data were collected through interviews. Patients provided signed informed consent. The study was performed in accordance with the Declaration of Helsinki and was approved by the local Research Ethics Committee (Protocol number 67198117.6.0000.5257).

Sociodemographic and clinical variables

Sociodemographic variables included age, sex, family income, religion, education, and socioeconomic status (Brazil Social Economic Stratum⁽¹⁰⁾). The clinical variables included disease duration, Montreal classification^(11,12), drug treatment, history of hospitalization or surgery, and presence of comorbidities. The Harvey & Bradshaw Index for Crohn's disease⁽¹³⁾ and the Mayo partial score for ulcerative colitis⁽¹⁴⁾ were used to measure clinical disease severity.

Evaluation of medication adherence

The Morisky Adherence scale (8 items) was modified to assess medication adherence⁽¹⁵⁾ and adapted by Trindade et al.⁽¹⁶⁾ for patients with IBD. The score ranges from <6 points (low adherence), 6–7 (average adherence), and >7 (high adherence).

Assessment of quality of life and mood disorders

Quality of life was assessed using the Inflammatory Bowel Disease Questionnaire (IBDQ), validated for use in Brazil⁽¹⁷⁾. The questionnaire consists of 32 questions and the score can vary from 32 to 224. According to the score, quality of life is classified as excellent (≥ 200), good (151–199), regular (101–150), or poor (≤ 100)⁽¹⁸⁾. The presence of anxiety and depression was assessed using the Hospital Scale for Anxiety and Depression (HADS)⁽¹⁹⁾. The HADS scale consists of 14 items and a score greater than eight is suggestive of anxiety or depression⁽¹⁹⁾.

Evaluation of the use of complementary and alternative medicine

The use of CAM was assessed through a specific questionnaire formulated for the study, through an interview by the study authors. The questionnaire was peer-reviewed and standardized for application at the two participating centers, with questions about the use of herbs or herbal medicine, teas, homeopathy, probiotics, omega 3/glutamine, and Chinese medicine (acupuncture, auriculotherapy, and reiki). For each type of CAM, the indication of use, frequency, and duration of use, current or previous use and patient satisfaction were evaluated. Patients were asked about the purpose of using CAM, whether as complementary therapy for IBD or for another indication.

Statistical analyses

The sample size was based on a convenience sample. Eleven patients were excluded as they did not fill in the questionnaires. Data are expressed as mean $\pm$ standard deviation or median (range) for continuous variables, and as frequency (proportion) for qualitative variables. Chi-square test and Fisher's exact test, as appropriate, were used to compare categorical data. Continuous data were compared using ANOVA and Tukey's multiple comparison test. Univariate logistic regression was performed to assess the association between the use of CAM and the clinical and psychological variables. A P -value < 0.05 was considered statistically significant. Statistical analyses were performed by using SAS version 9.3 for Windows (SAS Institute Inc., Cary, NC, USA). All authors had access to the study data. The statistical review of the study was performed by a biomedical statistician.

RESULTS

In total, 227 patients with IBD were evaluated; mean age was 41.19 ± 14.49 years, and the majority were female (57.27%). Regarding the clinical characteristics, 126 patients were in the CD group and 101 in the UC group, and the duration of the disease was 10.58 ± 7.50 years. Most patients were in clinical remission of the disease (CD, 75.40%; UC, 60.40%). The most used medications were azathioprine alone or in combination with biological therapy (42.29%), infliximab monotherapy (26.43%), aminosalicylates (25.55%), and adalimumab monotherapy (14.10%) (TABLE 1). It was observed that 28.24% of the patients had low medication adherence. Quality of life was classified as good (48.46%) or excellent (22.47%) in most patients, and there was a high percentage of anxiety (44.93%) and depression (31.72%) (TABLE 1).

The frequency of current use of CAM as complementary therapy for IBD or for another health problem was 32.16% of the sample. Considering the use of CAM as a complementary treatment for IBD, the frequency was low, with teas (5.29%), probiotics (5.29%), supplements such as omega 3 or glutamine (1.76%) being the most reported, followed by homeopathy (0.88%) and herbal medicines (0.44%) (TABLE 2). In terms of the use of CAM for other health problems, the use of herbal medicines (30%) was the highest, followed by Chinese medicine (26.92%), probiotics (25.53%), tea (23.33%), Omega 3 or glutamine (13.64%), and homeopathy (8.69%). Almost half of the patients had never used CAM (48.90%). Despite the low frequency of usage of CAM, patients were satisfied with their use (TABLE 2).

There was no association between the use of CAM and clinical variables such as age, sex, disease activity or the presence of anxiety

TABLE 1. Sociodemographic and clinical characteristics of patients with inflammatory bowel disease.

	IBD (n=227)		IBD (n=227)
Age (years)	41.19±14.49	Disease activity (CD)	
Female gender	130 (57.27)	Remission	95 (75.40)
Family income (BRL)	3107.79±2260.60	Mild	16 (12.70)
Christian religion	171 (75.33)	Moderate	14 (11.11)
Years of study		Severe	1 (0.79)
≤5	17 (7.49)	Partial Mayo score (points)	2.31±2.43
5 < x ≤9	49 (21.59)	Disease activity (UC)	
9 < x ≤12	104 (45.81)	Remission	61 (60.40)
>12	57 (25.11)	Mild	27 (26.73)
Social Economic Stratum*		Moderate	13 (12.87)
A	9 (3.97)	Medications in use	
B	114 (50.22)	5 ASA derivatives	58 (25.55)
C	97 (42.73)	Immunosuppressants	105 (46.25)
D	7 (3.08)	Steroid	7 (3.08)
Brazil State		Anti-TNF agents	94 (41.41)
Rio de Janeiro	84 (37)	Ustekinumab	1 (0.44)
São Paulo	143 (63)	Vedolizumab	1 (0.44)
Crohn's disease	126 (55.51)	No medication	3 (1.32)
Montreal Classification (CD)		Adherence to medication	
Age at diagnosis		High	68 (31.48)
A1 (<17 y)	20 (15.87)	Medium	87 (40.28)
A2 (17–40 y)	88 (69.84)	Low	61 (28.24)
A3 (>40 y)	18 (14.29)	Morisky adherence scale (points)	6.34±1.64
Disease location		Previous hospitalization	140 (61.67)
L1 (ileal)	40 (31.75)	Number of previous hospitalizations	1.38±0.49
L2 (colonic)	20 (15.87)	Previous surgery	69 (30.40)
L3 (ileocolonic)	66 (52.38)	Number of previous surgeries	2.20±2.31
Disease behavior		Comorbidities	71 (31.28)
B1 (non-stricturing, non-penetrating)	54 (42.86)	Quality of life (IBDQ)	
B2 (stricturing)	43 (34.13)	Excellent	51 (22.47)
B3 (penetrating)	29 (23.02)	Good	110 (48.46)
Perianal disease	44 (34.92)	Regular	47 (20.70)
Disease extent (UC)		Poor	19 (8.37)
Proctitis	20 (19.80)	IBDQ total score (points)	164.60±40.75
Left-sided colitis	25 (24.75)	Presence of anxiety	102 (44.93)
Pancolitis	56 (55.45)	HADS Anxiety (points)	7.15±4.82
Time since diagnosis (y)	10.58±7.50	Presence of depression	72 (31.72)
Harvey Bradshaw Index (points)	3.19±3.32	HADS Depression (points)	5.65±4.22

IBDQ: Inflammatory Bowel Disease Questionnaire; HADS: Hospital Anxiety and Depression Scale; BRL: Brazilian currency; CD: Crohn's disease; UC: ulcerative colitis.

Data are expressed as mean ± standard deviation or frequency (proportion). BRL, Brazilian currency. *Brazil Social Economic Stratum (ABEP - Associação Brasileira de Empresas de Pesquisa/Brazilian Market Research Association – 2016 – www.abep.org – abep@abep.org 1).

TABLE 2. Use and satisfaction with the use of CAM in patients with inflammatory bowel disease.

	Tea (n=60)	Probiotics (n=47)	Omega 3/ glutamine (n=22)	Homeopathy (n=23)	Herbal therapy (n=20)	Chinese medicine* (n=26)
Frequency of use in relation to the total number of patients	60/227 (26.43)	47/227 (20.70)	22/227 (9.69)	23/227 (10.13)	20/227 (8.81)	26/227 (11.45)
Current use for IBD	12/227 (5.29)	12/227 (5.29)	4/227 (1.76)	2/227 (0.88)	1/227 (0.44)	0
Current use for other indication	15 (25.0)	12 (25.53)	3 (13.64)	2 (8.69)	6 (30.0)	7 (26.92)
Previous use of CAM	33 (55.0)	23 (48.94)	15 (68.18)	19 (82.62)	13 (65.0)	19 (73.08)
Time of CAM use (months)	9.94±11.01	6.89±6.38	3.51±3.86	10.97±7.53	8.32±9.50	7.18±7.43
Frequency of CAM use						
Daily	34 (58.62)	31 (67.39)	20 (95.24)	17 (94.44)	16 (80.0)	0
Weekly or monthly	16 (27.59)	9 (19.57)	1 (4.76)	0	0	26 (100)
Sporadic use	8 (13.79)	6 (13.04)	0	1 (5.56)	4 (20.0)	0
Who indicated						
By yourself	26 (43.33)	24 (57.14)	9 (40.91)	5 (21.74)	3 (15.0)	7 (26.92)
Health team	6 (10.0)	13 (30.96)	12 (54.54)	13 (56.52)	10 (50.0)	9 (34.62)
Family or friend	28 (46.67)	5 (11.90)	1 (4.55)	5 (21.74)	7 (35.0)	10 (38.46)
Satisfaction with CAM use						
Pleased	40 (66.67)	15 (31.91)	11 (50.0)	9 (39.13)	12 (60.0)	16 (61.54)
Dissatisfied	6 (10.0)	5 (10.64)	1 (4.55)	5 (21.74)	4 (20.0)	6 (23.08)
Indifferent	14 (23.33)	27 (57.45)	10 (45.45)	9 (39.13)	4 (20.0)	4 (15.38)
Physician aware of the use	21 (35.0)	18 (38.30)	7 (31.82)	12 (52.17)	10 (50.0)	12 (46.15)

CAM: complementary and alternative medicine; IBD: inflammatory bowel disease.

*Chinese medicine includes the use of acupuncture (n=22; 84.62%), auriculotherapy (n=3; 11.54%) and reiki (n=1; 3.85%).

or depression (TABLES 3 and 4). However, there was an association between the use of CAM and the quality of life measured through the IBDQ (OR: 2.084; 95%CI: 1.147–3.786; $P=0.0159$) (TABLE 4), showing that patients with regular/poor quality of life are more likely to use CAM when compared to patients with good/excellent quality of life. Another factor associated with the use of CAM was the disease duration (OR: 0.956; 95%CI: 0.918–0.995; $P=0.0260$) (TABLE 4). Drug adherence was considered satisfactory among patients, with no difference between users and non-users of CAM for IBD.

DISCUSSION

Studies on the use of CAM in Latin America are scarce and the concepts and types used in practice, in addition to being very variable, have been modified according to the view of the practitioner, be it sociological, scientific, ideological, or economic⁽²⁰⁾. Historically, CAM has been defined as unconventional treatments and health practices, not included in the curriculum of medical schools, including Brazilian schools, and generally not used in hospitals, where there is a predominance of modern medicine. The use of CAM has progressively increased in developed countries aiming at disease prevention and health promotion, while in developing countries, the accessibility to this medicine is still very variable.

Brazil is a multiracial country with health practices influenced by indigenous beliefs and customs from Africa, culminating in the use of more natural and less expensive medicines in some regions, often with the use of natural plants and herbs. In recognition of

this practice, in 2006, CAM was incorporated into the SUS, the public health system, which started to make traditional Chinese medicine/acupuncture, homeopathy, herbal and herbal practices available to the population, in the form of Complementary and Integrative Practices of Brazil (PIC)⁽⁹⁾.

A recent Brazilian population study showed a 4.5% prevalence of CAM use by the adult population⁽⁵⁾. The data were obtained through a survey with interviews with the inclusion of 60,202 participants from different geographic regions, in the period 2013–2014. The profile of CAM users was characterized by the predominance of females, over 40 years old, higher educational level and residents in the North and South regions of the country. On the other hand, the use of CAM provided by SUS, a public health system, most popular and with the greatest impact on the most vulnerable populations, was more expressive in the Northeast and North regions of the country, used by women with a lower educational level, which can be explained by the more frequent use of popular practices in relation to the use of therapies with higher cost. The South and Southeast regions of the country, the most rich regions, were characterized with CAM provided by the private health service⁽⁵⁾.

The use of CAM among patients with IBD is a common practice around the world^(21–23), ranging from 21% to 60%⁽⁷⁾. The most used CAM were herbal or plant-based therapies⁽²²⁾, probiotics, fish oil, natural products and massage therapy⁽²¹⁾. In more than 50% of CAM users, an association of multiple types of alternative therapy was found^(21,22). In our sample, we found that the most used CAM were probiotics and homemade teas, perhaps due

TABLE 3. Sociodemographic and clinical characteristics of patients with inflammatory bowel disease according to CAM use.

	Use of CAM (n=73)	Non-use of CAM (n=154)	P-value
Age (years)	42.42±14.79	40.61±14.35	0.3794
Female gender	47 (64.38)	83 (53.90)	0.1357
Family income (minimum wage, BRL)	3.97±3.33	3.47±2.21	0.2191
Years of study >9 years	56 (76.71)	105 (68.18)	0.1862
Social Economic Stratum*			
A	2 (2.74)	7 (4.54)	0.2728
B	42 (57.53)	72 (46.75)	
C	28 (38.36)	69 (44.81)	
D	1 (1.37)	6 (3.90)	
Brazil State			
Rio de Janeiro	28 (38.36)	56 (36.36)	0.7715
São Paulo	45 (61.64)	98 (63.64)	
Crohn's disease	46 (63.01)	80 (51.95)	0.1171
Time since diagnosis (y)	8.95±6.91	11.35±7.66	0.0245
Disease activity (Crohn's disease)			
Remission	32 (69.57)	63 (78.75)	0.1243
Mild	5 (10.86)	11 (13.75)	
Moderate	9 (19.57)	5 (6.25)	
Severe	0	1 (1.25)	
Harvey Bradshaw Index, (points)	3.78±3.32	2.86±3.30	0.2964
Disease activity (ulcerative colitis)			
Remission	15 (55.56)	46 (62.16)	0.3490
Mild	10 (37.04)	17 (22.97)	
Moderate	2 (7.41)	11 (14.86)	
Partial Mayo score (points)	2.37±2.11	2.28±2.55	0.6734
Adherence to medication			
High	22 (30.99)	46 (31.72)	0.9081
Medium	30 (42.25)	57 (39.31)	
Low	19 (26.76)	42 (28.97)	
Morisky adherence scale (points)	6.36±1.61	6.33±1.65	0.8826
Quality of life (IBDQ)			
Excellent	14 (19.18)	37 (24.03)	0.0882
Good	30 (41.10)	80 (51.95)	
Regular	22 (30.14)	25 (16.23)	
Poor	7 (9.59)	12 (7.79)	
Quality of life (IBDQ)			
Excellent/good	44 (60.27)	117 (75.97)	0.0150
Regular/Poor	29 (39.73)	37 (24.03)	
IBDQ score (points)	159.2±40.59	167.1±40.71	0.1736
Presence of anxiety	35 (47.95)	67 (43.51)	0.5300
HADS Anxiety (points)	7.30±4.38	7.08±5.02	0.7521
Presence of depression	27 (36.99)	45 (29.22)	0.2403
HADS Depression (points)	5.89±4.12	5.53±4.27	0.5587

CAM: complementary and alternative medicine; BRL: Brazilian currency; IBDQ: Inflammatory Bowel Disease Questionnaire; HADS: Hospital Anxiety and Depression Scale. *Brazil Social Economic Stratum (ABEP - Associação Brasileira de Empresas de Pesquisa/Brazilian Market Research Association – 2016 – www.abep.org – abep@abep.org 1).

TABLE 4. Univariate logistic regression analysis for the use of complementary and alternative medicine among patients with inflammatory bowel disease.

	Odds ratio	95% confidence interval	P-value
Age (years)	1.009	0.989–1.028	0.3779
Gender (female vs male)	1.546	0.871–2.746	0.1369
Family income (BRL)	1.000	1.000–1.000	0.1561
Years of study (< 9y vs >9y)	0.651	0.343–1.234	0.1879
Brazil state (Rio Janeiro vs São Paulo)	1.089	0.613–1.935	0.7715
Crohn's disease vs ulcerative colitis	1.576	0.891–2.789	0.1183
Time since diagnosis (y)	0.956	0.918–0.995	0.0260
Disease activity vs remission (Crohn's disease)	2.005	0.941–4.274	0.0716
Harvey Bradshaw Index (points)	1.085	0.972–1.210	0.1449
Disease activity vs remission (ulcerative colitis)	1.314	0.538–3.209	0.5485
Partial Mayo score (points)	1.015	0.847–1.216	0.8734
Morisky adherence scale (points)	1.013	0.851–1.206	0.8823
Quality of life (IBDQ)			
Regular/poor vs excellent/good	2.084	1.147–3.786	0.0159
IBDQ score (points)	0.995	0.989–1.002	0.1739
Presence of anxiety	1.196	0.684–2.091	0.5302
HADS anxiety (points)	1.009	0.953–1.069	0.7508
Presence of depression	1.422	0.789–2.561	0.2413
HADS depression (points)	1.020	0.955–1.089	0.5570
Previous use of CAM	1.448	0.719–2.919	0.3000

BRL: Brazilian currency. IBDQ: Inflammatory Bowel Disease Questionnaire. HADS: Hospital Anxiety and Depression Scale. CAM: complementary and alternative medicine.

to economic status of patients from public hospitals. The main reason observed for the use an alternative therapy was the lack of effectiveness of conventional therapy, in addition to the presence of drug side effects⁽²¹⁾.

Patients report improvement in symptoms with the use of CAM, as well as a reduction of disease flares and a greater sense of well-being^(24,25). In the present study, we did not evaluate the positive or negative effects of using CAM among patients. Longitudinal studies should be performed and provide more reliable data on the benefits of using CAM on the disease symptoms.

These practices vary in different countries, as can be seen in a study carried out in Germany where there was a predominance of homeopathy (55%)⁽²³⁾, at rates much higher than those found in our study (0.88%). In a recent study in Portugal, 31% of the patients evaluated reported having used CAM at some point during the IBD treatment, while 12% reported to still use them⁽²⁶⁾. In Latin America, a Chilean study conducted with 200 IBD patients showed

a low prevalence of CAM use (25%), with phytotherapy being the most used (55%), followed by probiotics (42%)⁽²⁷⁾.

The absence of Brazilian studies on this topic demonstrates the need to expand this research, as we only approached two cities in the Southeast of Brazil. Despite the low rates of CAM use in the studied population, without a significant difference between the two cities ($P=0.77$), there was a higher frequency of use of CAM among the IBD patients seen in Botucatu (61.64%), a city from the interior of the state of São Paulo, which maintains some customs based on traditional medicine, when compared to patients treated in the city of Rio de Janeiro, a typically metropolitan region (38.36%).

The type of CAM used by the general Brazilian population varies according to regional sociodemographic conditions, probably related to accessibility and cost, with greater use of herbs and homemade teas being observed in inland cities and more modern practices such as acupuncture, aromatherapy, or Chinese medicine in large centers⁽⁵⁾.

Considering factors associated with use of CAM, among adult IBD population previous studies have shown that it is more prevalent in women ($P=0.03$), with high educational level ($P=0.02$), with a history of adverse events with conventional therapy ($P=0.000$) and active IBD ($P=0.005$)⁽²⁵⁾. A study carried out in Norway found that factors associated with the use of CAM among UC patients were age (OR: 0.97; 95%CI: 0.95–0.98; $P<0.001$), female gender (OR: 2.39; 95%CI: 1.45–3.94; $P<0.001$), educational level >12 years (OR: 2.25; 95%CI: 1.34–3.79; $P=0.02$), and presence of disease recurrence (OR: 3.81; 95%CI: 1.58–9.18; $P=0.003$). Among the CD patients, the associated factors were age (OR: 0.95; 95%CI: 0.93–0.98; $P=0.00$) and the presence of disease recurrence (OR: 5.58; 95%CI: 1.24–25.18; $P=0.03$)⁽²⁸⁾. At the beginning of the study, we postulated that these associated factors would be similar to the studies mentioned above, which was verified by the analysis performed. However, we observed no association between the use of CAM with the patient's sex, age, or educational level. However, the significant association in use of CAM in individuals with regular/poor quality of life suggests that patients seek improvement of the clinical condition in addition to the use of conventional IBD treatment. Therefore, we can assume the use of CAM is a consequential, and non-causal factor of worsening quality of life among IBD patients. In this study, we also observed that individuals with IBD with shorter duration of illness resorted to the use of CAM more frequently, possibly in an attempt to improve clinical outcomes faster, with less side effects, as adjuvants in IBD treatment. Despite this hypothesis, there was no association between disease activity assessed through clinical indexes and the use of CAM.

A previous study shows less medication adherence among patients who use CAM as a complementary therapy in IBD, in comparison to non-users of CAM or IBD patients who use CAM for other purposes⁽²⁴⁾. In the present study, drug adherence was not different between the CAM-users' and CAM-non-users' groups. Population studies with a larger number of patients should be carried out to assess the association between the use of CAM and its interference with medication adherence.

This study represents the initial step in assessing the CAM use as a complementary therapy in IBD in Brazil. We considered, as limitations of this study, the sample size, the inclusion of patients only from southeastern region of Brazil and the difficulty of verifying access to CAM through the government health system. For these reasons, the expansion of this study is justified with the inclusion of other referral centers for IBD from other Brazilian

geographic regions, mainly in the North and Northeast regions, which are places with greater tradition in the use of CAM⁽⁵⁾, and the better characterization of the use of CAM.

CONCLUSION

The prevalence of CAM use was low, and classified as satisfactory, according to our patients' opinion, among Brazilian IBD patients. The factors associated with CAM use were poor quality of life and shorter disease duration, hypothesizing that patients seek the use of these therapies as an alternative form of symptom control despite IBD treatment. Nationwide population studies should be carried out to better characterize the use of CAM among IBD patients in Brazil.

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Authors' contribution

All authors contributed to this manuscript. Sassaki LY and Zaltman C contributed to the conception and design of the study and drafting the article, Henriques DP, Oliveira RR, Vanni J, Lima HP, Otiti JV, Neves FRM and Hammerle MB contributed to the acquisition, analysis and interpretation of data, and drafting the article. All the authors revised it critically for important intellectual content and final approval of the version to be submitted.

Orcid

Débora Pereira Henriques: 0000-0003-1547-8157.

Rebeca Rodrigues de Oliveira: 0000-0002-2372-7216.

Jeslei Vanni: 0000-0002-8173-684X.

Henrique Patriota de Lima: 0000-0003-0377-758X.

Jean Vianney Otiti: 0000-0001-8615-9845.

Fabio Ricardo Monteiro Neves: 0000-0001-6242-6400.

Marcia Beiral Hammerle: 0000-0001-7319-9522.

Lígia Yukie Sassaki: 0000-0002-7319-8906.

Cyrila Zaltman: 0000-0002-5236-6501.

Henriques DP, Oliveira RR, Vanni J, Lima HP, Otiti JV, Neves FRM, Hammerle MB, Sassaki LY, Zaltman C. Uso de medicina complementar e alternativa em pacientes brasileiros com doença inflamatória intestinal. *Arq Gastroenterol*. 2022;59(3):375-82.

RESUMO – Contexto – O tratamento convencional da doença inflamatória intestinal (DII) é baseado na terapia medicamentosa, mas diferentes estudos têm mostrado aumento progressivo do uso de medicina complementar e alternativa (MCA) na abordagem dos pacientes. As modalidades de MCA mais usadas compreendem: acupuntura, medicina tradicional chinesa, medicina ayurvédica, homeopatia e fitoterapia, bem como práticas mais modernas, como aromaterapia e reflexologia. Os dados do uso de MCA no Brasil são escassos e não há estudos entre pacientes brasileiros com DII. **Objetivo** – O objetivo do estudo foi avaliar a frequência e os fatores associados com o uso de MCA entre pacientes com DII, além de estimar a satisfação com o uso de MCA. **Métodos** – Foi realizado estudo transversal em pacientes adultos ambulatoriais com DII oriundos de dois centros de referência no sudeste do Brasil, com amostra de 227 indivíduos. Foi aplicado questionário semiestruturado contendo produtos como – chá, probióticos, ômega 3 ou glutamina, homeopatia e fitoterapia, além de fatores associados ao uso de MCA e a satisfação do paciente. Utilizamos estatística descritiva, testes de associação ($P < 0,05$) e regressão logística para análise estatística. **Resultados** – No total, 126 pacientes com doença de Crohn e 101 com retocolite ulcerativa foram incluídos. A média de idade foi $41,19 \pm 14,49$ anos e 57,27% eram do sexo feminino. O tempo desde o diagnóstico foi de $10,58 \pm 7,5$ anos, e a maioria dos pacientes estava em remissão clínica. Vinte e nove pacientes (12,8%) relataram ter usado MCA para o tratamento de DII, como chá (5,29%), probióticos (5,29%), ômega-3 ou glutamina (1,76%), homeopatia (0,88%) e fitoterápicos (0,44%). Apesar da baixa frequência, os pacientes ficaram satisfeitos com o uso ($> 50\%$). Não houve diferença entre o uso de MCA entre os pacientes com doença de Crohn em comparação com pacientes com retocolite ulcerativa ($P = 0,1171$). Os fatores associados com o uso de MCA foram qualidade de vida regular ou ruim (Odds ratio 2,084; intervalo de confiança de 95% 1,147–3,786, $P = 0,0159$) e menor tempo desde o diagnóstico (Odds ratio 0,956; intervalo de confiança de 95% 0,918–0,995; $P = 0,0260$). **Conclusão** – A prevalência do uso de MCA foi baixa, mas satisfatória entre os pacientes com DII. O uso de MCA tem sido associada a baixa qualidade de vida e menor duração da doença.

Palavras-chave – Medicina complementar e alternativa; doença de Crohn; colite ulcerativa; doença inflamatória intestinal.

REFERENCES

1. Gomollón F, Dignass A, Annese V, Tilg H, Van Assche G, Lindsay JO, et al. European Evidence-based Consensus on the Diagnosis and Management of Crohn's Disease 2016: Part 1: Diagnosis and Medical Management. *J Crohns Colitis*. 2017;11:3-25. doi: 10.1093/ecco-jcc/jjw168.
2. Magro F, Gionchetti P, Eliakim R, Ardizzone S, Armuzzi A, Barreiro-de Acosta M, et al. European Crohn's and Colitis Organisation [ECCO]. Third European Evidence-based Consensus on Diagnosis and Management of Ulcerative Colitis. *J Crohns Colitis*. 2017;11:649-70. doi: 10.1093/ecco-jcc/jjx008.
3. Eisenberg DM, Davis RB, Ettner SL, Appel S, Wilkey S, Van Rompay M, et al. Trends in alternative medicine use in the United States, 1990-1997: results of a follow-up national survey. *JAMA*. 1998;11;280:1569-75.
4. Astin JA. Why patients use alternative medicine: results of a national study. *JAMA*. 1998;279:1548-53.
5. de Moraes Mello Boccolini P, Siqueira Boccolini C. Prevalence of complementary and alternative medicine (CAM) use in Brazil. *BMC Complement Med Ther*. 2020;20:51. doi:10.1186/s12906-020-2842-8.
6. National Center for Complementary and Alternative Medicine (NCCAM). What is complementary and alternative medicine? 2020. [Internet]. Available from: <http://nccam.nih.gov/health/whatiscam>
7. Lin SC, Cheifetz AS. The Use of Complementary and Alternative Medicine in Patients with Inflammatory Bowel Disease. *Gastroenterol Hepatol*. 2018;14: 415-25.
8. Torres J, Ellul P, Langhorst J, Mikocka-Walus A, Barreiro-de Acosta M, Basnayake C, et al. European Crohn's and Colitis Organisation Topical Review on Complementary Medicine and Psychotherapy in Inflammatory Bowel Disease. *J Crohns Colitis*. 2019;13:673-85e.
9. Brasil. Ministry of Health. National Policy for Complementary and Integrative Practices. Ordinance n. 971. Brasília: Brazilian Federal Register, n.84, section I; 2006. p. 20-4.
10. Brazilian Association of Research Companies / Brazilian Market Research Association - 2016 - www.abep.org - abep @ abep.

11. Silverberg MS, Satsangi J, Ahmad T, Arnott ID, Bernstein CN, Brant SR, et al. Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. *Can J Gastroenterol*. 2005;19:5A-36A.
12. Satsangi J, Silverberg MS, Vermeire S, Colombel JF. The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications. *Gut*. 2006;55:749-53.
13. Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. *Lancet*. 1980;315:514.
14. Lewis JD, Chuai S, Nessel L, Lichtenstein GR, Aberra FN, Ellenberg JH. Use of the noninvasive components of the Mayo score to assess clinical response in ulcerative colitis. *Inflamm Bowel Dis*. 2008;14:1660-6.
15. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. *J Clin Hypertens (Greenwich)*. 2008;10:348-54.
16. Trindade AJ, Ehrlich A, Kornbluth A, Ullman TA. Are your patients taking their medicine? Validation of a new adherence scale in patients with inflammatory bowel disease and comparison with physician perception of adherence. *Inflamm Bowel Dis*. 2011;17:599-604.
17. Pontes RM, Miszputen SJ, Ferreira-Filho OF, Miranda C, Ferraz MB. Qualidade de vida em pacientes portadores de doença inflamatória intestinal: tradução para o português e validação do questionário "Inflammatory Bowel Disease Questionnaire" (IBDQ). *Arq Gastroenterol*. 2004;41:137-143.
18. Irvine EJ. Quality of life--measurement in inflammatory bowel disease. *Scand J Gastroenterol*. 1993;199(Suppl):36-39.
19. Botega NJ, Bio MR, Zomignani MA, Garcia C, Pereira WA. Mood disorders among medical in-patients: A validation study of the Hospital Anxiety and Depression Scale (HAD). *Rev Saude Publica*. 1995;29:355-63.
20. de Barros NF, Nunes ED. Complementary and alternative medicine in Brazil: one concept, different meanings. *Cad Saude Publica*. 2006;22:2023-39. doi:10.1590/s0102-311x2006001000002
21. Weizman AV, Ahn E, Thanabalan R, Leung W, Croitoru K, Silverberg MS, Steinhart AH, Nguyen GC. Characterisation of complementary and alternative medicine use and its impact on medication adherence in inflammatory bowel disease. *Aliment Pharmacol Ther*. 2012;35:342-9.
22. Hilsden RJ, Verhoef MJ, Best A, Pocobelli G. Complementary and alternative medicine use by Canadian patients with inflammatory bowel disease: results of a national survey. *Am J Gastroenterol*. 2003;98:1563-8.
23. 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;6:19-26.
24. Nguyen GC, Croitoru K, Silverberg MS, Steinhart AH, Weizman AV. Use of Complementary and Alternative Medicine for Inflammatory Bowel Disease Is Associated with Worse Adherence to Conventional Therapy: The COMPLIANT Study. *Inflamm Bowel Dis*. 2016;22:1412-7. doi:10.1097/MIB.0000000000000773
25. Bertomoro P, Renna S, Cottone M, Riegler G, Bossa F, Giglio L, et al. Regional variations in the use of complementary and alternative medicines (CAM) for inflammatory bowel disease patients in Italy: An IG-IBD study. *J Crohns Colitis*. 2010;4:291-300.
26. Portela F, Dias CC, Caldeira P, Cravo M, Deus J, Gonçalves R, et al. The who-when-why triangle of complementary and alternative medicine use among Portuguese IBD patients. *Dig Liver Dis*. 2017;4:388-96.
27. Fernández A, Simian D, Quera R, Flores L, Ibáñez P, Lubascher J, et al. Complementary and alternative medicina in patients with inflammatory bowel disease: A survey performed in a tertiary center in Chile. *Complement Ther Med*. 2018;40:77-82.
28. Oheim R, Hoivik ML, Solberg IC, Moum B. The IBSEN Study Group. Complementary and alternative medicine in patients with inflammatory bowel disease: The results of a population-based inception cohort study (IBSEN). *J Crohns Colitis*. 2012;6:345-53.

