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Citalopram and metacognitive therapy for depressive symptoms and cognitive emotion regulation in patients with major depressive disorder: A randomized controlled trial

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Abstract:

BACKGROUND: Metacognitive therapy (MCT) is a new psychotherapy for depression. This study was conducted to compare the effectiveness of citalopram and MCT on major depressive disorders (MDDs).

MATERIALS AND METHODS: A total of 36 patients with MDD were randomly assigned into three groups of citalopram ($n = 12$), MCT ($n = 16$), and control ($n = 8$). MCT group received ten sessions of metacognition therapy. Citalopram group received 20–40 mg citalopram, and the control group did not receive any interventions. Outcomes were measured using the Beck Depression Inventory-II, Metacognition Questionnaire-30, and Cognitive-Emotion Regulation (CER) Questionnaire. Data were analyzed with ANCOVA using SPSS version 18.

RESULTS: Depression score reduction was significant in both citalopram and metacognitive groups ($P < 0.05$). However, there was only a statistically significant difference between MCT and control group in CER and metacognition.

CONCLUSION: MCT and citalopram both are effective in symptom reduction in MDD. Furthermore, MCT could lead to more improvement in metacognition, depression symptoms, and CER than citalopram, when treating MDDs.

Keywords:

Citalopram, emotional regulation, major depressive disorder, metacognition

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there is a specific relationship between ER strategies and depression.^[5,6] ER strategies can be classified as biological, social, behavioral, and conscious and unconscious cognitive processes.^[7] Cognitive strategies (cognitive-ER [CER]) have stronger effects on emotional problems compared to others.^[8] CER strategies include self-blame, others blame, rumination, catastrophizing, putting into perspective, positive refocusing, positive reappraisal, acceptance, and planning.^[9]

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MDD has high economic costs to individuals and societies.^[2] The number of incident cases of depression worldwide increased from 172 million in 1990 to 258 million in 2017, representing an increase of 49.86%.^[10]

Over the last few decades, some therapeutic methods were proposed to treat MDD.^[11] Some studies showed that antidepressant medications have the same efficacy in treating depression.^[12] According to a report from the WHO, selective serotonin reuptake inhibitors (SSRIs) are the first-line treatments for MDD. Among all, citalopram is the most common one due to its effectiveness and low drug interaction.^[13,14] Only about one-third of all the patients who receiving antidepressants, improve.^[12] In addition, not all patients with depression recover with available treatments.^[15] It needs to develop new treatments for greater short-term and long-term efficacy. Hence, it seems necessary to find new treatment methods for drug-resistant patients. A new treatment for depression is metacognitive therapy (MCT).^[16,17]

MCT is one new psychotherapy, which was developed based on the metacognitive model of psychological disorders.^[16] Since cognitive-emotional regulation problems and maladaptive cognitive styles have an important role in making depression, the treatment of depression should work on them. One of the psychotherapy methods that work on cognitive-emotional regulation strategies and metacognition is MCT. MCT by specific techniques such as the attention training technique detached mindfulness and postponement of rumination eliminates the cognitive-attentional syndrome (CAS), and it teaches patients new and more beneficial ways of relating to thoughts that act as triggers for rumination.^[16] The focus of MCT is on decreasing unhelpful cognitive processes and facilitating metacognitive modes of processes. It enables patients to interrupt rumination, decline unhelpful self-monitoring tendencies, and establish more adaptive styles of responding to thoughts and feelings. An important part of the treatment is modification of positive and negative metacognitive beliefs about rumination.

The strategy is to focus treatment on specific psychological mechanisms that directly maintain depressive symptoms as specified by the metacognitive model.

The metacognitive model of emotional disorder provides a basis for understanding the persistence and recurrence of depression. According to the model, persistence of disturbance is related to the activation of a particular style of thinking called the CAS. This includes repetitive thinking in the form of worry and rumination, which is used as a means of coping with threat. It also consists of an attentional strategy of excessively focusing on sources of threat, which are often internal (e.g., thoughts and

feelings). It includes coping behaviors (e.g., avoidance and thought suppression) that are unhelpful, because they negatively affect the interpersonal environment and prohibit the person from testing faulty beliefs.

In many cases, the person lacks metacognitive awareness or appropriate knowledge to facilitate effective control. In such cases, a recurrent vicious cycle of ruminative responses occurs that the person is unable to terminate. In summary, vulnerability to depression in the metacognitive model can be traced to the ease with which the patient activates the CAS in response to mood disturbances or stress. This, in turn, is linked to individual differences in metacognitive beliefs and the degree of flexible executive control overprocessing.^[16,18-21]

One study with a nonclinical sample reported that negative metacognitive beliefs about uncontrollability and danger of worry were a predictor of anxiety and depression independently of stressful life events.^[22] A meta-analysis of MCT for anxiety and depression showed that MCT is more effective than waiting list, and possibly cognitive-behavioral therapy (CBT).^[23]

Since the publication of the review of Normann *et al.* (2014), several studies on MCT for depression have been published.^[18,24-26]

Researchers found that MCT and CBT have similar positive results on symptom measures, but MCT develops better effects on improved executive control.^[17,24,27]

The study by Nordahl showed that the MCT had effect sizes of 2.25 for anxiety symptoms and 1.31 for depressive symptoms.^[28]

Our study hypothesis was that MCT could be effective as the same as citalopram in the treatment of depression by improving cognitive-emotional regulation and cognitive style. For evaluation of this hypothesis, we compared them with three items: depressive symptoms, metacognitive symptoms of depression, and CER.

Even though there is plenty of evidence about the effectiveness of MCT in diminishing depressive symptoms,^[18] there needs to be more studies to confirm its effectiveness in comparison to standard treatments, especially pharmacotherapies. In other words, in most of the previous studies, the efficacy of MCT was compared with waiting list or other methods of psychotherapy in depression. The supremacy of this study is comparison of this method with pharmacotherapy. This study was conducted to comparatively evaluate the impact of citalopram and metacognitive interventions on depression, metacognitive symptoms of depression, and CER in patients with MDD.

Materials and Methods

The present study is a randomized clinical trial. The participants were selected from outpatients in treatment centers and clinics of Isfahan with probable depression by convenient sampling based on the inclusion criteria. They were interviewed by a clinical psychologist and a psychiatrist based on Structured Clinical Interviews for Mental Disorders (SCID-I) to reach a definitive diagnosis of major depressive disorder. Inclusion criteria were diagnosis of MDD based on DSM-5, patients' age: 18–60 years, patients' educational level: higher than 3rd grade in junior high school, and no psychotherapy received for their MDD 6 months prior to the treatment. The exclusion criteria were diagnosis of bone mineral density, psychosis, drug abuse, organic disorders, and suicidal patients.

The eligible patients were randomly divided into three groups: MCT ($n = 16$), citalopram ($n = 12$), and control ($n = 8$). Then, metacognitive intervention was performed for MCT group for ten 1-h sessions by a trained psychologist. For the second experimental group, 10–60 mg citalopram (a well-known widely-used standard drug of SSRIs group of antidepressants) was administered, whereas the control group did not receive any interventions, and they were placed on a waitlist. All the groups were evaluated twice (pretest and posttest) by the Beck Depression Inventory-II, Metacognition Questionnaire-30, and CER questionnaire (CERQ). Furthermore, patients were asked to fill out a demographic form to reveal their age, gender, educational level, and occupation.

Measures

Beck Depression inventory-II

It includes 21 questions that evaluate the intensity of depression and determines depressive symptoms in psychiatric patients and normal population. The participants rated the severity of their symptoms on a scale of 0–3, and the range of total scores is 0–63. The reliability and validity of this questionnaire were approved in Iran.^[29]

Metacognition Questionnaire-30

It is a self-report scale comprising 30 questions and five domains: positive beliefs about worry, negative beliefs about thoughts concerning uncontrollability and danger, cognitive confidence (assessing confidence in attention and memory), negative beliefs concerning the consequences of not controlling thoughts, and cognitive self-consciousness (the tendency to focus attention on thought processes ($n = 6$ items for each subscale)). The items were responded using a Likert-type scale. This questionnaire has appropriate reliability and validity.^[30]

Cognitive-Emotion regulation questionnaire

This questionnaire is a 36-question self-assessment tool, which assesses nine different cognitive coping strategies (self-blame, other blame, rumination, catastrophizing, putting into perspective, positive refocusing, positive reappraisal, acceptance, and refocus on planning). CERQ can be used for both clinical and normal populations. Several studies were conducted on this questionnaire, all of which confirm its reliability and validity.^[31] Psychometric properties of this questionnaire are also confirmed in Iran.^[32]

To describe the data, we used descriptive statistics such as mean and its correspondence standard deviation for quantitative data and frequency (%) for qualitative data.

To analytical statistics, an ANCOVA model was used to compare outcomes such as depression, metacognition, and emotional regulation measures between the three groups of citalopram, MCT, and control controlling for baseline outcomes variables and age. To control baseline outcomes, we used the difference between pre-test and post-test measurements. Data were analyzed using SPSS 18.0 software (spss Inc, Chicago, IL, USA) $P < 0.05$ was considered to be statistically significant.

Results

The results of the demographic characteristics are demonstrated in Table 1.

In Table 1, even though most of the patients were female, married, homemakers, and with educational level of lower than bachelor's degree, the differences between the variables were not statistically significant ($P > 0.05$).

Variance equality and normality tests were used to evaluate the assumptions for using ANCOVA. The results of which indicated that adopting nonparametric tests were not required ($P > 0.05$).

Table 1: The percentile distribution of demographic variables in the three groups of pharmacotherapy, psychotherapy, and control (original)

Variable	Citalopram (%)	Metacognitive therapy (%)	Control (%)
Gender			
Male	16.7	6.3	12.5
Female	83.3	93.8	87.5
Marital status			
Single	41.7	28.6	35.3
Married, divorced	58.3	71.4	64.7
Educational level			
Bachelor's degree and higher	33.3	54.5	57.1
<Bachelor's degree	66.7	45.5	49.9

All the assumptions were fulfilled. Given the absence of any significant differences between the demographic variables in the three groups, controlling them for later evaluations was not required.

The results related to the comparison of the main output variables in the pretest and post test stages, and the results of ANCOVA test are presented in Table 2.

In Table 2, there was a significant difference between the groups in terms of depression, metacognition, and CER variables.

The results of tests indicated that MCT and citalopram both are effective in symptom reduction in MDD. In terms of metacognition, there was a significant difference between metacognitive intervention and control groups ($P = 0.005$).

There was a significant difference between the control group and metacognitive intervention groups ($P = 0.011$) in terms of depression.

Moreover, with respect to the CER variable, there was a significant difference between the metacognitive intervention and control groups ($P = 0.017$).

Discussion

This study was conducted to compare the effects of citalopram and metacognitive intervention on major depression, metacognitive beliefs, and CER.

Results indicate that citalopram is effective in assuaging depression. These findings are in accordance with those of previous studies.^[13,33,34]

Other findings of this study demonstrated that metacognitive intervention might treat MDD. These

results were congruent with the findings of other studies.^[16,18,20,26,30]

The metacognitive intervention for depression focused on the patient's depressive symptoms, rumination, addressed metacognitions, worry, and unhelpful coping behaviors that are related to psychological disorders.^[35]

Rumination is a more prominent process in maintaining depression than worry. Studies show that therapists should work on both ruminations and worry in MCT therapy, despite the fact that rumination may play an important role.^[22,35]

Furthermore, this study indicates the effectiveness of MCT on improving metacognitive beliefs and ER. Results showed a significant decrease in all metacognitive beliefs, confirm the idea that this may be the main mechanism of symptomatic change.^[27]

This result is in agreement with those of previous findings proposing that at the end of MCT course, patients with MDD used effective ER strategies.^[36,37]

According to the literature, the ER plays a mediatory role in depression.^[38]

Based on MCT, thinking style (or CAS) in MDD patients consists of repetitive processes such as rumination, worry, fixed attention toward threat, and maladaptive self-regulation strategies or coping behaviors.^[16] The cardinal feature of CAS is rumination,^[39] and evidence show that rumination plays an important role in depression.^[40] It seems that MCT can lead to depression decrease through focusing on thinking process, rumination, and changing the relationship between patients and problematic thoughts and emotions. MCT focuses on attention bias, cognition control, and the role of beliefs in the thought processing style.

Table 2: Means, standard deviations, and comparison of outcome measures at posttreatment in studied groups

Variables	Mean (SD)		Difference between groups Means (P)*	F	P
	Pretest	Posttest			
Depression*					
Citalopram (1)	45.6 (12.72)	27.6 (11)	Difference (1, 3)=-13.2 (0.095)	3.7	0.037
MCT (2)	37.2 (19.9)	13 (12.2)	Difference (2, 3)=-19.6 (0.011)		
Control (3)	19.9 (5.7)	18.4 (13.6)			
Metacognition*					
Citalopram (1)	89 (13.1)	74.5 (15)	Difference (1, 3)=-17.6 (0.193)	5.1	0.012
MCT (2)	82.4 (13.7)	47.1 (39.3)	Difference (2, 3)=-38.2 (0.005)		
Control (3)	71.1 (13.7)	71.7 (17.9)			
Cognitive emotion regulation*					
Citalopram (1)	91.2 (34.5)	90.3 (34.1)	Difference (1, 3)=147 (0.983)	5.7	0.008
MCT (2)	115.1 (24.5)	60.6 (51.2)	Difference (2, 3)=-54 (0.017)		
Control (3)	107.6 (7.4)	107 (8.4)			

*The results are obtained from fitting ANCOVA model in which the difference between pretest and posttest are as the outcome variables controlling for age. MCT: Metacognitive therapy, SD: Standard deviation

This method can treat depression and ER by reducing rumination.^[16] In other words, MCT for depression focuses on identifying and removing the CAS by challenging positive and negative metacognitive beliefs and eliminating dysfunctional behaviors.^[18]

MCT help patients to detach mindfulness and delay ruminations of all negative thoughts.^[27]

Self-regulatory executive function model is the base of MCT.^[41,42] This model has four main concepts that are important in persistence of negative thoughts and associated dysfunction in emotion. These are metacognitive beliefs, CAS, mental modes, and attention or executive control. The goal of MCT is to modify these factors.^[43]

In addition, MCT can improve metacognitive beliefs related to worry and catastrophizing.^[16] The tendency to worry, focuses attention on threat, and avoids from a normal adaptation process and leads to sustained thinking about danger and persistence of symptoms. In treating depression, MCT targets the process of rumination. Rumination in depression is a coping strategy, which follows an initial negative thought labeled a "trigger thought."^[16,17] Treatment consists of the attention training technique to interrupt repetitive styles of negative thought and regain flexible control over thinking styles. This is coupled with challenging negative metacognitive beliefs about the uncontrollability of depressive thinking and challenging positive beliefs about the need to ruminate as a means of coping and finding answers to sadness.^[44]

Conclusion

According to the obtained results, MCT and citalopram both had efficacy in treatment of depressive symptoms. Although MCT could lead to higher level of improvement in depression, CER and meta cognition (than citalopram). It means in the treatment of depressed patients with more prominent problems in cognitive-emotional regulation and metacognition (who have more rumination and worry) MCT could be more effective than citalopram. In none responder patients to drugs, patients with high recurrence on drug treatments, and patients that cannot tolerate drug side effects and who have more tendencies to psychotherapies method for treatment, our findings in this study can be useful. Depressed patients with more problems in cognitive-emotional regulation and metacognition are appropriate choices for MCT. The finding of this study can be applied for modification of positive and negative metacognitive beliefs about rumination in these patients, and this strategy treats depression and decreases relapses and results in adaptive style of thoughts and feelings.

Limitations

Three limitations of this study were: neglecting the role

of drug dose in recovery of depression and no follow-up with the patients, which can be evaluated in further studies. The third limitation is the small sample size that limits generalizability.

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Conflicts of interest

There are no conflicts of interest.

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