Original Article

Evaluation of the effect of bupropion on personality factors in depressed patients

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ABSTRACT

Introduction: 10 to 20 percent of the population and about half of outpatient and hospitalized patients suffer from personality disorder. Drug therapy is one of the effective therapies for personality disorders. The objective of this study 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 study evaluated the effect of bupropion, a widely-used drug in treatment of depression, on personality factors. Methodology: This is a randomized clinical trial study conducted on patients with major depression who referred to medical University Clinics in Yazd. A total of 30 depressed patients were included in this research. Then, they received Beck Inventory and 125 TCI test. The patients were followed-up in the clinic after 6 weeks of treatment. After being interviewed and examined by a psychiatrist, the patients received the TCI and Beck tests again. Finally, the results of each subject were submitted to the statistics consultant to analyze the data. Results: Based on Paired Sample Test and p-value test, there is a significant difference between the mean scores of Beck before and after the treatment and bupropion. In addition, the difference between mean scores of factors of novelty-seeking and reward dependence and self-directedness, cooperativeness, and self-transcendence before and after the treatment and bupropion are significant. Conclusion: Based on this study, treatment of depression with bupropion 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: Bupropion, personality factors, vulnerability, novelty-seeking, persistence, depressed patients.

Introduction

The personality refers to all the features making distinction between continuously evolving living creatures and a completely predictable machine object. By recognizing the personality of people, we can gain adequate knowledge on behavior and relationships among the people [1]. Recognizing the personality and its disorders differentiates it fundamentally from other branches of medicine. These disorders are very common in current community. Almost 10 to 20 percent of the community and about half of outpatient and hospitalized patients are afflicted with personality disorder. The importance of investigating the basic patterns of human behavior has been always emphasized and many explorations have been made in this path to achieve the main dimensions of personality. Personality disorder is often associated with other clinical syndromes such as depression. In addition, disorders such as mood disorder and anxiety disorder affect personality dimensions, but much of the personality is not related to mood and anxiety [2]. Enhancing the quality of life of psychiatric patients largely depends on positive developments in their personality. Psychiatric treatment should be directed towards improvement of mental health of the individual and reducing the negative symptoms of mental disorder [3, 4].

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) [1].

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Temperament components have a neurobiological basis 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 neuromodulator of persistence is glutamate and serotonin.

One of the effective treatments for personality disorders is drug therapy. Psychiatric drugs also affect the components of the personality by leaving effects on these neurotransmitters [1, 6]. The other treatment used in this regard is psychotherapy [7]. Given the inaccessibility of psychotherapy and its high cost, drug therapy has always been considered seriously in treatment of these patients [8, 9]. Tomita et al. (2015) examined TCI changes with paroxetine treatment study in a study conducted on 48 patients with major depression. The TCI and Montgomery Asberg depression rating scale were performed on week 0 and 6and patients were divided into three groups of responders and non-responders and early responders 6 weeks after treatment with paroxetine. Then, the TCI changes in these groups before and after treatment were compared. In the respondent group and early respondent group, TCI criteria did not change [10].

In a study conducted in 2010 on 98 patients with major depression, Kampman et al. examined the relationship between response to therapy and the temperament criteria in TCI. Six weeks before and after treatment with SSRI, patients received TCI questionnaire. HA was significantly higher before and after treatment compared to the normal population, and patients, especially men, had higher RD. Finally, it was found that HA was associated with response to treatment [11]. In 2004, Joyce et al examined the personality of patients with atypical depression. A total of 195 outpatient depressed patients were treated with nortriptyline and fluoxetine, which 16 of them with DSM 4 diagnosis received atypical depression, and then, personality types in people with and without atypical depression were compared.

In atypical depression, fluoxetine was more effective than nortriptyline, and atypical group showed more cohesion and lower persistence and more expected anxiety than other group [12]. In 2002, Hirano et al studied 108 depressed patients. First, their depression was evaluated by using Hamilton Test. Then, they underwent TCI test before and 16 weeks after antidepressant treatment. They found that the rate of depression had a direct relationship with the HA score, with a negative correlation with C and SD scores. These three criteria were changed in respondent group during the treatment and these changes were associated with change in intensity of depression [13]. 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 widely used drug of bupropion depression on personality factors.

Methodology

Research population and characteristics of subjects:

Sampling in this research was performed from September 2015 to September 2016 in patients with major depression referred to Shahid Sadoughi University Clinics in Yazd.

The research inclusion criteria include:

1-People aged above 18 years 2. Patients with major depression.

Research exclusion criteria include:

1-a psychiatric disorder other than depression, 2. Types of seasonal depression. 3. Sexual dysfunction at considerable level. 4. Patient undergoing treatment (passing 6 months of the last treatment, if treated before).

Research method

This study was conducted using randomized clinical trial.

Sampling method and sample size determination:

Convenient sampling method was used in this research. Sampling was performed on those referred to Shahid Sadoughi University Clinics. 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 score 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:

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

Variables and tools for data collection and analysis:

In this research, Beck inventory 2 was used to evaluate depression and 125-item TCI questionnaire was used to evaluate the personality factors. The personal information of the participants was recorded in this research.

TCI test

Temperament and Character Inventory 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 [3, 14].

Beck Inventory

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 the test is 78 and its validity is 70-90.

Procedure

In this research, patients with major depression referred to Shahid Sadoughi University Clinics of Yazd were examined. First, major depression was diagnosed clinically by the psychiatrist based on the DSM4-TR diagnostic criteria. After initial evaluation and ensuring the research inclusion criteria, the necessary explanations were provided for the patients on the research project and their written consent to participate in the research was taken from them.

Then, they received Beck inventory and the 125 TCI Test. Then, based on the order of the list of random numbers table prepared by the statistics consultant to achieve the desired homogeneity among the subjects and the type of the selected group (identified in numbers of 1 and 2), 30 People were included into bupropion-treated group. The patients were followed-up 6 weeks after treatment in clinic, so that patients underwent gain TCI and Beck tests after being interviewed and examined by a psychiatrist. Finally, results of each person were submitted to the statistics consultant to analyze the data.

Limitations and executive and moral problems of research

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 of the limitations of the study.

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 bupropion 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 referred to follow up the treatment and they were excluded from the study. Finally, intervention was performed on 30 patients receiving bupropion, and after 6 weeks, they were re-examined with Beck Inventory and TCI test. Finally, their data were analyzed. The results showed that the mean age of the bupropion-receiving group was 38.57 years.

In this research, 14 male and 16 female patients received bupropion. In the bupropion group, 9 subjects had elementary, 4 subjects had secondary, 7 subjects had high school, and 5 subjects had associate and 2 subjects had bachelor, and 3 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		Bupropion group
gender	male	14
	female	16
	total	30
Education level	Elementary	9
	secondary	4
	High school	7
	associate	5
	bachelor	2
	higher	3
	total	30

The mean score before treatment in the bupropion-receiving group was 33.73. In addition, the mean Beck Inventory score after treatment in the bupropion-receiving group was 19.33 (Table 2).

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

Variable	group	n
Beck test before drug use	bupropion	30
Beck test after drug use	bupropion	30

In the bupropion-treated group, the mean score of bupropion was 33.73 before treatment and it was 19.33 after treatment. Using paired samples and p-value = .000, the mean scores of Beck test before and after treatment were significant. The mean scores of NS before and after treatment in the bupropion group was 8.20 and 14.23, respectively, which showed a significant difference (P-value = .000).

The mean score of HA before and after treatment in bupropion group was 14.03 and 13.60 respectively, and there was no significant difference in this regard P-value = 0.248). The mean score of RD was 8.40 before treatment with bupropion and it was 10.50 after treatment, which it was significant with P-value = 0.000. The mean P score before and after treatment with

bupropion was 3.13 and 3.57, respectively, and there was no significant difference between them (P-value = 0.073).

In the bupropion group, the mean SD score was 8.00 before treatment and it was 11.70 after treatment, which this difference was significant (P value = .000). The mean score of CO was 15.47 before treatment and it was 16.57 after treatment, which this difference significant with P-value = 0.019. The mean score of ST was 10.47 before treatment with bupropion and it was 11.43 after treatment. The standard deviation before and after treatment with bupropion was 2.813 and 2.223, respectively, and this difference was significant with P-value = 0.022 (Table 3).

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

Variable	mean	SD	p-value
Beck before drug use	33.73	7.746	.000
Beck after drug use	19.33	11.360	
Novelty-seeking before drug use	8.20	2.709	.000
Novelty-seeking after drug use	14.23	3.104	
Harm avoidance before drug use	14.03	3.113	.248
Harm avoidance after drug use	13.60	3.058	
reward dependence before drug use	8.40	2.222	.000
reward dependence after drug use	10.50	2.301	
Persistence before drug use	3.13	1.634	.073
Persistence after drug use	3.57	1.305	
Self-directedness before drug use	8.00	4.119	.000
Self-directedness after drug use	11.70	4.244	
Cooperativeness before drug use	15.47	2.556	.019
Cooperativeness after drug use	16.57	2.837	
Self-transcendence before drug use	10.47	2.813	.022
Self-transcendence after drug use	11.43	2.223	

According to the above table, the Paired Sample Test and p-values presented, there is a significant difference between the mean scores before and after treatment with bupropion. Moreover, the difference between mean scores of novelty-seeking personality and reward dependence and self-directedness, cooperativeness, and self-transcendence before and after treatment with bupropion are significant.

In the bupropion group, the mean scores of NS, HA, RD, P, SD, CO, and ST were 8.20, 14.03, 8.40, 3.13, 8.00, 15.47, and 10.47, respectively, before treatment.

In the bupropion group, the mean scores of NS, HA, RD, P, SD, CO, and ST were 14.23, 13.60, 10.50, 3.57, 11.70, 16.57, and 11.43, 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
Novelty-seeking before drug use	bupropion	30	8.20
Novelty-seeking after drug use	bupropion	30	14.23
Harm avoidance before drug use	bupropion	30	14.03
Harm avoidance after drug use	bupropion	30	13.60
reward dependence before drug use	bupropion	30	8.40
reward dependence after drug use	bupropion	30	10.50
Persistence before drug use	bupropion	30	3.13
Persistence after drug use	bupropion	30	3.57
Self-directedness before drug use	bupropion	30	8.00
Self-directedness after drug use	bupropion	30	11.70
Cooperativeness before drug use	bupropion	30	15.47
Cooperativeness after drug use	bupropion	30	16.57
Self-transcendence before drug use	bupropion	30	10.47
Self-transcendence after drug use	bupropion	30	11.43

Out of 30 patients treated with bupropion, 18 were non-respondent to treatment and 12 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 bupropion drug*

Response to treatment	bupropion
NO	18
YES	12

*The response to treatment was considered to be a reduction of 50% or more in Beck score [15]

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. However, the P-value correlation between CO and the response to treatment in the bupropion group was 0.026 and significant. The only correlation between the CO factor before treatment and the response to treatment was significant in the bupropion group, but 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 bupropion group

Personality factors	Respondent to treatment
	bupropion 12

NS.B	.926
HA.B	.540
RD.B	.882
P.B	.411
SD.B	.293
CO.B	.026
ST.B	.847

The correlation between the response to treatment with bupropion and temperament was -254 with a P-value of .175. In addition, the correlation between response to treatment and bupropion and character was -338 with P-value = 0.068 (Table 7).

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

variable	Response to treatment	
	bupropion	P-value
Temperament	-.254	.175
character	-.338	.068

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

Discussion and Conclusion

Personality disorder is one of the most common disorders and its control has always been considered serious clinically. Drug therapy is an effective therapeutic treatment for personality disorders. Psychiatric drugs also affect the personality traits 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 widely used drug in bupropion on personality factors. The mean age of the participants in the bupropion group was 38.57 years.

In this study, bupropion caused a significant change in NS, RD, ST, C, but it had no significant effect on HA and P. No similar study was found on the effect of bupropion on personality factors. In this study, bupropion led to an increase in NS, which is expected due to the dominant effect of bupropion on dopamine. In the study conducted by Lyoo et al. in 2003 in South Korea, it was found that the temperament more than character was a function of treatment [16]. In the present study, in the bupropion group, no significant relationship was found between response to treatment and temperament and character. 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, significant correlation was found only between the CO factor before the treatment and response to the treatment in the bupropion group.

Hence, based on the present study, CO before the treatment might predict response to treatment with bupropion. In the study conducted by Sato et al., CO and SD were predictors of response to antidepressants [17]. In the study conducted by Kampman, HA was associated with the response to treatment [11]. In the study conducted by Baeken, SD score predicted response to rTMS treatment in depressed patients [18]. In this study, only NS personality factor significantly changed in respondents and non-respondents, and other personality factors did not change significantly in the respondents and non-respondents. In the study conducted by Tomita, only SD factor changed significantly in non-respondents, but there was no significant difference between the respondents and non-respondents [10].

The limitation of the present study was the low number of patients. The higher number of patients and the comparison 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 additional drugs might yield some important results. In this 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. 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 [7], 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 bupropion treatment.

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