

Evaluation of the Effect of Citalopram on Personality Factors in Depressed Patients (A Clinical Trial)

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Abstract

Recognizing the personality and its disorders differentiates it fundamentally from other branches of medicine. By recognizing the personality of people, we can gain adequate knowledge on behavior and relationships among the people. Enhancing the quality of life of psychiatric patients largely depends on positive developments in their personality. Considering the inaccessibility of psychotherapy and its costs, Drug therapy is always considered clinically in treating patients. The objective of this research was to evaluate the relationship between the use of medicine and personality factors, which could be helpful in the use of more effective drugs in the treatment of personality disorders. Hence, this research was conducted to evaluate the effect of citalopram, as a widely used drug for treating depression on personality factors. This is a randomized clinical trial study conducted since September 2015 to September 2016 on 30 patients with major depression who referred to Shahid Sadoughi University Clinics in Yazd. First, major depression was clinically examined and diagnosed by physician based on DSM4 diagnostic criteria. Then, they received Beck Inventory and 125 TCI test. Then, they were treated with citalopram. After that, they were followed-up in clinic after 6 weeks of treatment. After being interviewed and examined by a psychiatrist, the patients re-received the TCI and Beck tests. Finally, the results of each subject were submitted to the statistics consultant to analyze the data. Based on Paired Sample Test and p-value test, there is a significant difference between the mean scores of Beck test before and after treatment and citalopram. In addition, the difference between the mean scores of factors of novelty-seeking, harm avoidance, reward dependence, self-directedness, cooperativeness, and self-transcendence before and after treatment and citalopram is significant. Based on this study, treatment of depression with citalopram causes changes in personality factors. The results of this research can be helpful in treatment of patients with personality disorders. However, further investigations are required to examine the effects of other psychotropic drugs on the treatment of personality disorders, such as antipsychotics and other antidepressants.

Keywords: Citalopram, Personality Factors, Self-Directedness, Cooperativeness, Self-Transcendence, Depressed Patients.

Introduction

The personality refers to all individual characteristics, which include fixed intellectual, emotional, and behavioral patterns. The personality can be divided into three parts of temperament, character, and psyche. The four main attributes of the temperament include novelty seeking (NS), harm avoidance (HA), Persistence (P), and reward dependence (RD), and three attributes of character include self-directedness (SD), cooperativeness (C) and self-transcendence (ST) (Benjamin et al., 2009). Temperament components have a neurobiological base and are inherited and the components of the character reflect the cultural and social education. All components of temperament are specific to the activity of the neurotransmitter system (5). The main neuromodulator of the vulnerability is the Gaba neurotransmitter and serotonin, and the neuromodulator of novelty seeking is dopamine. The neuromodulator of reward dependence is norepinephrine and serotonin and the neuromodulators of Persistence are glutamate and serotonin (Lyoo et al., 2003). Psychiatric treatment should be directed towards improvement of the psychological well-being of the patient and reduce the negative psychological symptoms (Kaviani et al., 2005; Cloninger et al., 1997), Drug therapy is one of the effective treatments for personality disorders. Psychiatric drugs also affect the components of the personality by leaving effects on these neurotransmitters (Benjamin et al., 2009). Even if a psychiatrist wants to only treat the diseases rather than having comprehensive approach to the patient, the assessment of personality disorder in the clinic will be still necessary since such disorders are nowadays very common in community. Almost 10 to 20 percent of the population and about half of outpatient and hospitalized patients suffer from personality disorder.

Personality disorder is often associated with other clinical syndromes such as depression. In addition, disorders such as mood and anxiety disorders affect personality dimensions, but major part of the personality is not associated with mood and anxiety (Brown et al., 1992). Psychotherapy is another treatment used in this regard (Cloninger, 2002). Given the inaccessibility of psychotherapy and its high cost, drug therapy has always been considered seriously in treatment of these patients (Furukawa et al., 216; Patel K et al., 216)

Tomita et al (2014) conducted a study to evaluate paroxetine treatment in patients with major depression using TCI. A total of 73 patients performed TCI and monitoring test before and after six-week treatment with paroxetine. After treatment, patients were divided

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into two groups: respondents and non-respondents. The results of the research revealed that only 10 TCI items were effective in prediction of response to treatment (Tomita et al., 2014).

Mazza et al (2009) evaluated the effect of SSRI on temperament and character in fibromyalgia patients. In this research, 60 patients with fibromyalgia were tested by TCI-Beck test and patients were re-evaluated 6 months after treatment with citalopram or fluoxetine or paroxetine and their results were compared with those of control group. Patients had higher HA and lower SD compared to control group subjects before and after treatment (Mazza et al., 2009). Boz et al (2007) evaluated the effect of serotonergic anti-depressant therapy on temperament and character in patients with chronic tension headache. 45 patients with chronic tension headache were assessed by TCI test and Beck inventory before treatment and 4 months after prophylactic treatment with serotonergic antidepressants and one control group, similar to their age and gender and education level, was selected. Comparing two groups before treatment showed that patients had higher HA and lower SD compared to control group. After treatment, HA decreased and SD increased, while HA was higher and SD was still lower than those in control group (Boz et al., 2007). Lyoo et al (2003) evaluated change in TCI in OCD patients 4 months after treatment. 35 patients diagnosed with OCD by DSM4 received TCI test and Beck inventory before treatment and 4 months after treatment. HA decreased after treatment while SD did not change; RD also increased after treatment.

In general, this research revealed that temperament more than character is subordinate of the treatment (Lyoo et al., 2003). Allgulander et al (1998) evaluated change in TCI with paroxetine treatment in a study on 29 subjects with a generalized anxiety disorder. Patients were assessed by TCI test before treatment and 4 and 6 months after treatment. Reduction in HA and increase in SD were seen after treatment (Allgulander et al., 1998).

The objective of this research was to evaluate the relationship between the use of drugs and personality factors, which could be helpful in the use of more effective drugs in the treatment of personality disorders. Hence, this research was conducted to evaluate the effect of the citalopram, a widely used drug in treatment of depression, on personality factors.

Methodology

This is a randomized clinical trial study conducted since September 2015 to September 2016 on patients with major depression who referred to Shahid Sadoughi University Clinics in Yazd. The research subjects were selected using convenient sampling method. Given the significance level of 5% and the test power of 80%, and considering the standard deviation of scores of 7 domains of TCI (3.5) and to achieve the minimum significant difference in the mean scores of HA in each group, sample size was determined to be 30 people. The formula to calculate sample number required for this research is as follows:

$$N = \frac{(Z_{\alpha/2} + Z_{\beta})^2 \times 2S^2}{(X_1 - X_2)^2}$$

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The research inclusion criteria included people aged above 18 years and patients with major depression and the research exclusion criteria included a psychiatric disorder other than depression, types of seasonal depression, sexual dysfunction at considerable level, and undergoing treatment (passing 6 months of the last treatment, if treated before).

In this research, Beck inventory 2 was used to evaluate depression and 125-item TCI inventory was used to evaluate the personality factors. The personal information of the participants was recorded in this research. Temperament and Character Inventory or TCI is a psychological test used for evaluation of personality and it has been developed by Cloninger based on the personality bio-social model. TCI has been designed based on self-report. This test assesses the four dimensions of temperament of novelty seeking, harm avoidance, reward dependence, Persistence, and three dimensions of character, including cooperativeness, self-directedness and self-transcendence. The questionnaire used in this research included 125 questions, answered based on two options of true and false. This test has good validity and reliability in Iranian population (Kaviani & Pournasah, 2005). Beck-Depression Inventory-2 is a depression screening test focusing on cognitive, behavioral, and physical symptoms. Beck Test is able to assess the severity of depression and is sensitive to change; so, it is used to assess response to treatment. The reliability coefficient of test is 78 and its validity is 70-90.

In this research, patients with major depression referred to Shahid Sadoughi University Clinics of Yazd were examined and diagnosed clinically by the psychiatrist based on the DSM4-TR diagnostic criteria. After initial evaluation and ensuring that they met the research inclusion criteria, the necessary explanations were provided for the patients on the research project and written consent to participate in the research was taken from them. Then, they received Beck inventory and the 125 TCI Test. In the next stage, 30 subjects were treated with citalopram. The patients were followed-up 6 weeks after treatment in clinic, so that patients received TCI and Beck tests again, after

being interviewed and examined by a psychiatrist. Finally, results of each person were submitted to the statistics consultant to analyze the data. One of the most important problems in this research was the large number of questions of the inventory, led to patients' unwillingness to cooperate and lack of giving adequate response owing to requiring much time to complete it. Non-tolerance of drug by some of the samples or side effects led to the discontinuation of treatment by patients as well as the lack of follow-up of treatment by some patients led to their exclusion from study were some other limitations of this research.

Results

In this research, a total of 74 patients over the age of 18 with major depression referred to Yazd Shahid Sadoughi University Clinics since September 2015 to September 2016 who did not meet the exclusion criteria of research and were willing to participate in the study were examined. All patients were interviewed and examined clinically by a Beck Inventory and TCI test. Then, 36 patients were treated with citalopram using a random number table. Finally, 14 patients were excluded from the study. Five patients had to replace the drug owing to drug side effects and non-tolerance, and 9 patients did not refer to follow up the treatment and they were excluded from the study. Finally, intervention was performed on 30 patients receiving citalopram, and after 6 weeks, they were re-examined with Beck Inventory and TCI test. Finally, the data were analyzed. The results showed that the mean age of the citalopram -receiving group was 36.20 years.

In this research, 13 male and 17 female patients received citalopram. In the citalopram-receiving group, 6 subjects had elementary, 3 subjects had secondary, 8 subjects had high school, and 3 subjects had associate and 6 subjects had bachelor, and 4 had education higher than bachelor (Table 1).

Table 1: Determination and comparison of frequency distribution of gender and educational level in the study group

variable		Citalopram group
gender	male	13
	female	17
	total	30
Education level	Elementary	6
	secondary	3
	High school	8
	associate	3
	bachelor	6
	higher	4
	total	30

The mean score was 34.17 in the citalopram -receiving group before treatment. In addition, the mean Beck Inventory score was 20.93 in the citalopram -receiving group after treatment (Table 2).

Table 2: Determination and comparison of mean score of Beck test before and after treatment in two study groups

Variable	group	n	mean	p-value
Beck test before drug use	citalopram	30	34.17	.815
Beck test after drug use	citalopram	30	20.93	.538

In the citalopram -treated group, the mean score of Beck was 34.17 before treatment and it was 20.93 after treatment. Using paired samples and p -value = .000, the change in mean scores of Beck test before and after treatment was significant. The mean scores of NS before and after treatment in the citalopram group was 8.60 and 10.07, respectively, which showed a significant difference (P -value = .015).

The mean score of HA before and after treatment was 13.07 and 9.30 respectively, in citalopram group and there was a significant difference in this regard (P -value = 0.000). The mean score of RD was 9.57 before treatment with citalopram and it was 10.93 after treatment, which was significant with P -value = 0.002. The mean P score before and after treatment with citalopram was 3.20 and 3.40, respectively, and there was no significant difference between them (P -value = 0.351).

In the citalopram group, the mean SD score was 7.37 before treatment and it was 10.23 after treatment, which this difference was significant (P value = .000). The mean score of CO was 15.67 before treatment and it was 17.47 after treatment, which this difference was significant with P -value = 0.001. The mean score of ST was 7.70 before treatment with citalopram and it was 9.27 after treatment.

The standard deviation of this factor before and after treatment with citalopram was 3.485 and 2.545, respectively, and this difference was significant with P-value = 0.000 (Table 3).

Based on Table 3 and Paired Sample Test and p-values, there is a significant difference between the mean scores before and after treatment with citalopram. Moreover, there is a significant difference in the mean scores of factors of novelty-seeking personality, harm avoidance, reward dependence, self-directedness, and cooperativeness and self-transcendence before and after treatment with citalopram.

Table 3: Determination and comparison of mean scores of Beck and TCI tests before and after treatment with citalopram

variable	mean	SD	p-value
Beck before drug use	34.17	6.502	.000
Beck after drug use	20.93	8.428	
Novelty-seeking before drug use	8.60	3.191	.015
Novelty-seeking after drug use	10.07	3.194	
Harm avoidance before drug use	13.07	3.248	.000
Harm avoidance after drug use	9.30	2.818	
reward dependence before drug use	9.57	2.725	.002
reward dependence after drug use	10.93	2.288	
Persistence before drug use	3.20	1.095	.351
Persistence after drug use	3.40	1.003	
Self-directedness before drug use	7.37	4.230	.000
Self-directedness after drug use	10.23	3.875	
Cooperativeness before drug use	15.67	3.594	.001
Cooperativeness after drug use	17.47	3.776	
Self-transcendence before drug use	7.70	3.485	.000
Self-transcendence after drug use	9.27	2.545	

In the citalopram group, the mean scores of NS, HA, RD, P, SD, CO, and ST were 8.60, 13.07, 9.57, 3.20, 7.37, 15.67, and 7.70, respectively, before treatment. In the citalopram group, the mean scores of NS, HA, RD, P, SD, CO, and ST were 10.07, 9.30, 10.93, 3.40, 10.23, 17.47, and 9.27, respectively, after treatment (Table 4).

Table 4: Determining and comparison of the score of personality factors before and after treatment in the study group

variable	group	n	mean	t-Test result
Novelty-seeking before drug use	citalopram	30	8.60	.603
Novelty-seeking after drug use	citalopram	30	10.07	.000
Harm avoidance before drug use	citalopram	30	13.07	.244
Harm avoidance after drug use	citalopram	30	9.30	.000
reward dependence before drug use	citalopram	30	9.57	.074
reward dependence after drug use	citalopram	30	10.93	.467
Persistence before drug use	citalopram	30	3.20	.853
Persistence after drug use	citalopram	30	3.40	.581
Self-directedness before drug use	citalopram	30	7.37	.559
Self-directedness after drug use	citalopram	30	10.23	.167
Cooperativeness before drug use	citalopram	30	15.67	.805
Cooperativeness after drug use	citalopram	30	17.47	.301
Self-transcendence before drug use	citalopram	30	7.70	.001
Self-transcendence after drug use	citalopram	30	9.27	.001

Out of 30 patients treated with citalopram, 23 were non-respondent to treatment and 7 were respondent to treatment. The appropriate response was considered to be a reduction of 50% or more in Beck score (Table 5).

Table 5: Response to treatment with citalopram drug *

Response to treatment	citalopram	bupropion	total
NO	23	18	41
YES	7	12	19

*The response to treatment was considered to be a reduction of 50% or more in Beck score (Kheirkhah et al., 2010)

P-value of the correlation between factors NS, HA, RD, P, SD, ST before treatment and response to treatment with any of the drugs was not significant. The P-value correlation between CO and the response to treatment in the citalopram group was not significant. Other factors did not show a significant relationship with the response to treatment (Table 6).

Table 6: Relationship between factors before treatment and response to treatment in the citalopram group

Personality factors	Respondent to treatment
	Citalopram 7
NS.B	.145 (P-value)
HA.B	.229
RD.B	.743
P.B	.772
SD.B	.096
CO.B	.740
ST.B	.096

The correlation between the response to treatment with citalopram and temperament was .120 with a P-value of .528. In addition, the correlation between response to treatment with citalopram and character was -.432 with P-value = 0.017. By assessing the correlation of response to treatment and character, response to treatment showed significant and reverse relationship with character in citalopram group (Table 7).

Table 7: Correlation * between the response to treatment and temperament and character

variable	Response to treatment	
	citalopram	P-value
Temperament	.120	.175
character	-.432	.068

The correlation number is between -1 and +1, in which the negative number indicates the reverse relationship and the positive number indicates the direct relationship between two factors.

Discussion and Conclusion

Personality disorder is one of the most common disorders that challenges psychiatrists and its control has always been considered clinically. Drug therapy is one of the effective treatments for personality disorders. Psychiatric drugs also affect the personality components through leaving an effect on neurotransmitters. The objective of this research was to evaluate the relationship between the use of drugs and personality factors, which could be helpful in the use of more effective drugs in the treatment of personality disorders. This research was conducted to evaluate the effect of the citalopram, a widely used drug in treatment of depression, on personality factors. The mean age of participants in the citalopram group was 36.20 years.

In the current research, citalopram caused a significant change in NS, RD, SD, C, and HA but it had no significant effect on P statistically. In the study conducted by CR et al on 29 people with generalized anxiety disorder and treated with citalopram, the patients were re-assessed 4 and 6 months and the results showed the reduction in HA and increase in SD after treatment (Cloninger et al., 1997) which was in line with the result of our study. In a study conducted by Boz et al with serotonergic antidepressants, HA and SD increased after the treatment (Boz et al., 2007). In a study conducted by Tomita et al in 2015 on 48 patients with major depression, they were treated with paroxetine and results in contrast to those of our study were obtained. In the Tomita study, the follow-up was also performed after 6 weeks of treatment. The patients were divided into three groups: respondents and non-respondents and early respondents. In the respondent group and early respondent group, TCI criteria did not change with treatment (Tomita et al., 2015).

In a study conducted by Lyoo et al in 2003, it was found that temperament more than character is a function of treatment (Lyoo et al., 2003). In the present study, in the bupropion group, response to treatment and temperament showed direct relationship but it was not significant. However, response to treatment showed reverse relationship with character and this relationship was significant. Some studies have been conducted on personality dimensions as predictors of response to treatment with antidepressants in major depression, but they have not yielded consistent results. In the current study, only the personality factor of novelty-seeking (NS) changed significantly in respondents and non-respondents and other personality factors did not change significantly in respondents and non-

respondents. In the study conducted by Tomita, the only factor of SD changed significantly in non-respondents, but no significant change was found in the rest of dimensions between respondents and non-respondents (Tomita et al., 2015).

The limitation of the present study was a small number of patients. The higher number of patients and comparing them with healthy people might yield more useful results. Another limitation was that only the acute phase depression treatment was evaluated in this study and longer treatment might yield different results. In addition, the effects of other drugs such as benzodiazepine and anti-psychotics were not considered in the treatment of anxiety and insomnia, and the analysis of more other might reveal some important results. In the present study, if the patient underwent anti-depressant treatment, she or he would be excluded from the study, unless 6 months passed since the completion of treatment while it is not clear that how long the effect of previous drugs remains on personality factors.

A number of studies have indicated the relationship between SSRIs and changes in personality factors of TCI in MDD patients. There are few reports on evaluation of TCI in patients with major depression disorder with SSRIs (Gunasekara et al., 1998), and this is strength of this study. One another strength of this study was that other comorbidities were not diagnosed and not studied by clinical interviews. Finally, the results of this study revealed that personality factors change in patients with major depression disorder through treatment with citalopram and the mechanism of action of this drug in treatment of depression varies.

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