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DIFFERENCES IN MEN AND WOMEN WITH BIPOLAR-I DIAGNOSED PATIENTS

BİPOLAR BOZUKLUK TIP I TANILI HASTALARDA KADIN VE ERKEK FARKLILIKLARI

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Abstract

The importance of gender on phenomenology and course of bipolar illness has been an increased focus of study over recent years. The purpose of present study was to examine whether gender differences exist in the sociodemographic characteristics, age of onset, severity of disease, number & type of episodes, symptomatology and treatment response of bipolar disorder. The life charts of 300 (193 female; 107 male) patients with BD type-I were evaluated retrospectively. BD diagnosis of patients was given by two experienced clinicians in accordance with DSM-IV-TR criteria. A semi-structured chart which was developed to assess sociodemographic and clinical features of patients and “mirror design” method was utilized for the assessment of patients’ response patterns to maintenance treatment. Bipolar women were significantly more likely to have history of (at least one) any mood episode than bipolar men. However no significant gender differences emerged in number of manic or mix episodes; whereas, women had more depressive episodes. Frequency of psychotic episodes (at least one episode during lifetime) was higher for men than women. There was also no significant gender difference in terms of response to lithium and anticonvulsant maintenance treatment, mean episode severity and age of onset. The results of the present study show that some gender differences may be evident in patients with BD-I. In the highlight of that investigators studying bipolar disorder may need to consider gender as a variable for assessment and treatment strategies.

Keywords: bipolar disorder, female, male

Özet

Cinsiyetin bipolar hastalığın fenomenolojisi ve seyri üzerine önemi son yıllarda artan bir çalışma odağı olmuştur. Bu çalışmanın amacı, cinsiyet farklılıklarının sosyodemografik özellikler, başlangıç yaşı, hastalığın şiddeti, episodların sayısı ve tipi, semptomatoloji ve bipolar bozukluğun tedaviye yanıtı üzerinde etkisinin var olup olmadığını incelemektir. Bipolar bozukluk tip-I’li 300 (193 kadın, 107 erkek) hasta retrospektif olarak incelendi. Bipolar bozukluk tanılarını DSM-IV-TR kriterlerine göre iki deneyimli klinisyen tarafından verildi. Hastaların sosyodemografik ve klinik özelliklerini değerlendirmek için geliştirilen yarı yapılandırılmış bir grafik ve sürdürüm tedavisine yanıt biçimlerini değerlendirmek için “ayna dizaynı” yöntemi kullanılmıştır. Bipolar kadınlarda bipolar erkeklere göre herhangi bir duygudurum atak öyküsü (en az bir) olma ihtimali daha yüksekti. Bununla birlikte, manik veya karışık atak sayısında anlamlı bir cinsiyet farklılığı ortaya çıkmamışken kadınlarda daha fazla depresif dönemler mevcuttu. Psikotik atak sıklığı (yaşam boyu en az bir dönem) erkeklerde kadınlardan daha yüksekti. Lityum ve antikonvülsan sürdürüm tedavisine yanıt, ortalama episod şiddeti ve başlangıç yaşı açısından cinsiyetler arasında anlamlı bir farkı yoktu. Bu çalışmanın sonuçları, BD-I’li hastalarda bazı cinsiyet farklılıklarının görülebileceğini göstermektedir. Bipolar bozukluğu çalışan araştırmacıların değerlendirmede ve tedavi stratejilerinde cinsiyeti için bir değişken olarak kabul etmeleri gerekebilir.

Anahtar Kelimeler: bipolar bozukluk, kadın, erkek

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1. Introduction

Bipolar disorder is an important disease with an estimated lifetime prevalence of 0.6% for bipolar disorder type I, 0.4% for bipolar disorder type II, and 2.4% for bipolar spectrum disorders due to a recent studies (Merikangas et al., 2011). Lifetime prevalence of bipolar disorder appears to be equal in both genders (Grant et al., 2005). Although the importance of gender on the phenomenology and course of bipolar illness has been an increased focus of study over the recent years, results are controversial. Some studies with clinical samples report that female with bipolar disorder (BD), compared to male with BD, may be more likely to experience fewer manic episodes and more episodes of depression (Roy-Byrne et al., 1985; Tondo & Baldessarini, 1998), to have the rapid cycling subtype (Tondo & Baldessarini, 1998; Hendrick, 2000), psychotic episodes (Yildiz & Sachs, 2003) and later age of onset (Leibenluft, 1996). A majority of studies also shows that women are more likely than men to be diagnosed with the BP II subtype, and to experience hypomanic and mixed episodes (Diflorio & Jones, 2010). However, not all studies report finding these gender differences (Hendrick, 2000; Baldassano, 2005.; Kawa et al., 2005) The seasonal pattern of manic admissions is also associated with male gender and the presence of psychotic features, thus might be associated with more severe form of the disorder (Hochman, 2016). When we look gender differences in suicidal risk factors among individuals with mood disorders men had greater suicide risk than women. In addition, factors that predicted suicide risk differed by gender. Childhood adversity was more strongly associated with suicide risk for women than for men while anxiety predicted suicide risk for men but not for women. Severity of depression was the primary predictor for both sexes (Weiss et al., 2016). In addition, women with bipolar disorder have greater comorbidity of physical diseases, especially thyroid diseases. Drug abuse is more common in men with bipolar disorder, whereas women with bipolar disorder tend to have more eating and anxiety disorders (Arnold, 2003). There is a range of treatment options for bipolar disorder, including mood stabilizers such as lithium, both first and second generation neuroleptics. There is no clear evidence about treatment response to these options differs between women and men, and so no justification for adjusting the treatment of bipolar disorder due to gender (Hendrick, 2000; Kawa et al., 2005).

The purpose of the present study was to examine whether gender differences exist in the sociodemographic characteristics, age of onset, severity of disease, type of episodes, symptomatology and treatment response of bipolar disorder.

2. Methods

The life charts of 300 (193 female; 107 male) out patients with BD type I who have been traced in Haseki Research and Training Hospital, Psychiatry Department between May 2016 and May 2017 were evaluated retrospectively. The files were sorted according to the examination date of the patients and taken into study according to this order. BD diagnosis of the patients admitted to the unit was given experienced clinicians through a detailed semi-structured clinical assessment in accordance with Diagnostic and Statistical Manual of Mental Disorders – 4th ed. (DSM-IV)

(APA, 1994). All patients were treated in the outpatient service, which constitutes our study's academic setting.

Inclusion criteria were patients diagnosed with bipolar disorder type I, who applied to the clinic and volunteered to participate in the study. Exclusion criteria were bipolar disorder type II, mental retardation, mental disorder based on physical medical condition, education and language problems severe enough to prevent psychiatric interview and assessment. The study design is retrospective. The ethics committee approval of this study was obtained.

A semi-structured interview chart which was developed by the authors that assess sociodemographic and clinical features (family history; presence of psychotic features; age of onset; number and type of episodes; type, duration and outcome of maintenance treatments etc.) of the patients based on data obtained from the patient and/or his/her family on admission and previous medical records, as well as "mood chart" that includes graphical records for the outcome of the disorder and outcome of treatments since the onset of the BD are filled. These charts are updated during the follow-up of the patients. Charts of the patients were screened for the present study and missing parts were completed when necessary. Age of onset was the age that met mood episode criteria of DSM-IV for the first time.

Maintenance treatment response: In the present study, "mirror design" method (Vieta et al. 2008) was utilized for the assessment of patients' response patterns to the maintenance treatment. Zero point was indicated to be the time when maintenance treatment has started, and maintenance treatment period was compared to a same drug-free period prior to zero point. For patients whose multiple maintenances were investigated, response type was assessed for each prophylaxis separately and each prophylaxis period was compared with the same drug-free untreated period prior to treatment period.

Based on their response features, patients were divided into two groups;

Treatment responder group: It was composed of patients who never had any recurrence (good response) or those who had a recurrence during maintenance treatment period with a decrease in severity, duration and frequency (moderate response) in regard to the same period prior to maintenance treatment.

Treatment non-responder group: It included patients who had a recurrence during maintenance treatment period similar or even worse in severity, duration and frequency in regard to the period prior to maintenance treatment (poor response). Minimum duration for the maintenance treatment was 1 year. However, shorter durations were included if a clear conclusion can be made according to the mirror design when treatment changed earlier because of recurrences.

2.1. Statistical analysis

Descriptive statistics are computed as mean±SD (standard deviation), count and percent frequencies. The data were analyzed using either Student's t-tests for continuous variables and chi-square or Fisher-Freeman-Halton exact test when appropriate for categorical variables. A P-value of <0.05 was considered statistically significant. All statistical analyses were carried out using the PASW (ver.18).

3. Results

Demographic and clinical characteristics of the samples are shown in Table 1. Findings can be summarized as follows: Compared with bipolar women, men were significantly more educated and number of unmarried man was significantly higher than in women but number of divorced women was higher than man (p values are <0.001 and 0.013 respectively). Bipolar women were significantly more likely to have history of (at least one) any mood episode than bipolar men ($p=0.024$). No significant gender differences emerged in number of manic or mix episodes; whereas, women had significantly more depressive episodes than man ($p<0.001$). There was no significant gender difference in terms of response to lithium and anticonvulsant (AC) maintenance treatment (valproic acid or carbamazepine). However, rate of response to lithium treatment and response to AC monotherapy was higher for man. No significant differences between men and women about mean episode severity. In addition when we look at the history of psychiatric illness in first degree relatives, the rate of the any affective disorder, rate of suicide and rate of bipolar disorder are not significant differences between men's and women's relatives. Psychotic symptoms in men are significant higher than women ($p=0.010$). Men and women differences about age at onset is not significant.

Table 1: Demographic and clinical characteristics for the sample

Categorical characteristics	Women (N=193)	Men (N=107)	p
	n (%)	n (%)	
Marital status			
Married	92 (47.7)	52 (48.6)	0.013
Divorced	37 (19.1)	8 (7.5)	
Unmarried	64 (33.2)	47 (43.9)	
Psychiatric history in first degree			
Bipolar disorder	47 (24.3)	22 (20.6)	0.478
Any affective disorder	66 (34.2)	28 (26.2)	0.156
Suicide	6 (3.1)	3 (2.8)	0.882
Mean episode severity (severe)	108 (55.9)	70 (65.4)	0.113
Psychotic symptoms	138 (71.5)	91 (85.0)	0.010
Prophylactic treatment response			
Lithium monotherapy (R/U)*	100/148 (67.6)	60/76 (78.9)	0.086
Anticonvulsan monotherapy (R/U)	48/80 (60.0)	25/32 (78.1)	0.082
Numerical characteristics			
	Mean±SD	Mean±SD	
Age	42.7 (13.2)	40.6 (12.0)	0.034
Age at onset	24.6 (9.1)	24.1 (8.3)	0.482
Education (year)	11.0 (3.0)	12.4 (2.0)	<0.001
No. total episode	11.0 (9.8)	9.4 (7.4)	0.024
No. manic episode	4.8 (4.7)	5.3 (4.6)	0.188
No. mix episode	0.5 (1.5)	0.4 (1.1)	0.352
No. depressive episode	3.2 (4.8)	1.9 (2.8)	<0.001

*: R/U: number of maintenance treatment Responders/number of that maintenance treatment Users. $p<0.05$. The data were analyzed using either Student's t-tests for continuous variables and chi-square or Fisher-Freeman-Halton exact test when appropriate for categorical variables

3. Discussion

Education and marital status differences among female and male bipolar patients might be related with sociocultural characteristics of our country. In Turkey, mean education level is lower for women than men. Also, women get married earlier than men. Chronic psychiatric disorders of men might be tolerated better culturally within marriage. A considerable amount of research has been directed towards examining gender differences in unipolar depression. Overall, this study indicates that women are at increased risk for depression, with a sex ratio of approximately 2:1. In contrast to unipolar depression, epidemiological studies indicate that frequency of BD-I is approximately equal in men and women. But in bipolar patients, some studies with clinical samples report that women with BD compared to men with BD experience fewer manic episodes and more episodes of depression (Roy-Byrne et al., 1985; Tondo & Baldessarini, 1998). Also, in our study it was found that number of life time depressive episode is higher for women than men. Depression may have a relation with factors specific to female gender among both unipolar and bipolar patients.

In our study, the total number of attacks in women was significantly higher than men. Increasing the number of mood episodes in bipolar disorder increases the recurrence risk (Perlis et al., 2006). In addition, psychotic symptoms were found more frequently in males in our study. Some studies found that while psychotic symptoms in bipolar disorder occur frequently in women (Bräunig et al., 2009; Yildiz & Sachs, 2003) and later age of onset, some studies have not found a significant difference (Leibenluft, 1996). The high frequency of psychotic manic episodes in male patients in our study may be due to the high proportion of unmarried males. As it is known, chronic illnesses like bipolar disorder may be severe when there is no social support like marriage. (Pelivan, 2006)

According to DSM-IV, mixed episodes are seen more frequently in women, and according to DSM-5, manic episodes with mixed feature are more common in women, and there is no gender difference for depressive episodes with mixed feature. (Vieta & Valenti, 2013). In our study, we could not find such a meaningful difference. There was no difference in the incidence of mixed periods in women and men. However, since we did not evaluate DSM-5, we could not see whether the dominant period was manic or depressive. Accordingly, we may not be able to adequately assess gender differences here. Bipolar disorder (BI) is a recurrent and serious disease and the frequency of suicide attempts in particular is high. Suicide risk, being 0.2-0.4% per year in bipolar patients, is almost 20-30 times higher than the total population (Pompili et al., 2013; Søndergård et al., 2008). It is estimated that approximately 10-15% of patients die due to suicide (Schaffer, 2015). In our study, suicide rates were 3.1% for women and 2.8% for men. These findings are higher than the general population, even though they are lower than estimated suicide rates.

It is accepted that suicide attempt is more frequent in females than males (Vonborczyskowski, 2011). The rate of suicide attempt in female bipolar patients is reported to be twice the same rate in males (Pompili et al., 2013). However, in our study, we could not find any difference between male and female bipolar patients.

Very little is known about possible sex-based differences for the effectiveness of mood-stabilizing agents in BD. Some studies suggest that there may be gender differences in response to mood stabilizers (Hendrick 2000; Leibenluft, 1996) even though this has not been always confirmed (Viguera et al., 2000). In our study, there was no significant gender difference in terms of response to lithium and AC maintenance treatment. However, rate of response to lithium treatment was higher for men than women; whereas rate of response to AC monotherapy was higher for men than women. In a review article, response rates of women and men to lithium (65% and 61%, respectively) were not similar to our findings. (Viguera et al., 2000; Geoffroy et al., 2016)

A major limitation of our study is the retrospective nature of data collection. The reliability and validity of patients' reports of clinical history, such as age of onset or number of prior episodes is unknown. However, the large sample size and follow-up of patients in a specific unit strengthen the results of our study. Also, previous large studies generally have assessed patients with BD-I, BD-II and sometimes BD not otherwise specified within the same category (Hendrick, 2000; Baldassano, 2005; Kawa et al., 2005; Holtzman, 2016). In our study, additional psychiatric disorders to bipolar diagnoses of patients and their association with bipolar disorder were not evaluated. Patients with bipolar disorder type II are not included in our study because of their difficulty in recognizing and confusion with personality disorders, especially borderline personality disorder (Akiskal, 1981). The retrospective nature of our work also puts this process in great difficulty.

However, our study included a more specific group composed of only BD-I patients. The results of the present study show that some gender differences may be evident in patients with BD-I. In the highlight of that investigators studying bipolar disorder may need to consider gender as a variable in interpreting their results. Also, the investigation of gender differences is likely to further our understanding of BD in general, and may provide important insights into the development of optimum assessment and treatment strategies for this chronic and often debilitating condition.

It would not be wrong to say clear evidence of specific differences between the two sexes, in terms of differences in clinical presentation and course of bipolar disorder have been elusive. It is also important to stress that any attending psychiatrist at a busy mental hospital has probably experienced the need to employ altering clinical approaches to male female patients, even when the difficulty presented by female bipolar patients of reproductive age is excluded. In order to satisfactorily address varying challenges presented by sex difference, one must first define those differences.

Ethical Considerations

Authors confirmed the compliance with all relevant ethical regulations.

Conflict of Interest

No conflict of interest

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