Clinical and Mucosal Improvement With Specific Carbohydrate Diet in Pediatric Crohn Disease

*Stanley A. Cohen, *Benjamin D. Gold, ‡Salvatore Oliva, *Jeffery Lewis, *Angela Stallworth, *Bailey Koch, †Laura Eshee, and §David Mason

ABSTRACT

Objective: The aim of the study was to prospectively evaluate clinical and mucosal responses to the specific carbohydrate diet (SCD) in children with Crohn disease (CD).

Methods: Eligible patients with active CD (Pediatric Crohn's Disease Activity Index [PCDAI] ≥ 15) underwent a patency capsule and, if passed intact, capsule endoscopy (CE) was performed. Patients taking SCD were monitored for 52 weeks while maintaining all prescribed medications. Demographic, dietary, and clinical information, PCDAI, Harvey-Bradshaw Index (HBI), and Lewis score (LS) were collected at 0, 12, and 52 weeks. CEs were evaluated by an experienced reader blinded to patient clinical information and timing.

Results: Sixteen patients were screened; 10 enrolled; and 9 completed the initial 12-week trial—receiving 85% of estimated caloric needs before, and 101% on the SCD. HB significantly decreased from 3.3 ± 2.0 to 0.6 ± 1.3 ($P = 0.007$) as did PCDAI (21.1 ± 5.9 to 7.8 ± 7.1, $P = 0.011$). LS declined significantly from 2153 ± 732 to 960 ± 433 ($P = 0.012$). Seven patients continued the SCD up to 52 weeks; HB (0.1 ± 0.4) and PCDAI (5.4 ± 5.5) remained improved ($P = 0.016$ and 0.027 compared to baseline), with mean LS at 1046 ± 372 and 2 patients showed sustained mucosal healing.

Conclusions: Clinical and mucosal improvements were seen in children with CD, who used SCD for 12 and 52 weeks. In addition, CE can monitor mucosal improvement in treatment trials for pediatric CD. Further studies are critically needed to understand the mechanisms underlying SCD's effectiveness in children with CD.

Key Words: capsule endoscopy, Crohn disease, mucosal healing, nutritional therapy, specific carbohydrate diet

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The impact of nutrition as a therapeutic option for active Crohn disease (CD) in pediatric patients has received relatively little attention in the United States compared with the efforts that have been applied to evaluate pharmacotherapy for this chronic lifelong disease. Concerns for both the short- and long-term risks of medical therapy for CD in children warrant investigations of safer, sustainable, effective treatment strategies.

In contrast to the United States, enteral therapy is often the initial management approach for new-onset CD in Canada, Europe, and Japan (1,2). Two independently published meta-analyses demonstrated exclusive enteral nutrition to be at least as effective as corticosteroids in inducing disease remission in children with CD (3,4), achieving normalization of inflammatory markers and clinical remission rates in >80% of subjects (5), irrespective of disease phenotype (6).

The specific carbohydrate diet (SCD), developed in the 1920s (7) and popularized beginning in the 1940s (8,9), restricts complex carbohydrates and eliminates refined sugar from the diet, based on the rationale that the sugars and complex carbohydrates are malabsorbed and could eventuate in bacterial dysbiosis contributing to the intestinal inflammation of inflammatory bowel disease (IBD) (7–9). The SCD has had passionate adherents and advocates for the use of this diet as an intervention for a variety of different conditions, including IBD, irritable bowel syndrome, celiac disease, and autism (10). A retrospective clinical review of 7 patients with pediatric CD, naïve to immunosuppression, demonstrated clinical improvement (symptomatic and in inflammatory markers) within 3 months of diet initiation, and continuing for a duration from 5 to 30 months (14.6 ± 10.8 months) (11). No prospective studies have, however, been performed to date, which evaluate SCD efficacy in IBD.

Mucosal healing has become an important endpoint in prospective clinical IBD trials (12,13). Mucosal healing may be a cost-effective endpoint for biologic therapy (14) in adult CD, and when achieved, is associated with less inflammatory activity (15), less steroid use (15,16), and a decreased rate of bowel resection and hospitalization (16). Improvement of the intestinal surface, and specifically mucosal healing, is rarely sought as a primary outcome in prospective pediatric trials. Assessment of mucosal healing is particularly challenging in the pediatric CD population because 80% have small bowel (SB) involvement, with approximately 38% isolated to the SB as determined by colonoscopy and SB radiography (16). Capsule endoscopy (CE) has been shown in adults to be an effective method of evaluating mucosal healing in CD (17). In addition, CE safety and efficacy have been well documented in adult CD and, particularly, in pediatric IBD (18,19).

Thus, as a result of positive anecdotal results using the SCD in our own practice, this prospective, pilot short- and long-term study was designed as an initial attempt to evaluate the impact of the SCD on pediatric-onset CD. Furthermore, by using CE, in addition to standard clinical research scoring methods, this trial evaluated mucosal improvement and healing in the SB before introduction of the SCD and after 12 and 52 weeks. Moreover, the SCD was the sole intervention evaluated for these pediatric patients with CD during the short- and long-term phases of the study, because there were no

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From the *Children's Center for Digestive Health Care, †Children's Healthcare of Atlanta, Atlanta, GA, the ‡Department of Pediatrics, Pediatric Gastroenterology Unit, ''La Sapienza'' University of Rome, Rome, Italy, and §Given Imaging, Yoqneam, Israel.

Address correspondence and reprint requests to Stanley A. Cohen, MD, Children's Center for Digestive Healthcare, Children's Healthcare of Atlanta, Atlanta, GA 30342 (e-mail: scohen@gicareforkids.com).

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changes in concurrent medications or new medications introduced during the course of the study.

METHODS

Subject Demographics and Inclusion/Exclusion Criteria

This study was approved by the institutional review board at Children's Healthcare of Atlanta. Subjects between 10 (the lower age limit for Food and Drug Administration–approved CE at the onset of the study) and 21 years of age, with active CD (Pediatric Crohn's Disease Activity Index [PCDAI] $\geq$ 15, mild defined as 15–30 and moderate disease defined as >30) (20), requesting alternatives to standard pharmacologic therapy for newly diagnosed disease or escalation of pharmacologic treatment during a flare, were considered eligible for this trial. After obtaining informed consent (from the subject or the legal guardian) and assent from patients between 10 and 18 years old, subjects were assessed for eligibility to participate based on the inclusion and exclusion criteria listed in the following section.

Subjects were excluded from entering the study if they were unable to swallow the video capsule; were known or suspected to have intestinal obstruction; had motility disorders, known enteric infection, or prior abdominal surgery of the gastrointestinal tract, including SB or colonic resection (other than uncomplicated appendectomy or uncomplicated cholecystectomy); had diabetes mellitus type 1 or 2; were pregnant; had a pacemaker or other implanted electromedical device; had any condition that precluded compliance with the study and/or device instructions; had any life-threatening condition; or were concurrently participating in another clinical study. Patients and their parents received a full explanation of the requirements of the study by the study coordinator (A.S.), supervised by the referring physician and the investigators. Furthermore, subjects were instructed to remain on all prescribed medications (IBD and non-IBD) throughout the trial and the extension. The patency capsule (Given Imaging, Yoqneam, Israel) was ingested at week 0, and, if passed intact within 48 hours, CE was performed at baseline. The subjects who passed an intact patency capsule, indicating functional intestinal patency (21), were fully instructed in the SCD, adapted from the Crohn's and Colitis Foundation of America Web site (22) (Table 1), by a registered dietitian with certification as a specialist in pediatrics (B.K.). The specialist also obtained 3-day dietary records at baseline and again at 12 weeks. Patients were monitored at 4-week intervals and had access to a dietitian throughout their participation in the study to assist with any issues regarding the trial or the diet. Demographic information was collected at baseline. Dietary and clinical information on all of the patients were collected at weeks 0 and 12. Routine clinical examinations, assessments, and laboratory evaluations, including complete blood count count with differential, sedimentation rate, and metabolic profile at weeks 0 and 12, were evaluated. Because the first patients and families in the study responded well clinically to SCD and asked to continue the diet, the protocol was extended to 52 weeks, with clinical and laboratory data collected at that visit. The PCDAI and Harvey-Bradshaw Index (HBI) scores were calculated at each visit.

TABLE 1. Specific carbohydrate diet instructions

Foods that may be eaten
Fresh/frozen vegetables and legumes
Fresh/raw/dried fruits, unsweetened juices (not from concentrate)
Navy beans, lentils, peas, split peas, most nuts (unroasted preferably nuts coming directly from shells so that nothing is added), natural peanut butter (with no sugar), lima beans, string beans
Fresh/frozen meats, poultry, fish, eggs
Some (natural/hard) cheeses (cheddar, Colby, Swiss, Havarti), homemade yogurt fermented >24 hours (no sugar added), dry curd cottage cheese
Honey
Tea, coffee, mustard, vinegar, most oils
Foods to avoid
Canned vegetables
Canned fruits, unless packed in own juices
All grains, including flours
Potatoes, yams, parsnips
Chickpeas, bean sprouts, soybeans, mung beans, fava beans, and garbanzo beans
Seaweed and byproducts, including agar and carageenan
Processed, canned, breaded, smoked meats/fish
All milk, buttermilk, commercially prepared yogurt and sour cream, heavy cream, soy/rice/potato/oat/hemp milk
Instant tea or coffee, coffee substitutes, beer
Canola oil, mayonnaise (due to additives), cornstarch, chocolate or carob, bouillon cubes or instant soup bases, all products made with refined sugar, sugar substitutes, Stevia, pectin, ketchup, ice cream, molasses, corn or maple syrup, baking powder, medication containing sugar, all seeds, balsamic vinegar, fructo-oligo saccharides

Capsule Endoscopy

Those passing the patency capsule intact within 48 hours then ingested a small intestinal PillCam Capsule (Given Imaging) of the same size. Patients were asked to remain on a clear liquid diet from noon the day before. Patients were then also given polyethylene glycol-3550 on the evening before capsule ingestion, with dosing based on their age. Patients aged <12 years received 4 capfuls (68 g) of polyethylene glycol 30 minutes apart. Patients ages 12 and older received 8 capfuls (136 g) 30 minutes apart. All of the patients were to begin taking polyethylene glycol at approximately 2 PM the day before the PillCam SB. At the time of the CE, the child ingested 160 mg of simethicone to decrease intestinal gas. Patients were kept nil per os for 2 hours and then were able to drink water. Four hours after swallowing the capsule, per our center's routine CE protocol, patients were able to consume a dairy-free, nonred fruit–based smoothie, while following their normal daily routine.

After completion, the capsule studies were deidentified and evaluated by 1 of 2 experienced readers (S.C., J.L.) not involved in the care of the patient. To add consistency and further rigor, the results were independently scored by a single reviewer (S.O.) from a different institution, who was blinded to timing of the CE during the course of the study (ie, week 0, 12, or 52) and to all of the patient's personal health information (ie, age, demographics, name, date of birth), and the patient's clinical condition. In addition to a full reading of the CE download, focusing on inflammatory lesions in the small and large intestine, the reader also assigned a Lewis score (LS) for each one-third of the SB (SB tertile) and the entire SB using indexing software embedded into CE system. As a validated, weighted index of 3 parameters, stenosis, ulceration, and villous edema, the LS has a range of 8 to 4800 points, with <135 reflecting normal mucosa and $\geq$790 reflecting moderate-to-severe inflammatory change (23,24).

Statistics and Data Analysis

Summary statistics including the mean, standard error of the mean (SE), and frequency (%) are presented for demographic and other baseline patient characteristics for the total study population.

Means and SEs are reported here for a small number of patients enrolled. All results are reported on an intention-to-treat analysis of the 10 enrolled in the study. The LS assigned by the independent CE reader was used for analysis. For the outcome variables of the PCDAI, HBI, LS, caloric intake and individual laboratory studies, nonparametric analysis with the Wilcoxon signed-rank test was used to evaluate the significance of these individual factors at the measured time points, because of the small sample size. Regression analysis was used to evaluate associative phenomena and covariance, with analysis of variance then used to evaluate for variable dependency.

RESULTS

Participation in this study of the SCD was offered to 16 patient families who preferred alternative therapy for CD. Three declined because of the perceived stringency of the SCD; 3 were unable to unable to ingest the video capsule, with 10 being enrolled and then analyzed for this report. One (a 20-year-old girl) dropped out of the study at 8 weeks because of difficulty maintaining the SCD while at college. Nine (7 boys, 2 girls, average age 13.6 years, disease duration 3.2 years) completed the 12-week trial (Table 2). Three patients were newly diagnosed and naïve to any medication. Four were taking immunomodulators; 1 was taking mesalamine and 1 was taking budesonide. None were taking biologics or other steroids.

The 9 completers were receiving an average of 85% of their estimated caloric needs before SCD, and subsequently 101% of estimated caloric needs on the SCD at week 12. There was wide variability in patients' ability to meet estimated daily caloric requirements and 3 (33%) lost weight (Table 3). The dietitian (B.K.) and coordinator (A.S.) maintained telephone contact as needed to support the implementation of SCD such that most of the patients (9/10) completed the study and remained on the diet through the extension period. Weight gain was variable and appeared to be independent of intake or prior medication; however, weight gain for the 12 weeks was inversely related to the change in PCDAI ($r = -0.763$, covariance -26.528), but then that correlation was lost during the extension when the weight for the remaining participants returned to baseline ($r = -0.2110$, covariance -12.38). Body mass index remained essentially unchanged and showed no correlation with PCDAI at any time point ($r = -0.4236$, 0.1041, and 0.1275 at 0, 12, and 52 weeks, respectively). As seen in Table 4, improvements in hemoglobin (Hgb), white blood cell count, erythrocyte sedimentation rate, and albumin were observed during the course of the study and extension, yet the differences were small and not statistically significant. During the 12-week initial period, HBI decreased from 3.3 ± 2.0 to 0.6 ± 1.3 ($P = 0.007$) and the PCDAI declined from 21.1 ± 5.9 to 7.8 ± 7.1 ($P = 0.011$), whereas the LS dropped from 2153 ± 732 to 960 ± 433 ($P = 0.012$), with a decline in 3 patients to <135, a level consistent with normal intestinal mucosa (23) (Table 5). Small intestinal ulcers seen on initial CE in 4 subjects were not seen on the 12-week CE, with LS decreasing in 8 patients. In 1 patient not rigidly adherent to the SCD, the number of stenotic areas decreased and the LS declined; however, in this patient additional apthous ulcers developed in a new location. The PCDAI of patient 9 (with isolated colonic CD) increased, whereas the HBI decreased and the normal SB mucosa on initial CE remained unchanged on the second examination.

Seven patients proceeded to the extension period (Fig. 1 details the clinical and laboratory parameters at 0, 12, and 52 weeks). One patient (17-year-old boy, disease duration 6 years) whose PCDAI rose at week 12 did not continue on the diet; another patient (15-year-old boy, disease duration 4.2 years) was lost to follow-up. The HBI (0.1 ± 0.4) and PCDAI (5.4 ± 5.5) dropped further for the remaining participants ($P = 0.016$ and 0.027, respectively). None of the patients required medication change or dosage adjustment through the initial trial or the extension period. The LS at the 52-week visit (1046 ± 372) was higher than at the 12-week visit, with 4 of the patients having higher LS, whereas 2 showed mucosal healing and 1 other continued to show mucosal improvement.

DISCUSSION

This is the first prospective trial of the SCD in pediatric patients with CD, and the first in which SB mucosal healing was assessed as a primary outcome of a single (dietary or medication) intervention. At both the 12-week endpoint and the extension period out to 52 weeks, we observed clinical improvement assessed by PCDAI, HBI, in 8 of the 10 subjects enrolled, with 6 patients (60%) having achieved clinical remission (PCDAI < 10) by 12 weeks. Sustained clinical remission was seen in 6 of the 7 patients who remained on the diet to 52 weeks, with none of the patients requiring medication change or dosage adjustment. Although the numbers were small for statistical comparison, this improvement was demonstrated both in newly diagnosed patients with CD and in patients with established CD having an exacerbation despite taking medication, including immunomodulators.

Of the 10 patients enrolled, 1 dropped out owing to the stringency of the diet and inability to maintain compliance with the SCD while in college. Patients were observed to have difficulty adjusting to the diet initially, both in terms of restricting various carbohydrates and in finding suitable caloric substitutes; however, during the course of the trial, the 9 reported here adapted to the requirements of the SCD and continued to successfully maintain the dietary restrictions. Most patients increased their overall caloric intake by the 12-week visit, which may be in part related to their

TABLE 2. Population demographics and clinical information

Patient	Age, y	CD duration, y	Disease location	Other CD medications
1	13	1.3	Ileum, R colon	Azathioprine 150 mg
2	10	8.0	Ileum, cecum	No CD meds
3	15	4.2	Duodenum, ileum, R colon	Methotrexate 25 mg
4	16	4.6	Duodenum, ileum, cecum, rectosigmoid	6-Mercaptopurine 75 mg
5	11	1.2	Duodenum, ileum, rectosigmoid	Azathioprine 100 mg
6	13	0.2	Ileal, duodenal, R colon	No CD meds
7	14	3	Ileum, jejunum	No CD meds
8	14	0.2	R colon, TI, cecum, duodenum	Budesonide 6 mg
9	17	6	Colonic	Balsalazide 2250 mg
Mean	13.6	3.2		

CD = Crohn disease; meds = medications; TI = terminal ileum.

TABLE 3. Dietary results

	Week 0				Week 12			Week 52	
Patient	kcal/kg needs	kcal/kg actual	Weight, kg	BMI, %	kcal/kg actual	Weight, kg	BMI, %	Weight, kg	BMI, %
1	55	48	35.4	3	84	35.7	3	35.9	1
2	70	53	35.2	48	56	35.4	48	37.2	37
3	27	21	58.1	90	32	52.2	88	n/a	n/a
4	40	24	51.8	11	22	49.1	7	52.2	37
5	68	119	27.7	13	67	30	13	34.1	15
6	55	33	57	37	43	60.5	37	64.5	26
7	66	58	46.8	5	79	50	5	54.5	2
8	55	43	55.9	13	77	57.2	13	59.8	8
9	53	31	66.8	50	39	56.8	50	n/a	n/a
Mean	54	48	48.3	30.0	55	47.4	29.3	48.3	14.7
SE	4.6	9.9	4.3	28.9	7.5	3.7	28.7	4.1	13.0

BMI = body mass index; SE = standard error of the mean.

overall clinical improvement and a subsequent increase in appetite. Although strict dietary assessments and characterization were not collected at the 52-week visit, many of the patients admitted to intentional ''cheating'' with non-SCD foods. Of note, the majority of the subjects in this initial study gained weight during the trial and the extension period (Table 3). Of note, weight gain was inversely associated with the PCDAI at the 12-week visit, although this did not appear to be sustained through the 52-week visit. The lack of inverse correlation of the weight and PCDAI at the end of the study, at least in part, is related to data loss for 2 of the heavier subjects who were no longer participating at that time point. All of the other subjects had maintained their weight or gained, but the absence of these 2 subjects skewed the remaining data, decreasing the mean weight and body mass index.

As characterized by CE independently reviewed in a blinded fashion, 4 of the 10 patients (40%) achieved mucosal healing (LS < 135), with 8 of 10 showing significant mucosal improvement ($P = 0.012$) at 12 weeks when compared with baseline; however, mean LS rose at the 52-week visit, with 3 of the patients having higher LS scores, although 2 achieved the mucosal healing and 1 patient continued to show mucosal improvement. The degree of mucosal healing as ascertained by the CE did not correspond with the extent of clinical remission in all of the subjects; 6 patients achieved clinical remission (PCDAI ≤ 10), whereas only 3 had normal mucosa at the end of the 12-week trial (LS < 135). Of the 4 patients who achieved mucosal healing, 1, whose PCDAI increased while HBI decreased, had nearly normal SB mucosa on initial CE but showed even less ulceration on the 12-week examination. Two of the others with mucosal healing had the lowest LS at enrollment, although they did not have the lowest clinical scores (Table 5). Of note, SB CE and the LS do not assess colonic disease, and thus may understate the diet's impact because patient 9 had only colonic disease, and assessment by the Children's Center for Digestive Health Care reviewers paralleled that of the blinded readers.

Although clinical improvement persisted through the entire 52 weeks in those subjects completing the entire study, as measured by both HBI and PCDAI, mucosal change was less consistent in the 7 patients remaining on the diet. While mucosal improvement in 8 of the 10 patients over the initial time frame, at 52 weeks, 2 patients continued to improve and 3 others had LS lower than baseline, although the LS mean rose at that time point.

Mucosal improvement was observed both in newly diagnosed, treatment-naïve patients, and in those who experienced flares of existing disease at enrollment This observation lends strength to proving the hypothesis that the use of the SCD improves disease for some pediatric patients with CD, with improvement of mucosal inflammation. It, however, remains unclear whether this

TABLE 4. Results of measured parameters

	Week 0		Week 12		Week 52	
Parameter	Mean	SE	Mean	SE	Mean	SE
Weight	48.3	4.3	47.4	3.7	48.3	4.1
BMI, %	30.0	28.9	29.3	28.7	14.7	13.0
kcal/kg	48	9.9	55	7.5		
Hgb	12.4	1.4	13.3	1.0	13.5	1.2
WBC	7.5	1.6	6.2	1.6	6.4	1.6
ESR	9.7	9.9	4.1	1.5	7.1	10.3
Albumin	4.1	0.4	4.3	0.2	3.9	1.1
PCDAI	21.1	5.9	7.8	7.1	5.4	5.5
HB	3.3	2.0	0.6	1.3	0.1	0.4
LS	2153	732	960	433	1046	372

BMI = body mass index; ESR = erythrocyte sedimentation rate; HB = Harvey-Bradshaw; Hgb = hemoglobin; LS = Lewis score; PCDAI = Pediatric Crohn's Disease Activity Index; SE = standard error of the mean; WBC = white blood cell count.

TABLE 5. Clinical and endoscopic scores for reported patients

	Week 0			Week 12			Week 52		
Patient	PCDAI	HB	LS	PCDAI	HB	LS	PCDAI	HB	LS
1	30	3	337	5	0	0	5	0	0
2	15	3	225	5	1	0	0	0	135
3	20	2	1358	5	0	1350	n/a	n/a	n/a
4	15	2	6228	10	1	3720	15	0	1312
5	30	2	4492	10	0	247	10	0	1012
6	15	3	2080	0	0	143	0	0	0
7	22.5	5	712	5	0	712	5	1	1912
8	22.5	2	3813	5	0	112	2.5	0	2952
9	20	8	135	25	4	112	n/a	n/a	n/a
Mean	21.1	3.3	2153	7.8	0.6	711	5.4	0.1	1046
P vs week 0				0.011	0.007	0.012	0.027	0.016	0.091

HB = Harvey-Bradshaw; LS = Lewis score; PCDAI = Pediatric Crohn's Disease Activity Index.

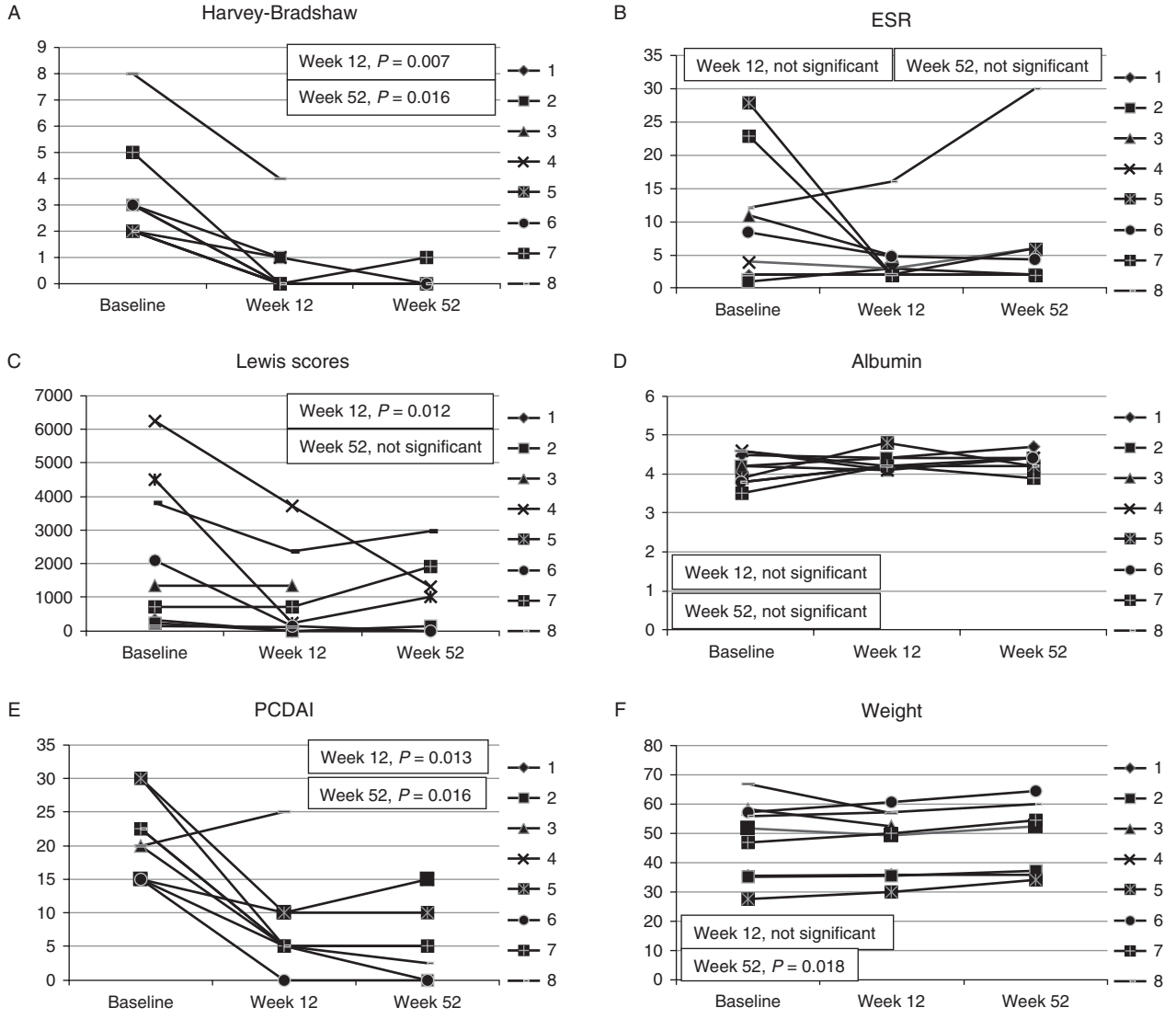

FIGURE 1. Individual patients' clinical parameters at baseline and at 12 and 52 weeks on the specific carbohydrate diet: (A) Harvey-Bradshaw Index; (B) erythrocyte sedimentation rate (ESR); (C) Lewis capsule endoscopy score; (D) serum albumin; (E) Pediatric Crohn's Disease Activity Index (PCDAI); (F) weight in kilograms.

improvement is the result of the diet itself, some specific SCD component, a resultant increase in caloric intake, or a possible change in microbiota that can accompany dietary alteration (25–27).

Conversely, the small number of patients enrolled, the lack of a control population, the dietary monitoring methodology used, and assessment limited to clinical parameters and the SB mucosal surface do limit the interpretation and broader application of this initial trial. Despite the small numbers of patients, the lack of homogeneity in disease phenotype, and the mixture of newly diagnosed, treatment-naïve patients with established patients who were flaring, the overwhelming resolution of disease by the majority of outcome variables assessed mandates a larger subsequent clinical trial, one that addresses both treatment effects and mechanisms of disease resolution in children with IBD with changes in nutrients, the microbiome, and clinical markers measured prospectively. Additionally, clinicians and families pursuing the SCD should be fully cognizant that in the first weeks, at least in our pilot study, some of the patients decreased their intake and lost weight, and that imposing such a restrictive diet on a child can be psychologically stressful (22), although a number of the patients in this trial are continuing the SCD or their personal modifications of the diet. Moreover, specific dietary deficiencies in folate, thiamine, and vitamin B_6 can arise from limiting grains; calcium and vitamin D deficiency can occur from dairy avoidance; and vitamins C, A, and potassium deficiency are possible as a result of limiting fruits and vegetables (28).

A number of hypotheses have been raised regarding why dietary interventions may be as successful, if not more so, than pharmacological therapy for IBD. In particular, the premise that IBD results from a combination of environmental influences that alter the microbiome and trigger specific susceptibility proinflammatory genes within the mucosa raises important hypotheses as to why dietary modification such as that in the SCD could be effective.

By using CE, this trial evaluated mucosal improvement and healing in the SB before the introduction of the SCD and after 12 and 52 weeks in which other medications were not introduced or

adjusted. Because the readers at our institution were both actively involved in recruiting patients and may have some bias, a totally objective view was obtained by an independent reader to benefit the intent of the study, The study suggests that CE, with a miss rate of 1% for SB ulcers in IBD (29), and the LS may be able to characterize differences in small intestinal mucosa for a relatively short time frame (ie, 12 weeks), and provides objective evidence of change to complement standard clinical IBD research scoring methods that can be affected by the subjective reports from the patients and their families.

In summary, this initial pilot study involving 10 patients and 9 completing the trial, 3 with newly diagnosed CD and 6 with exacerbation of established IBD, showed statistically significant mucosal healing and clinical improvements in the majority of patients when using the SCD for 52 weeks. The SCD therefore shows promise as an alternative therapy for this chronic disease. Further studies are, however, critically needed with larger, phenotypically well-characterized cohorts to understand the changes associated with the SCD, the pathobiological mechanisms behind them, and whether certain components of the SCD are particularly important. In addition, our study demonstrates that CE can be used to monitor mucosal improvement in an intervention trial for pediatric CD, and thus, subsequent studies should consider routinely using CE as a methodology to further and better characterize SB mucosal change in intervention trials.

REFERENCES

1. Ruemmele FM, Roy CC, Levy E, et al. Nutrition as primary therapy in pediatric Crohn's disease: fact or fantasy? *J Pediatr* 2000;136:285–91.
2. Konno M, Kobayashi A, Tomomasa T, et al. Guidelines for the treatment of Crohn's disease in children. *Pediatr Int* 2006;48:349–52.
3. Heuschkel RB, Menache CC, Megerian JT, et al. Enteral nutrition and corticosteroids in the treatment of acute Crohn's disease in children. *J Pediatr Gastroenterol Nutr* 2000;31:8–15.
4. Dziechciarz P, Horvath A, Shamir R, et al. Meta-analysis: enteral nutrition in active Crohn's disease in children. *Aliment Pharmacol Ther* 2007;26:197–806.
5. Zachos M, Tondeur M, Griffiths AM. Enteral nutritional therapy for induction of remission in Crohn's disease. *Cochrane Database Syst Rev* 2007;1:CD000542.
6. Buchanan E, Gaunt WW, Cardigan T, et al. The use of exclusive enteral nutrition for induction of remission in children with Crohn's disease demonstrates that disease phenotype does not influence clinical remission. *Aliment Pharmacol Ther* 2009;30:501–7.
7. Haas SV. Value of banana in treatment of celiac disease. *Am J Dis Child* 1924;28:421.
8. Haas S. The treatment of celiac disease with the specific carbohydrate diet: report on 191 additional cases. *Am J Gastroenterol* 1955;23:344–60.
9. Gottschall E. *Breaking the Vicious Cycle: Intestinal Health Through Diet.* Baltimore, Canada: Kirkton Press; 1987.
10. *http://www.breakingtheviciouscycle.info*. Accessed February 10, 2013.
11. Suskind DL, Wahbeh G, Gregory N, et al. Nutritional therapy in Crohn's disease: the specific carbohydrate diet. *J Pediatr Gastroenterol Nutr* 2014;58:87–91.
12. Sandborn WJ, Feagen BG, Hanauer SB, et al. A review of activity indexes indices and efficacy endpoints for clinical trials of medical therapy in adults with Crohn's disease. *Gastroenterology* 2002;122:512–30.
13. D'Haens GR, Fedorak R, Lemann M, et al. Endpoints for clinical trials evaluating disease modification and structural damage in adults with Crohn's disease. *Inflamm Bowel Dis* 2009;15:1599–604.
14. Aranthakrishnan AN, Korzenik JR, Hur C. Can mucosal healing be a cost-effective endpoint for biologic therapy in Crohn's disease? A decision analysis. *Inflamm Bowel Dis* 2013;19:37–44.
15. Froslie KR, Johnsen J, Mourn BA, et al. Mucosal healing in inflammatory bowel disease: results from a Norwegian population-based cohort. *Gastroenterology* 2007;133:412–22.
16. Griffiths AM. Specificities of inflammatory bowel disease in childhood. *Best Pract Res Clin Gastroenterology* 2004;18:509–23.
17. Triester SL, Leighton JA, Leontiadis GI, et al. A meta-analysis of the yield of capsule endoscopy compared to other diagnostic modalities in patients with non-stricturing small bowel Crohn's disease. *Am J Gastroenterol* 2006;101:954–64.
18. Cohen SA, Klevens AI. Use of capsule endoscopy in diagnosis and management of pediatric patients, based on meta-analysis. *Clin Gastroenterol Hepatol* 2011;9:490–6.
19. Cohen SA. Pediatric capsule endoscopy. *Tech Gastrointest Endosc* 2013;15:32–5.
20. Turner D, Griffiths AM, Walters TD, et al. Appraisal of the Pediatric Crohn's Disease Activity Index on four prospectively collected datasets: recommended cutoff values and clinimetric properties. *Am J Gastroenterol* 2010;105:2085–92.
21. Caunedo A, Romero J, Herrerias J. Patency and PC capsules. *World J Gastroenterol* 2008;14:5269–73.
22. Gordon D. The specific carbohydrate diet: does it work? http//www.ccfa.org/resources/specific-carbohydrate-diet.html. Accessed February 10, 2013.
23. Gralnek IM, Defranchis R, Seidman E, et al. Development of a capsule endoscopy scoring index for small bowel mucosal inflammatory change. *Aliment Pharmacol Ther* 2008;27:146–54.
24. Rosa B, Moreira MJ, Rebelo A, et al. Lewis score: a useful clinical tool for patients with suspected Crohn's disease submitted to capsule endoscopy. *J Crohn's Colitis* 2012;6:692–7.
25. Lambert B, Lemberg DA, Leach ST, et al. Longer-term outcomes of nutritional management of Crohn's disease in children. *Dig Dis Sci* 2012;57:2171–7.
26. Lionetti P, Callegari ML, Ferrari S, et al. Enteral nutrition and microflora in pediatric Crohn's disease. *J Parenter Enteral Nutr* 2005;29:S173–5.
27. Shiga H, Kajiura T, Shinozaki J, et al. Changes of faecal microbiota in patients with Crohn's disease treated with an elemental diet and total parenteral nutrition. *Dig Liver Dis* 2012;44:736–42.
28. Hwang C, Ross V, Mahadevan U. Popular exclusionary diets for inflammatory bowel disease: the search for a dietary culprit. *Inflamm Bowel Dis* 2014;20:732–41.
29. Lewis BS, Eisen GM, Friedman S. A pooled analysis to evaluate results of capsule endoscopy trials. *Endoscopy* 2005;37:960–5.