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A randomized trial of inulin for bowel symptoms, depression and quality of life in constipation predominant IBS

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This study was conducted to evaluate the effect of inulin on bowel symptoms, depression and quality of life in individuals with constipation-predominant irritable bowel syndrome. This study was designed as a randomized, single-blind, placebo-controlled clinical trial with a parallel design and a 1:1 allocation ratio. Individuals ($n = 34$) aged between 21 and 63 years with constipation-predominant IBS were included in the study. Individuals were randomly assigned to two groups: the prebiotic group ($n = 17$), which received a 50%/50% mixture of inulin/oligofructose (4.6 g twice daily, for a total daily dose of 9.2 g), and the placebo group ($n = 17$), which total received 9.2 g of maltodextrin per day. The intervention period was 8 weeks. Bristol Stool Scale, IBS-Visual Analogue Scale (IBS-VAS), IBS-Symptom Severity Score Scale (IBS-SSS), IBS-Quality of Life Scale (IBS-QoL) and Beck Depression Scale were administered to the participants at the beginning, 1st month and 2nd month. As a result, total IBS-QoL score increased in the prebiotic group (61.0 ± 19.4 to 77.4 ± 15.1 ; $p < 0.006$), whereas total IBS-SSS score decreased (267.3 ± 56.0 to 195.8 ± 59.0 ; $p < 0.026$). In the prebiotic group, significant improvement was observed in the IBS-VAS parameters of constipation status (2.2 ± 2.3 to 4.9 ± 2.5 ; $p < 0.042^{\text{group} \times \text{time}}$), psychological state (7 ($2-10$) to 9 ($5-10$); $p < 0.006$). It is thought that inulin may have beneficial effects on reducing symptom severity and frequency and on quality of life in individuals with IBS in whom constipation is predominant.

Keywords Bowel symptoms, Depression, Inulin, Constipation, Irritable bowel syndrome, Quality of life

Irritable bowel syndrome (IBS) is a chronic and recurrent functional gastrointestinal disorder characterised by recurrent abdominal pain, bloating, gas and changes in bowel habits¹. According to Rome IV criteria, IBS is classified into four subtypes: IBS-C (constipation-predominant), IBS-D (diarrhoea-predominant), IBS-M (mixed), and IBS-U (unspecified)². IBS affects approximately 4.0% of the world's population and is twice as common in women as in men³. It is one of the most commonly diagnosed gastrointestinal disorders^{3,4}. According to Fond et al., individuals with IBS tend to have higher levels of depression and anxiety⁵. A clinical investigation found that 37.1% of individuals with IBS had depression and 31.4% had anxiety⁶.

Even though IBS is the most prevalent gastrointestinal system condition seen in clinics, its mechanism is not entirely understood. Various factors such as changes in gastrointestinal motility, genetic predisposition, visceral hypersensitivity, environmental factors, psychological factors, dietary habits, food intolerance and changes in intestinal microbiota (dysbiosis) are involved in its pathophysiology. It has been reported that the interaction between diet and gut microbiota has a potential contribution to the pathophysiology of IBS^{7,8}. On the other hand, patients report that their eating habits have an effect on the symptoms and severity of IBS. Therefore, many patients tend to turn to nutritional approaches such as removing certain foods from their diet or consuming more on their own^{9,10}. However, the relationship between IBS symptoms and food intake seems to be quite complex. Although there are nutritional therapy approaches to treat symptoms, there is not yet a specific diet to manage IBS, especially constipation-predominant IBS^{11,12}. Therefore, healthy dietary recommendations are generally recommended for these patients¹³. In recent years, it has been reported that pro/prebiotics have a therapeutic effect on intestinal microbiota in IBS¹⁴. It is thought that inulin, a prebiotic component, may also have a beneficial effect in individuals with constipation-predominant IBS. Inulin is a complex carbohydrate belonging to a class

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of compounds known as fructan. It is found and obtained from plant sources such as chicory, yam, garlic, leek and onion¹⁵. Inulin is resistant to hydrolysis by digestive enzymes. Thus, it reaches the colon undigested and is selectively fermented by colonic microbiota¹⁶. Inulin intake can regulate intestinal peristalsis, colon transit time, stool consistency and frequency of defecation by changing the composition of the intestinal microbiota¹⁴. Studies show that inulin intake may not only have potential benefits on bowel function and quality of life in individuals with constipation-predominant IBS, but also exert positive effects on psychological symptoms by modulating the gut microbiota through the brain–gut axis—a bidirectional communication system that plays a key role in the pathophysiology of anxiety and depression commonly observed in IBS patients^{14,16–21}. The current study, conducted within this scope, is one of the randomised controlled trials evaluating the effects of inulin supplementation on gut symptoms, depression, and quality of life in individuals with constipation-predominant IBS-C. This study comprehensively addresses not only gut complaints but also psychological status and quality of life. Based on this information, the aim of the study was to evaluate the effect of inulin supplementation on bowel symptoms, depression and quality of life in individuals with constipation predominant IBS.

The hypotheses of the study are as follows.

Primary hypothesis

H1 Inulin supplementation significantly reduces symptom severity, as assessed by the total score on the IBS-Symptom Severity Score Scale (IBS-SSS), in individuals with constipation-predominant IBS.

Secondary hypotheses

H2 Inulin supplementation significantly improves quality of life, as measured by the IBS-Quality of Life Scale (IBS-QoL), in individuals with constipation-predominant IBS.

H3 Inulin supplementation significantly reduces depression levels, as assessed by the Beck Depression Scale, compared to the placebo group.

H4 Inulin supplementation significantly improves bowel movement frequency and consistency, as assessed by the Bristol Stool Form Scale, in individuals with constipation-predominant IBS.

H5 Inulin supplementation significantly reduces symptom-specific discomfort levels, as measured by the IBS Visual Analogue Scale (IBS-VAS), compared to the placebo group.

Materials and methods

Study design

This study was planned as a randomised, single-blind, placebo-controlled clinical trial. This study utilized a parallel design with a 1:1 allocation ratio. Single blinding: It was conducted as a study in which only the researcher knew which group the participant was in, but the participants did not know which group they were in. In this study, participants were blinded to group assignments. The researcher was not blinded to group assignments. The doctor who diagnosed IBS was blinded to participant group assignments. However, he was not involved in the intervention or assessments. The study was conducted with individuals aged between 21 and 63 years who applied to the Gastroenterology Department Clinic of Mardin Education and Research Hospital affiliated to Mardin Artuklu University, diagnosed with constipation-predominant IBS and volunteered to participate in the study (November 2021–April 2023). The total intervention period for the participants was determined as 8 weeks. Ethical approval of the study was obtained from Izmir Bakırçay University Non-Interventional Clinical Research Ethics Committee (Date: 03/11/2021, Decision No: 377). In addition, the study was conducted within the framework of the Helsinki Declaration Principles and informed consent and approval were obtained from the participants. The study was registered at www.clinicaltrials.gov (NCT06610188) (24/09/2024).

Patients and randomization

Inclusion criteria were that the individuals were between 19 and 65 years of age, volunteered to participate in the study, and were diagnosed with IBS by a physician according to Rome IV criteria. According to the Rome IV criteria, the diagnosis of IBS includes recurrent abdominal pain present at least 1 day a week for the last 3 months and accompanied by at least two of the three criteria: (1) related to defecation; (2) related to changes in stool frequency; (3) related to changes in stool shape. These criteria must have been present for the last 3 months and the symptoms must have started at least 6 months before the diagnosis. In order to identify the constipation-predominant subtype of IBS, patients' stool types were assessed using the Bristol Stool Form Scale, and only individuals with type 1 and 2 stools were included in the study.

Exclusion criteria were a history of gastrointestinal surgery (except appendectomy and cholecystectomy), inflammatory bowel disease, lactose malabsorption, gastroenteritis, celiac disease, gastric and duodenal ulcer, metabolic diseases (cardiac, hepatic and renal diseases, diabetes, etc.), history of malignancy, pregnancy and lactation, use of intestinal motility and antidepressant drugs, involuntary body weight loss of more than 5 kg in the last 3 months, use of dietary fibre supplements in the last 3 months, use of antibiotics in the last 3 months, low compliance (compliance rate below 80%), use of prebiotic and probiotic supplements in the last 3 months. The randomised flow chart is given in Fig. 1.

Individuals were blinded to groups. Individuals were randomly assigned by the researcher to one of two groups: prebiotic (n = 17) and placebo (n = 17) groups. Randomisation was conducted among individuals who met the inclusion criteria using a random numbers table (<https://www.randomizer.org>). Participants were assigned to prebiotic and placebo groups according to the numbers generated in the programme.

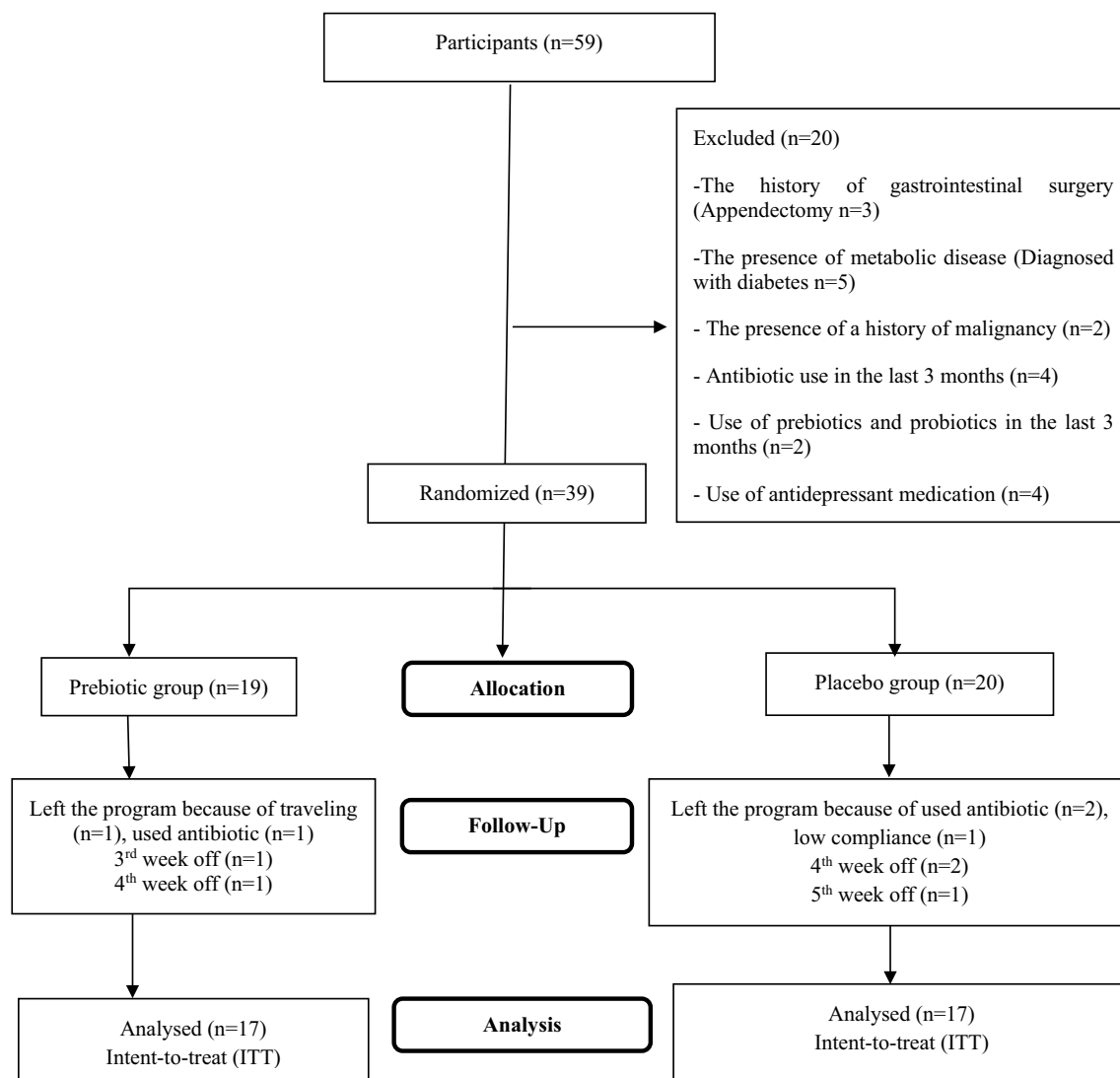


Fig. 1. Flowchart of participants.

Data collection

The research data were collected by the researcher using a questionnaire form and face-to-face interview technique. Primary outcomes of interest are changes in IBS symptoms, including IBS-SSS, depression and quality of life. Secondary outcomes include Bristol stool scale and IBS-VAS measurements. The Bristol Stool Scale developed by Lewis and Heaton (1997) was used to determine the type of IBS through stool forms. The Bristol Stool Scale, developed by Lewis and Heaton (1997), was used to determine the type of IBS using stool forms²². This scale aims to predict the stool form through seven different stool forms.

Constipation-predominant IBS was evaluated over the first 4 stool forms, and it is understood that there is improvement as the stool forms of the individuals approach the type 4 form. The severity of IBS symptoms was assessed using the IBS-Visual Analogue Scale (IBS-VAS) developed by Bengtsson et al.²³. The scale, which consists of ten questions in total, is preferred for converting non-numerical values into numerical form. In this scale, the parameter to be evaluated is defined at both ends of a 100 mm line and there are cuts that will enable scoring from 1 to 10. The scoring on the scale indicates that 1:very bad, 10:very good. The Irritable Bowel Syndrome Symptom Severity Score (IBS/SSS) was developed by Francis et al. to assess the severity of gastrointestinal symptoms in individuals with IBS²⁴. It consists of 5 questions in total and each question is scored between 0 and 100. The IBS-SSS scale has a maximum score of 500 points, which is classed as '75–174 points = mild IBS', '175–299 points = moderate IBS', and '> 300 points = severe IBS'. The quality of life levels were assessed using the Irritable Bowel Syndrome Quality of Life Scale (IBS-QoL). IBS-QoL developed by Patrick et al. is divided into 8 sub-parametres, 34 questions in total and the lowest score is 34, while the highest score is 170²⁵. The increase in the total score obtained from the scale indicates a decrease in the quality of life associated with the disease. The Beck Depression Scale was used to evaluate the depression status of the individuals. It is a 21-question (multiple-choice) self-report scale developed by Aaron T. Beck to provide a quantitative assessment of depression severity²⁶. Tegin (1980) and Hisli (1989) evaluated its validity and reliability in Turkish^{27,28}. It

provides a four-point likert-type measurement. The score scale ranges from 0 to 3 for each question. Total score varies between 0 and 63. Higher scores obtained from the scale indicate more depressive symptoms. According to the validity and reliability article of the scale for Turkish, it was stated that the cut-off score was accepted as 17²⁸. In this study, the data were divided into two groups as depressed and non-depressed according to the scale using a cut-off score of 17. The evaluations were performed three times in total, at the beginning of the study, at the 4th week and at the 8th week.

Intervention

In the study, products containing a total of 9.2 g (4.6 g twice a day) inulin/oligofructose (50/50) mixture (prebiotic group) or maltodextrin (placebo group) that individuals should consume daily were delivered to individuals in identical opaque bags. The amount of inulin/oligofructose mixture supplementation in the study was determined by considering the amounts recommended in the literature and the amounts contained in the content of 1 sachet product^{29–31}. The product used in the study has no taste, colour or odour and does not change the smell and colour of the foods it is mixed with. One sachet contains 4.6 g of pulp. Maltodextrin used as placebo was preferred because it is a fully digestible carbohydrate and has a similar taste and appearance to chicory inulin and has been used in many studies^{29,32–34}. Inulin/oligofructose mixture and maltodextrin supplements were obtained from a private company. The duration of supplementation in the study was determined as 8 weeks based on the studies in the literature^{35,36}. Individuals were requested to take the supplements twice a day, in the morning (4.6 g) and evening (4.6 g), while fasting for eight weeks³⁷. Usage status was questioned by weekly follow-ups. Participants were verbally informed about the use of the products. Because it may affect the results of the study, individuals were requested to continue their routine eating habits and not to use supplements other than those given. In line with the general recommendations at the end of the study; participants were verbally informed about proper nutrition, physical activity recommendations and stress management in IBS. If an adverse event occurred, the person would be excluded from the study, but no patient reported an adverse event.

Sample size

The population of the study consisted of individuals between the ages of 19–65 who applied to the Gastroenterology Department Clinic of Mardin Education and Research Hospital and were diagnosed with IBS. The sample size was determined using G*Power version 3.1.9.7, based on a repeated measures ANOVA (within-between interaction) with two groups and three measurements. The effect size (f) was set to 0.5, representing a moderate effect, based on findings from previous clinical trials that assessed the impact of prebiotic and probiotic interventions on IBS symptom severity scores^{21,38,39}. With an α error probability of 0.05, power ($1-\beta$) of 0.80, and a correlation among repeated measures of 0.5, the required total sample size was calculated to be 24 participants (12 per group), achieving an actual power of 0.82.

Statistical analysis

The data obtained in the study were analyzed using SPSS (Statistical Package for the Social Sciences) 26.0 package software. The suitability of the data for normal distribution was examined by Kolmogorov–Smirnov and Shapiro–Wilk tests and histogram graphs, and it was determined that the data showed normal distribution. In descriptive statistics, the number of individuals (n) and percentage (%) for qualitative variables and mean $\pm$ standard deviation ($\bar{X} \pm SD$) for quantitative variables were given. Pearson Chi-Square test was used to examine the relationship between two categorical variables, and Fisher's Exact Test, Continuity or Pearson Chi-Square tests were used to examine the relationship between more categorical variables according to the expected value. When the quantitative variables met the assumption of normal distribution, Repeated measures ANOVA (General linear model) and Bonferroni correction in the post-hoc test were used for intra-group comparisons, and Independent Sample t Test was used for inter-group comparisons. When the quantitative variables did not fulfil the assumption of normal distribution, Repeated Measures Friedman Test and Wilcoxon in the post-hoc test, Mann–Whitney U Test was used in inter-group comparisons. In the comparison of differences between groups, P_{group} , P_{time} and $P_{\text{group} \times \text{time}}$ interaction effect were evaluated. P_{time} value indicates the comparison of any quantitative variable within the group in terms of time periods. The P_{group} value indicates the comparison of the study groups by averaging any quantitative variable in different time periods. $P_{\text{group} \times \text{time}}$ value indicates the comparison between the groups depending on the time period of the quantitative variable. It expresses whether the study groups have superiority over each other in any variable during the intervention. Pearson Correlation Analysis was used to see whether there was a statistical relationship between two quantitative variables. In statistical tests, 95% confidence interval and significance level $p < 0.05$ were accepted.

Results

General characteristics

The socio-demographic characteristics of the individuals participating in the study according to the groups are shown in Table 1. Among the participants, 76.4% were female and 64.7% were not employed. According to the Chi-square analysis results, a statistically significant difference was found between the groups in terms of education status ($\chi^2 = 9.167$, $p = 0.027$), indicating that individuals in the placebo group were more likely to have only primary school education. Although no statistically significant differences were observed in employment status ($p = 0.055$) and job description ($p = 0.078$).

When the Bristol stool scale scores of the individuals were examined, there was no significant difference between the groups at baseline, first month and second month measurements ($p > 0.05$). At the end of the study, improvement was observed in the stool type of the prebiotic group. When the baseline and 1st month results of the prebiotic group were examined, it was observed that most of the participants had type 2 stool type, while the majority of the individuals had type 3 stool type at the end of the 2nd month. However, there was no significant

Individual characteristics	Prebiotic (n = 17)		Placebo (n = 17)		X ² /p
Mean age (years) ($\overline{X} \pm SD$)	38.58 ± 2.03		38.05 ± 3.17		
Min–Max	27–63		21–62		
	n	%	n	%	
Gender					
Male	4	23.6	4	23.6	0/1
Female	13	76.4	13	76.4	
Education status					
Primary school	1	6.0	7	41.0	9.167/0.027
Middle school	–	–	1	6.0	
High school	8	47.0	2	12.0	
Graduate and postgraduate	8	47.0	7	41.0	
Employment status					
Employee	11	64.7	6	35.3	3.694/0.055
Unemployed	6	35.3	11	64.7	
Job description	(n = 11)		(n = 6)		
Civil servant	9	81.9	3	50.0	6.804/0.078
Self-employment	–	–	2	33.3	
Worker	2	18.1	1	16.7	
The factors affecting IBS disease*					
Stress	10	58.8	12	70.5	
Family problems	2	11.8	1	5.9	
Foods	8	47.0	6	35.2	
The change of environment	2	11.8	2	11.8	
Menstrual period	1	5.9	2	11.8	
Economic situation	1	5.9	1	5.9	

Table 1. Socio-demographic characteristics. *More than one answer was given. $\bar{X}$: mean, SD: Standard deviation, Min: minimum, Max: maximum, IBS: Irritable Bowel Syndrome) X²: Chi-Square analysis.

difference ($p > 0.05$). At the end of the study, an increase in type 2 stool type was observed in the placebo group (not shown data).

At the end of the study, a significant improvement was observed in the VAS parameters of the effect of symptoms such as constipation status (2.2 ± 2.3 to 4.9 ± 2.5 ; $p_{\text{group} \times \text{time}} < 0.042$), psychological state (7 (2–10) to 9 (5–10); $p < 0.006$) in individuals using inulin. It was determined that the statistical difference in these parameters originated from the 1st and 2nd month scores and was higher than the baseline scores. No significant difference was found between the prebiotic and placebo groups in terms of feeling that the bowel was not completely emptied after the toilet at baseline, first month and second month ($p > 0.05$) (Table 2).

When the IBS-SSS was evaluated, it was determined that abdominal pain (50 (0–75) to 25 (0–75); $p < 0.004$), the frequency of abdominal pain (20 (10–70) to 10 (10–60); $p < 0.007$), abdominal bloating (50 (25–75) to 30 (25–50); $p < 0.001$), dissatisfaction with bowel habits (75 (50–100) to 50 (25–100); $p < 0.001$) showed a significant decrease in the prebiotic group and this statistical difference was due to the fact that the 1st and 2nd month measurements were lower than the baseline measurements ($p < 0.05$). The prebiotic group's total IBS-SSS score was 267.3 ± 56.0 at baseline and decreased to 217.6 ± 64.4 in the 1st month of the study and to 195.8 ± 59.0 in the 2nd month ($p < 0.001$). When the interaction effect of group and time on the total IBS-SSS score was assessed, it was found to be statistically significant ($p_{\text{group} \times \text{time}} = 0.047$) (Table 3).

Table 4 shows the classification of IBS-SSS by group. According to IBS-SSS classification, a significant difference was found between the groups at the first month ($p < 0.05$).

Table 5 shows intra- and intergroup data for the quality of life scale and its sub-dimensions. In the prebiotic group, it was determined that dysphoria, activity, health concern, social reaction and social relationship sub-dimensions increased over time compared to baseline ($p_{\text{time}} < 0.05$). It was observed that the statistical difference in dysphoria ($p_{\text{time}} = 0.001$) and social reaction scores ($p_{\text{time}} = 0.013$) was due to the 2nd month scores, which were higher than the baseline and 1st month scores. In addition, the group and time interaction effect of dysphoria (prebiotic: 53.3 ± 23.6 to 76.1 ± 21.3 ; placebo: 26.8 ± 25.3 to 62.1 ± 22.5 ; $p_{\text{time} \times \text{group}} = 0.022$) and food avoidance (prebiotic: 48.1 ± 26.6 to 63.2 ± 18.1 ; placebo: 51.9 ± 25.1 to 44.1 ± 17.8 ; $p_{\text{time} \times \text{group}} = 0.008$) sub-dimensions was statistically significant. In the prebiotic group, while the total IBS-QoL score was 61.0 ± 19.4 before the intervention, it increased to 71.8 ± 17.8 in the 1st month of the study and to 77.4 ± 15.1 in the 2nd month and the difference was found to be significant ($p_{\text{time}} = 0.009$).

Figure 2 illustrates the progression of symptom severity (IBS-SSS) and quality of life (IBS-QoL) in both study groups. In the prebiotic group, there was a steady and pronounced reduction in IBS-SSS scores over time, with the largest change observed between baseline and the second month ($\Delta = -71.47 \pm 40.68$), significantly greater

VAS parameters		Baseline		1st Month		2nd Month		p ^{*,λ}	Post hoc
Abdominal pain ($\bar{X} \pm \text{SD}$)	Prebiotic	3.8 ± 3.2		5.3 ± 2.6		5.0 ± 2.5		0.665 ^g 0.006 ^t 0.702 ^{g*†}	1 < 2,3
	Placebo	4.1 ± 3.5		5.5 ± 3.3		5.8 ± 3.3			
	p	0.840		0.820		0.454			
Constipation status ($\bar{X} \pm \text{SD}$)	Prebiotic	2.2 ± 2.3		4.4 ± 2.3		4.9 ± 2.5		0.466 ^g 0.001 ^t 0.042 ^{g*†}	1 < 2,3
	Placebo	2.6 ± 2.4		4.0 ± 3.1		3.2 ± 2.9			
	p	0.615		0.664		0.078			
Bloating/gas ($\bar{X} \pm \text{SD}$)	Prebiotic	2.8 ± 2.6		4.5 ± 2.7		4.8 ± 2.3		0.191 ^g 0.008 ^t 0.215 ^{g*†}	1 < 2,3
	Placebo	2.6 ± 2.4		3.1 ± 2.9		3.1 ± 3.1			
	p	0.732		0.171		0.102			
Nausea/vomiting [Median (IQR)]	Prebiotic	10 (3–10)		10 (5–10)		10 (5–10)		0.497	-
	Placebo	10 (0–10)		10 (3–10)		10 (3–10)		0.005	1 < 2,3
	p	0.065		0.089		0.472			
Psychological state [Median (IQR)]	Prebiotic	7 (2–10)		10 (3–10)		9 (5–10)		0.006	1 < 2,3
	Placebo	6 (0–10)		7 (0–10)		7 (0–10)		0.529	-
	p	0.250		0.099		0.032			
Impact of symptoms on daily life ($\bar{X} \pm \text{SD}$)	Prebiotic	3.8 ± 2.8		4.9 ± 2.5		4.9 ± 2.0		0.467 ^g 0.001 ^t 0.710 ^{g*†}	1 < 2,3
	Placebo	2.8 ± 2.3		4.5 ± 3.1		4.6 ± 2.6			
	p	0.326		0.630		0.665			
		Yes	No	Yes	No	Yes	No		
The sensation that the bowels are not completely empty after defecation ^a (n (%))	Prebiotic	16 (94.1)	1 (5.9)	16 (94.1)	1 (5.9)	16 (94.1)	1 (5.9)	p = 0.997 χ ² = 0.366	
	Placebo	15 (88.2)	2 (11.8)	14 (82.4)	3 (17.6)	15 (88.2)	2 (11.8)		
	p	0.997 χ ² = 0.366		0.601 χ ² = 1.133		0.997 χ ² = 0.366			

Table 2. The evaluation of visual analogue scale (VAS) parameters according to groups. [#]Friedman test, ^λRepeated measures ANOVA, [†]Independent sample t test, ^aFisher's Exact Test, ^mMann Whitney U test, ^gGroup, ^tTime, ^{g*†}Group $\times$ time interaction, Post hoc: 1 = Baseline, 2 = 1st month, 3 = 2nd month, $\bar{X}$: mean, SD: standart deviation, IQR: Inter quantile range).

IBS-SSS		Baseline	1st	2nd	p ^{*,λ}	Post hoc
Abdominal pain [Median (IQR)]	Prebiotic	50 (0–75)	25 (0–75)	25 (0–75)	0.004	1 > 2,3
	Placebo	50 (0–75)	25 (0–75)	25 (0–100)	0.809	
	p ^m	0.198	0.657	0.723		
The frequency of abdominal pain [Median (IQR)]	Prebiotic	20 (10–70)	10 (0–30)	10 (10–60)	0.007	1 > 2
	Placebo	50 (0–70)	20 (0–60)	20 (0–60)	0.121	
	p ^m	0.071	0.059	0.008		
Abdominal bloating [Median (IQR)]	Prebiotic	50 (25–75)	50 (25–75)	30 (25–50)	0.001	1,2 > 3
	Placebo	50 (25–100)	50 (0–100)	50 (0–100)	1.00	
	p ^m	0.827	0.076	0.002		
Dissatisfaction with bowel habits [Median (IQR)]	Prebiotic	75 (50–100)	75 (25–100)	50 (25–100)	0.001	1 > 2,3; 2 > 3
	Placebo	100 (30–100)	100 (25–100)	100 (25–100)	0.834	
	p ^m	0.793	0.031	0.002		
Impact on general life [Median (IQR)]	Prebiotic	75 (0–100)	75 (25–100)	75 (25–100)	0.156	–
	Placebo	75 (25–100)	75 (0–100)	75 (25–100)	0.296	
	p ^m	0.906	0.942	0.770		
Total IBS-SSS score ($\bar{X} \pm SD$)	Prebiotic	267.3 $\pm$ 56.0	217.6 $\pm$ 64.4	195.8 $\pm$ 59.0	0.070 ^g 0.001 ^t 0.047 ^{g*†}	1 > 2,3
	Placebo	280.2 $\pm$ 70.5	269.7 $\pm$ 93.7	257.6 $\pm$ 92.1		
	p ^t	0.558	0.068	0.026		

Table 3. The evaluation of IBS-SSS according to the groups. [#]Friedman test, ^λRepeated measures ANOVA, ^mMann Whitney U test, [†]Independent sample t test, ^gGroup, ^tTime, ^{g*†}Group $\times$ time interaction, Post hoc: 1 = Baseline, 2 = 1.month, 3 = 2.month, $\bar{X}$: Mean, SD: Standart deviation, IQR: Inter quantile range.

	Baseline			1. Month			2. Month		
	Prebiotic	Placebo		Prebiotic	Placebo		Prebiotic	Placebo	
IBS-SSS*	n (%)	n (%)		n (%)	n (%)		n (%)	n (%)	
Remission	–	1 (5.9)	0.378	–	1 (5.9)	0.027	–	1 (5.9)	0.081
Mild	–	1 (5.9)		5 (29.4)	1 (5.9)		5 (29.4)	1 (5.9)	
Middle	11 (64.7)	7 (41.2)		11 (64.7)	8 (47.1)		11 (64.7)	10 (58.8)	
Severe	6 (35.3)	8 (47.1)		1 (5.9)	7 (41.2)		1 (5.9)	5 (29.4)	

Table 4. Classification of IBS-SSS according to groups. IBS-SSS Irritable Bowel Syndrome-Symptom Severity Score. *Fisher's Exact Test.

Scale sub-dimensions		Baseline	1. Month	2. Month	p ^λ	Post hoc
Dysphoria ($\bar{X} \pm SD$)	Prebiotic	53.3 ± 23.6	68.9 ± 25.1	76.1 ± 21.3	0.343 [§]	3 > 1,2
	Placebo	26.8 ± 25.3	58.3 ± 24.3	62.1 ± 22.5	0.001 [†]	
	p [†]	0.680	0.217	0.073	0.022 ^{§*†}	
Activity ($\bar{X} \pm SD$)	Prebiotic	62.8 ± 22.3	71.8 ± 21.5	78.3 ± 16.4	0.091 [§]	3 > 1
	Placebo	58.6 ± 23.3	60.1 ± 23.6	61.9 ± 17.7	0.026 [†]	
	p [†]	0.595	0.139	0.009	0.177 ^{§*†}	
Body image ($\bar{X} \pm SD$)	Prebiotic	55.8 ± 19.3	66.2 ± 17.4	68.1 ± 16.6	0.146 [§]	–
	Placebo	55.8 ± 21.9	55.5 ± 17.9	55.1 ± 15.8	0.135 [†]	
	p [†]	0.997	0.088	0.028	0.093 ^{§*†}	
Health concern ($\bar{X} \pm SD$)	Prebiotic	57.8 ± 19.4	69.6 ± 16.4	75.9 ± 14.6	0.001 [§]	3 > 1
	Placebo	44.1 ± 23.2	45.1 ± 22.1	49.5 ± 21.1	0.010 [†]	
	p [†]	0.070	0.001	0.001	0.162 ^{§*†}	
Food avoidance ($\bar{X} \pm SD$)	Prebiotic	48.1 ± 26.6	56.9 ± 22.1	63.2 ± 18.1	0.223 [§]	
	Placebo	51.9 ± 25.1	49.1 ± 15.3	44.1 ± 17.8	0.478 [†]	
	p [†]	0.661	0.237	0.004	0.008 ^{§*†}	
Social reaction ($\bar{X} \pm SD$)	Prebiotic	73.9 ± 23.9	83.5 ± 19.0	87.5 ± 14.3	0.085 [§]	3 > 1,2
	Placebo	67.3 ± 22.6	69.5 ± 25.4	73.5 ± 20.3	0.013 [†]	
	p [†]	0.413	0.079	0.027	0.322 ^{§*†}	
Sexuality ($\bar{X} \pm SD$)	Prebiotic	83.8 ± 24.9	90.4 ± 20.9	91.9 ± 18.7	0.256 [§]	–
	Placebo	80.1 ± 28.6	80.8 ± 25.4	80.1 ± 25.4	0.407 [†]	
	p [†]	0.692	0.241	0.135	0.442 ^{§*†}	
Social relationship ($\bar{X} \pm SD$)	Prebiotic	68.6 ± 21.6	76.5 ± 20.6	83.8 ± 15.7	0.347 [§]	3 > 1
	Placebo	65.6 ± 25.3	71.5 ± 29.0	71.0 ± 27.0	0.022 [†]	
	p [†]	0.718	0.575	0.105	0.274 ^{§*†}	
Total IBS-QoL score ($\bar{X} \pm SD$)	Prebiotic	61.0 ± 19.4	71.8 ± 17.8	77.4 ± 15.1	0.071 [§]	3 > 1
	Placebo	58.9 ± 19.3	60.1 ± 18.9	61.7 ± 15.5	0.009 [†]	
	p [†]	0.748	0.074	0.006	0.064 ^{§*†}	

Table 5. Evaluation of the total IBS-QoL and sub-categories of individuals according to groups. ^λRepeated measures ANOVA, [†]Independent sample t test, [§]Group, [†]Time, ^{§*†}Group × time interaction, Post hoc: 1 = Baseline, 2 = 1.month, 3 = 2.month, $\bar{X}$: Mean, SD: Standart deviation.

than in the placebo group ($\Delta = -22.64 \pm 72.43$). Conversely, IBS-QoL scores improved more substantially in the prebiotic group, with a cumulative increase of 16.34 ± 17.95 points over two months, while the placebo group showed a minimal change ($\Delta = 2.85 \pm 16.96$).

Table 6 shows the comparison of Beck depression scale scores according to the groups. According to the baseline, 1st month and 2nd month total Beck score averages in both groups, it was determined that depression was not observed in the majority of the individuals. Beck depression scale scores of the prebiotic group were lower in the 1st and 2nd month measurements compared to the placebo group. While the pre-intervention depression score was 9.4 ± 4.8 in the prebiotic group, it was determined that the depression score was 6.8 ± 4.3 and 5.5 ± 3.3 (respectively) in the 1st and 2nd month of the intervention. In the prebiotic group, a statistically significant decrease was observed in the depression score after the intervention depending on time ($p_{\text{time}} = 0.007$). When the group and time interaction effect of total Beck score was analysed, there was no significant difference ($p > 0.05$).

There is a negative and moderate correlation between the 2nd month IBS-SSS scores and quality of life scores of the placebo group ($r: -0.577$; $p = 0.015$). There was a negative and moderate correlation between Beck

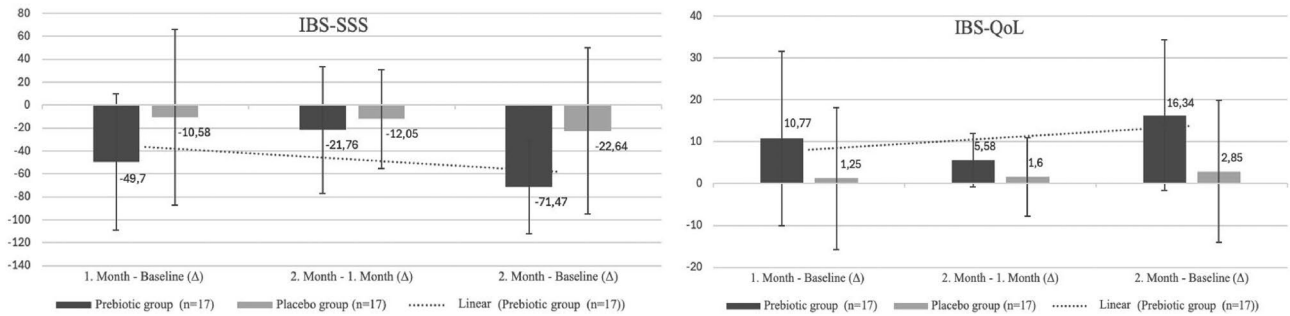


Fig. 2. Changes in IBS Symptom Severity Score (IBS-SSS) and Quality of Life (IBS-QoL) over time in the prebiotic and placebo groups. Bar graphs represent the mean differences from baseline to 1st month, 2nd month, and between months, with error bars showing standard deviations. The dotted lines represent the trend in the prebiotic group.

	Groups	Baseline	1. month	2. month	p ^λ	Post hoc
Total BECK score	Prebiotic	9.4 ± 4.8	6.8 ± 4.3	5.5 ± 3.3	0.009 ^g	1 > 3
	Placebo	12.1 ± 5.2	12.6 ± 8.1	9.1 ± 5.9	0.007 ^t	
	p ⁱ	0.128	0.015	0.038	0.344 ^{g*†}	

Table 6. Comparison of Beck depression scale scores of individuals according to groups. ^λRepeated measures ANOVA, [†]Independent sample t test, ^gGroup, ^tTime, ^{g*†}Group × time interaction, Post hoc: 1 = Baseline, 2 = 1. month, 3 = 2.month.

		IBS-QoL					
		Prebiotic (n = 17)			Placebo (n = 17)		
Scales		Baseline	1.Month	2.Month	Baseline	1.Month	2.Month
IBS-SSS	r	−0.125	−0.146	−0.013	−0.170	−0.327	−0.577
	p	0.634	0.575	0.961	0.514	0.199	0.015
Beck depression Scale	r	−0.432	−0.640	−0.162	−0.218	−0.577	−0.055
	p	0.083	0.006	0.536	0.401	0.015	0.833

Table 7. Correlation between the scores of individuals on the IBS-QoL scale and the IBS-SSS and Beck Depression Scale scores. Pearson Correlation, *IBS-QoL* Irritable Bowel Syndrome-Quality of Life Scale, *IBS-SSS* Irritable Bowel Syndrome- Symptom Severity Score.

depression and quality of life scores of both prebiotic and placebo groups at the 1st month ($r_{\text{prebiotic}}: -0.640$, $p_{\text{prebiotic}}: 0.006$; $r_{\text{placebo}}: -0.577$, $p_{\text{placebo}}: 0.015$) (Table 7).

Discussion

This randomized controlled intervention study was conducted to examine the effect of inulin on bowel symptoms, depression and quality of life in individuals with constipation-predominant IBS admitted to the Gastroenterology Department Clinic of Mardin Education and Research Hospital.

Studies have reported that individuals with IBS have significantly more stress than those without IBS^{40–42}. Stress is strongly associated with symptom onset and symptom severity in individuals with IBS and causes exacerbation of symptoms⁴³. Symptoms are not continuous and periods of remission occur intermittently⁴⁴. In terms of the factors affecting the course of IBS in this study, stress affected 58.8% of the prebiotic group and 70.5% of the placebo group. In another study conducted in female university students, it was determined that students with IBS had higher stress levels and lower quality of life⁴⁵. A similar result was found in a study conducted in medical students, and it was determined that the stress level was statistically higher in students with IBS compared to healthy individuals (63.6%)⁴⁶. It is seen that stress has a two-way effect in individuals with IBS. Stress may trigger the onset of symptoms, and the presence and severity of symptoms may lead to an increase in stress levels of individuals and thus a decrease in their quality of life⁴³.

Inulin intake, which is a type of soluble fiber, is associated with intestinal peristalsis, colonic transit time, stool consistency and frequency of defecation because it causes changes in the composition and activity of intestinal microbiota, immune response, mineral absorption, and hunger-satiety response¹⁹. Therefore, it is thought that inulin supplementation may be an alternative method in the management of IBS symptoms. In a pilot study conducted by Isakov et al. with individuals with constipation-predominant IBS, it was shown that individuals

who consumed inulin-enriched yogurt (1.23 g/100 g) compared with traditional yogurt consumption; stool frequency, stool type assessed using the Bristol Stool Scale, satisfaction with bowel habits (bloating, feeling of incomplete emptying of the intestine, straining) and colon transit time improved²⁰. In addition, in a randomized controlled study conducted by Pilipenko et al. with 49 individuals with constipation-predominant IBS for 2 weeks, one group (control group) was given a standard diet, while the other group was given a functional drink containing 4 g inulin, 4 mg menthol and 2 mg pyridoxine twice a day in addition to the standard diet. It was shown that stool parameters (stool frequency and stool type), abdominal pain severity, bloating, feeling of incomplete bowel emptying and quality of life improved in the group consuming the functional drink. However, the functional drink has been reported to cause heartburn in individuals, and its composition should be modified to reduce its side effects⁴⁷.

In a randomized crossover case-control study with 47 individuals with constipation-predominant IBS, individuals were randomized to receive one group constipation diet and the other group constipation diet + Stoptoxin® (5 g inulin, 37 mg choline and 40 mg silymarin) for 4 weeks. At the end of 4 weeks, the groups were crossed and assigned to the other diet group and followed with this diet for 4 weeks. It was determined that the intake of Stoptoxin® (5 g inulin, 37 mg choline and 40 mg silymarin) in addition to the constipation diet improved the severity of abdominal pain by 68.3% ($p=0.004$) and the severity of abdominal bloating by 34.8% ($p=0.040$), and the number of weekly stools and stool consistency according to the Bristol Stool Scale improved. However, statistical significance was not found between the groups ($p>0.05$)⁴⁸. In another randomized controlled study involving 40 women with constipation-predominant IBS, one group was given 220 ml kombucha tea enriched with inulin (2.53 g/220 ml) and vitamins (0.59 mg B₁, 0.55 mg B₂, 5.9 mg B₃, 0.7 mg B₆, 81.4 mcg folic acid/220 ml) for 10 days, and a significant increase in defecation frequency was observed in the tea-consuming group compared to the control group consuming only water. The mean values of Bristol Stool Scale scores increased in the kombucha group (3.0 ± 1.2 to 4.4 ± 1.0 ; $p=0.001$), whereas they remained unchanged in the control group (2.9 ± 1.2 versus 3.4 ± 1.2 ; $p=0.6$). There was also a significant decrease in the feeling of incomplete bowel emptying in the kombucha group (1.88 ± 0.78 vs. 1.41 ± 0.56 points; $p=0.015$), which was not observed in the control group⁴⁹. In this study, it was determined that abdominal pain, abdominal bloating, dissatisfaction with bowel habits and total IBS-SSS scores of the prebiotic group showed a significant decrease over time and this statistical difference was due to the fact that the 1st and 2nd month measurements were lower than the baseline measurements ($p<0.05$). In the prebiotic group, the baseline total IBS-SSS score decreased in the 1st and 2nd months of the study and the difference was found to be statistically significant ($p<0.001$). At the end of the study (2nd month), it was determined that the total IBS-SSS score was lower in the prebiotic group compared to the placebo group and the difference was significant ($p<0.05$). Significant improvement was observed in the effect of symptoms such as abdominal pain, constipation, bloating/gas problems on daily life at the end of the study ($p_{\text{time}}<0.05$). It is thought that inulin supplementation may benefit individuals with constipation-predominant IBS by positively changing intestinal peristalsis, colonic transit time, stool consistency and frequency of defecation.

IBS is associated with a significant deterioration in quality of life compared to other chronic diseases. Symptom severity in IBS negatively affects general health and quality of life⁵⁰. Constipation-predominant IBS is associated with poorer health-related quality of life, greater loss of work productivity, and greater utilization of health care resources⁵¹. Quality of life is an important measure that evaluates the personal and social lives of individuals with IBS⁵². In a meta-analysis by Wilson et al. examining the effect of prebiotic use on quality of life in individuals with IBS, it was reported that prebiotic use did not affect quality of life in individuals with IBS, and prebiotic use of ≤ 6 g and >6 g per day did not change quality of life compared to placebo³¹. In this study, it was determined that dysphoria, activity, health concern, social reaction and social relationship sub-dimensions increased in the prebiotic group in a time-dependent way compared to baseline ($p_{\text{time}}<0.05$). It was observed that the statistical difference in dysphoria and social reaction scores was due to the 2nd month scores, which were higher than the baseline and 1st month scores ($p_{\text{time}}<0.05$). In addition, the group and time interaction of dysphoria and food avoidance sub-dimensions was statistically significant ($p_{\text{time} \times \text{group}}<0.05$). In the prebiotic group, the total IBS-QoL score before the intervention increased during the study ($p_{\text{time}}<0.05$). The low values at the beginning of the study indicate that constipation-predominant IBS negatively affects quality of life. At the end of the study, quality of life improved similarly in both groups. However, the quality of life score of the prebiotic group was higher than the placebo group ($p_{\text{time}}<0.05$). This result suggests that prebiotic use may have a positive effect on quality of life. In addition, it can be said that the duration of the study, the amount given and the type of prebiotic used were effective.

It is stated that the severity and frequency of IBS symptoms can negatively affect the quality of life of individuals⁵³. In the study by Choghakhori et al., there is a strong negative correlation between the IBS-QoL and IBS-SSS, and there is also a moderate negative correlation between the IBS-QoL and abdominal pain, bloating, gas, dissatisfaction with bowel habits and general gastrointestinal symptoms⁵⁴. In a study by Andrae et al. to determine the correlation between quality of life and IBS symptoms in IBS patients, it was observed that there was a strong negative correlation between IBS-QoL and IBS-SSS and a moderate negative correlation with abdominal pain⁵⁵. In this study, it was found that the total IBS-SSS scores of the prebiotic and placebo groups decreased over time, but the decrease was significant only in the prebiotic group. When the effect of symptom severity score (IBS-SSS) on quality of life (QoL) was evaluated in the study, a negative and moderate relationship was found between the 2nd month IBS-SSS scores and IBS-QoL scores in the placebo group ($p<0.05$). It is thought that prebiotic (inulin/oligofructose) supplementation may be effective in reducing symptom severity and frequency and improving quality of life, and thus may be beneficial in individuals with constipation-predominant IBS.

According to the Diagnostic and Statistical Manual of the American Psychiatric Association, depression is defined as the presence of psychological complaints accompanied by impaired functioning. Symptoms include changes in weight or appetite, sleep disturbance, abnormal physical movements such as agitation or

retardation, feeling of fatigue and difficulty concentrating⁵⁶. In a study, it was reported that approximately 25.7% of individuals with IBS had borderline and clinically significant depression according to the Hospital Anxiety and Depression Scale score⁵⁷. In another study conducted with Korean individuals with IBS using the same scale, this rate was slightly higher (38.6%). It has also been reported that depression negatively affects individuals' quality of life and symptom pain severity⁵⁸. It has been reported that approximately half of individuals with IBS have anxiety and/or depression. Individuals with constipation-predominant IBS are reported to experience psychological disorders at a higher rate than other categories of IBS⁵⁹. In a meta-analysis of 27 studies including 2293 individuals with IBS and 4951 healthy controls from East Asia, America and Europe, it was reported that the incidence of depression and anxiety was higher in individuals with IBS. In addition, the prevalence of depression and anxiety is higher in individuals with constipation-predominant IBS compared to diarrhea-predominant IBS⁶⁰. This is associated with intestinal serotonin imbalance and decreased sensitivity to serotonin in the central and peripheral regions of these patients⁶¹. In this study, while the pre-intervention Beck depression scale score in the prebiotic group was 9.4 ± 4.8 , it decreased to 6.8 ± 4.3 and 5.5 ± 3.3 (respectively) in the 1st and 2nd month of the intervention. Although depression was not determined according to the scale in both groups, the decrease in the score is a positive situation. In the prebiotic group, there was a significant decrease in the Beck depression scale score after the intervention depending on time ($p_{\text{time}} < 0.05$). There was no significant difference in the interaction effect of group and time for total Beck score ($p > 0.05$). IBS is a disease that includes both physical and mental components and should be managed by two disciplines, gastroenterology and neurology. It is important for physicians to evaluate and address psychological symptoms in all patients with functional gastrointestinal disorders.

Strengths and limitations

One of the strengths of the study is its randomised controlled design. In addition, the diagnosis of IBS and the effectiveness of the treatment were evaluated by the clinician. The fact that individuals had constipation-predominant IBS subtype is important in terms of study design and homogeneity. In the study, the researcher contacted the patient once a week via telephone, thus ensuring patient follow-up and compliance with the treatment. Not only intestinal symptoms but also depression, which can be commonly seen together, were questioned. The participants' quality of life was also assessed.

Despite the strengths of this study, it has some limitations. In this study, stool samples of individuals with constipation-predominant IBS were not examined and therefore the effectiveness of the inulin/oligofructose mixture on gut microbiota could not be observed. Since the same amount of inulin/oligofructose supplementation was given to the prebiotic group, the effect of different amounts of inulin/oligofructose could not be evaluated.

The clinical efficacy of a low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) diet in IBS is well known but was not the main aim of this study and was not administered to patients. The IBS-QoL scale and Beck Depression Scale are self-report scales and therefore may cause bias during data collection.

Conclusion

It may be appropriate for individuals with IBS to be aware of their disease, to apply lifestyle changes, to determine the topics to be regulated in their diet, to encourage physical activity and to provide psychological support to reduce their stress in order to manage the disease, reduce symptoms and improve quality of life after diagnosis. Dietary restrictions in individuals with IBS may lead to energy and nutrient deficiencies. Therefore, it is of great importance that the nutrition of individuals should be evaluated by a dietitian from the first moment of diagnosis and their nutritional treatment should be followed up. In this study, only the effect of inulin supplementation was examined. It may be recommended to first determine the adverse conditions that may be related to the disease in the diet of individuals and then consider supplementation. In this study, inulin supplementation was found to improve bowel symptoms and quality of life, but had no superior effect on symptoms of depression and stool type compared to the placebo group. A significant reduction in IBS-SSS scores was observed and improvement was observed especially in symptoms such as abdominal pain, bloating and dissatisfaction with defecation habits. Therefore, it is thought to be useful in individuals with constipation-predominant IBS. Since the quality of life of individuals with IBS is negatively affected, psychological comorbidities such as anxiety and depression may develop. In this study, stress was found to be the most common factor affecting the progression of IBS. Therefore, a multimodel perspective that includes psychological support (cognitive behavior therapy, stress management strategies, etc.) in addition to lifestyle changes (dietary changes, etc.) may be useful in the treatment of IBS. In this study, inulin supplementation in individuals with IBS and gastrointestinal symptoms can be said to have a potential beneficial effect by reducing IBS-SSS and increasing IBS-QoL score.

Data availability

Materials described in the manuscript will be available upon contacting the contact author, Dr. Çağlar Akçalı.

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Author contributions

Conceptualization, Ç.A. and A.U.; methodology, Ç.A., A.U. and K.A.; software, Ç.A.; formal analysis, Ç.A.; investigation, Ç.A., A.U. and K.A.; data check, Ç.A. and K.A.; writing—original draft preparation, Ç.A., and A.U.; writing—review and editing, Ç.A. and A.U. All authors have read and agreed to the published version of the manuscript.

Declarations

Competing interests

The authors declare no competing interests.

Ethical approval

Ethical approval of the study was obtained from Izmir Bakırçay University Non-Interventional Clinical Research Ethics Committee (Date: 03/11/2021, Decision No: 377). In addition, the study was conducted within the framework of the Helsinki Declaration Principles and informed consent and approval were obtained from the participants.

Registration: The study was registered at www.clinicaltrials.gov (NCT06610188) (24/09/2024).

Additional information

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