Open-longitudinal study of the effect of dissociative symptoms on the response of patients with panic disorder to venlafaxine

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Abstract

The relationship between Panic Disorder (PD) and dissociation is well known. In this study we aimed to investigate whether or not dissociative experiences affect the response to PD drug treatment. For this purpose, standart dose of venlafaxine was preferred for treatment. 63 patients with PD were included in the study. Venlafaxine treatment with increasing dose was administered to each patient during a 10-week period. The Panic Disorder Severity Scale (PDSS) and the Dissociation Questionnaire (DIS-Q) were applied to the patients at the beginning of the study. Patients were divided into two groups based on DIS-Q scores. PDSS was applied again to both groups at the end of 10-week treatment.

No difference between sociodemographic data and PDSS scores of two groups – patients with low DIS-Q scores (<2.5) and high DIS-Q scores (>2.5) – was found at the beginning. At the end of the study, a significant decrease in PDSS scores measured in both groups was detected. However, the decrease in PDSS score for the group with lower DIS-Q score was at a higher percentage (z = −3.822, p = 0.0001).

These results depict that dissociative symptoms accompanying PD affect psychopharmacological treatment in a negative way. Reevaluation of dissociative symptoms at the beginning and end of treatment would help in planning personal therapy.

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1. Introduction

Panic disorder (PD) is a frequent disease causing disability and decreased quality of life and characterized by panic attacks. Despite slight differences between treatment guidelines, venlafaxine treatments, which are selective serotonin (SSRI) and serotonin–norepinephrine reuptake inhibitors, are regarded as first-line agents in panic disorder owing to their treatment efficacy and advantages in side effect profiles [1]. There are many studies on the demonstrable efficacy of PD treatment based on pharmacological evidence [2–4]. However, number of patients nonresponsive to treatment or with clinically significant residual symptoms is still considerably high. Quite a few studies were performed on the factors that negatively influence the treatment of PD. In these studies, separation anxiety [5,6], Cluster C and Cluster A personality disorders [7], presence of comorbid depression and drug addiction or drug abuse [8], age of onset of panic symptoms, degree of comorbid social anxiety and agoraphobic avoidance [9] were found to be amongst factors having negative influence on psychotherapy treatment. On the other hand, factors that were found to negatively affect medical treatment of panic attack include comorbid personality pathology [10], high comorbidity of obsessive compulsive disorder, major depression and high ratio of anxiety, and phobic and depressive symptoms [11]. Demographic data collected in a study conducted by measurement of electric neural activity showed that age, sex, employment status, duration of disease and level of dissociation were influential on the response to the treatment of PD [12].

The spectrum model associated with panic and agoraphobia is rather flexible and comprehensive [13]. In Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV-TR), dissociation is defined as “a disruption in the usually integrated functions of consciousness, memory, identity, or...
perception of environment” and also as a complex psychopathological process that occurs on a continuum ranging from minor normative dissociations to psychiatric conditions [14].

In a study on an outpatient psychiatric population, dissociative disorders that were not clinically diagnosed before were found at a high percentage [15]. Dissociative symptoms may co-exist with many psychiatric diseases such as borderline personality disorder [16,17], conversion disorder [18], obsessive–compulsive disorder [19,20], schizophrenia [21] or, especially, PD [22]. In a study by Sierra et al. it was claimed that dissociative symptoms might be observed at a frequency between 10% and 60%, and might change based on culture [23]. In another study it was found that dissociative experiences affected outcome of cognitive behavioral therapy negatively in patients with obsessive–compulsive disorder [20].

Studies regarding the effects of dissociative symptoms on the treatment of PD were detected by reviewing related literature. Results of these studies depict that dissociative symptoms with comorbid PD negatively affect psychotherapeutic [24,25] and psychopharmacologic [26] treatment outcomes.

When related literature was reviewed, it was reported that dissociative symptomatology can be a very important factor in not responding to treatment. This condition can involve only treatment resistance to psychotherapy. In this study we aimed to investigate whether or not dissociative experiences affect the response to PD drug treatment. We hypothesized that: people with a low dissociation score at baseline have a much better response to standardized drug treatment than do people with a high dissociation score; and dissociation scores at baseline also influence treatment outcome. For this purpose, 10-week, open ended-longitudinal venlafaxine treatment at standard dose was administered to the patients.

2. Method

2.1. Subjects

92 patients with PD, who had consulted our clinic between May 2012 and March 2013 or who had not consulted for psychiatric complaints before, were included in the study. 29 patients were excluded; treatment of 14 patients was changed due to side effects of venlafaxine. 9 patients stopped their treatment and six patients reported that they did not want to participate to study. The study population was composed of 45 (71.4%) female and 18 (28.6%) male patients.

2.2. Procedure

Patients diagnosed with PD by another clinician and using venlafaxine 37.5 mg treatment for less than one week were called for interview on the phone and included in the study after implementing related scales. Doses of venlafaxine were increased to 75 and 150 mg by 4-week intervals after 2-week treatment with venlafaxine 37.5 mg.

Included patients were diagnosed with PD by 3 psychiatrists in accordance with DSM-IV TR diagnosis criteria. DIS-Q and PDSS scales were applied to the patients at the beginning of the study. Based on the cutoff score, 2.5-average, of DIS-Q scale, patients were divided into two groups as low and high score groups. PDSS scale was re-applied at the end of 10-week treatment period. The difference between PDSS scores obtained at the beginning and end of the study was calculated and the decreases in scores of high and low DIS-Q groups were compared as percentage. PD and agoraphobia symptoms were assessed via PDSS.

After the participants were informed about the aim of the study and the tests to be implemented, their consents in writing were collected. The ethical approval for the study was received from the Turkey Ministry of Health, Drug and Medical Device Institution (Confirmation number: 26247029-514-05-01). 2.3. Measures

2.3.1. Dissociation Questionnaire (DIS-Q)

This scale was developed by Vanderlinden et al. [27]. It is used in surveillance of dissociative symptoms and experiences and measurement of their severities. It is a self-rating scale that can be utilized in follow-up of dissociative symptoms in patients with psychiatric diseases and traumatic experiences. It is comprised of 63 questions in total and each question has a score between 1 and 5. Total mean score is calculated by dividing sum of all scores by 63 [28]. Sar et al. [29] calculated validity and reliability of Cronbach’s α coefficient of the scale for Turkey as 0.98. A high correlation was found between DES and DIS-Q scores ($r = 0.90$, $P < 0.001$). As a result of studies performed in Turkey, probability of presence of dissociative disorder is high for individuals whose average total score is 2.5 or more.

2.3.2. Panic Disorder Severity Scale (PDSS)

PDSS is a scale developed by Shear at al. [30]. Being tested for reliability and validity [31], it features evidence-based guidelines for interpreting the scores [32]. Panic Disorder Severity Scale is a simple and effective method developed for clinicians to evaluate severity of panic disorders. Advantages of PDSS include perfect interrater reliability, moderate internal consistency and favorable levels of validity and sensitivity to change. Convergent and discriminant validity of individual items is reasonable. Based on the analysis, a two-factor model is in the best compliance with the data. Monkul et al. [33] performed validity and reliability.

2.4. Statistical investigations

The Statistical Package for Social Sciences, version 17 (SPSS), was used for all statistical analyses. Comparisons of sociodemographic and clinical variables among groups were conducted using Mann–Whitney U, Student t and one way ANOVA tests for continuous variables and chi-squared ($\chi^2$) test for categorical variables. The Wilcoxon Signed Rank
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