

Smartphone application for celiac patients: assessing its effect on gastrointestinal symptoms in a randomized controlled clinical trial

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Abstract

Background: We aimed to study the effectiveness of information provided via smartphone application on gastrointestinal symptoms in patients with celiac disease (CD).

Methods: In the present randomized controlled clinical trial, 60 patients with CD were randomly assigned to receive education through a smartphone application (n=30) or conventional clinical education (n=30). The patients were asked to use it for obtaining the required information for three months. We assessed gastrointestinal symptoms using the gastrointestinal symptom rating scale (GSRS) questionnaire at baseline and three months after interventions. The GSRS total score, celiac disease GSRS (CD-GSRS) score, abdominal pain, reflux, diarrhea, constipation, and indigestion scores were calculated.

Results: Out of 60 randomized patients, 58 patients completed the study. The mean age of the participants was 37.49 ± 9.32 years, and the mean disease duration was 4.57 ± 3.36 years. There were no significant differences between the two groups regarding the baseline values. In comparison to baseline, the mean CD-GSRS score ($p=0.001$) and indigestion subscore score ($p<0.001$) were significantly decreased in the intervention group. The results of the between-group comparisons showed that although the mean GSRS and CD-GSRS total scores were lower in the intervention group than in the standard care group, the differences were not statistically significant. In terms of GSRS subscores, there was a significant difference between the two groups only in the mean score of indigestion ($P=0.002$).

Conclusion: According to the results, using smartphone application for providing information to patients with celiac disease had only a significant positive effect on indigestion symptoms compared with routine clinic education, and we did not observe any significant differences in GSRS and CD-GSRS scores between the two groups.

Trial registration: The protocol of the study was registered in the Iranian registry of clinical trials (IRCT code: IRCT20170117032004N2). trial registry webpage: <https://www.irct.ir/user/trial/40187/view>. Trial registry date: 2019.6.26

Background

Celiac disease (CD) is an autoimmune enteropathy characterized by gluten intolerance¹. It is associated with the destruction of the small intestine mucosa and accompanied by different gastrointestinal (GI) and non-GI symptoms¹. Eliminating gluten-containing foods from the diet is the only available treatment for these patients². However, due to different reasons, such as lack of knowledge, inadequate labeling and high cost of gluten-free products, strict compliance with a gluten-free diet (GFD) is challenging³. In Iran, vouchers are given to patients to buy essential gluten-free products such as bread and flour. However, lack of knowledge about gluten-containing products is one of the main problems. Although individualized education by an expert dietitian is considered the standard of care, it is costly and time-consuming. Therefore, different methods were studied to overcome these limitations. In this regard, the positive effect of online education programs has been shown in previous studies. For example, Sainsbury et al showed that six weekly online

modules, including a combination of education, validated behavior change techniques and cognitive behavior therapy, were effective in improving adherence to GFD in adult patients with celiac disease⁴. Moreover, in children with celiac disease⁵, the interactive e-learning module was shown to be effective in increasing patients' knowledge about GFD. However, online methods depend on internet access and are not available wherever you need them. Text-message intervention is another method of providing information to patients with celiac disease, and its efficacy in improving patient quality of life has been shown⁶. This method was limited by the fact that very little data can be transferred through it. Therefore, it seems that there is a need for a more appropriate method that covers the limitations of previous methods. Recently, due to the global increase in the use of smartphones, transferring health messages through smartphone applications has grown. This method was used for promoting health-related behaviors in different studies⁷⁻¹¹. In terms of diet therapy, the positive effect of a smartphone application in weight reduction programs has been shown¹²⁻¹⁴. Therefore, we hypothesized that this method may also be an effective method of transferring GFD information to celiac patients. Previously, an English language smartphone application, "MyHealthyGut", was developed for celiac patients¹⁵, and its positive effect on gastrointestinal symptoms had been reported¹⁶. However, concerning the differences in the list of gluten-free products between countries, a specific application should be developed for each culture and country. There is no inclusive Persian application for celiac patients that covers all aspects of the GFD. Therefore, we developed a Persian-language application for patients with celiac disease and confirmed its positive effect on patients' knowledge and adherence to the GFD¹⁷. In the present study, we aimed to study the effectiveness of a three-month educational intervention delivered via smartphone application compared with standard care on decreasing gastrointestinal Symptom Rating Scale (GSRS) scores in patients with celiac disease. Moreover, in a post hoc analysis, the scores of three domains that are most relevant to celiac disease were compared between groups.

Methods

Participants:

In the present two-arm, parallel design randomized controlled clinical trial, the patients were selected randomly from the East-Azerbaijan celiac disease registry database based on the following criteria: age > 18 years, being at least 6 months postdiagnosis, and use of a smartphone. Patients who had other chronic inflammatory GI diseases, diabetes, psychiatric, or neurological disease that could interfere with assessments were excluded. All patients were diagnosed based on positive serology markers (including anti-tissue transglutaminase (tTG) antibodies, endomysial antibodies (EMA) and deamidated gliadin peptide (DGP) antibodies) confirmed by compatible duodenal histological findings.

In the present study, 65 celiac patients were randomly selected out of 80 patients who had eligibility criteria. Five patients did not consent to participate in the study, and 60 patients were randomly assigned into two groups using the GraphPad randomization software tool. The randomization process was conducted by a third person not involved in the research protocol. All patients received GFD recommendations in the celiac clinic of Imam Reza Hospital with the help of leaflets before the study. An

expert nutritionist designed the leaflets. The patients in the intervention group (n=30) received the “celiac” application, and they were asked to use it for three months to obtain the required information. The patients in the control group (n=30) continued their weekly routine education with the help of leaflets in the clinic. Both programs (application or leaflet) had identical topics and included information about disease, gluten-free food items, gluten-free drugs, gluten-free food labeling, and gluten-free cooking. The outcome assessor and statistician were blind to group allocation.

“celiac” is a Persian language application designed by our research team based on the Analysis, Design, Development, Implementation, Evaluation (ADDIE) model¹⁸.

In the first phase, we reviewed the published articles, various health and diet-related applications, and interviewed patients with celiac disease to gather the relevant information to define the education scopes and purposes of the application and create the main contents and sub-contents of application. Then, based on this information, a professional Web producer developed the first draft of an application. A team of gastroenterologists and expert nutritionists evaluated the first version. In addition, with the help of five patients with celiac disease, the usability of the application was checked. Based on the experts' and patients' comments, minor modifications were made, and the “celiac” was developed.

The “celiac” is the free android-based application that can be used both on smartphones and android tabs and provides different information regarding CD and GFD in seven sections, including “about disease”, “gluten-free diet”, “gluten-free drugs and supplements”, “gluten-free food labeling”, “gluten-free cooking”, “calculations” and “celiac centers in Iran”. In the “about disease” section, various information, such as disease causes, symptoms, diagnosis, and treatments, was provided. In the “gluten-free diet” section, more than 150 foods were marked by three colors: green for allowed foods, red for prohibited foods, and orange for suspicious foods. The generic name and factory name of the gluten-free drug list introduced by Iran's Food and Drug Organization were provided in the “gluten-free drugs and Supplements” section. In “gluten-free food labeling”, the names of different food ingredients that may contain gluten were provided. In “gluten-free cooking”, the cooking methods of different foods with gluten-free ingredients were provided. The calculation section allowed patients to calculate their body mass index (BMI) and to register their tissue transglutaminase antibodies for follow-up. Finally, the “Celiac Disease Centers” section listed the address of CD clinics and gluten-free food providers in different provinces of Iran for more access of patients to gluten-free foods when they are on the journey. The patients were asked to use it for obtaining the required information for three months and informed us about the probable difficulties.

Outcome measure:

The difference in the severity of gastrointestinal symptoms between the two groups was the outcome of interest that was assessed by the Gastrointestinal Symptom Rating Scale score (GSRS) questionnaire. This questionnaire is a seven-point Likert scale with 15 questions that has response options ranging from “no problem (0)” to “severe discomfort (6)”. The questionnaire is divided into 5 domains that cover the gastrointestinal system: diarrhea (3 questions; score range: 0-18), constipation (3 questions; score range: 0-18), abdominal pain (3 questions; score range: 0-18), reflux (2 questions; score range: 0-12), and

indigestion (4 questions; score range: 0-24). The questionnaire was translated into the Persian language and validated in our population previously¹⁹. In a post hoc analysis, the three domains that are most relevant to celiac disease were evaluated separately using celiac disease-GSRS (CD-GSRS). This modified questionnaire contains 10 questions from the GSRS and includes the following domains: diarrhea (3 questions; score range: 0-18), abdominal pain (3 questions; score range: 0-18), and indigestion (4 questions; score range: 0-24)²⁰. Higher scores represent worse symptoms.

This study adheres to CONSORT guidelines.

Statistical analysis:

Originally, the study was designed and powered to detect the effects of a smartphone application on patients' knowledge and adherence level, which were taken as the primary endpoints (data were presented in our previous publication). In this study, we presented the secondary outcome variables and the gastrointestinal effects of our intervention. Using the results of a previous study that assessed the effect of education on celiac patient adherence score (CDAT score)⁶, assuming a significance level of 0.05 and power of 80%, the minimum sample size needed to detect a significant between-group difference in adherence level was 24 participants in each group. Considering the probability of a 20% attrition rate, the desired sample size was 30 patients in each group.

SPSS 21.0 was used for statistical analysis. Skewness and kurtosis were used to test the assumption of normality. The continuous values were reported as the mean and standard deviation, and the nominal and categorical variables such as sex, educational status, occupation categories, family history, comorbidities presence, and March categories were reported in frequency and percentage. A paired t-test was used to compare the changes in each score before and after the interventions. The differences in baseline values between two groups were compared by independent sample t-test. One-way analysis of covariance (ANCOVA) with adjustment for age, sex, disease duration, educational level, and baseline values was used to compare the after intervention values between the two groups. For comparing the nominal and ordinal variables, the chi-square and Mann-Whitney U tests were used. Test results are reported as significant for $P < 0.003$, adjusted for multiplicity (Bonferroni's correction $0.05/14$)²¹.

Results

In the present study, out of 60 patients who were randomly divided into two groups, the questionnaire of one patient in the intervention group was incomplete, and one patient in the standard care group was lost to follow-up (Figure 1). The data were analyzed on 29 patients in each group. Table 1 presents the baseline characteristics of the patients. As indicated, the baseline characteristics were not significantly different between groups ($P > 0.05$).

The mean changes from baseline of GSRS scores and subscores stratified by groups are shown in Figure 2. As depicted, in comparison to baseline, the mean CD-GSRS score ($p = 0.001$) and indigestion subscore

($p < 0.001$) were significantly decreased in the intervention group. In the standard care group, compared to baseline, no significant changes were observed.

Table 2 shows the comparison of the mean GSRS total score and subscores between the two groups. There were no significant differences between the two groups at baseline. Three months after the intervention, the mean GSRS and CD-GSRS total scores were lower in the intervention group than in the standard care group; however, the differences were not statistically significant. In terms of subscores, the indigestion score was significantly lower in the Application group than in the standard care group ($P = 0.002$).

None of the patients reported any problems regarding downloading or use of the application.

Discussion

Increasing the knowledge of celiac patients about gluten-free food, drugs, and commercial products is considered an important way of increasing their adherence to GFD and alleviating disease symptoms²². In the present study, to overcome the limitations of the previous methods, we designed a smartphone application and assessed its efficacy in decreasing GI symptoms in celiac patients. We showed that a smartphone application was significantly more effective in decreasing the indigestion score compared with the standard care group. These results were consistent with the findings of a previous study that used the “MyHealthyGut” smartphone application in celiac disease. Dowd et al showed that one-month use of application had a significantly more positive effect on GI symptoms in celiac patients compared with the standard care group¹⁶. These findings may be due to the specific characteristics of smartphone applications that increase the patient’s adherence to the diet. A large amount of information can be transferred through applications²³ and considering the mobility feature of them, by just installing the applications, they can be used whenever somebody needs it²⁴. In addition to the gluten content of foods, other information, such as gluten-related labeling and gluten-free drug lists, was also provided to patients through applications. Previously, a lack of knowledge about the gluten content of commercial foods and drugs was reported as a barrier to GFD adherence²². However, using this application, this information can easily be used during shopping and dining outside the home and could increase the patient’s adherence to the diet.

Although the GSRS total score and some subscores (reflux, abdominal pain, diarrhea, and constipation) were lower in the intervention group than in the standard care group, they did not reach standard levels of significance. Although symptoms of celiac disease improve within weeks after strict adherence to GFD, not all patients have adequate adherence to GFD from the beginning of the study. Therefore, we assume that a longer follow-up period would be associated with significant differences. Moreover, the possibility that education via application was not superior to standard care cannot be excluded.

We acknowledge the limitations of the present study, such as the short duration of the follow-up and low sample size. Moreover, assessing GI symptoms was the secondary endpoint of this clinical trial, and the

power calculation was not performed for this aim. Additionally, we only included patients who had the ability to read and had a smartphone that limits its generalizability to all celiac patients.

Conclusions

In conclusion, a smartphone application was significantly more effective than routine clinic education in relieving indigestion symptoms. However, in terms of other symptoms, there were no significant differences between groups. Considering the limitations of the study, further investigations with longer follow-up durations are needed to prove that providing information via smartphone application would be sufficient to help patients feel better.

Declarations

Ethics approval and consent to participate: The present study was approved by the Ethics Committee of Tabriz University of Medical Sciences (IR.TBZMED.REC.1397.697). Written informed consent was obtained from all participants.

Consent to publish: Not applicable

Availability of data and materials: The datasets supporting the conclusions of this research are included within the article.

Competing interests: The authors declare no conflicts of interest.

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Authors' contributions: **ZN:** Conceptualization; Funding acquisition, Supervision, Methodology, Writing-review & editing, Formal analysis; **ZAN:** Project administration, Software, Writing - review & editing; **MSH:** Project administration, Writing - review & editing.

All authors have read and approved the manuscript.

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Abbreviations

CD: Celiac disease; GFD: Gluten-free diet; GSRS: gastrointestinal symptom rating scale; CD-GSRS: celiac disease-gastrointestinal symptom rating scale (GSRS); ANCOVA: one-way analysis of covariance

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Tables

Table 1: The baseline characteristics of participants stratified by groups

Variable	Intervention (n=29)	Control (n=29)	p-value
Age (Mean±SD) Years	36.04±8.54	38.62±9.88	0.28#
Sex n (%) male/female	8 (27.5)/ 21 (72.4)	10 (34.4)/ 19 (65.5)	0.22##
Education n (%)			
≤ Diploma	15 (51.72)	20 (68.9)	0.18##
College education	14 (48.27)	9 (31.0)	
Marital status			0.32##
Single	8 (27.58)	7 (24.1)	
Married	21 (72.4)	22 (75.8)	
Occupation			0.62##
Employed	10 (34.4)	11 (37.9)	
Student	3 (10.3)	3 (10.3)	
House wife	16 (55.1)	15 (51.7)	
Positive Family history	2 (6.8)	1 (3.4)	0.38##
Marsh			0.35##
I	4 (13.79)	3 (10.34)	
II	6 (20.68)	5 (17.24)	
IIIa	6 (20.68)	9 (31.03)	
IIIb	8 (27.58)	7 (24.13)	
IIIc	5 (17.24)	5 (17.24)	
Presence of comorbidities	6 (20.68)	9 (31.0)	0.55##
Disease duration (years)	5.32±4.05	3.51±2.26	0.16#

BMI: Body mass index; SD: standard deviation

#P-value of independent t-test

P-value of chi-square

Table 2: The comparison of the GSRS total scores and subscores between studied groups.

Variables	Application group (n=29)		Placebo (n=29)		p-value#	p-value##
	Before	After	Before	After		
GSRS total score	33.64±18.44	27.28±15.69	36.93±23.47	35.09±19.05	0.57	0.36
CD-GSRS	25.32±13.62	17.48±11.13	25.31±16.92	22.09±13.21	0.99	
Abdominal pain	6.04±4.76	5.04±5.64	7.80±6.01	5.65±4.35	0.24	0.31
Reflux	3.04±3.22	3.75±4.02	3.93±4.05	6.06±4.22	0.38	0.09
Indigestion	13.84 ±5.96	8.20±5.3	13.23±7.89	12.36±7.91	0.40	0.002
Diarrhea	5.91±7.16	4.62±6.10	6.96±6.75	4.89±6.24	0.58	0.40
Constipation	5.62±4.79	6.45±6.97	8.46±6.30	7.82±7.92	0.07	0.47

GSRS: Gastrointestinal Symptom Rating Scale; CD-GSRS: celiac disease-gastrointestinal Symptom Rating Scale;

#p-value of independent t-test

##p-value of one-way ANCOVA with adjusting to age, sex, disease duration, and baseline values

Figures

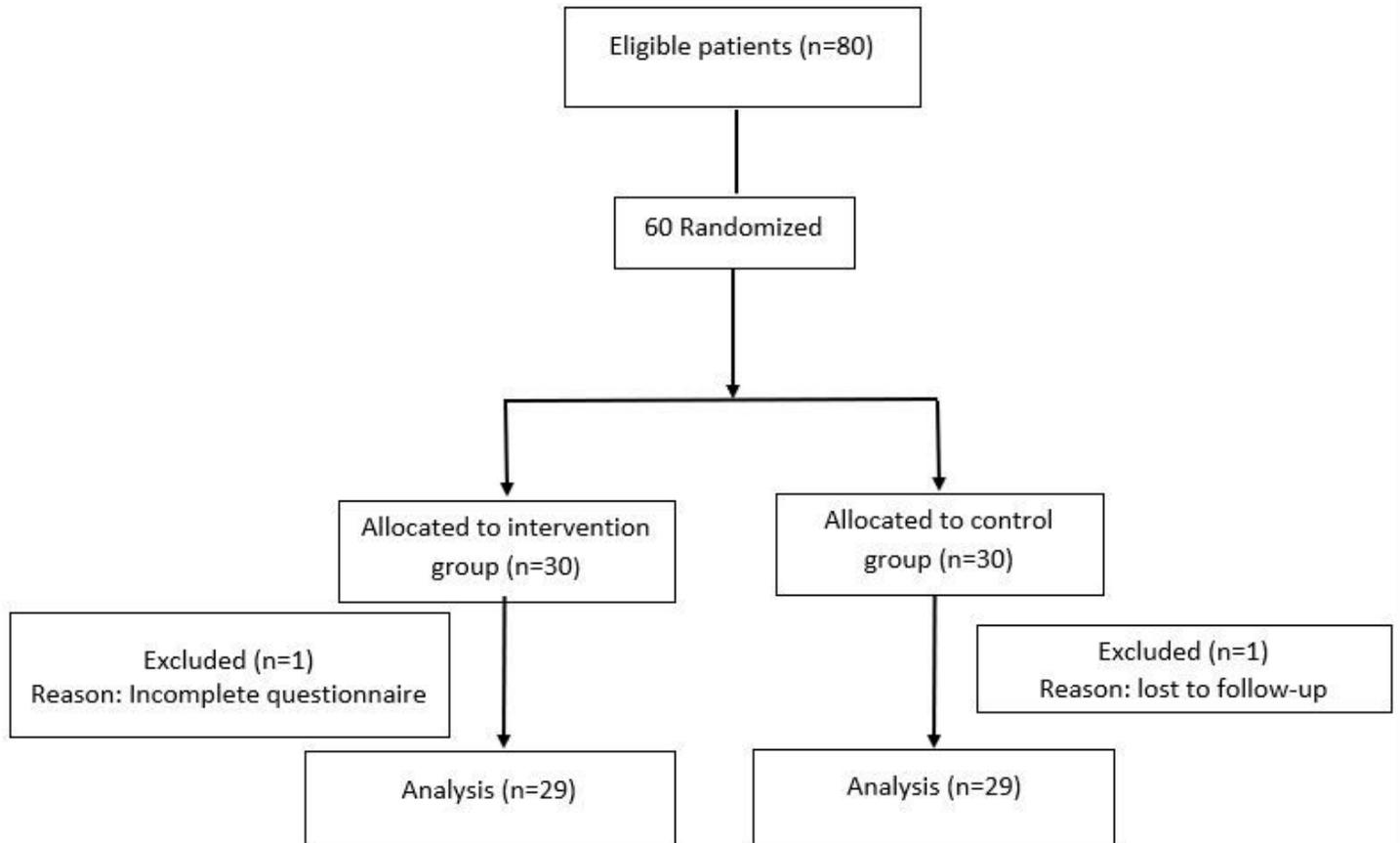


Figure 1

Flow chart for patient enrolment, randomization, and retention

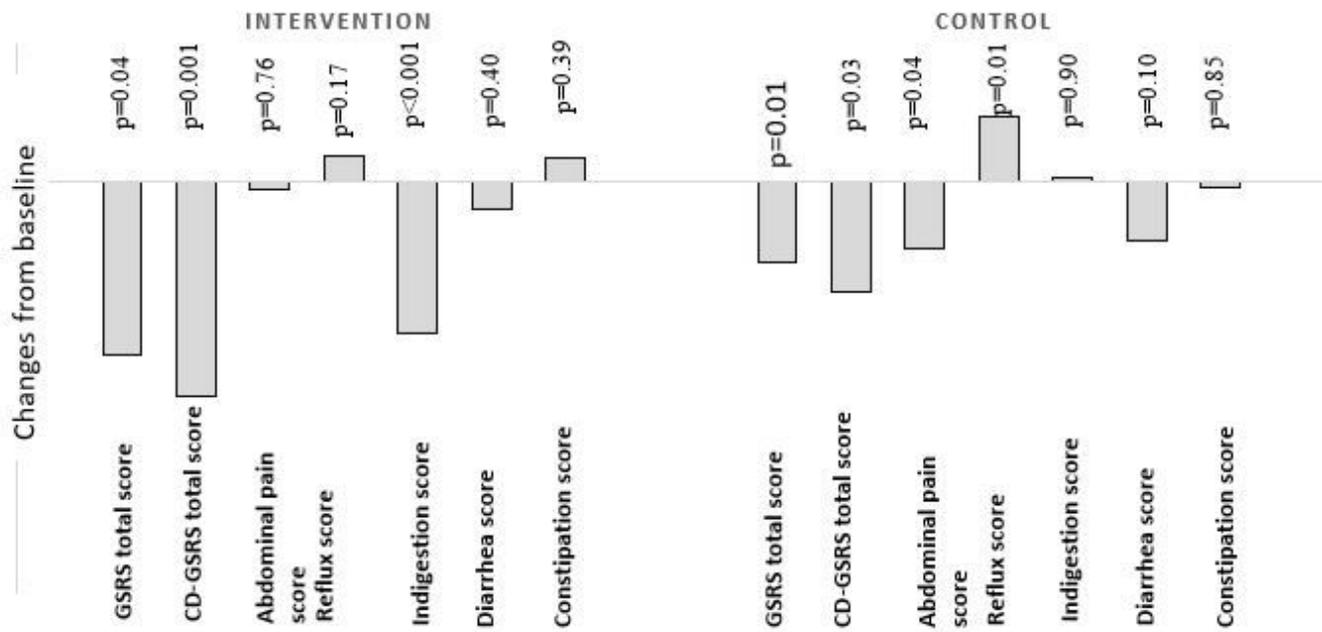


Figure 2

Mean changes from baseline of GRS and subscores stratified by groups CD: celiac disease *p-value of paired t-test comparing the mean changes from baseline of GRS scores and subscores