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Brief Report / Kısa Araştırma

Comparison of Sociodemographic and Clinical Characteristics of Bipolar Type 1 Patients on Single or Double Mood Stabilizers Treatment

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ABSTRACT

Comparison of sociodemographic and clinical characteristics of bipolar type 1 patients on single or double mood stabilizers treatment

Objective: Purpose of the current study is to compare the demographic and clinical characteristics, prognoses and episode characteristics between patients on a single mood stabilizer treatment and those on double mood stabilizer treatment.

Methods: The follow-up files of 167 patients who met DSM-IV-TR criteria for bipolar-I disorder were examined retrospectively. Patients were divided into two groups, with 136 patients on a single mood stabilizer and 31 patients on double mood stabilizer treatment. Sociodemographic and clinical characteristics of the groups were evaluated. The data derived from the study were analyzed with SPSS (Statistical Package for Social Sciences) for Windows 17.0. The data were evaluated with chi-square and t test.

Results: The number of women was significantly higher in the single mood stabilizer group. The total number of episodes and hospitalizations were higher in patients on double mood stabilizer treatment compared to the single mood stabilizer group. When comparing within the single medication group, the total number of episodes and hospitalizations in patients using Lithium were significantly lower than in patients on valproat.

Conclusion: Patients medicated with double mood stabilizer may be more difficult to treat and have a poorer prognosis than patients medicated with a single mood stabilizer. The number of female patients was greater in the single mood stabilizer group, which may indicate a generally more positive outcome in women. However, this research was cross-sectional and had a relatively low sample size, making it rather difficult to come to a more definite conclusion. Therefore, follow-up studies with a greater number of patients on a single mood stabilizer over an extended period of time are required.

Keywords: Bipolar disorder, clinical characteristics, mood stabilizer

ÖZET

Tek ve ikili duygudurum dengeleyici ile koruma altındaki iki uçlu bozukluk tip 1 tanılı hastaların sosyodemografik ve klinik özelliklerinin karşılaştırılması

Amaç: Bu çalışmada İki Uçlu Bozukluk tanısıyla tek bir duygudurum dengeleyici kullanan hastalar ile ikili duygudurum dengeleyici kullanan hastaların demografik ve klinik özellikleri ile hastalık seyri ve dönem özelliklerinin karşılaştırılması amaçlanmıştır.

Yöntem: İki Uçlu Bozukluk Tip 1 tanısıyla takip edilen 167 hastanın ayaktan takip dosyaları geriye dönük olarak incelenmiştir. Hastaların 136'sı tek duygudurum dengeleyici ve 31'i çift duygudurum dengeleyici kullanmaktaydı. Grupların sosyodemografik ve klinik özellikleri kayıtlanmış, elde edilen veriler SPSS (Statistical Package for Social Sciences) 17.0 programı kullanılarak analiz edilmiştir. Veriler değerlendirilirken Ki kare ve t testi kullanılmıştır.

Bulgular: Tek ilaçla koruma tedavisi alan hastalarda anlamlı olarak kadınlar daha fazlaydı. İkili ilaç kullanan hastaların toplam dönem sayısı ve hastaneye yatış sayısı, tek ilaç kullananlara kıyasla yüksekti. Tek ilaç grupları kendi aralarında karşılaştırıldıklarında lityum alan hastaların toplam dönem sayısı ve hastaneye yatış sayısı valproat kullanan hastalara kıyasla anlamlı derecede düşük bulundu.

Sonuç: İkili duygudurum dengeleyici ile koruma altındaki hastalarda hastane yatış ve dönem sayısı yüksekliği bu hastaların daha zor tedavi edilen, daha kötü seyirli bir grup olduğuna işaret edebilir. Tek ilaç kullanan hastalarda kadın cinsiyet oranlarının yüksekliği kadınlarda hastalık seyrinin daha iyi olduğuna işaret edebilir. Ancak araştırmamızın kesitsel olması ve görece düşük örneklem sayısı nedeniyle daha fazla yorum yapmak güçleşmektedir. Bu nedenle bu alanda özellikle tek ilaç kullanan hasta sayısının daha fazla olduğu uzunlamasına izlem çalışmalarına gereksinim vardır.

Anahtar kelimeler: İki uçlu bozukluk, klinik özellikler, duygudurum dengeleyici

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INTRODUCTION

Bipolar (BP) disorder is a chronic disease exhibiting mood swings, with a course consisting of relapse and improvement episodes. Studies on BP disorder have found a prevalence of between 1 and 3% (1-3). As this disease correlates to a high suicide rate and causes significant morbidity and mortality, also leading to a marked loss of competence, it represents a relevant public health concern (4).

Previous studies have found that BP disorder patients were more often unemployed compared to healthy controls, many patients were not able to get married throughout their lives, and divorce rate was high (5). With long-term treatment, a significant improvement of life quality and functionality can be achieved. Therefore, in treating the disease, long-term therapy as another step is at least as important as treatment during an acute episode. To prevent recurrence and relapses, basic aims of maintenance treatment are the removal of subsyndromal symptoms and maintenance of patients' premorbid functionality levels (6). For this purpose, lithium and certain antiepileptics (valproate, carbamazepine, lamotrigine) are used as mood stabilizers (MS) (6). Recently, certain atypical antipsychotics have also been selected by clinicians for the maintenance treatment of BP disorders (7-10).

One of the cornerstones of BP disorder treatment is lithium, though its mode of action is not fully understood. Its positive effect on depressive and manic episodes, too, has not yet been fully clarified (11,12). In the treatment of acute mania, 70-80% of patients receiving lithium monotherapy respond positively; the lithium response rate decreases in mixed episodes, rapidly cycling courses, psychotic mania, and substance abuse, as well as in the presence of cerebral pathologies (13). Valproate, in addition to its anti-manic effect, also reduces the frequency of manic episodes in BP disorder, its anti-manic effect setting on some days after reaching an effective blood level (14). While the effectiveness rate of valproate is 60% on average, especially in rapidly cycling BP disorder, mixed mania, late-onset mania and manias accompanied by organic diseases (15), it is not as effective in depressive episodes as it is in manic episodes (16). The literature shows that the long-term effect of valproate compared to lithium is good. Therefore, in all treatment guidelines valproate has been listed as an alternative choice to lithium. The effectiveness of carbamazepine in maintenance therapy has not been entirely clarified. Crossover studies showed that carbamazepine is less effective than lithium in maintenance therapy (17).

Which MS drug to choose in which patients, and which patients requires more than one MS drug, are still important topics of clinical debate, where no agreement has been reached. Thus, determining the sociodemographic and clinical characteristics predicting therapy response in BP patients will make the doctor's task easier. Therefore we aimed to compare sociodemographic and clinical characteristics between those using single and those using double MS drug.

METHOD

The study population consisted of around 800 patients diagnosed with Bipolar Disorder according to the criteria of the DSM-IV-TR receiving treatment at the Rasit Tahsin Mood Center of the Bakirkoy Prof. Dr. Mazhar Osman Hospital for Mental and Nervous Diseases (BRSHH). Having received approval of the BRSHH ethics committee (Nr. B.10.1.TKH.4.34.R. AT.0.01/47894-239, dated Nov. 13, 2012), we analyzed the files of 167 outpatients above the age of 18 diagnosed with Bipolar I Disorder, with an illness duration and mood stabilizer use of at least one year, who were currently in remission. Patients with mental retardation, concurrent alcohol and psychoactive substance abuse, neurological diseases or change of diagnosis during follow-up were not included in the study. In the group of single MS users, 99 patients used Li, 31 VPA, and 6 carbamazepine; the double MS users (n=31) received lithium and valproic acid. Drug compliance was assessed (yes/no) using analyses from the doctors who had followed the patients during the previous year and considering if the plasma level of the MS drug used by the patient was lower than 3 or more consecutive maintenance therapy values.

Statistical Analysis

Results were analyzed using SPSS (Statistical Package for Social Sciences) for Windows 17.0. In the data analysis, descriptive methods (number, percentage) were used; to establish correlations between descriptive data, chi-square test and t-test were performed.

RESULTS

Demographic and Clinical Characteristics of the Groups

Comparing the sociodemographic characteristics of the single and double MS drug treated patients, the rate of females was significantly higher in the group of single MS users (p=0.014). On the other hand, patients were similar regarding age, familiar disease history, total education period, and marital and employment status (Table 1).

Comparing the clinical characteristics of the single and double MS drug treated patients, no significant differences were found between the patients regarding onset age of the disease (p=0.65), type of first episode (p=0.45), history of suicide attempt (p=0.27), drug compliance (p=0.39), seasonal course (p=0.48), or presence of episodes with psychotic features (p=0.15). However, among the patients being treated with double MS, total number of episodes (p=0.001) and hospitalizations (p=0.006) were significantly higher than among patients using a single MS (Table 2).

Comparison of Clinical Characteristics

Among the participating patients, no significant relation between the groups was found for age at onset of disease (p=0.56), type of first episode (p=0.49), history of suicide attempt (p=0.56), drug compliance (p=0.54), seasonal course (p=0.61), and history of episodes with psychotic features (p=0.079). However,

Table 1: Relations Between Kinds of Medicine and Demographic Characteristics in Study Participants Using Single Mood Stabilizers or Double Mood Stabilizers

	Single Drugs		Double Drugs			
	n	%	n	%	χ^2	p
Sex						
Female	85	87.6	12	12.4	5.87	0.014*
Male	51	72.9	19	27.1		
Marital status						
Married	71	82.6	15	17.4	0.32	0.850
Single	48	81.4	11	18.6		
Divorced	17	77.3	5	22.7		
Employment status						
Unemployed	11	78.6	3	21.4	5.53	0.240
Not working	10	76.9	3	23.1		
Housewife	49	89.1	6	10.9		
Working/student	60	80.0	15	20.0		
Incapacitated	6	60.0	4	40.0		
Household members						
Parents	43	78.2	12	21.8	0.68	0.710
Spouse, child	81	83.5	16	16.5		
Child	12	80.0	3	20.0		
Known family history of bipolar disorder						
Absent	65	80.2	16	19.8	0.15	0.430
Present	71	82.6	15	17.4		
	mean±SD		mean±SD			
Age	40.58±10.87		43.16±9.52			0.230
Duration of education	8.32±4.02		8.68±4.09			0.660

χ^2: Chi-square value, mean: mean value, SD: Standard deviation, *p<0.05 level of significance

Table 2: Comparison of Clinical Characteristics Between Patients Using Single Mood Stabilizers and Double Mood Stabilizers

	Single Drugs		Double Drugs			
	n	%	n	%	χ^2	p
Type of first episode						
Mania	75	78.1	21	21.9	2.66	0.450
Depression	49	84.5	9	15.5		
Mixed	7	100.0	0	0.0		
Hypomania	5	83.3	1	16.7		
Suicide attempt						
No	118	82.5	25	17.5	0.77	0.270
Yes	18	75.0	6	25.0		
Drug-compliant						
No	90	80.4	22	19.6	0.26	0.390
Yes	46	83.6	9	16.4		
Seasonal specificity of episodes						
No	128	81.0	30	19.0	0.35	0.480
Yes	8	88.9	1	11.1		
Psychotic feature of episodes						
No	9	100.0	0	0.0	2.17	0.150
Yes	127	80.4	31	19.6		
	mean±SD		**mean±SD**			
Age at disease onset	23.34±8.69		24.1±7.06			0.650
Total number of episodes	3.68±2.04		6.03±3.40			<0.001
Number of hospitalizations	1.77±1.50		3.26±2.76			0.006

χ^2: Chi-square value, mean: mean value, SD: Standard deviation, p<0.05 level of significance

among patients treated with VPA, total number of episodes (p=0.02) and number of hospitalizations (p=0.01) were significantly higher compared to patients treated with lithium only.

DISCUSSION

In this retrospective study of outpatient follow-up files, patients' sociodemographic and clinical characteristics have been compared. The great majority of participants (51.4%) consisted of married housewives. In studies with BP disorder patients, the rate of married status was found to be low and divorce rates were high (18), whereas in our study most of the patients were married. This observation might be explained by the fact that most of our participants were women, the disease generally manifested itself after marriage; and because of a traditional trend in Turkey not to dissolve the family structure.

Apart from gender, our study showed no significant difference between the sociodemographic data of single and double mood stabilizer groups in maintenance treatment regarding age, educational status, employment situation, cohabiting persons, or presence of family history. As to the gender factor, we found that female patients were significantly more often taking single drug therapy. Altamura et al. found that generally women used more drugs than men (19). By contrast, Masi et al. (20), comparing gender and age between patients using either only lithium or a group of drugs including lithium, found that only the mean age constituted a significant difference. Levine et al. (21) found that age, gender, marital status, and level of education did not represent important factors in the use of prescription medicine in BP disorder. Even if this indicates that the course of the disease in women could be better, it is difficult to comment further on this situation, given the small size of our sample, especially of the group using single MS drugs. The differences between this result and those in the literature indicate that more research is required.

The reason why we did not find a relation between sociodemographic characteristics and treatment with single or dual mood stabilizer might be related to the

fact that most of the patients were housewives with the same average period of education (mostly elementary school level) and a similar employment status. In many participants, a family history was found, and some studies established that a genetic load can lead to treatment-resistance, deterioration of the clinical course, and necessity for dual therapy (22). However, our study did not find anything of this kind. This shows that more research is needed to study the effect of family history on the therapy, because a primary choice of mood stabilizer in response to family history could be approached as an effective method in case of therapy-resistance.

Another result of our study is that the number of disease episodes and hospitalizations is significantly higher in patients with dual MS therapy. It has been shown that the most common reason for adding a second MS drug to the therapy is an insufficient effectiveness of a single MS during a disease episode or an increase in the frequency of episodes. Our result is consistent with Cole et al.'s findings in rapidly cycling therapy resistance (22). In addition, numbers of episodes and hospitalizations are lower in lithium users than in patients using valproic acid, which is also consistent with the literature (23); however, in order to decide if this situation is due to the protective effect of lithium use or because clinicians prefer valproic acid in cases of more treatment-resistant presentations, further follow-up studies are required. The trend to choose preferably valproic acid in rapidly cycling manic episode presentations with psychotic symptoms (24) might also be explained with the relation between use of valproic acid and number of episodes and hospitalizations. Our findings indicating a positive correlation between the use of multiple mood stabilizers and number of hospitalization also show that therapy resistance is an effective factor for clinicians' tendency towards polypharmacy.

Finally, as a distinctive effect in the transition to multiple maintenance therapy the specification of episode frequency has been established. In order to be able to evaluate the effect of sociodemographic data on drugs, it is necessary to analyze prospective studies with larger patient numbers. Specific limitations of our study were the retrospective design, not having analyzed the patients' use of other drugs, such as antipsychotics, alongside mood stabilizer drugs, and the inability to assess the reasons for the selection of mood stabilizer drugs definitively. Follow-up studies overcoming these limitations will be more helpful to understand the stages in choosing single or dual MS therapy.

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