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Original Research Report

Psychotherapy for Medically Unexplained Pain: A Randomized Clinical Trial Comparing Intensive Short-Term Dynamic Psychotherapy and Cognitive-Behavior Therapy

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Background: *The efficacy of intensive short-term dynamic psychotherapy (ISTDP) for medically unexplained pain remains open to debate because of a paucity of high-quality studies.* **Objectives:** *This study sought to evaluate ISTDP as a treatment for medically unexplained pain in outpatients by comparing it with the established evidence-based cognitive-behavioral therapy (CBT) in a randomized clinical trial.* **Methods:** *A total of 341 adults with medically unexplained pain were randomly assigned to 16 sessions of individual manualized CBT (N = 164) or ISTDP (N = 177). The groups were assessed at baseline, after 16 weeks of treatment, and at the 3-month follow-up. The primary outcome was perceived pain assessed using the numerical pain rating scale. The secondary outcomes were psychologic distress, depression, and cognitive variables. The cognitive variables included self-efficacy, catastrophizing, and coping strategies.* **Results:** *In the intention-to-treat analysis, the ISTDP and CBT groups both showed improvement in the primary outcome after treatment. Pain symptoms in both conditions were significantly reduced. Both ISTDP and CBT groups demonstrated reductions in psychologic distress, depression and catastrophic thinking, and also increases in the use of relaxation as a coping strategy. The CBT group showed an improvement in self-efficacy that was not obtained in the ISTDP group. However, significant differences were not observed in the primary and secondary outcomes at the 3-month follow-up compared with posttreatment. Overall, both treatments were equally effective at the 3-month follow-up.* **Conclusion:** *Our results suggest that ISTDP may provide an effective alternative therapy for medically unexplained somatic symptoms of pain.*

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Key words: intensive short-term dynamic psychotherapy, medically unexplained pain, cognitive-behavioral therapy, randomized controlled trial.

INTRODUCTION

Chronic pain is a common issue worldwide and remains a big challenge to physicians, particularly when the underlying causes are unexplained. Such medically unexplained pain (MUP) that lacks an integrated diagnosis in medicine has a high psychiatric comorbidity, such as depression, and will require a multidisciplinary treatment strategy.[1]

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Psychosocial factors play an important role in pain and associated physical and psychosocial disabilities.[2] In fact, 4 of the 8 nonpharmacologic treatments recommended for persistent back pain include mind-body components.[2] One of these, intensive short-term dynamic psychotherapy (ISTDP), has demonstrated effectiveness for medically unexplained somatic symptoms of pain.[3]

Different randomized controlled trials (RCTs) provide support for the acceptability and feasibility of ISTDP as an alternative treatment for MUP outpatients.[4–6] More recently, we conducted an RCT to examine the effectiveness of ISTDP and mindfulness-based stress reduction for patients with MUP. At the end of the treatment and at the 3-month follow-up, the ISTDP group reported significantly lower pain intensity than mindfulness-based stress reduction at posttreatment.[4] We have also demonstrated the effect of Internet-delivered ISTDP for MUP using video teleconferencing. The results show that in-person ISTDP participants had significantly lower pain intensity than Internet-delivered ISTDP participants, both immediately after the intervention and at the 12-month follow-up.[5] In another study, we investigated the efficacy of Internet-delivered ISTDP for MUP through Skype in comparison with a treatment as usual condition. ISTDP delivered through Skype was deemed successful, as evidenced by the significant reductions in pain severity and depression, anxiety, and stress levels. However, a greater increase in emotion regulation functioning, mindfulness, and quality of life was observed after the treatment and at the 6-month follow-up.[6]

Despite these encouraging findings, it is worth mentioning that most of the available studies on ISTDP have significant methodologic shortcomings. A main shortcoming of these studies concerns the lack of a control group or the comparison between ISTDP and inactive control groups (i.e., waiting lists or treatment as usual), and fewer studies have compared ISTDP with other well-established active treatments. In connection to this, no study has yet compared ISTDP with cognitive-behavioral therapy (CBT) as a recommended treatment for chronic pain.[7]

The efficacy of CBT for individuals with chronic pain has been evaluated in RCTs for more than 3 decades—primarily in samples of adults with chronic back pain,[8] headache,[9] orofacial pain,[10] or arthritis-related pain.[11] Two recently published meta-analyses demonstrated that CBT is one of the best documented psychologic treatments for patients with chronic medically-unexplained symptoms.[12,13] As some patients do not like this form of treatment, thus there is a need for a different approach such as ISTDP. This RCT is the first attempt to assess the efficacy of ISTDP compared with CBT in a large sample of patients with MUP.

METHOD

Design

This study was a mixed between-within subjects' design with an allocation ratio of 1:1 for CBT and ISTDP. All of the patients also received their usual medical care including physiotherapy and medication. There were no changes to the trial design after its commencement. The study design was approved by the ethics committee of the Baqiyatallah Medical Sciences University's Research Deputy.

Participants

Participants were recruited through patient self-help groups and news media, and referrals from a multidisciplinary pain and rheumatology clinic, a neurology clinic, and a gastroenterology clinic at an academic health center in Tehran, Iran. For this study, MUP was defined as any current principal somatic pain reported by patients for which no definite medical diagnosis could be found by physical examination and appropriate investigation. The physician's opinion was determined by the final diagnosis stated in the clinical case notes. Patients were recognized as having MUP when their physicians gave a diagnosis of "functional," or continued to defer the diagnosis because of no detected physical abnormality. These were considered indications that the pain symptoms were medically unexplained. To evaluate the reliability of the assessment, a different assessor reviewed 16% of all written clinical interviews, resulting in an inter-rater agreement of $r = 0.88$ for the diagnosis of MUP. On a diagnosis of MUP, eligible participants were asked to complete a battery of preassessment questionnaires.

Inclusion criteria were 18–45 years of age, at least 1 MUP with for duration of 6 months, fluency in Farsi and provision of consent. The exclusion criteria were acute drug/alcohol abuse, psychotic or bipolar disorders, anorexia nervosa, acute suicidality, and pregnancy.

Interventions

Participants were randomly allocated to either CBT or ISTDP condition. Both psychotherapies comprised 16 individual sessions within 22 weeks and were conducted according to published treatment manuals.[4,14]

Cognitive-Behavioral Therapy

CBT was based on the principles described by Turk et al.[14] The CBT program consisted of the following components, all supported by written materials: education concerning pain, disuse, drugs, and sleep; exercise routines for fitness, flexibility and muscle minimum strength, and increasing gradually on a quota system; goal-setting across all activities with quota increases and activity-rest scheduling (pacing); psychology sessions to improve problem-solving, change maladaptive behaviors and to maintain those changes, with cognitive techniques to identify unrealistic and unhelpful thoughts and beliefs, and to challenge and change them; drug reduction applied to all pain-related drugs, which had neither achieved analgesia nor improved function, with the usual aim of abstinence by discharge; applied relaxation; relapse prevention and planning for crises; and sleep hygiene.

Intensive Short-Term Dynamic Psychotherapy

ISTDP uses an active technique. After the defensive system is rapidly identified, the patient is made acquainted with it and its self-sabotaging consequences in his life. Thus, the patient turns himself against his defenses, and mobilizes his own will, which becomes a decisive force in the treatment. The patient perceives the therapist relentlessly but with respectful confrontations, and sees him as a solid partner in the struggle to overcome the pathogenic forces. Through this process, an unconscious therapeutic alliance emerges.[15] At the same time, this work with defenses mobilizes unresolved feelings in the transference, and triggers corresponding anxiety.

Davanloo noted 3 main neurobiologic discharge pathways of unconscious anxiety and the process of motor conversion. The first, striated (voluntary) muscle unconscious anxiety, is observable as hand clenching and sighing respirations: accompanying this pathway, he noted that clients primarily used what he called as isolation of affect with intellectual awareness devoid of emotional experience. The second level is smooth (involuntary) muscle unconscious anxiety affecting the muscles of the gastrointestinal tract, blood vessels, and airways, resulting in problems such as migraines, irritable bowel syndrome, and hypertension: accompanying this pathway, he noted instant repression of emotions and major depression where emotions were channeled directly into the body before reaching consciousness. The third level is cognitive perceptual disruption where the person experiences visual blurring, mental confusion, and hallucinations: these clients tend to use projection and projective identification as primary major defenses. Clients with motor conversion, with focal or global muscle weakness, also experience repression of emotions.[16]

A crucial element in ISTDP is the continuous observation of the neurobiologic channels of anxiety, and the knowledge of how they indicate the patient's tolerance capacity, to keep the process securely within the patient's capacity. The process results in the patient's inner experience of his repressed feelings in the transference with a subsequent shift to the person in his life, toward whom the repressed feelings originally were generated. The corresponding feelings of rage, guilt, and grief, but also affection, can be directly worked through, the defensive system can be overcome, and the tolerance capacity gets improved. Based on the patient's will, it poses a challenge and pressure to overcome defenses and anxiety, and pressure to the inner experience of the repressed feelings.[17]

Psychotherapists

To avoid contamination among treatment arms, different therapists, who were all skilled at the underlying therapeutic approach, provided 2 approaches. Psychotherapists in both treatment conditions were psychiatrists or psychologists with at least a master's degree who completed either a 3-year core training program in ISTDP or a 100-hour basic CBT training course. Moreover, all therapists adequately conducted at least 1 intensively supervised therapy case in

accordance with the relevant treatment manual as judged by a study supervisor. Treatment integrity and adherence to ISTDP principles were continuously checked in the bimonthly group supervisions by first author. In addition, videotapes of all individual sessions were available for systematic adherence and competence evaluation.

Differences in the mean number of years that the supervisors had been conducting their respective modalities were minimal (CBT = 8.9 years [standard deviation {SD} = 9.3]; ISTDP = 8.7 years [SD = 4.4]) but somewhat larger with respect to mean years conducting supervision (CBT = 13.3 years [SD = 11.3]; ISTDP = 6.6 years [SD = 2.2]), although neither difference was significant.

Overall, 9 CBT therapists and 8 ISTDP therapists were involved, on average, 17.1 patients and 16.3 patients, respectively. No differences among treatment conditions were found regarding the average number of times a patient was discussed in supervision (CBT = 4.6; ISTDP = 4.2) or the mean number of therapy sessions patients received (CBT = 11.2; ISTDP = 11.9; mean numbers are lower than the maximum of 16 because of premature termination, dropout, and patients missing sessions). Regarding therapist protocol adherence, CBT therapists reported a mean score of 7.1 (scale range: 0–10) more than 1218 CBT sessions. Conditions did not differ regarding the mean number of years of clinical experience therapists had after completing their master's degree or medical degree (CBT = 7.3 years [SD = 6.4]; ISTDP = 7.4 years [SD = 7.3]), but CBT was more often conducted by psychiatrists, and ISTDP was more often conducted by psychologists ($\chi^2 = 103.66$, df = 1, $p < 0.001$). Furthermore, CBT was conducted more often by a female therapist than was ISTDP ($\chi^2 = 14.54$, df = 1, $p < 0.001$). We, therefore, conducted a sensitivity analysis controlling for therapist sex and profession, either a psychologist or a psychiatrist.

Outcome Measures

We took the following measurements at 3 timepoints: at a baseline assessment (before randomization); immediately after treatment (after 16 sessions); and after 3 months. All the instruments used were self-reported. Diagnostic evaluations were done according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition[18] by trained assessors on staff. The Mini International Neuropsychiatric Interview[19] was used for assessing Axis I diagnoses at pretreatment.

Pain intensity as a primary outcome was assessed using an 11-point numerical pain rating scale (NPRS) with anchors of 0 = "no pain" to 10 = "worst pain." Patients were asked to mark the number that best represented the severity of their pain in the last week.[20] The psychometric properties of the NPRS have been established in a sample of adults with persistent pain.[21]

Secondary measures assessed the following areas of functioning: emotional, cognitive, and coping. General psychologic distress was assessed using the Hospital Anxiety and Depression Scale (HADS), a 14-item questionnaire.[22] The global HADS score is the sum of the anxiety (7 items) and depression (7 items) scales and is considered to be an index of emotional disturbance.[23] The alpha coefficient for global HADS is 0.86.[24] The Beck Depression Inventory-II (BDI-II) has 21 items and was used to assess depression.[25] Catastrophizing was assessed using the pain catastrophizing scale (PCS).[26] This questionnaire has 13 items, with a global score of catastrophizing and 3 scales, namely, rumination (4 items), magnification (3 items), and helplessness (6 items). Coefficient alpha for the total PCS was 0.87. Self-efficacy was assessed using the chronic pain self-efficacy scale (CPSS).[27] This 22-item questionnaire included several self-efficacy indices: global, pain (5 items), physical function (9 items), and coping with symptoms (8 items). Coefficient alpha were 0.88, 0.87, and 0.90. To assess coping, the chronic pain coping inventory (CPCI) 64-item patient version was used.[28] The CPCI evaluated several coping strategies, including illness-focused coping and wellness-focused coping. It has 8 scales: guarding (9 items), resting (7 items), asking for assistance (4 items), seeking social support (8 items), relaxation (7 items), task persistence (6 items), exercise/stretch (12 items), and coping self-statements (11 items). The CPCI scales showed an adequate stability with alpha ranging from 0.74–0.91.

Randomization

Patients were randomized in blocks by a computer algorithm.[29] Block size was randomly chosen to include either 3 or 6 patients. Information regarding eligible patients entering the trial was sent to a study manager who otherwise had no contact with the

patients. The study manager then determined block size and randomized the patients, but only if there were enough patients to fill the next block.

Allocation Concealment Mechanism

The allocation sequence was concealed from the research assessor. An e-mail confirming the treatment allocation was sent directly to the therapist.

Implementation

The research assessor enrolled participants in the trial and gained written informed consent for their participation in the trial as well as treatment.

Statistical Methods

All data were entered into the SPSS version 21 for Windows. The analysis of efficacy was based on the "intention to treat," using data from those participants who provided baseline and follow-up data regardless of whether they completed the treatment. To reduce the amount of missing data from partially filled-in questionnaires, the average score was computed for questionnaires where only 1 item was missing. To correct for multiple missing-item data for questionnaires with 2 or more missing items, and in some cases for entire missing measures, multiple imputation was used.[30] The group, baseline NPRS, BDI, HADS, PCS, CPSS, and CPCI scores were entered into the model as predictors of missing data, and 30 imputations were run.

Differences in clinical and sociodemographic variables were analyzed using the χ^2 and t-test, as appropriate. Changes in psychologic measures over the study period were analyzed using the repeated measures analysis of variance. Analyses from baseline (T0) to (T1) corresponding to the end of the treatment program and from (T0) to (T3) corresponding to the 3-month follow-up period from baseline periods were included. Significance was set at a $p \leq 0.05$, two-tailed.

For the main outcome, the treatment effects in both groups were tested across the 3 measurements using linear mixed models by analyzing the differences between baseline and end of treatment or 3-month follow-up, respectively, and controlling for age and education. Secondary outcomes were reported equally. We calculated Cohen's d as a within-group effect size (standardized effect size) reflecting differences between pretreatment and 3-month follow-up by computing the mean difference and dividing this by the SD at baseline.

Power Analysis

An *a priori* power analysis indicated that 300 participants were required ($\alpha = 0.05$, $1-\beta = 0.80$) to answer our primary research question.[31] To detect the 10% difference in remission rates among conditions that constituted the noninferiority margin ($\alpha = 0.05$, $1-\beta = 0.80$), 341 participants were needed (using SPSS SamplePower for equivalence studies, one-tailed). Power to detect an outcome difference of a Cohen's d value of 0.30 for continuous outcome measures was 0.87.

RESULTS

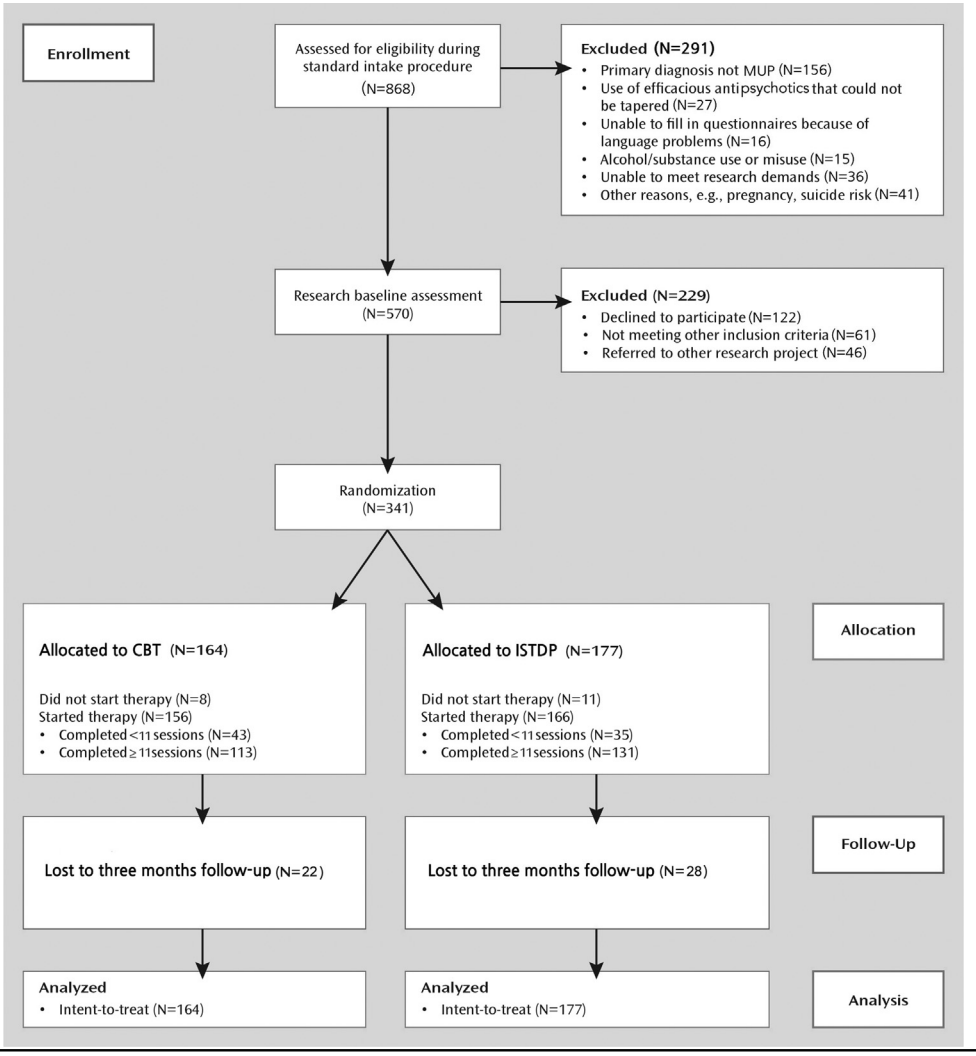
Participants

The CONSORT diagram for the study is presented in the Figure. Overall, 868 patients were assessed for eligibility during a standard intake procedure; 570 (65.6%) were found to be potentially eligible and invited for baseline assessment. Of these patients, 229 (40.1%) did not meet inclusion criteria or were not willing to participate. Therefore, 341 patients were randomly assigned to CBT (N = 164) or ISTDP (N = 177). Demographic and clinical characteristics of the sample are summarized in Table 1. No significant differences were found between 2 treatment conditions.

Nearly, all the patients were stabilized on a psychiatric medication (e.g., antidepressant, anxiolytic, and antiepileptic) and analgesics. The number of patients on medication was similar across both groups, with no alterations to the prescription throughout the duration of the study. However, no significant differences were found among treatment conditions regarding the proportion of patients who did not complete treatment (CBT = 11.1%; ISTDP = 12.9%). Most patients who dropped out missed treatment appointments without specifying a reason (9.9%).

The blinded ratings of session recordings for the CBT group indicated that there was a mean of 15.5 (SD = 3.6) components of CBT per session and 0 components of ISTDP per session [t (49) = 14.74; $p < 0.001$]. For the ISTDP group, there was a mean of 14.64 (SD = 6.62) components of ISTDP

FIGURE. CONSORT Diagram of Participants in a Study of the Efficacy of Intensive Short-Term Dynamic Psychotherapy Relative to Cognitive Behavioral Therapy.



per session and a mean of 0.21 (SD = 0.50) components of CBT per session [t (49) = 13.71; $p < 0.001$]. There were, therefore, no violations of the condition that CBT should not be used in ISTDP and vice versa. In blinded ratings of the therapeutic relationship, CBT (mean = 3.41, SD = 0.84) did not differ to ISTDP [mean = 3.17, SD = 0.44; t (49) = 1.42; p = 0.35]. Equally, for therapist directiveness, CBT (mean = 3.23, SD = 0.54) did not differ with ISTDP [mean = 3.33, SD = 0.57; t (49) = –0.39; p = 0.49].

Treatment Effects

Table 2 provides means, SD and effect sizes for each group, across measurement points, and the Cohen d effect size between CBT and ISTDP for all outcome measures. In the within-group analysis of CBT and ISTDP, there was a significant decrease in NPRS, BDI, HADS, PCS measures, and improvement in the CPSS measure at week 16 and after the 3-month follow-up.

For the primary outcome (the NPRS score), both CBT group [t (1, 341) = 41.96, $p < 0.001$] and ISTDP group [t (1, 341) = 47.16, $p < 0.001$] showed improvement. For the secondary outcomes, the following results were obtained: (1) psychologic distress improved in the CBT [t (1, 341) = 53.92, $p < 0.001$] and ISTDP groups [t (1, 341) = 66.16, $p < 0.001$]; (2) BDI improved in the CBT [t (1, 341) = 73.08, $p < 0.001$] and ISTDP groups [t (1, 341) = 39.37, $p < 0.001$]; (3) PCS, catastrophizing improved in the

TABLE 1. Baseline Demographic and Clinical Characteristics of Participants in a Study of the Efficacy of Intensive Short-Term Dynamic Psychotherapy Relative to Cognitive-Behavioral Therapy

Characteristic	Total sample (N = 341)		CBT group* (N = 164)		ISTDP group (N = 177)		Statistic†
	Mean	SD	Mean	SD	Mean	SD	
Demographic							
Age (y)	36.23	10.43	37.32	10.12	38.78	10.66	0.82
	N	%	N	%	N	%	
Sex							
Male	102	29.9	51	31.1	51	28.8	0.65
Female	239	70.1	113	68.9	126	71.2	
Marital status							
Married	80	23.7	45	27.4	35	20.1	0.75
Divorced	69	20.4	34	20.7	35	20.1	
Widowed	10	3.0	4	2.4	6	2.4	
Never married	176	52.1	80	48.8	96	55.2	
Other	3	0.9	1	0.6	2	1.1	
Education level							
Low	67	20.0	35	21.5	32	18.6	0.64
Intermediate	159	47.5	71	43.6	88	51.2	
High	101	30.1	55	33.7	46	26.7	
Other	8	2.4	2	1.2	6	3.5	
Previous treatment for current pain							
No	218	65.3	118	68.2	100	62.1	0.29
Yes	116	34.7	55	31.8	61	37.9	
Pain location							
Face	36	10.4	12	7.7	24	13.6	0.69
Head	139	41.7	63	38.5	80	45.5	
Abdomen	212	62.5	114	69.2	95	54.5	
Chest	99	29.2	38	23.1	63	36.4	
Low back	119	35.4	63	38.5	56	31.8	
Spine	64	18.8	31	19.2	32	18.2	
Shoulder or neck	78	22.9	38	23.1	39	22.7	
Arm or hand	35	10.4	25	15.4	8	4.5	
Leg or foot	64	18.8	44	26.9	15	9.1	
Duration of pain (y)							
Once of disease	5.2	2.05	5.5	1.8	5.6	2.1	0.64
Since diagnosis	1.5	0.3	1.8	0.5	1.9	0.4	
Baseline pain score	7.3	1.2	7.98	0.7	7.7	0.9	
Drug intake							
Antidepressant	91	26.6	41	25	50	28.2	0.52
Anxiolytic	58	17.1	32	19.5	26	14.6	
Antiepileptic	36	10.5	16	9.7	20	11.2	
Analgesic	40	11.7	21	12.8	19	10.7	
Comorbid axis I disorder							
Major depression disorder	153	44.8	71	43.2	82	46.3	0.69
Dysthymic disorder	78	22.8	43	26.2	35	19.7	
Generalized anxiety disorder	128	37.5	69	42.1	59	33.3	
Panic disorder	65	19.1	23	14.1	42	23.7	
Social anxiety	69	20.2	43	26.2	26	14.6	
Obsessive-compulsive disorder	57	16.7	39	23.7	28	15.8	
Eating disorder	27	7.9	16	9.7	11	6.2	

SD = standard deviation.

* CBT = cognitive-behavioral therapy; ISTDP = intensive short-term dynamic psychotherapy.

† Differences between conditions for demographic and other baseline characteristics (p values) were assessed using chi-square (χ^2) tests of independence for categorical or ordinal variables and Student t tests for interval variables.

CBT [$t\,(1, 341) = 17.98, p < 0.001$) and ISTDP groups [$t\,(1, 341) = 4.97, p < 0.03$]; rumination improved in the CBT [$t\,(1, 341) = 18.57, p < 0.001$] and ISTDP groups [$t\,(1, 341) = 8.14, p < 0.001$]; helplessness improved only in the CBT group [$t\,(1, 341) = 12.75, p < 0.001$]; magnification improved in the CBT [$t\,(1, 341) = 5.36, p < 0.02$] and ISTDP groups [$t\,(1, 341) = 39.37, p < 0.001$]; (4) CPSS, pain self-efficacy improved only in the CBT group [$t\,(1, 341) = 15.57, p < 0.001$); for coping symptoms, self-efficacy improved only in the CBT group [$t\,(1, 341) = 4.73, p < 0.03$); there were no significant differences in any group for physical function self-efficacy; global self-efficacy increased in the ISTDP [$t\,(1, 341) = 4.04, p < 0.05$) and CBT groups [$t\,(1, 341) = 4.37, p < 0.001$]; (5) CPCI, there were no significant differences in any group for guarding; (6) resting improved only in the CBT group [$t\,(1, 341) = 7.28, p < 0.01$); (7) there were no significant differences in any group for asking for assistance and seeking social support; (8) relaxation improved in the CBT [$t\,(1, 341) = 31.90, p < 0.001$) and ISTDP groups [$t\,(1, 341) = 10.22, p < 0.02$); and (9) no significant differences were found in any group for the task persistence, exercise/stretch and coping self-statements.

Posttreatment Effects

To obtain additional information, the follow-up data at 3 months were analyzed in relation to the posttreatment scores to determine whether the improvements at the end of treatment were maintained. The posttreatment effects were analyzed in the CBT and ISTDP groups. The results obtained at posttreatment were maintained or improved in the CBT group: NPRS ($p < 0.05$; $d = 0.91$), BDI ($p < 0.05$; $d = 1.34$), psychologic distress ($p < 0.05$; $d = 1.12$), and PCS ($p < 0.05$; $d = 0.98$). In the CBT group, some measures were lower compared with the posttreatment levels: PCS, magnification ($p < 0.015$); and CPSS, physical function self-efficacy at 3 months ($p < 0.019$). However, the results obtained at posttreatment were maintained or improved in the ISTDP group: NPRS ($p < 0.05$; $d = 0.97$), BDI ($p < 0.05$; $d = 1.12$), psychologic distress ($p < 0.05$; $d = 0.82$), and PCS ($p < 0.05$; $d = 0.98$). In the CBT group, some measures were lower compared with the posttreatment levels: PCS, rumination ($p < 0.015$); and physical function self-efficacy at 3 months ($p < 0.019$).

Table 3 shows the linear change in dependent variable scores from baseline to week 16 and the interaction between group and time for all outcome measures. There was a significant group × time interaction for the primary outcome (NPRS score) and other measures (HADS and PCS) at week 16. There was no group × time interaction for depression (BDI) or CPCI score.

Adverse Events

Adverse events occurred in 4 patients (1%) during the trial, including major depression (3 in the CBT group and 1 in the ISTDP group) and panic disorder (1 in the ISTDP group). Given the small number of participants with adverse events and serious adverse events, no significance tests were performed.

DISCUSSION

Although there is some overlap between CBT and ISTDP, there are considerable differences in the approach. Broadly, the focus of CBT is on the contribution of core beliefs and automatic thoughts in the here and now, whereas in ISTDP, experiences of core emotion from the past is seen as the transformative vehicle and the therapist relies on non-interpretive techniques such as encouragement to feel; challenge to take responsibility to change; and confrontation of resistance to change.[15–17]

We used a randomized clinical design to compare the efficacy of CBT and ISTDP for MUP in a large sample of patients in outpatient clinics. In the intention-to-treat analysis, pain symptoms in the both groups were significantly reduced at the posttreatment and follow-up assessments. Our findings are in line with previous studies that reported the efficacy of CBT[32] and ISTDP [4–6] in decrement of pain intensity among patients with MUP.

Secondary outcomes at posttreatment showed improvements in the CBT and ISTDP groups for psychologic distress (HADS scores) and depression (BDI scores). In this regard, the reduction in psychologic distress has been documented in a CBT [33–35] and ISTDP groups.[36,37] In addition, our findings are in line with previous studies that reported the improvement in pain intensity, depression, and anxiety observed posttreatment did remain in the follow-up period.[4–6]

TABLE 2. Means ± SD, Within-Group Comparisons and Between-Group Effect Sizes (Cohen's *d*) for Primary and Secondary Outcome Measures at Baseline, Posttreatment (week 16) and at the 3-month Follow-up*

	Within-group comparisons										
	CBT group (N = 164)						ISTDP group (N = 177)					
	Mean ± SD			Differences (statistics)		Cohen *d*†	Mean ± SD			Differences		Cohen's *d*
	BL	PT	FU	BL-PT	BL-FU		BL	PT	FU	BL-PT	BL-FU	
NPRS	8.4 ± 0.9	3.6 ± 1.1	3.1 ± 0.5	$p < 0.001$ $d = 1.37$	$p < 0.001$ $d = 1.15$	1.49	8.2 ± 0.4	3.1 ± 0.8	3.1 ± 0.1	$p < 0.001$ $d = 1.67$	$p < 0.001$ $d = 1.77$	1.41
BDI	15.3 ± 1.6	6 ± 0.9	4.7 ± 1.4	$p < 0.001$ $d = 1.67$	$p < 0.001$ $d = 1.45$	1.36	14.3 ± 1.1	5.7 ± 1.9	3.7 ± 1.3	$p < 0.001$ $d = 1.32$	$p < 0.001$ $d = 1.65$	1.16
HADS (psychologic distress)	14.2 ± 3.1	5.4 ± 0.8	4.9 ± 1	$p < 0.0001$ $d = 1.45$	$p < 0.001$ $d = 1.43$	1.26	15.2 ± 2.2	5.1 ± 0.3	4.4 ± 1.1	$p < 0.001$ $d = 1.65$	$p < 0.001$ $d = 1.63$	1.16
PCS												
Catastrophizing	14.3 ± 1.9	5.1 ± 1.2	5.2 ± 1.8	$p < 0.001$ $d = 1.44$	$p < 0.001$ $d = 1.73$	1.34	15.1 ± 2.2	5.1 ± 1.3	5.1 ± 0.8	$p < 0.001$ $d = 1.24$	$p < 0.001$ $d = 1.33$	1.25
Ruminations	16.2 ± 0.9	6.1 ± 2.2	5.1 ± 1.5	$p < 0.001$ $d = 1.64$	$p < 0.001$ $d = 1.63$	1.37	16.1 ± 1.2	6.6 ± 1.1	6.1 ± 1.8	$p < 0.001$ $d = 1.54$	$p < 0.001$ $d = 1.53$	1.27
Helplessness	12.4 ± 2.3	6.4 ± 2.5	5.1 ± 2.1	$p < 0.001$ $d = 1.74$	$p < 0.001$ $d = 1.73$	1.24	12.2 ± 1.8	6.6 ± 1.1	6.1 ± 0.4	$p < 0.001$ $d = 1.54$	$p < 0.001$ $d = 1.63$	1.26
Magnification	18.4 ± 3.3	9.4 ± 4.5	8.9 ± 3.2	$p < 0.001$ $d = 1.66$	$p < 0.001$ $d = 1.63$	1.24	18.5 ± 3.1	9.3 ± 2.8	9.4 ± 3.4	$p < 0.001$ $d = 1.76$	$p < 0.001$ $d = 1.43$	1.39
CPSS (self-efficacy)												
Coping with symptoms	22.4 ± 7.3	16.4 ± 5.5	15.1 ± 5.3	$p < 0.001$ $d = 1.38$	$p < 0.001$ $d = 1.83$	1.24	22.1 ± 6.8	16.6 ± 2.2	16.7 ± 5.4	$p < 0.001$ $d = 1.58$	$p < 0.001$ $d = 1.69$	1.26
Physical function	22.2 ± 4.3	14.4 ± 3.5	15.5 ± 5.4	$p < 0.001$ $d = 1.78$	$p < 0.001$ $d = 1.83$	1.11	22.4 ± 4.8	16.3 ± 3.3	16.4 ± 4.4	$p < 0.001$ $d = 1.69$	$p < 0.001$ $d = 1.39$	1.17
Global	32.4 ± 11.1	22.4 ± 7.5	25.3 ± 9.2	$p < 0.001$ $d = 1.84$	$p < 0.001$ $d = 1.83$	1.24	32.3 ± 11.3	26.6 ± 8.1	16.1 ± 0.4	$p < 0.001$ $d = 1.54$	$p < 0.001$ $d = 1.63$	1.17
CPCI												
Guarding	8.4 ± 1.2	4.4 ± 0.8	3.9 ± 0.2	$p < 0.001$ $d = 1.22$	$p < 0.001$ $d = 1.23$	1.14	8.5 ± 1.3	3.3 ± 0.8	3.4 ± 0.7	$p < 0.001$ $d = 1.16$	$p < 0.001$ $d = 1.13$	1.11
Resting	8.1 ± 1.3	4.2 ± 0.5	4.6 ± 1.7	$p < 0.001$ $d = 1.59$	$p < 0.001$ $d = 1.71$	1.12	8.2 ± 2.1	4.4 ± 0.7	4.1 ± 0.2	$p < 0.001$ $d = 1.56$	$p < 0.001$ $d = 1.55$	1.19
Relaxation	8.8 ± 0.5	3.4 ± 0.5	3.4 ± 0.5	$p < 0.001$ $d = 1.44$	$p < 0.001$ $d = 1.23$	1.43	8.2 ± 0.2	3.7 ± 1.1	3.4 ± 1.4	$p < 0.001$ $d = 1.77$	$p < 0.001$ $d = 1.44$	1.19
Asking for assistance	8.4 ± 1.5	4.3 ± 5.5	4.1 ± 3.5	$p < 0.001$ $d = 1.48$	$p < 0.001$ $d = 1.63$	1.39	8.6 ± 3.1	4.3 ± 2.8	4.4 ± 3.4	$p < 0.001$ $d = 1.65$	$p < 0.001$ $d = 1.53$	1.15
Seeking social support	10.3 ± 1.2	6.6 ± 1.2	6.3 ± 3.3	$p < 0.001$ $d = 1.86$	$p < 0.001$ $d = 1.16$	1.05	10.5 ± 2.1	7.3 ± 3.8	7.4 ± 4.4	$p < 0.001$ $d = 1.45$	$p < 0.001$ $d = 1.33$	1.09
Task persistence	18.4 ± 3.3	9.4 ± 4.5	8.9 ± 3.2	$p < 0.001$ $d = 1.66$	$p < 0.001$ $d = 1.63$	1.34	18.5 ± 3.2	9.3 ± 2.8	9.4 ± 3.4	$p < 0.001$ $d = 1.76$	$p < 0.001$ $d = 1.43$	1.09

Exercise/stretch	10.4 ± 1.3	7.4 ± 6.5	7.9 ± 2.4	$p < 0.001$ $d = 1.76$	$p < 0.001$ $d = 1.83$	1.29	10.5 ± 2.1	7.3 ± 2.8	7.4 ± 3.3	$p < 0.001$ $d = 1.46$	$p < 0.001$ $d = 1.44$	1.09
Coping self-statements	11.4 ± 3.3	7.4 ± 3.5	7.9 ± 1.2	$p < 0.001$ $d = 1.56$	$p < 0.001$ $d = 1.67$	1.27	11.5 ± 3.3	7.6 ± 2.5	7.4 ± 3.8	$p < 0.001$ $d = 1.78$	$p < 0.001$ $d = 1.48$	1.08

CPSS = chronic pain self-efficacy scale; SD = standard deviation.

* BDI = Beck Depression Inventory; BL = baseline; CBT = cognitive-behavioral therapy; CPCI = Chronic Pain Coping Inventory; FU = 3-month follow-up; HADS = Hospital Anxiety and Depression Scale; ISTDP = intensive short-term dynamic psychotherapy; NPRS = Numerical Pain Rating Scale; PCS = Pain Catastrophizing Scale; PT = posttreatment (week 16).

† Effect size given as Cohen's standards: small effects as $d = 0.2$–0.5, medium effects as $d = 0.5$–0.8, and large effects as $d > 0.8$.

Physical symptoms are common in major depression and may lead to chronic pain and complicate treatment.[38] Because depression and pain share a common neurochemical pathway in that they are both influenced by serotonin and norepinephrine, depression, and associated painful physical symptoms must be treated together to achieve remission. In fact, research has shown that physical symptom improvement was correlated with the improvement of other depression symptoms, which suggests that the patient's ability to achieve depression remission may be directly related to the reduction of painful physical symptoms.[39]

In this study, self-efficacy was only observed in the CBT group. It is possible that a more independent manner of interacting with the CBT treatment can increase self-efficacy. There is sufficient evidence to demonstrate that CBT can increase self-efficacy in psychosomatic patients.[40] Relaxation and coping increased after treatment in both conditions. This preference for the use of relaxation skills was the main characteristic of CBT in Rendondo et al.[41]

Strengths and Limitations

There is a general paucity of studies regarding the effectiveness of brief dynamic therapy, such as ISTDP in the treatment of MUP and limiting the evidence base of this treatment method. More specifically, this study compares 2 psychotherapy treatments, which have never been directly compared before. This study relates to research questions unanswered so far. Secondly, this is, to our knowledge, the largest RCT to date comparing ISTDP with active treatments in the treatment of MUP (N = 341). Third, several elements contribute to the generalizability of the study's findings. Treatment was provided in regular outpatient clinics by a large number of therapists. Patients were not only recruited by advertisement but also referred by general practitioners. Moreover, patients with relatively low socioeconomic status were included.

This study also has a number of limitations. Firstly, a substantial number of patients did not complete treatment or were lost to assessment. Secondly, we could not prevent patients from seeking additional treatment during the follow-up period, and a nonsignificant finding suggested that patients in the CBT group might have returned to treatment more

TABLE 3. Linear Growth Models for Change in Outcomes Over Time*

Growth parameter	Baseline to posttreatment (week 16) parameter estimates			
	β	SE (*β*)	*p* value	95% CI
NPRS				
Treatment	3.99	3.25	0.127	4.34–8.15
Time	−3.82	1.48	0.232	4.13–8.11
Treatment × time	−4.17	2.16	0.189	4.27–8.17
BDI				
Treatment	5.98	5.21	0.786	4.41–8.22
Time	−7.12	2.16	0.065	4.16–8.31
Treatment × time	−8.54	3.12	0.346	4.22–8.12
HADS (psychologic distress)				
Treatment	7.89	2.76	0.786	10.26–16.27
Time	−4.78	1.44	0.386	11.42–16.46
Treatment × time	−7.32	2.11	0.323	11.38–16.24
PCS				
Treatment	3.14	4.67	0.007	12.62–17.35
Time	−6.90	2.54	0.323	12.23–18.78
Treatment × time	−6.19	3.87	0.423	13.11–17.25
CPSS (self-efficacy)				
Treatment	−5.12	3.82	0.387	12.34–18.12
Time	−0.34	1.54	0.875	13.45–18.56
Treatment × time	2.12	0.33	0.146	12.78–17.43
CPCI				
Treatment	−3.21	0.24	0.754	1.8–5.5
Time	−1.22	0.22	0.332	0.67–4.4
Treatment × time	1.34	0.33	0.187	0.56–4.8

CPSS = Chronic Pain Self-efficacy Scale; SE, standard error.

* BDI = Beck Depression Inventory; CPCI = Chronic Pain Coping Inventory; HADS = Hospital Anxiety and Depression Scale; NPRS = Numerical Pain Rating Scale; PCS = Pain Catastrophizing Scale.

than those in the ISTDP group. However, controlling for additional treatment in the follow-up period did not change the general pattern of results. Thirdly, the study uses a *comparative strategy*, which directly compares 2 fully realized clinically representative treatment packages. Although this strategy is beneficial to the external validity, it is impossible to identify specific operative aspects within the treatment. Consequently, this study does not focus on these aspects. Fourth limitation of the current study is the absence of a treatment-as-usual or waiting list conditions makes it difficult to know whether both groups improved owing to effects of the intervention, nonspecific therapeutic effects, placebo effect, treatment-as-usual, or the passage of time or both. Besides the ethical considerations of withholding patients from treatment for 16 weeks, it was practically very difficult to incorporate such a condition into this design. A fifth limitation is the fact that outcome assessors were not blinded for treatment conditions. Although blinding undoubtedly would have contributed to the internal validity of this study, it is by definition impossible to blind patients and therapists for psychotherapy treatment conditions. Because the independent research assessors work in small-scale clinics, it was impossible to prevent them from knowing the therapists' treatment conditions. Therefore, the independent research assessors could not be blinded. Nonetheless, statistical analyses will be performed blindly to minimize bias.

Finally, psychodynamic therapy adherence was not assessed using an adherence measure, but manual fidelity in both conditions was monitored using intensive supervision.

Further research is required to compare both treatments at the same endpoint beyond 16 weeks, and to determine a long-term follow-up of 1 year or more to better consider the efficacy of treatments. CBT and ISTDP are a complex intervention, and there is a need to unbundle specific modules to determine their effectiveness and contribution. This is not surprising, given the chronicity of their problems, previous failure of treatment and frequent comorbidity. Further

research is required to compare ISTDP with CBT difficult-to-treat population, such as patients with MUP, comorbid with personality disorders. Lastly, it would be helpful to determine the cost effectiveness of ISTDP in comparison with CBT.

CONCLUSIONS

Among adults with MUP, treatment with ISTDP or CBT, resulted in improvement in perceived pain, psychologic distress, depression, and cognitive variables. This included self-efficacy, catastrophizing, and coping strategies at 16 weeks, with almost no significant differences in outcomes between ISTDP and CBT. These findings suggest that ISTDP may be an effective treatment option for patients with medically unexplained somatic symptoms of pain.

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