ORIGINAL ARTICLE

Depression and Anxiety and the Effectiveness of Cognitive Behavioural Therapy in IBS Patients: A Randomized Controlled Trial

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Abstract

Backgrounds: Anxiety and depression are found to be the major contributors to irritable bowel syndrome (IBS). The present study aimed to measure the effect of a specifically designed cognitive behavioural therapy (CBT) program on the severity of the symptoms and quality of life of patients with chronic IBS, and also define whether anxiety and depression in patients with IBS at baseline affect their response to CBT.

Methods: The participants were randomly allocated to conventional treatment only (n=25, control) or CBT plus conventional treatment (n=25, intervention) group. The intervention group attended an eight-session group stress management training course conducted by a psychologist in a meeting room at a gastrointestinal clinic at Yasuj University of Medical Sciences. Pre- and post-interventions and 3-month follow-up visits were scheduled and conducted by an experienced healthcare worker to measure the primary outcomes and levels of depression and anxiety in the patients. The study was conducted on 2011.

Results: The Raw Group Difference (RGD) and Standardised Mean Differences (SMD) for the post-treatment scores of the intervention group, when compared with those of the control group, indicated a considerable improvement in the severity of IBS symptoms (RGD=−10.48, SMD=−1.23), anxiety (RGD=−9.90, SMD=−0.725), depression (RGD=−9.57, SMD=−0.785) and patient's quality of life (MD=−16.81, SMD=−0.469). No association (and interaction with CBT) was found between anxiety/depression at baseline and post-treatment or follow-up scores of the outcomes.

Conclusion: Although CBT improved anxiety, depression, severity of IBS and quality of life of patients with IBS, its effect was independent of the initial level of anxiety and depression of the patients.

Trial registration number: IRCT201102195868N1

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Introduction

It is estimated that about 11% of the people around the world suffer from irritable bowel syndrome (IBS), the most prevalent digestive functional disorder.[1] This disorder is characterised by chronic abdominal pain, alteration in bowel habits, bloating, and discomfort.[2] IBS is also associated with several psychological and

social problems including stress, anxiety, sleeping disorder, sexual dysfunction and sick leave.[3,4] However, as suggested by Cremonini and Talley, social and psychological problems can predict IBS.[5] For example, Dean and colleagues reported that 50%–90% of the patients with IBS who participated in their study had experienced psychological disorders earlier in their life.[6] In other words, a bidirectional causal relationship may exist between IBS and psychological disorders.[5]

Based on a biopsychosocial model introduced by Drossman and colleagues, gastrointestinal illnesses are influenced by interactions between a wide and diverse range of social, biologic and psychological factors.[7] Of these influential factors, stress is strongly associated with gastrointestinal conditions, including IBS.[8] Lackner suggested the following three pathways that explain the mechanism of the effect of psychological distress on IBS: directly through biological system, adaptation of illness behaviours and mediating the risk of IBS onset.[9] Based on a neurobiological model, sustained stress has been noted to cause chronic alterations in central stress and arousal circuits, which are referred to as emotional motor system (EMS), including sympathetic and parasympathetic, endogenous pain modulation and ascending aminergic pathways. Alterations in the EMS system can in turn initiate or worsen the IBS symptoms.[10] Accordingly, psychological and specifically designed behavioural interventions, including cognitive behavioural treatments, can be effective in the management of IBS symptoms.[9,11] Based on Lackner's theory, there are two sets of behavioural intervention strategies: direct behaviour alteration techniques (e.g. assertiveness training), which work by directly altering the behaviour or environmental contingency, and respondent techniques (e.g. cognitive behavioural interventions), which work by providing the patients with the ability to manage their psychological arousal.[9] Briefly, cognitive behavioural therapy (CBT), which can be applied on individual or group bases, are specifically designed methods to change the way in which a person thinks and behaves to manage his/her defined problems.[12,13] As a result of the ability to manage psychological arousal, the patients can control IBS symptoms via the brain-gut axis.[11]

The positive effects of cognitive and behavioural interventions on several aspects of psychosomatic conditions have been investigated by experimental studies, and many of them have supported the significant effect of CBT on the clinical aspects of IBS.[14] For example, in a randomised trial, Jones and colleagues examined the pathways of the association between CBT and severity of IBS.[15] They concluded that CBT affects IBS via indirect pathways involving alteration in anxiety and depression following significant changes in mood, which in turn improves anxiety and depression. In other words, CBT helps individuals to manage excess physical or emotional reactions when facing social or emotional situations by changing the way in which individuals think, believe or act.[16] These chains of effects are suggested to be responsible for the relief from the severity of IBS. However, despite all these conclusive experimental and theoretical studies suggesting better therapeutic effect of CBT on IBS, when compared with that of conventional medicine, few studies have found no or slight superiority of CBT. For example, Blanchard and colleagues, in two consecutive studies, failed to find significant superiority of CBT over conventional treatments.[17,18]

In 2010, Reme and colleagues conducted a randomised controlled trial (RCT) to define the predictors of the outcomes of two types of treatments, namely mebeverine hydrochloride and mebeverine+CBT, in patients with acute IBS.[19] Interestingly, they found better outcome in the mebeverine hydrochloride (control) group when the baseline levels of depression and anxiety were lower and improved outcome in the mebeverine+CBT group when psychological distress was higher. Accordingly, they concluded that anxiety and depression at baseline are significant predictors of the outcome measures.

Based on the proposed contributions of anxiety and depression to the effect of CBT, the present study evaluated the impact of a stress management training program and its interaction with anxiety or depression on IBS. Only chronic patients who did not respond to conventional medical treatments were selected, assuming that their clinical conditions are more susceptible to their psychological distress.[19]

Methods

The study was approved by the research ethics committee of Yasuj University of Medical Sciences (trial register number: IRCT201102195868N1). On 2011, gastrointestinal specialists were contacted and asked to introduce interested patients with diagnosis of IBS for more than 6 months who did not show satisfactory response to conventional treatments during this period.

Participants

A total of 50 patients with chronic IBS symptoms (lasting for more than 6 months) and showing no response to conventional medical treatments were referred to the study office located at Yasuj University of Medical Sciences by their physicians. Written informed consent was obtained from the patients before they were randomly allocated to either intervention or control groups (25 participants each). However, 8 patients (16%, 4 participants each in the intervention and control groups) did not attend the sessions or post-intervention appointment. No

significant differences in the background variables and baseline measures were observed between the dropouts and study patients. The participants were predominantly young (mean age 32.9 years, range 15–55 years), male (57.1%), married (69%) and had a university degree (47.6%). The mean duration of IBS symptoms among the patients was 65 months (range 6–288 months).

Inclusion Criteria

The patients were included if their conditions were diagnosed as IBS by gastrointestinal specialists (the diagnosis was made based on Rome III criteria). Other inclusion criteria included suffering from IBS for at least 6 months, recurrent abdominal pain for at least 3 days in the last 3 months, no satisfactory response to treatments prescribed by their physicians (gastrointestinal specialists) and willingness to participate in the study.

Exclusion Criteria

The exclusion criteria were the presence of any underlying pathological evidence, severe psychological disorders or family history of colon cancer. Furthermore, the patients were also excluded if they reported any history or concurrent non-medical (i.e. psychological) treatment for their condition.

Primary Outcomes and Other Measures

Self-report Irritable Bowel Syndrome Quality of Life Questionnaire (QOL–IBS 34) was used to measure the impact of IBS on various aspects of the patient's quality of life. The score for each question was based on a five-point Likert response scale, with lower score indicating better quality of life. Furthermore, self-report Bowel Symptoms Severity and Frequency Scale (BSS-FS) was used for measuring the severity of IBS. This scale consists of 20 questions (in Farsi) and measures the severity of IBS based on Rome III criteria. The scale has been reported to be reliable and valid.[20] Further information on the BSS-FS scale and its validity and reliability has been presented elsewhere.[21] The anxiety and depression levels of the participants were measured by Beck depression and anxiety inventory questionnaires. The scores of anxiety and depression are considered as indicatives of those symptoms and not as diagnostic measures. Data on age, sex, education and duration of the disease of the participants were provided by the participants during the baseline visit. All these questionnaires are available in Farsi version and are evaluated and widely used for research purposes.[22-24] The questionnaires were completed by an interviewer before the first and after the last sessions as well as about 3 months after the intervention during routine visits in the physicians' offices. The participants in the intervention and control groups were invited for the interview through an invitation letter and a reminder phone call. The interviewer was particularly trained and familiar with the study questionnaires and was not among the research team members (Figure 1).

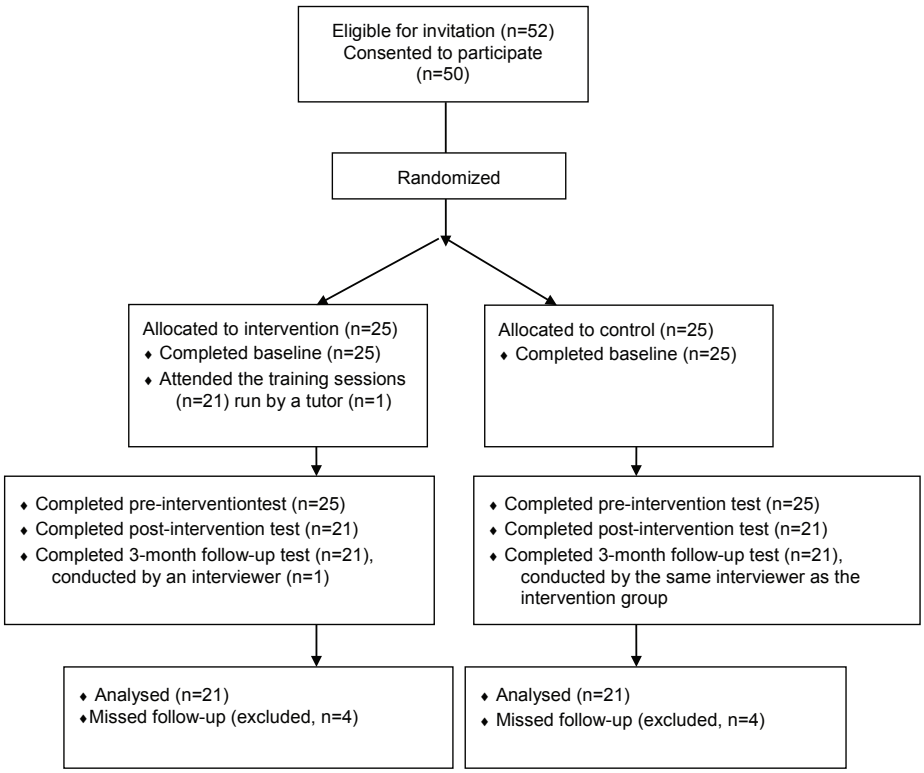

Figure 1: The follow-up process

Intervention

The participants were randomly allocated to either intervention or control groups using block randomization in an un-blinded manner. The control-group participants continued taking routine medicine prescribed by their physicians during the study period (medicine was the only treatment prescribed by the physicians). The intervention-group participants, in addition to the treatment, attended an eight-session group based on stress management training program (7 patients in each group, each session conducted for 2 h a week). The program was based on CBT principles according to a predefined and widely used training protocol with a slight modification to meet patient-specific requirements.[25,26] Sessions were run by a professional and experienced psychologist at a gastrointestinal clinic at Yasuj University of Medical Sciences. Briefly, the patients were given an introduction about the disease and its symptoms, followed by an opportunity to learn and practice relaxation, anger management and social support skills. The scheduled outlines and an overview of each session are presented in Table 1. After each session, a checklist was completed by the tutor to assess the content coverage of that session and uncovered issues were addressed at the start of the next session. To ensure that the participants attended their scheduled appointments, a call was made to all participants a day before each session to remind them the time and place of their appointment. Study visits and training sessions were scheduled to align with the participants' medical appointments. No further CBT or other complementary intervention was provided to the participants after the intervention. The program was organized and supervised by a team consisting of three experienced psychologists. Neither the participants nor the interviewer was blinded to the assignment of the intervention.

Randomization was conducted by a person independent of the research team using computer-generated random number list.

Power Calculation and Analysis

A post-hoc power analysis was conducted on the baseline measurements and the results indicated that a sample size of 42 (21 patients each in the intervention and control groups) provided 80% power to detect half of the SD difference in the severity of the symptoms between the study groups. Raw Group Difference (RGD) in the mean and Standardized Mean Difference (SMD) were calculated to measure the effect size of CBT based on post-intervention measures. Bivariate and multivariate analyses were performed using Chi-square, independent and paired t-tests and generalized linear model for repeated measures. To measure the interaction between intervention and baseline levels of anxiety and depression, the scores of anxiety and depression were included in the models as covariates and interaction terms.

Results

Of the eligible participants, 16% dropped out of the follow up because they did not attend the training sessions or post-intervention and follow-up appointments (4 patients each in the intervention and control groups). As expected, no significant difference was observed between the participants in the intervention and control groups regarding age, sex, education, scores of quality of life, depression and anxiety as well as the duration and severity of IBS symptoms at the baseline visit (Table 2). Bivariate comparison of post-intervention measures between the two study groups indicated significant improvements in the primary outcomes of the patients owing to the intervention ($P<.05$ for all measures, the results are not presented). Accordingly, the RGD and SMD±$CI_{95\%}$ indices for the post-treatment measures of the intervention group, when compared with those of the control group, indicated considerable improvements in the severity of IBS symptoms (RGD=10.48; SMD=1.18; $CI_{95\%}$=0.52,1.83), anxiety (RGD=9.90; SMD=0.73; $CI_{95\%}$=0.10,1.35),

Table 1: Sessions of the intervention

Session 1	Understanding IBS	1- Patients introduced themselves to their group 2- Understanding physiology of the digestive system, effects of psychological factors on IBS and its severity and complications. 3- Understanding the goals and expectations of the program
Session 2	Facts and non-rational believes about the disease	The session started with relaxation exercise according to Jacobson's relaxation method followed by changing irrational to rational believes and development of a personal model of IBS.
Session 3	As session2	As session2
Session 4	Problem solving skills	Step by step training and practicing problem solving and social support skills
Session 5	As session4	As session 4
Session 6	Anger management	Step by step training and practicing methods of anger management
Session 7	Social support	Step by step training and practicing methods of social support
Session 8	Review	Review of the whole sessions and introducing useful books and reading materials

Table 2: Sample characteristics by group

	Control (n=21)	Intervention (n=21)	P value
Sex male (%)	12 (57.0)	6 (28.6)	0.59
Age (Year) mean±SD	34.410.6±	31.39.0±	0.32
Duration of IBS(month) mean±SD	62.350.9±	67.873.5±	0.78
Education <compulsory (%)	9 (43)	3 (14)	0.91
Compulsory (%)	5 (24)	5 (24)	
Higher (%)	7 (33)	13 (62)	
Severity of symptoms mean±SD	18.37.9±	19.58.8±	0.65
Depression mean±SD	21.910.6±	20.411.2±	0.91
Anxiety mean±SD	24.511.3±	24.014.4±	0.66
Quality of life mean±SD [a]	112.530.9±	100.839.1±	0.31

[a] Lower score indicates better quality of life.

depression (RGD=9.57; SMD=0.79; $CI_{95\%}$=0.16,1.41), and participant's quality of life (RGD=16.81; SMD=0.47; $CI_{95\%}$=0.14,−1.08). Comparisons of the pre- and post-treatment measures of the control and intervention groups suggested deterioration or marginal improvement in the control-group participants (P>.05 for all measures), but a significant improvement in the participants in the intervention-group. Accordingly, the mean differences between the pre- and post-treatment measures of the intervention-group participants indicated considerable improvements in the severity of IBS symptoms (9.00; $CI_{95\%}$=4.52,13.48, P<0.001), anxiety (7.00; $CI_{95\%}$=0.76,13.24, P=0.03), depression (6.48; $CI_{95\%}$=1.25,11.70, P=0.02), and participant's quality of life (21.95; $CI_{95\%}$=8.11,35.80, P=0.004). Furthermore, no significant difference was observed between the post-treatment and follow-up measures in either of the groups (P>0.05 for all measures). The results of GLM for repeated measures analysis with age and baseline score of a given scale as covariates indicated similar results, i.e. significant improvements in IBS symptoms (P=0.04), quality of life (P=0.03), anxiety (P=0.005), and depression (P=0.009) in the intervention group, when compared with those in the control group (Table 3). The interaction of the baseline anxiety and depression with CBT on the primary outcomes (severity of the symptoms and quality of life of the patients) was tested and no significant result was noted (P=0.24).

Discussion

To date, no biochemical, structural or serologic abnormality has been found to be associated with IBS, leaving adequate possibility for significant contribution of psychological factors to IBS. The disorder often causes chronic and disturbing side effects, including psychological problems,[27] and the severity of the psychological problems and symptoms are directly associated.[4,28,29] Although several medical remedies are recommended for controlling IBS symptoms, conventional treatment is sometimes insufficient especially when the symptoms are severe or chronic.[27] Among the non-medical interventions, stress management programs are believed to improve IBS[30] through several biopsychosocial mechanisms,[7,8,15] and CBT is more effective in patients with no satisfactory response to conventional therapies.[19] Accordingly, depression and anxiety share important roles in the resistance of IBS to medicine.

Similar to previous studies, the results of the present study suggested that a cognitive-behavioural stress management program for patients with IBS not only reduces the severity of the IBS symptoms and other psychological comorbidities, namely, stress and anxiety, but also improves the quality of life of the patients affected by the disorder. Also, the improvement could last for at least a few months after the CBT program.[31]

Table 3: Comparison of the outcome measures for the intervention and control groups during the study period

Groups		Before Mean±SD	After Mean±SD	Follow up Mean±SD	P Value [a]
Depression	Intervention	20.4±11.2	13.9±13.7	11.6±12.3	0.009
	Control	21.9±10.5	23.5±10.5	22.5±12.2	
Anxiety	Intervention	24.0±14.4	17.0±13.9	15.1±14.2	0.005
	Control	24.5±11.3	26.9±13.4	25.0±12.2	
Quality of life [b]	Intervention	112.1±30.9	90.1±40.5	76.9±41.1	0.03
	Control	100.8±39.1	106.9±30.3	102.733.2±	
Symptoms	Intervention	19.5±8.8	10.7±9.3	11.19.0±	0.02
	Control	18.3±7.9	20.9±8.0	18.79.3±	

[a]P value for between groups effect of intervention based on GLM repeated measures analysis. Measures at baseline and age were used as covariate in the analysis. [b]Lower score indicates better quality of life.

Based on the hypothetical mechanism of the effect of CBT on IBS and the results of interventional and observational studies regarding the importance of psychological distress in the severity and management of the symptoms, significant interactions were expected between depression/anxiety and CBT.[11,15,19,32] However, the results of the present study on patients with IBS who are resistant to conventional interventions revealed that the effect of CBT on IBS is independent of the levels of anxiety and depression. In other words, irrespective of the levels of depression or anxiety, CBT was found to be effective in the control of IBS symptoms. The application of Rome III diagnosis criteria and widely used and validated scales as well as the similarities between the findings of the present study and those reported previously with different populations and settings support the external validity of the results. Nevertheless, further studies are needed to understand the mechanism of action of CBT on IBS, and RCTs with active control groups are highly recommended.

The participants attended this study voluntarily. The non-probability sampling strategy may cause more susceptibility to selection bias. Of the assigned participants (50), 8 patients (4 patients each in the intervention and control groups) did not finish the training sessions or did not attend post-test assessment. Although, based on the calls that were made to five of the dropout cases, incomplete participation was not related to the disease status or study intervention of the dropouts, and no significant difference in the background variables or baseline outcomes was observed between the dropout cases and patients who completed the study, the incomplete participation rate might have caused bias in the estimates of the effect size of the intervention. In addition, the attrition rate also reduced the sample size and, consequently, the power of statistical analysis. Furthermore, although the current trial applied well-known and widely used self-reported scales, the use of self-reported scales to obtain required information is generally prone to more measurement error and bias. Lastly, the present study was not blinded and the control group was inactive.

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Conflict of Interest: None declared.

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