

The Effect of Psychotherapy in Improving Physical and Psychiatric Symptoms in Patients with Functional Dyspepsia

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Objective: Functional Dyspepsia (FD) is a common symptom of upper gastrointestinal discomfort. Few data are available on the role of psychotherapy in the treatment of dyspeptic syndromes. This study assesses whether brief core conflictual relationship theme (CCRT) psychoanalytic psychotherapy improves gastrointestinal and psychiatric symptoms in patients with functional dyspepsia.

Methods: A randomized, controlled trial was planned in two educational hospitals in city of Babol .

Forty-nine patients with FD were randomly assigned to receive standard medication treatment with CCRT psychotherapy (24 participants) or standard medication treatment alone (25 participants). The participants completed the Patient Assessment of Upper Gastrointestinal Symptom Severity Index (PAGI-SYM) and Symptom Checklist-90-Revised (SCL-90-R) questionnaires before the trial, after the treatment and at 1 and 12-month follow-ups. The mixed-effects (regression) model was used to analyze the data.

Results: The results showed that CCRT psychotherapy improved all of the FD symptoms (heartburn/regurgitation, nausea/vomiting, fullness, bloating, upper abdominal pain, and lower abdominal pain) and many of the psychiatric symptoms (depression, anxiety, somatization, interpersonal sensitivity and paranoid ideation) after the treatment and at 1-month and 12-month follow-ups.

Conclusion: Brief CCRT psychoanalytic psychotherapy can serve as an effective intervention for promoting gastrointestinal and psychiatric symptoms in patients with functional dyspepsia.

Keywords: *Functional dyspepsia, Psychiatric Symptoms, Core Conflictual Relationship Theme*

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Functional dyspepsia (FD) is a clinical syndrome defined by chronic or recurrent upper abdominal pain in the absence of an underlying organic disease that can explain the symptoms (1). The prevalence of FD in the general population has been reported to range from 17-29%. (2,3). FD is a common morbid condition that impacts absenteeism as well as direct and indirect healthcare costs (4). Unfortunately, the symptomatic improvement of patients with FD after pharmacological interventions remains controversial (5,6). Research has demonstrated the influence of psychological processes on gastrointestinal sensorimotor functions and symptoms (7). Geeraerts et al. (2005) showed that experimentally induced

anxiety in healthy volunteers was associated with impaired gastric compliance and accommodation (8). Van Oudenhove et al. (2007) showed negative correlations between anxiety levels and compliance in FD patients (9). It has been fairly well established that the comorbidity of mood and anxiety disorders in functional disorder patients is higher than in the general population, with rates up to 50% or higher, depending on the population studied as previously reviewed (7,10, 11).

In addition, few data are available on the role of psychotherapy in dyspeptic syndromes. However, Haug (2002) suggested cognitive therapy for symptom reduction in patients with FD (12). Hamilton et al. (2000) reported that psychodynamic-

interpersonal psychotherapy may be effective in FD patients (13). Previous studies have shown that the prevalence of psychiatric symptom is high among FD patients (10,14), and many FD patients have relationship disturbances (15). The CCRT model focuses on interpersonal conflicts and emotional changes. It seems that a release from interpersonal conflicts will improve psychiatric symptoms. A recent study showed that an improvement in interpersonal problems following psychotherapy in patients with functional gastrointestinal disorders appears to be associated with reduced psychological distress and improved health status (16).

In this study, we compared the outcome of combined CCRT and standard medication therapy with the outcome of standard medication therapy alone in patients with FD. The effects of CCRT on FD symptoms and psychiatric symptoms were investigated.

Material and Methods

Participants and Procedure

The study is registered at the Iranian Registry of Clinical Trials, number IRCT 201102285931N1. It is noteworthy to mention that the results of this article is a part of an extended project that was implemented in the Social Determinants of Health Research Center of the Babol University of Medical Sciences (2010-2011). The effect of CCRT on alexithymia and defense mechanisms has been reported in previous studies (17). This article focuses on improving psychiatric symptoms. Patients were recruited from two gastroenterology clinic hospitals of Babol University of Medical Sciences from April 2010 to September 2011. Inclusion criteria were as follows: age range of 20- 40 years, having a high school diploma or a university degree, having recurrent or persistent upper abdominal pain or discomfort more than 2-3 days per week for at least 3 months, and two gastroenterologists confirmed FD diagnosis according to Rome III criteria (18). Biochemical, ultrasonographic and endoscopic examinations were used to diagnose any structural organic gastrointestinal diseases. Patients with peptic ulcer, gastroesophageal reflux, biliary tract disease and gastric cancer were excluded. All participants with the diagnosis of FD were interviewed by a psychoanalytic psychotherapist who had sufficient experience with the CCRT psychotherapy to assess exclusion criteria (psychosis or borderline, highly dependent, schizoid or paranoid personalities)(19). An investigator with no clinical involvement in the trial randomly assigned the patients into two groups by a paper list (odd numbers were assigned to the standard medication therapy group and even numbers to the CCRT psychotherapy group). The experimental group received CCRT psychotherapy developed by Book 1998 (20).

Of the 155 patients who were assessed for eligibility at the beginning of the study, 49 (34 women, 15

men) were eligible and entered the study. Twenty patients from each group completed the trial period. At the beginning of the study, the participants of both groups were asked to complete the Patient Assessment of Upper Gastrointestinal Symptom Severity Index (PAGI-SYM) and Symptom Checklist-90-Revised (SCL-90-R) questionnaires. The serial evaluations of patients' symptoms with the two mentioned questionnaires were done for the two groups at the beginning of the study (baseline), at post-treatment (18 weeks after the baseline), at follow-up1 (1 month after the post-treatment) and at follow-up 2 (12 months after the post-treatment). All aspects of this protocol were approved by the Medical Ethics Committee.

FD Treatment

Patients with Positive H. pylori (31 persons) were given a combination of bismuth subcitrate (3×500 mg), metronidazole (3×250 mg), amoxicillin (3×500 mg) and either omeprazole (2×20 mg) or ranitidine (2×150 mg) for two weeks. Then, omeprazole (2× 20 mg) or ranitidine (2 ×150 mg) was only continued for four weeks. Patients with negative H. pylori (18 persons) were given omeprazole (2×20 mg) or ranitidine (2×150 mg) for six weeks.

CCRT Psychotherapy

CCRT psychotherapy can be determined by examining three aspects of the relationship episode including "What the patient wanted from other people, how the other person reacted, and how the patient reacted to their reactions" (21). Wish (W) is defined as "What the individual wanted from the interaction". The response from the other person (RO) is the second aspect. The third component to the CCRT is the response of the self (RS). The CCRT is originated from a number of relationship episodes (REs), which are stories that patients tell about their interaction with others. After a review of multiple REs, a common or overarching theme often emerges. This theme lies in the heart of the client's symptoms and interpersonal difficulties representing a repetitive and interpersonal concern, for which the patient seeks treatment (22).

In this study, the experimental group received 16 individual sessions (50 minutes each) once a week over four months. The therapist had two sessions with each patient before the start of the formal psychotherapy. During the first two sessions, the therapist took a history, carried out a mental status examination and listened to the relationship episodes of the patients to extract and build the main conflictual relationship theme (23).

Book (2007) divides the 16 sessions into three phases. Sessions 1 to 4 (the first phase), which involves identifying the CCRT with the patient, determining the goals for the therapy and providing the treatment rationale. During sessions 5 to 12 (the second phase), the primary focus is working through the RO by examining the childhood roots of this pattern. Sessions 13-16 (the third phase) of the

therapy involves dealing with termination issues. Separation anxiety or fantasies of the patient about why treatment is ending should be explored (22).

Measures

PAGI-SYM

Gastrointestinal symptoms were evaluated using the Patient Assessment of Upper Gastrointestinal Symptom Severity Index (PAGI-SYM), which is a self-report questionnaire. It contains 20 items and 6 subscales that cover heartburn/regurgitation (7 items), nausea/vomiting (3 items), postprandial fullness/early satiety (4 items), bloating (2 items), upper abdominal pain (2 items), and lower abdominal pain (2 items). The subscale scores vary from 0 (none or absent) to 5 (very severe). The construct validity of the PAGI-SYM subscale scores was confirmed by previous studies. Also, the internal consistency reliability ($\alpha = 0.79-0.91$) and test-retest reliability ($\alpha = 0.60-0.82$) were high (24). In this sample, the internal consistency reliability of the PAGI-SYM was calculated using the scores at pretreatment. Cronbach's alpha coefficient was 0.93.

SCL-90-R

The psychological symptoms were assessed with the widely-used Symptom Checklist-90-Revised (SCL-90-R), a self-rating inventory with 9 clinical scales for somatization, interpersonal sensitiveness, obsessive-compulsiveness, hostility, phobic anxiety, paranoid ideation, depression, anxiety and psychoticism. The total scores are considered to be measures of overall psychological symptoms. The SCL-90-R is a reliable and valid measure of psychological symptoms and is widely used in psychosomatic research (25). A valid Persian version of the SCL-90-R was used in this study (26). In this sample, the internal consistency of SCL-90-R was calculated using the scores at pretreatment. Cronbach's alpha coefficient was 0.91.

Statistical Analysis

The characteristics of the two subject groups were compared using the student' T test for the continuous variables and the χ^2 test for the categorical variables. The results were analyzed using the mixed-effects model with fixed-effects approach. The mixed-effects (regression) model has important advantages over traditional method of repeated-measurement analysis of variance. It uses all available data on each subject, it is unaffected by randomly missing data, it can flexibly model time effects, and it allows the use of realistic yet parsimonious variance and correlation patterns for particular applications (27). To examine the effect of CCRT therapy on the course of FD symptoms, we used mixed-effects model with time, treatment and time \times treatment interaction. By using this model, we considered 4 times (baseline, post-treatment, follow-up1, and follow-up2) as a repeated factor and group (CCRT and control) as a fixed factor. This model was used for all the dependent variables to assess whether the interaction effect time

\times group was significant. For each group of trials, mixed-effects models, with four times (baseline, post-treatment, follow-up1, and follow-up2), as a fixed factor, was used to determine the changes in the dependent variables during the 4 series measurements. Bonferroni tests were conducted to explore pairwise comparisons at each time of administration. A Bonferroni correction to the level of significance was applied, 0.013 (0.05/4). All of the statistical analyses were performed using SPSS software, version 18; $P < 0.01$ was regarded as statistically significant.

Results

Table 2 demonstrates the trend of changes in the mean scores of the gastrointestinal symptom scores in the two groups over the trial period. Mixed-effects model on PAGI-SYM subscales revealed a significant interaction effect for group \times time in all of the gastrointestinal symptoms. There were differences between the CCRT and control group in terms of improving all dyspepsia symptoms over the trial period including heartburn/regurgitation, nausea/vomiting, postprandial fullness/early satiety, bloating, upper abdominal pain, lower abdominal pain and total gastrointestinal symptom scores ($p < 0.001$). The mixed-effects model on each group over the time of the trial revealed that the CCRT group significantly improved all of the mean scores of FD symptoms from pretreatment to post-treatment and to the two follow-ups ($p < 0.01$). Medication therapy did not improve gastrointestinal symptoms from pretreatment to post-treatment and to the two follow-ups ($P > 0.05$).

Psychiatric Symptoms

Table 3 presents the trend of changes in the mean scores of the psychiatric symptoms in the two groups over the trial period. Mixed-effects model on SCL-90-R subscales revealed a significant interaction effect for group \times time in several of the psychological symptoms. There were differences between the CCRT and control group in improving all psychological symptoms over the time of the trial: depression ($p < 0.01$), anxiety ($p < 0.001$), somatization ($p < 0.001$), interpersonal sensitivity ($p < 0.001$), paranoid ideation ($p < 0.01$) and total SCL scores ($p < 0.001$). The interaction effect for group \times time in three SCL subscales, obsessive-compulsiveness, psychosis and phobic anxiety were not significant. Mixed-effects model on each group over the time of the trial revealed that the CCRT group significantly improved the mean scores of several psychological symptoms from pretreatment to post-treatment and to two follow-ups: depression, anxiety, somatization, interpersonal sensitivity, paranoid ideation and total SCL scores. CCRT did not significantly improve the mean score of the psychosis and hostility subscales from pretreatment to post-treatment and to the two follow-ups.

Medication therapy did not improve the psychiatric symptoms from pretreatment to post-treatment and to the two follow-ups ($P>0.05$).

Discussion

The results of this randomized controlled trial revealed that CCRT therapy is more effective than standard medication therapy in improving all of the dyspepsia symptoms by the end of the treatment and that this effect persisted at the 1- and 12-month follow-ups. Few published studies have reported the effects of psychotherapy on the symptoms of FD. Haug (2002) reported that a CBT group exhibited a

greater reduction in the number of days of epigastric pain, nausea and heartburn compared to controls, but the improvements in the epigastric discomfort score and in the extent of bloating were not greater in the therapy group than in the control group (12). Hamilton et al.

(2000) reported that patients who received the psychodynamic interpersonal therapy showed a significantly greater improvement in FD symptoms including upper abdominal pain, fullness, bloating and total scores than those receiving the control treatment (13).

Table 1: Demographic and characteristics of study sample

	CCRT		Control	
	Women (n=17) N (%)	Men (n=7) N (%)	Women (n=17) N (%)	Men (n=8) N (%)
Age (Mean, SD)	31.6 (7.0)	32.7(7.6)	32.8 (5.7)	34.1(4.5)
Education				
High school	9.0 (18.4)	3.0 (6.1)	11.0 (22.5)	5.0 (10.2)
College degree	8.0 (16.3)	4.0 (8.2)	6.0 (12.2)	3.0 (6.1)
Occupational status				
Employed	6.0 (12.2)	7.0 (14.3)	10.0 (20.4)	7.0 (14.3)
Unemployed	11.0 (22.5)	0.0 (0.0)	7.0 (14.3)	1.0 (2.0)
Marital status				
Single	5.0 (10.2)	1.0 (2.0)	3.0 (6.1)	1.0 (2.0)
Married	12.0 (24.6)	6.0 (12.2)	14.0 (28.6)	7.0 (14.3)
Helicobacter status				
Positive	11.0 (22.5)	4.0 (8.2)	11.0 (22.5)	5.0 (10.2)
Negative	6.0 (12.2)	3.0 (6.1)	6.0 (12.2)	3.0 (6.1)
Duration of symptoms				
≤2 years	3.0 (6.1)	2.0 (4.1)	4.0 (8.2)	1.0 (2.0)
>2 years	14.0 (28.6)	5.0 (10.2)	13.0 (26.5)	7.0 (14.3)

Table 2: Gastrointestinal symptom scores in two groups over the trial period

PAGI-SYSM	Baseline		Post treatment		p-value	Follow- up1		P-value	Follow-up2		P-value
	CCRT (N=24)	Control (N=25)	CCRT (N=21)	Control (N=22)		CCRT (N=20)	Control (N=21)		CCRT (N=20)	Control (N=20)	
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)	
Heartburn/regurgitation	12.8 (8.1)	13.9 (8.5)	5.6 ^a (5.3)	12.3 (8.3)	0.004	4.7 ^a (4.2)	12.3 (8.1)	0.030	4.9 ^a (4.3)	12.1 (8.5)	0.003
Nausea/Vomiting	4.0 (3.5)	4.5 (3.6)	1.0 ^a (1.5)	4.4 (3.9)	0.000	0.7 ^{a,b} (0.9)	4.2 (3.0)	0.040	0.9 ^a (1.2)	4.6 (3.1)	0.002
Post-prandial fullness	10.7 (4.5)	10.5 (5.9)	4.3 ^a (2.5)	9.7 (5.6)	0.000	4.1 ^a (3.1)	10.5 (4.9)	0.000	4.4 ^a (2.7)	9.6 (5.3)	0.000
Bloating	6.5 (3.1)	5.8 (2.3)	3.2 ^a (2.0)	6.9 (4.1)	0.000	3.1 ^a (2.1)	5.8 (2.1)	0.000	3.6 ^a (2.3)	6.4 (3.3)	0.005
Upper abdominal pain	5.7 (2.9)	6.9 (2.8)	2.3 ^a (1.7)	7.3 (2.9)	0.003	2.5 ^a (2.1)	7.4 (2.5)	0.007	2.5 ^a (1.9)	7.4 (2.8)	0.040
Lower abdominal pain	3.7 (3.5)	4.1 (3.7)	1.3 ^a (1.5)	4.0 (3.5)	0.002	1.2 ^a (1.9)	3.6 (3.2)	0.030	1.4 ^a (2.0)	4.0 (3.4)	0.030
Total mean score	43.6 (12.4)	45.9 (20.6)	17.8 ^a (10.9)	42.4 (21.0)	0.000	19.4 ^a (11.7)	44.1 (17.9)	0.000	17.8 ^a (10.8)	44.3 (19.5)	0.000

NOTE. **Ranges:** heartburn/regurgitation, 0-35; nausea/vomiting, 0-15; post-prandial fullness/early satiety, 0-20; bloating, 0-10, upper abdominal pain, 0-10, lower abdominal pain, 0-10; total scores, 0-100

Mixed-effects analysis: Within-group values with alphabetic superscripts for each measure are statistically significant at each phase of administration; **a**, post treatment and two follow-ups with baseline; **b**, post treatment with follow-up1; **c**, post treatment with follow-up2. Values with numeric

Table 3: Psychiatric symptom scores in two groups over the trial period

SCL-90-R	Baseline		Post treatment			Follow-up1			Follow-up2		
	CCRT (N=24)	Control (N=25)	CCRT (N=21)	Control (N=22)	P- value	CCRT (N=20)	Control (N=21)	P- value1	CCRT (N=20)	Control (N=20)	P- value
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)	
Depression	28.2 (9.8)	26.3 (10.3)	19.0 ^{ac} (8.1)	23.7 (7.6)	0.040	16.4 ^a (9.4)	23.1 (8.2)	0.030	15.8 ^{ac} (8.9)	21.9 (8.3)	0.030
Anxiety	18.0 (5.7)	18.4 (5.5)	11.1 ^a (4.6)	16.7 (5.9)	0.000	10.5 ^a (4.9)	17.4 (6.0)	0.000	10.4 ^a (4.9)	17.0 (5.5)	0.000
Somatization	20.9 (7.9)	21.4 (7.5)	13.9 ^a (4.9)	18.1 (7.6)	0.030	12.0 ^a (4.9)	17.4 (6.1)	0.000	10.4 ^a (4.9)	17.0 (5.5)	0.000
Obsessive- compulsion	21.5 (8.4)	21.1 (7.5)	18.3 (7.9)	19.5 (6.4)	0.070	16.0 (6.4)	19.5 (8.1)	0.130	16.1 (6.9)	18.4 (7.3)	0.120
Interpersonal sensitivity	16.4 (7.3)	17.0 (4.7)	13.1 ^{ac} (8.0)	16.8 (3.4)	0.030	10.6 ^a (6.0)	15.7 (5.4)	0.040	10.0 ^{ac} (5.3)	15.2 (4.5)	0.020
psychoticism	14.1 (6.0)	13.4 (6.3)	12.0 (5.5)	12.5 (5.6)	0.090	11.9 (5.9)	12.8 (6.3)	0.080	11.9 (5.7)	12.7 (5.4)	0.270
paranoid ideation	10.3 (3.6)	11.0 (4.5)	8.8 ^a (4.5)	11.9 (5.5)	0.030	7.5 ^a (2.3)	10.4 (5.5)	0.040	8.4 ^a (4.7)	11.2 (5.6)	0.30
Hostility	8.7 (4.3)	11.8 (5.4)	8.0 (4.4)	10.3 (5.9)	0.090	6.4 (3.2)	11.1 (6.4)	0.090	6.7 (2.8)	10.7 (5.9)	0.150
phobic anxiety	6.6 (4.2)	6.5 (4.2)	6.1 (3.4)	7.8 (5.0)	0.102	5.8 (3.6)	7.6 (5.5)	0.070	5.4 (3.3)	7.9 (5.1)	0.170
Total of mean score	159.5 (46.1)	157.9 (45.6)	120.7 ^{ab} (44.7)	147.4 (31.0)	0.020	106.2 ^{ab} (42.5)	148.3 (45.4)	0.010	124.6 ^a (49.0)	143.6 (39.2)	0.000

Ranges of scores: depression, 0-52; anxiety, 0-40; Somatization, 0-48; obsessive-compulsion, 0-40; interpersonal sensitivity, 0-36; psychoticism, 0-40; paranoid ideation, 0-24; hostility, 0-24; phobic anxiety, 0-28; total score of SCL-90; 0-360

Mixed-effects analysis: Within-group values with alphabetic superscripts for each measure are statistically significant at each phase of administration; **a**, post treatment and two follow-ups with baseline; **b**, post treatment with follow-up1; **c**, post treatment with follow-up2. Values with

Our findings revealed that the comorbid psychiatric symptoms of FD patients, including depression, anxiety, somatization, interpersonal sensitivity, paranoid ideation and the total SCL-90 score can be improved by CCRT therapy. Similar results have been reported in a few studies that assessed limited symptoms. The benefits of psychotherapy with respect to the psychological symptoms of the FD patients at the end of the treatment included the followings: enhancing the flexibility of coping (28), improving anxiety and depression (29) and improving anxiety and family problems (12). The findings of this study are not consistent with those of some prior studies. Some research has reported that the mean SCL-90-R global symptom index score did not significantly change (either at the end of the treatment or at a one-year follow-up) when group counseling psychotherapy (30) or individual psychodynamic interpersonal therapy (13) was provided to patients with functional gastrointestinal disorders. Our study had methodological differences with that of Hamilton (2000) in some aspects and this may have led to obtaining different outcomes. Hamilton study included patients with chronic symptoms of FD who had failed to respond to conventional pharmacologic treatments, whereas the present study included typical FD patients. Also, in the Hamilton study, experimental patients received psychodynamic-interpersonal therapy developed by Hobson 1987 that all focused more on the therapist-patient relationship, whereas the present study used CCRT (31). In addition, in Hamilton study,

the control group received supportive therapy, whereas the control group in the present study received medication therapy.

Due to some limitations, generalizations of these results should be made with caution. The low cooperation of men in entering or continuing the study was another limitation of this study. Approximately 27.2% of the men who were eligible to participate in the study refused participation. In addition, 33% of the men who were enrolled did not complete the trial. Thus, the question may be raised whether this male sample is representative of the population of FD patients. We recommend further research with a larger sample, particularly males. Another limitation refers to the control condition. The CCRT group received more treatment, and the positive results obtained may be due to the additional treatment (e.g., more contact, common factors, etc.) rather than anything specific about CCRT. Further research is needed with a third group of patients who are receiving no treatment, but are on a waiting list to see a physician.

In conclusion, brief CCRT psychoanalytic psychotherapy improved the physical and psychiatric symptoms in patients with functional dyspepsia.

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