An Autoimmune Protocol Diet Improves Patient-Reported Quality of Life in Inflammatory Bowel Disease

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Background: Prior studies suggest dietary modification may improve clinical response or remission rates in patients with inflammatory bowel disease (IBD). Our aim was to examine whether an autoimmune protocol diet improves quality of life in patients with active Crohn disease (CD) and ulcerative colitis (UC).

Methods: We conducted an uncontrolled clinical trial of the autoimmune protocol diet in adult patients with active IBD (Harvey–Bradshaw Index ≥ 5 for CD or partial Mayo score ≥ 3 for UC, and erosions/ulcers on endoscopy and/or elevated fecal calprotectin). The dietary intervention consisted of a 6-week elimination phase, followed by a 5-week maintenance phase. Short Inflammatory Bowel Disease Questionnaire (SIBDQ) was completed at baseline, and weeks 3, 6, 9, and 11.

Results: The final cohort included 6 UC and 9 CD participants. Mean SIBDQ score improved significantly from baseline (46.5) to weeks 3 (54.0, $P = 0.02$), 6 (53.3, $P = 0.02$), 9 (62.0, $P = 0.03$), and 11 (60.5, $P = 0.05$). Among participants completing all 5 surveys, mean SIBDQ increased from 46.5 to 61.5 by week 11 ($P = 0.03$). By week 3, participants experienced significant improvements in bowel movement frequency (36%, $P = 0.04$), stress (28%, $P = 0.01$), and ability to perform leisure/sport activities (29%, $P = 0.02$). Effects were not significantly different between CD and UC participants.

Conclusions: Dietary modification can improve quality of life as early as week 3 in patients with active IBD. Larger randomized controlled trials are needed to examine dietary interventions in IBD.

Key Words: autoimmune protocol, Crohn disease, diet, inflammatory bowel disease, quality of life, ulcerative colitis

BACKGROUND

Inflammatory bowel diseases (IBD), including Crohn disease (CD) and ulcerative colitis (UC), are chronic disorders of the gastrointestinal tract affecting approximately 1.5 million people in the United States, and increasing in developing countries.[1] The etiology of IBD is multifactorial, attributed to gut dysbiosis, genetic susceptibility, and environmental triggers such as Westernization of diet, lifestyle, tobacco use, stress,

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Registry: This trial has been registered on ClinicalTrials.gov, NCT03512327.

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Synopsis: Our aim was to examine whether the autoimmune protocol diet improves quality of life (QOL), as measured by Short Inflammatory Bowel Disease Questionnaire (SIBDQ), in patients with active Crohn's disease and ulcerative colitis. We found that mean SIBDQ score increased significantly during the dietary intervention, with improvements in QOL observed as early as week 3.

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infections, and medications.[2] IBD can manifest with a range of symptoms, including diarrhea, abdominal pain, gastrointestinal bleeding, weight loss, and fatigue, which substantially impact a patient's quality of life (QOL), both physically and psychosocially.[3] Unfortunately, rates of clinical remission and mucosal healing, the 2 primary goals of IBD therapy, remain low, despite targeted biological and small molecule therapies for moderate-to-severe IBD.[3] With increasing understanding of the complex interaction between diet, the microbiome, and the immune system, dietary modification has become a key target for the symptomatic and therapeutic modulation of IBD.

A major stimulus for targeting diet comes from IBD patients, who identify and often avoid foods that exacerbate their symptoms. Advice from healthcare providers regarding diet and nutrition varies.[4] High-quality evidence is lacking, and few studies have systematically studied the relationship between specific dietary factors and IBD activity. Several observational studies have examined the association between dietary factors and onset of IBD. For example, a Western diet—high in omega-6 fatty acids, processed foods, and red meats, and low in fiber, fruits, and vegetables—is associated with the development of IBD.[5–7] Small, nonrandomized clinical studies of exclusion diets in patients with established and active IBD are promising. The specific carbohydrate diet, which restricts grains, dairy, and refined sugar intake, improved both clinical outcomes and laboratory biomarkers in pediatric IBD patients.[8–10] Other elimination diets, such as an anti-inflammatory diet, Crohn disease exclusion diet with or without partial enteral nutrition, low "Fermentable Oligo-, Di-, Mono-saccharides And Polyols" (FODMAP) diet, and the recent "Crohn's Disease-TReatment-with-EATing" (CD-TREAT) diet have demonstrated improvement in symptoms among patients with IBD.[11, 12]

The autoimmune protocol (AIP) diet, an extension of the Paleolithic diet,[13] involves elimination of foods that may act as antigens, stimulate mucosal inflammation, and/or trigger dysbiosis within the gastrointestinal tract.[13] The diet involves an initial elimination phase of multiple food groups, including grains, legumes, nightshades, eggs, dairy, nuts and seeds, coffee, alcohol, refined/processed sugars, and industrial seed oils, as well as food additives and nonsteroidal anti-inflammatory drugs.[13, 14] The preparation and consumption of fresh, nutrient-dense foods, fermented foods and probiotics, and bone broth is emphasized during this initial phase, while lifestyle factors such as physical activity, stress management, sleep, and support system formation are also addressed. The initial elimination phase is followed by a maintenance phase, during which elimination of these food groups is sustained, until individuals symptomatically improve. Staged reintroduction of eliminated food groups is the last phase, which allows individuals to identify unique foods or food groups associated with symptoms and possibly also disease aggravation.[13]

Despite data supporting clinical improvements using dietary therapy in IBD, we have fewer data evaluating the impact of dietary interventions on patient-reported QOL. Food-related quality of life (FRQoL) is a newer concept that specifically evaluates the psychosocial factors surrounding eating behaviors and was recently examined in both IBD and irritable bowel syndrome patients.[15] The highest FRQoL was reported in IBD patients in remission, whereas the use of more dietary treatments (eg, number of diets, types of diets) was associated with decreased FRQoL for both IBD and IBS patients, suggesting both clinical and dietary factors can influence QOL measures.[15]

We recently conducted an uncontrolled clinical trial to examine the efficacy of the AIP diet in adults with active IBD.[16] Here, we sought to examine the effect of the AIP diet on patient-reported QOL in patients with active CD and UC. This article presents the QOL analyses from the primary study.[16]

METHODS

We conducted a single-center, open-label, uncontrolled trial to examine the efficacy of an AIP diet in patients with active CD and UC as previously described.[16]

Adults (>18 y of age) with CD and a Harvey–Bradshaw Index (HBI) score ≥ 5, or UC and a partial Mayo score ≥ 3, as well as objective evidence of active disease (ulcerations/erosions on endoscopy within 7 mo and/or elevated fecal calprotectin [FC; >50 µg/g] within 1 month of enrollment) were eligible for the study. Exclusion criteria included pregnant or breast-feeding women; known celiac disease or history of positive tissue transglutaminase antibody; evidence of untreated infection (eg, *Clostridium difficile*); presence of a stoma or J-pouch; bowel surgery within 12 weeks prior to enrollment or deemed likely during the study period; and use of tube or enteral feeding, elemental diet, or parenteral alimentation within 4 weeks of study initiation. Dosage of medications being used to treat IBD prior to enrollment was advised to remain stable during the study period, with the exception of corticosteroid taper. The study was approved by the Scripps Institutional Review Board and registered on ClinicalTrials.gov (identifier NCT03512327).

Dietary Intervention

The AIP dietary intervention consisted of both a 6-week elimination phase, with staged elimination of grains, legumes, nightshades, dairy, eggs, coffee, alcohol, nuts and seeds, refined/processed sugars, oils, nonsteroidal anti-inflammatory drugs, and food additives; followed by a 5-week maintenance phase, during which food group reintroduction was not allowed. All participants began the study on September 5, 2016 and completed the study on December 10, 2016. A certified health coach supervised the dietary intervention and educated participants on the importance of nutrient density and fermented foods, whereas a registered dietitian provided one-to-one feedback to participants. Participants were asked to review their dietary intake with the health coach and dietitian during the study and were contacted once weekly with the dietary protocol for the following week. Dietary compliance was assessed at office visits

at weeks 6 and 12 with their healthcare provider. Handouts were also provided on forming a support system, grocery shopping and food preparation, sleep and sleep hygiene, stress management, and physical activity on a weekly basis. A private Facebook group was utilized to conduct health and group-based coaching, as well as dietary counseling. Investigators and study staff were excluded from the Facebook group, which study participants could use to communicate with one another, as well as the health coach and dietitian, as frequently as needed. Information from this private group remained blinded to the investigators, including after study completion.

Surveys

During the 11-week study, participants completed the Short Inflammatory Bowel Disease Questionnaire (SIBDQ), as well as open-ended questions, through an online survey portal. Surveys were conducted at baseline, and weeks 3, 6, 9, and 11. The SIBDQ is one of the most commonly utilized tools for evaluating QOL in patients with IBD, though its use is mainly in clinical trials.[17] It is a validated 10-item questionnaire that assesses IBD disease activity subjectively across multiple domains.[17] Total score ranges from 10 to 70, and patients with SIBDQ scores ≥ 50 are considered to have good health-related QOL.[18] In addition to the SIBDQ, the online survey also included open-ended questions regarding diet prior to study enrollment, sleep and exercise habits, and other health concerns. At baseline and follow-up office visits, additional information was collected regarding adherence to the diet protocol, IBD activity, and medication use. The partial Mayo score (for UC) or HBI (for CD) was utilized to examine clinical IBD activity at baseline, and weeks 6 and 11.

Statistical Analyses

Quantitative data analysis was performed using SPSS 24.0 (IBM Corporation, Armonk, NY). Descriptive statistics, including frequencies, percentages, means, and modes, were analyzed. Total SIBDQ scores for each participant were assessed at each survey time point—baseline, week 3, week 6, week 9, and week 11. Results of a 2 (CD/UC) × 3 (baseline/week 3/week 6) mixed design analysis of variance (ANOVA) indicated a significant effect of time ($F(2,6) = 9.45$, $P = 0.01$, $\eta_p^2 = 0.76$) during the elimination phase. Relationships between bivariate categorical variables, including diet adherence and IBD type, were tested using chi-square or Fisher exact test, if any cell of the contingency table contained a value of less than 5. Due to attrition at weeks 9 and 11, 2 (CD/UC) × 3 (baseline/week 3/week 6) mixed design ANOVAs examined changes over time, comparing the 2 IBD types with post hoc Bonferroni corrected *t*-tests used to examine where difference occurred. Differences were examined for participants completing measures at each time point using 1-way repeated-measures ANOVA. SIBDQ score was also analyzed as a dichotomous variable, with good health-related QOL defined as SIBDQ score ≥ 50, to determine whether a statistically significant change in QOL occurred over time. Results were considered significant if the *P* value was less than or equal to 0.05.

RESULTS

A total of 18 adult participants were enrolled, but 3 withdrew before the start of the study, due to an inability to commit to the proposed diet (Fig. 1). The final cohort included 9 participants with CD and 6 with UC (Table 1). Average disease duration was 19 years (SD 14.6). Seven participants (46.7%) were on biologic therapy at the start of the study, with mean duration of biologic use before study start 1.8 years (SD 2.5), and regimens as follows: adalimumab monotherapy (n = 2), infliximab monotherapy (n = 2), vedolizumab monotherapy (n = 1), and vedolizumab in combination with methotrexate (MTX; n = 1) or thiopurine (n = 1). Two participants were initiated on infliximab or vedolizumab within 3 months of starting the study. One participant with severe UC started infliximab 20 days before study initiation, whereas another participant with ileocolonic CD with postoperative recurrence and anastomotic stricture, maintained on oral MTX, started vedolizumab therapy (in addition to MTX) 75 days before study start. Mean duration of biologic use before study initiation, excluding these 2 participants, was 2.5 years (SD 2.7).

Review of Clinical Outcomes From Primary Study

In our primary study, 73% of participants achieved clinical remission by week 6 and maintained remission through the 5-week maintenance phase.[16] Among participants with complete follow-up data at weeks 6 and 11, mean partial Mayo score in those with UC (n = 6) significantly improved from 5.8 (SD 1.2) to 1.2 (SD 2.0) and 1.0 (SD 2.0), whereas mean HBI in those with CD (n = 7) significantly improved from 7.0 (SD 1.5) to 3.6 (SD 2.1) and 3.4 (*SD* 2.6).[16] We also identified decreases in serum C-reactive protein (CRP) from 3.9 (SD 5.2) at baseline to 3.4 (SD 5.3) at week 11 ($P = 0.82$), and FC from 471 (SD 562) at baseline to 112 (SD 104) at week 11 ($P = 0.12$). Among those with a baseline FC > 50 µg/g (n = 4), mean FC decreased from 701 (SD 563) at baseline to 139 (SD 113) by the end of the study ($P = 0.09$). Furthermore, endoscopic improvements were noted in the majority of participants completing endoscopic reassessment. At week 11, among those that completed follow-up endoscopy (UC, n = 5; CD, n = 2), Mayo endoscopy subscore improved by ≥1 point among 80% (4/5) of participants with UC, and in both participants with Crohn disease, by Rutgeerts score or Simple Endoscopic Score for Crohn disease.[16]

Survey Completion and Diet Adherence

A total of 13 participants filled out the baseline SIBDQ survey. Survey completion rate declined as the study progressed,

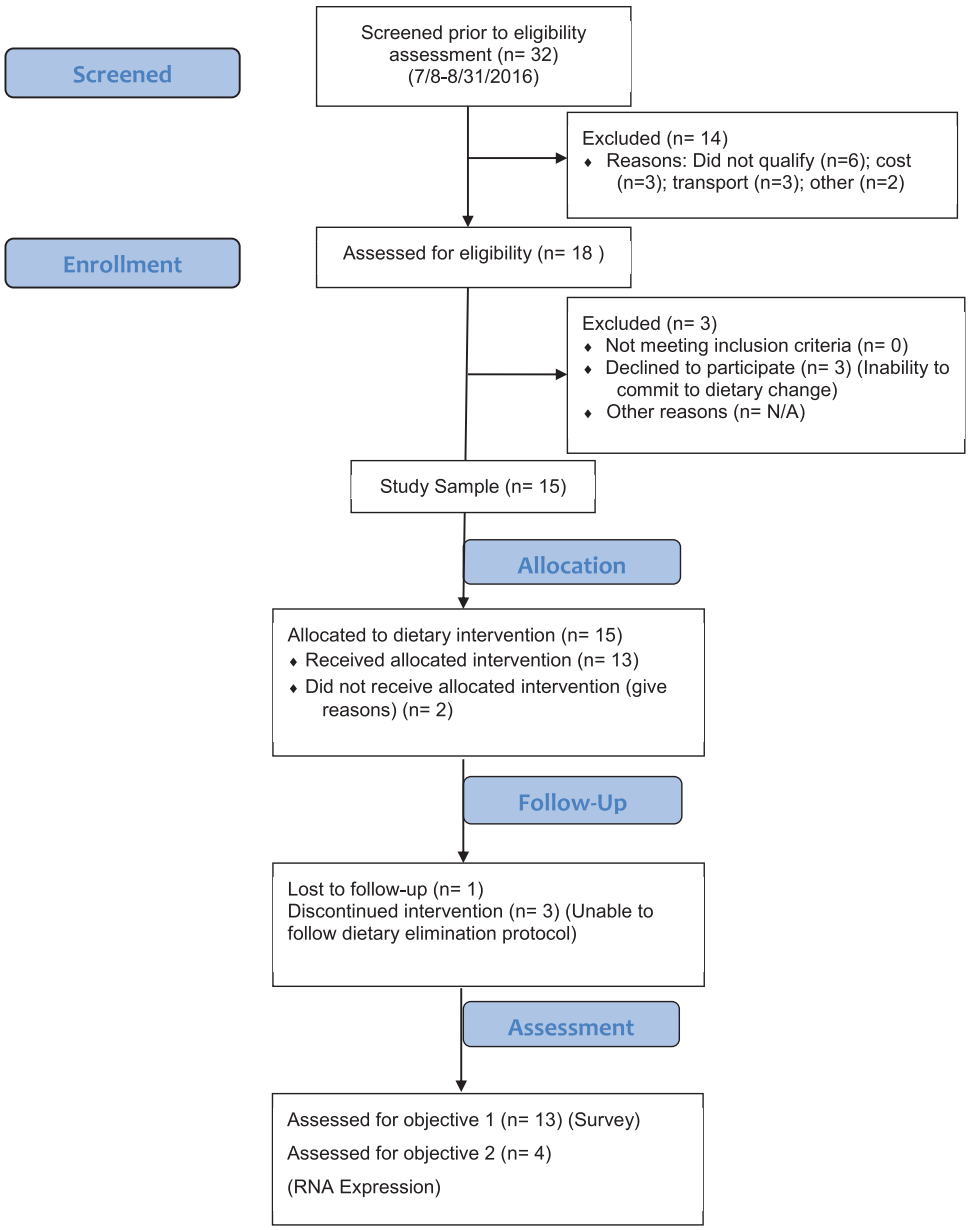

FIGURE 1. CONSORT flowchart.

from 86.7% (n = 13) at baseline, to 60% (n = 9) at week 3, 40% (n = 6) at week 6, and 26.7% (n = 4) at weeks 9 and 11.

At week 6 (end of elimination phase), 60% of participants (n = 9) had eliminated all prohibited foods, whereas 13.3% (n = 2) chose to eliminate all of these food groups within the first 2 weeks of the study, for an overall adherence rate of 73.3% at week 6. Three study participants (20%) were unable to follow the elimination protocol as advised, whereas 1 participant was lost to follow-up. When stratified by IBD type, 83.3% of UC participants (n = 5) and 66.7% of CD participants (n = 6) had eliminated all prohibited food groups by week 6 of the study (P_{exact} = 0.42 for difference in adherence between UC and CD). In the primary study, examination of clinical response rates by dietary adherence indicated that 66.7% of participants following the protocol (ie, elimination of specified food groups over a 6-wk period) achieved clinical remission at week 6, whereas 77.8% achieved remission at week 11 (end of maintenance phase and study).[16] Both participants eliminating all food groups within 2 weeks had documented clinical remission at weeks 6 and 11. There was no statistically significant association between pattern of adherence and clinical remission at week 6 or 11.

TABLE 1. Characteristics of Study Participants

	Crohn Disease (n = 9)	Ulcerative Colitis (n = 6)	Total Cohort (n = 15)
Age (y), mean (SD)	45 (22)	41 (15)	44 (19)
Female, n (%)	7 (78)	4 (67)	11 (73)
IBD duration (y), mean (SD)	21.4 (15.0)	15.3 (14.6)	19.0 (14.6)
IBD location	Ileal (n = 4) Colonic (n = 2) Ileocolonic (n = 2) Ileocolonic with perianal disease (n = 1)	Rectum (n = 1) Left side (n = 2) Pancolitis (n = 3)	n/a
Tobacco use			
Never, n (%)	5 (56)	6 (100)	11 (73)
Current, n (%)	0 (0)	0 (0)	0 (0)
Former, n (%)	4 (44)	0 (0)	4 (27)
IBD medication use			
Mesalamine, n (%)	2 (22)	5 (83)	7 (47)
Immunomodulator, n (%)	2 (22)	0 (0)	2 (13)
Biologic, n (%)	6 (67)	1 (17)	7 (47)
Systemic steroid, n (%)	1 (11)	2 (33)	3 (20)
Fecal calprotectin (µg/g), mean (range)	404 (0–1269)	376 (25–1177)	392 (0–1269)
C-reactive protein (mg/L), mean (SD)	7.6 (13.0)	6.7 (6.9)	7.3 (10.7)

n/a, not available.

SIBDQ Data

Total SIBDQ improved from baseline score (mean ± SD) of 46.5 ± 12.5 to week 3 (54.0 ± 7.7, $P = 0.02$), week 6 (53.3 ± 10.9, $P = 0.02$), and week 9 (62.0 ± 3.3, $P = 0.03$) (Table 2). Among the 4 participants with complete follow-up data (eg, surveys completed at all 5 time points), mean SIBDQ score increased from 46.5 at baseline to 61.5 at week 11 ($P = 0.07$). A repeated-measures ANOVA with a Greenhouse–Geisser correction, due to a violation of sphericity, determined that mean SIBDQ score in these 4 participants significantly improved over the time points ($F(1.30,3.91) = 10.05$, $P = 0.03$, $\eta_p^2 = 0.77$).

At baseline, mean SIBDQ score was 48.2 (SD 13.4) in UC participants and 45.5 (SD 12.8) in CD participants ($P_{diff} = 0.77$; Fig. 2). Results of a 2 (CD/UC) × 3 (baseline/week 3/week 6) mixed design ANOVA indicated a nonsignificant effect of IBD type ($F(1,3) = 3.03$, $P = 0.18$, $\eta_p^2 = 0.50$). At the start of the study, average SIBDQ score was 45.2 (SD 12.6) in female participants and 54.0 (SD 12.7) in male participants ($P_{diff} = 0.32$). Scores between female and male participants from baseline to any of the time points were unable to be compared, due to small numbers.

SIBDQ score was also analyzed as a dichotomous variable, with good health-related QOL defined as SIBDQ score ≥ 50. An exact McNemar test demonstrated no significant difference in the proportion of participants achieving good health-related QOL from baseline to week 3 ($P = 0.13$). However, 4 study participants with baseline poor QOL (eg, SIBDQ < 50) achieved increases in their score to ≥50 by week 3; conversely, none of the participants with baseline SIBDQ score ≥ 50 dropped below 50 at week 3. Similarly, there was no statistically significant difference in subjects who had a baseline score of SIBDQ ≥ 50 to week 6 ($P = 0.25$). Three study participants with poor QOL at baseline had increases in their score to ≥50 by week 6. The 4 participants who completed surveys at all time points achieved SIBDQ ≥ 50 at weeks 9 and 11, increased from a baseline mean score of 47.5 (SD 9.5).

Answers to individual questions on the SIBDQ were also analyzed. Compared with baseline, there were significant improvements in bowel movement frequency (36%, $P = 0.04$), stress (28%, $P = 0.01$), and ability to perform leisure/sport activities (29%, $P = 0.02$) at week 3. There was again a significant improvement in the performance of leisure/sport activities (31%, $P = 0.01$) at week 9, though other results were not statistically significant as the study progressed, likely due to the small sample size.

Intent to Treat Analysis

To account for missing data due to survey nonresponse, a missing values analysis was performed. This demonstrated that neither IBD type nor gender affected the distribution of missing data. Furthermore, a Little's Missing Completely at Random (MCAR) test suggested that the data were likely missing completely at random ($P = 0.35$).

An intent to treat approach was taken with participants' last available scores moved forward to evaluate the impact of

TABLE 2. Trend in Average SIBDQ Scores Over Time

	Week 0	Week 3	Week 6	Week 9	Week 11
Total responses, n	13	9	6	4	4
Ulcerative colitis, mean (SD), n	48.2 (13.4), 5	60.7 (2.1), 3	54.8 (13.6), 4	63.3 (2.3), 3	62.7 (2.5), 3
Crohn disease, mean (SD), n	45.5 (12.8), 8	50.7 (7.3), 6	50.5 (3.5), 2	58.0 (n/a), 1	54.0 (n/a), 1
Female, mean (SD), n	45.2 (12.6), 11	53.6 (8.1), 8	53.4 (12.1), 5	63.3 (2.3), 3	62.7 (2.5), 3
Male, mean (SD), n	54.0 (12.7), 2	57.0 (n/a), 1	53.0 (n/a), 1	58.0 (n/a), 1	54.0 (n/a), 1
Overall SIBDQ score, mean (SD)	46.5 (12.5)	54.0 (7.7)	53.3 (10.9)	62.0 (3.3)	60.5 (4.8)
SIBDQ ≥ 50, n (%)	4 (30.8)	6 (66.7)	4 (66.7)	4 (100)	4 (100)

n/a, not available.

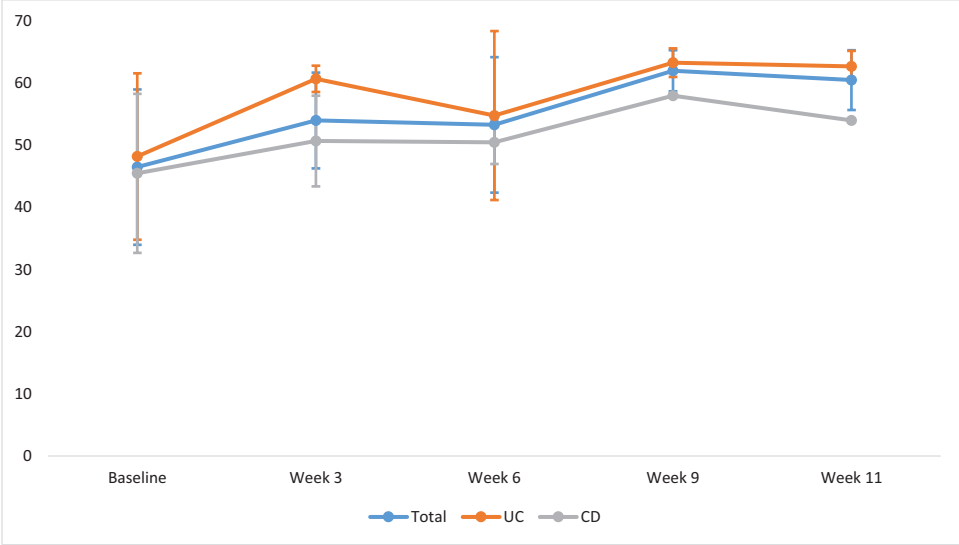

FIGURE 2. Effect of AIP diet on mean SIBDQ score.

the decline in survey participation as the study progressed. Results of a 2 (CD/UC) × 5 (baseline/week 3/week 6/week 9/week 11) mixed design ANOVA with a Greenhouse–Geisser correction continued to indicate a significant main effect of time ($F(4,44) = 7.98$, $P = 0.01$, $\eta_p^2 = 0.42$), with improvement in scores over the course of the study, and a nonsignificant effect of IBD type ($F(1,11) = 0.82$, $P = 0.39$, $\eta_p^2 = 0.07$).

Adverse Events

One participant with ileal CD with an ileocecal valve stricture withdrew before the end of elimination phase due to worsening symptoms, and an assessment at week 6 could not be made. Another participant with postoperative recurrence of ileal CD with known ileocolonic anastomotic stricture developed partial small bowel obstruction, requiring hospitalization, approximately 3 weeks into the study. This was attributed to a significant increase in consumption of raw vegetables, salad, and meat, and exacerbated by a lack of communication with the health coach and dietitian regarding his diet in the setting of known stricture. The participant's hospitalization was brief, with rapid clinical improvement with the use of intravenous steroids. He was discharged on a rapid steroid taper, but was subsequently lost to follow-up, and assessments were not made at weeks 6 or 11.

DISCUSSION

Dietary modification in IBD, common among patients with IBD, is gaining increasing awareness in the medical community as a potential modulator of symptoms and/or inflammatory burden. Although multiple studies have demonstrated an association between a Western diet and IBD development,[2, 5, 6] conclusive data demonstrating a role for dietary modification as an adjunct to IBD treatment is limited. In this study, we found that patients with clinically and objectively active IBD experienced improvements in symptoms and QOL after incorporating an AIP diet.

Previous studies have examined the effect of various elimination diets on IBD symptoms and QOL. A case series by Kakodkar et al[19] demonstrated that patients with IBD who

followed the specific carbohydrate diet (SCD), which restricts grains, dairy, and refined sugar intake, achieved a high QOL with a mean SIBDQ score of 60.9. Thirty-three (66%) participants had complete resolution of their symptoms after a mean of 9.9 months. However, all 50 participants were in remission, per the HBI or St. Mark Index score, and reported following the SCD prior to the onset of the study, so no baseline measurements were obtained for comparison.[19] Two recent studies by Suskind et al also examined the SCD for patients with IBD.[10, 20] In a survey-based study, 33% participants reported clinical remission after 2 months on SCD, and up to 42% at both 6 and 12 months.[20] A second prospective study evaluated the SCD among pediatric patients with mild-moderate IBD.[10] In this study, a dietitian provided dietary protocol education, counseling, resources, and meal/snack recommendations. Patients were able to contact the dietitian throughout the study, and compliance was assessed through 3-day food intake records before each clinical visit.[10] After 12 weeks, improvements in pediatric UC and CD disease activity index scores (PUCAI and PCDAI, respectively), as well as CRP, were demonstrated. Similar to the experience of SCD, the AIP diet appears to improve both clinical disease activity scores and objective markers of IBD.[16] The present study further describes temporal changes in QOL during the dietary intervention by comparing post-AIP elimination and maintenance phase results to baseline measurements among patients with active IBD.

The Crohn's Disease Exclusion Diet (CDED) is similar to the AIP diet, in that it aims to eliminate dietary components that may alter innate immunity, affect barrier function, and/or result in dysbiosis.[21] Two recent studies examined this diet among children and adults with active CD (pediatric CD activity index > 7.5 or HBI ≥ 4).[21, 22] After 6 weeks, 70% participants achieved remission, with majority normalizing CRP.[22] A subsequent study examined CDED, in combination with partial enteral nutrition (PEN), in children and adult CD patients non-responsive to therapy with infliximab or adalimumab.[21] Clinical remission was obtained in 61.9% of participants, whereas HBI and CRP significantly decreased.[21] Most recently, a multicenter randomized controlled trial was performed comparing exclusive enteral nutrition (EEN) to CDED, in combination with PEN, in children with mild-to-moderate CD, with a primary endpoint of dietary tolerance.[23] The protocol involved support with a dietitian, through education, provision of dietary instructions and recipes, and phone calls to support patients and assess adherence.[23] EEN was tolerated by 73.6% of participants, compared with 97.5% tolerance in those receiving a combination of CDED and PEN.[23] At the end of the 12-week study, 75.6% of participants receiving CDED and PEN were in steroid-free remission, versus 45.1% of those given EEN.[23] Similarly, in a case series by Olendzki et al,[11] disease activity was assessed in IBD patients who followed an anti-inflammatory diet. All participants who followed the anti-inflammatory diet were able to discontinue at least one of their prior IBD medications. Mean HBI score decreased by 9.5 and Modified Truelove and Witts Severity Index (MTLWSI) decreased by 7 for CD and UC, respectively.[11] Taken together, these studies suggest that elimination diets, with or without enteral nutrition, can be tolerable and effective, reducing subjective and objective measures of inflammation. Additional data is needed to examine sustainability of dietary modification, particularly given low adherence[4] to enteral nutrition among adults, and its effects on patient-reported QOL. Specifically, FRQoL may be a useful construct to determine the effects of dietary therapy, as it correlates with QOL measures. Through a reduced questionnaire (FRQoL-29), it has also been shown to be both reliable and valid across multiple IBD-related QOL measures, such as fatigue, mood, and social functioning.[24]

This study has several strengths. Participants were followed closely by a certified health coach and registered dietitian during the 11-week dietary intervention, during which time adherence was monitored and support was provided. Although the effect of these interactions on QOL was not examined, this should be a consideration in future studies. Prior work has demonstrated face-to-face education and written information materials provided to IBD patients improves disease-related patient knowledge,[25] which suggests regular follow-up with a health care provider and dietitian (in the context of dietary therapy) may positively influence QOL. SIBDQ surveys were administered approximately every 3 weeks, providing an opportunity to evaluate effects on QOL during both elimination and maintenance phases, and separately for CD and UC. Additionally, approximately half of the participants were on immunosuppressive agents prior to study enrollment, and the other half on mesalamine or no therapy at baseline, suggesting that the AIP diet may be used effectively with varying severities of IBD. Two participants (1 with CD and 1 with UC) initiated biologic therapy within 3 months of study start, but sensitivity analyses performed on the clinical outcomes from the primary study demonstrated that this did not alter the final results.[16]

Our study has several potential limitations as well. A study cohort of 15 participants is a relatively small sample size, and a control group was not incorporated, though we aimed to conduct a pilot study focused on examining the potential efficacy of the AIP diet. Despite the small sample size, significant results were still observed as early as week 3 with respect to QOL measures. Additionally, blinding is difficult to achieve in dietary studies, and participants' knowledge of the study goals may have introduced bias. We considered that participants willing to enroll in a study evaluating dietary therapy may be more likely to respond, which could have affected the generalizability of the results. In addition to the dietary intervention, education was also provided on sleep hygiene and stress management, which may have affected QOL outcomes. Future studies should investigate the role of these lifestyle factors on QOL and their effect on diet behavior, as well as the

role that regular follow-up with a healthcare provider and/or dietitian may play in outcomes. Last, we observed a progressive decline in survey participation, which limited examination of our results, though an intent to treat analysis demonstrated that results were preserved over time.

Our study suggests that the AIP diet has the potential to significantly improve QOL within a relatively short time frame, including during the elimination phase of dietary therapy. Effects were also sustained during the maintenance phase. The data suggest the clinical benefits are similar in both CD and UC patients, regardless of current IBD medication use. Therefore, the AIP diet, similar to other elimination diets, has the potential to be an effective adjunct to conventional IBD therapy. Larger randomized controlled trials are necessary to assess long-term efficacy and effects on QOL of dietary therapy for IBD.

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