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Clinical correlates of treatment adherence and insight in patients with schizophrenia

Şizofreni hastalarında tedavi uyumu ve içgörünün değerlendirilmesi

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Abstract

Aim: The aim of this study was to assess clinical correlates of the treatment adherence and insight in patients with schizophrenia.

Methods: That cross-sectional study included 229 outpatients with schizophrenia who were admitted to the Psychiatry Outpatient Clinic of Health Sciences University Dışkapı Yıldırım Beyazıt Training and Research Hospital. All participants were administered a socio-demographic form, Morisky Medication Adherence Questionnaire, Schedule for Assessing the three components of insight, Brief Psychiatric Rating Scale, Positive and Negative Symptoms Rating Scale, Calgary Depression Scale for Schizophrenia, and Global Assessment of Functioning Scale. Collected data were analyzed with descriptive statistics, Pearson Correlation Analysis, and logistic regression analysis.

Results: Poor treatment adherence was associated with male gender, lower insight level, more severe psychotic symptoms, and lower functionality level. The insight score was negatively correlated with the severity of psychotic symptoms, duration of the disorder, and mean antipsychotic dose; but positively correlated with advanced age of onset, and higher functionality level. The logistic regression analysis revealed that functionality level was more predictive on poor medication adherence.

Conclusion: Poor treatment adherence and lower insight level were closely associated with more severe clinical symptoms and lower functionality level. It was noteworthy that adherence and insight levels both showed a high predictivity for wellbeing of the patients. Therefore, psychotherapeutic interventions should be implemented to increase treatment adherence and insight in schizophrenia even if the psychotic symptoms show resistance. Further research is needed to clarify clinical associations of the treatment adherence and insight level in patients with schizophrenia.

Keywords: treatment adherence, schizophrenia, insight

Öz

Amaç: Bu çalışmanın amacı şizofreni hastalarında tedaviye uyumu ve içgörü ile ilişkili klinik değişkenleri değerlendirmektir.

Yöntemler: Kesitsel nitelikteki bu çalışmaya Sağlık Bilimleri Üniversitesi Dışkapı Yıldırım Beyazıt Eğitim ve Araştırma Hastanesi Psikiyatri Polikliniği'ne başvuran 229 şizofreni hastası dahil edildi. Tüm katılımcılara sosyodemografik veri formu, Morisky Tedaviye Uyum Ölçeği, İçgörünün Üç Bileşenini Değerlendirme Ölçeği, Kısa Psikiyatrik Değerlendirme Ölçeği, Pozitif ve Negatif Belirtileri Değerlendirme Ölçeği, Calgary Şizofrenide Depresyon Ölçeği ve İşlevselliğin Genel Değerlendirilmesi Ölçeği uygulanmıştır. İstatiksel analizde tanımlayıcı analizler, Pearson Korelasyon Analizi ve lojistik regresyon analizi kullanıldı.

Bulgular: Şizofrenide düşük tedavi uyumu bulunması erkek cinsiyet, düşük içgörü düzeyi, yüksek psikotik belirti şiddeti ve düşük işlevsellik düzeyi ile ilişkili bulundu. İçgörü düzeyi ise psikotik belirti şiddeti, hastalığın süresi ve ortalama antipsikotik ilaç dozu ile negatif korelasyon gösterirken; geç başlangıç yaşı ve yüksek işlevsellik düzeyi ile pozitif korelasyon gösterdi. Lojistik regresyon analizinde ise işlevsellik düzeyinin düşük tedavi uyumunu öngörmede daha etkili olduğu belirlendi.

Sonuç: Düşük tedavi uyumu ve içgörü düzeyi yüksek klinik belirti şiddetiyle ve düşük işlevsellik düzeyiyle güçlü korelasyon gösterdi. Tedavi uyumu ve içgörü düzeyi hastaların iyilik durumu üzerinde önemli prediktif faktörler olarak saptandı. Bu nedenle psikotik belirtiler dirençli olsa dahi şizofreni hastalarında tedavi uyumu ve içgörüyü arttırmaya yönelik psikososyal tedaviler uygulanmalıdır. Şizofreni hastalarında tedavi uyumu ve içgörü düzeyi ile ilişkili klinik değişkenlerin daha iyi anlaşılması için gelecekte yapılacak çalışmalar önemli olacaktır.

Anahtar Kelimeler: tedavi uyumu, şizofreni, içgörü

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Introduction

Schizophrenia is a chronic disorder and shows poor clinical outcomes. One of the main reasons affecting on the clinical course of schizophrenia is poor treatment adherence. Many patients with schizophrenia drop out the medication in less than one year, and full adherence to treatment in patients with schizophrenia is not common [1]. Treatment adherence is defined as regular use of the drugs and compatibility with implemented suggestions of the healthcare staff [2]. Good treatment adherence is a necessity for the patients with schizophrenia to maintain improvement, however, there is a high rate of poor medication adherence in schizophrenia patients. Poor medication adherence in schizophrenia is associated with more relapses, increased number of hospitalizations, and poor clinical course [3].

Clinical course of schizophrenia is affected by several clinical factors, such as characteristics of the disorder, comorbid psychiatric disorders, and medication adherence [4]. Insight level is also a predictive factor on clinical course of schizophrenia [5]. Insight is basically defined as awareness of the disorder and signs of exacerbation. The insight concept also includes ability to interpret clinical symptoms as pathological and acceptance of the treatment [6,7]. A recent study assessed the impact of psychoeducation on knowledge level about the disorder and insight in patients with schizophrenia. That study revealed that psychoeducation did not have a significant impact on insight but provided a significant improvement on clinical symptoms [8]. Even if better insight level is not improved by the clinical interventions, the interventions might improve clinical outcomes in schizophrenia patients [8, 9].

Poor treatment adherence and low insight level often show a good clinical association in schizophrenia; however, poor medication adherence can be found in patients with good clinical insight [9,10]. Besides that, some patients with lower insight can be provided an adequate antipsychotic treatment [11]. Taken together, there are some differences between clinical associations of the medication adherence and insight. As both are major predictive factors on clinical course of schizophrenia, it is important to clarify clinical associations of the treatment adherence and insight in schizophrenia. A better understanding on the clinical associations of those two variables might improve clinical outcomes and therefore it was aimed to assess correlates of the treatment adherence and insight in patients with schizophrenia.

Material and methods

This study was carried out in Dışkapı Yıldırım Beyazıt Training and Research Hospital. The patients aged between 18 and 60 with the diagnosis of schizophrenia according to Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) who applied to the outpatient Psychiatry Clinic of the Hospital between December 2017 and June 2018 were enrolled into the study [12]. The patients with remission and partial remission were included and patients who are not in remission/ partial remission (n=21) were not got involved. In addition, those with organic brain disorders (n=8), neurodevelopmental disorders (n=2), and alcohol or substance use disorders (n=5) were excluded. Therefore, 229 patients were included as participants. The study was carried out in compatibility to the Declaration of Helsinki. Written informed consents were obtained from all of the participants, and Ethical Commission of the Dışkapı Training and Research Hospital approved the study (06.11.2017-4210).

Instruments

Brief Psychiatric Rating Scale (BPRS): The BPRS is used to evaluate general symptom severity in patients with schizophrenia. It was developed by Overall and Gorham in 1961 [13]. It is an 18-item Likert scale, and all items are scored between 1 (absent) and 7 (severe) points. Its Turkish validity and reliability were made by Soykan et al. in 1989 [14].

Scale for the Assessment of Negative Symptoms (SANS): The SANS measures negative symptom severity such as anhedonia, avolition, and the items are rated from 0 to 5. It was developed by Andreasen in 1990 and its Turkish validity and reliability study was conducted by Erkoç et al. in 1991 [15,16].

Scale for the Assessment of Positive Symptoms (SAPS): The SAPS assesses severity of positive symptoms like hallucinations, delusions, and the total score of the SAPS is 170. It was developed by Andreasen in 1990 and its Turkish validity and reliability study was conducted by Erkoç et al. in 1991 [15, 17].

Morisky 8-item medication adherence questionnaire (MMAS-8): Good medication adherence is a key factor on the treatment response to the antipsychotics in schizophrenia. There is a high rate of low treatment adherence in patients with schizophrenia, and low adherence is one of the most important reasons of poor clinical course in schizophrenia [3]. The MMAS-8 assesses if there is a poor compliance to medication intake because of forgetfulness, carelessness or stopping the drug voluntarily [2, 7]. It is a self-rated questionnaire consisting of eight questions and first seven elements of the questionnaire include yes/no answers while the eighth element has five answers [18]. When the answer indicates a negative adherence issue, a score of 1 is recorded. A score of 3 and higher on the MMAS-8 indicate a poor medication adherence in patients with schizophrenia while a score of 2 and lower on the scale show a good medication adherence. It was developed by Morisky et al. [18] and Turkish validity and reliability study was performed by Hacıhasanoglu Asılar et al. in 2014 [18, 19].

Schedule for Assessing Insight Scale (SAI): The SAI is a likert scale and it is used to measure the insight level of the patients. Its items are rated from 0 to 2 and it has 7 items. It was developed by David et al. [20] and its Turkish validity and reliability study was made by Arslan et al. in 2000 [20, 21].

Calgary Depression Scale for Schizophrenia (CDSS): The CDSS is a nine-item structured interview scale, and it is used to measure the depression level within last two weeks in patients with schizophrenia. It was developed for the assessment of depressive symptoms by Addington et al. [22]. Turkish validity and reliability study were made by Oksay et al. in 2000 [22, 23].

Global Assessment of Functioning Scale (GAF): Functionality in schizophrenia is defined as the ability to work full-time, to have good social relationships and communication skills, and being able to accomplish daily tasks by himself/herself in society. The GAF scale is a widely used scale for assessment of the functionality level of the patients with schizophrenia and it was used in the present study. The scale is scored between 0 to 100, and it was developed by Endicott et al. [24] and it was included in Diagnostic and Statistical Manual of Mental Disorders (4th ed.; DSM-IV) [24, 25].

Statistical Analysis

Clinical data were presented as mean ± standard deviation (SD). Demographic and clinical characteristics of the patients with good and poor adherence were compared with descriptive statistics. Pearson correlation analysis was used to assess clinical correlations of the treatment adherence and insight level. Logistic regression analysis was carried out to determine which clinical variables were more predictive on the treatment

adherence. The statistical analyses were carried out with the Statistical Package for the Social Sciences (SPSS) version 21. All probability values (p values) were computed as two - sided, and p< 0.05 was considered statistically significant.

Results

The sample included 229 patients with a mean age of 38.96 ± 10.36 years, and 30 % (n= 69) of the sample was female while 28 % (n=64) of the individuals were married. About 24 % (n=55) of the patients was classified as having poor medication adherence according to the MMAS-8 scale while 76 % (n=174) of the patients showed good medication adherence. The poor adherence rate was 13 % in female patients, whereas it was 29 % in male patients. The difference in adherence rate between the male and female was significant (p< 0.05). Mean onset age of the disorder was 23.50±6.41years, and mean duration of the disorder was 15.49±6.41 years in the patients with good adherence. On the other hand, they were 21.91±5.09 and 15.73±8.49 years in the poor adherence group. Comparison of the onset age, duration of the disorder, and CDSS score did not show a significant difference between the groups (p> 0.05). In addition, no significant difference was seen between the two groups in terms of age, marital status, and education level (p> 0.05). Poor treatment adherence was associated with male gender, more severe BPRS, SANS, SAPS scores, and lower functionality level (p< 0.05). The BPRS scores were 26.45 ± 5.86 and 21.97 ± 8.27 in poor and good adherence groups, respectively (p< 0.05). Also, the patients with poor adherence demonstrated more severe positive and negative symptoms compared to those with good adherence (SAPS: 32.82 ± 6.85, 28.16 ± 7.85; SANS: 32.51 ± 6.28, 28.50 ± 7.06, respectively, p< 0.05). However, mean equivalent dose of chlorpromazine and severity of the depressive symptoms did not show a significant difference between the patients with poor and good adherence (p> 0.05). Table 1 shows the comparison between the two groups in terms of the main sociodemographic and clinical characteristics.

The SAI score was higher in good adherence group and the difference between two groups was significant (10.03 ± 1.72, 9.11 ± 1.44, respectively, p< 0.05). Age, gender, marital status, and education level were not associated with the insight level (p> 0.05). The SAI score was negatively correlated with duration of the disorder and mean antipsychotic dose; but positively correlated with advanced age of onset and higher GAF score. The severity of BPRS, SAPS, and SANS symptoms were all negatively correlated with the SAI score (r=-0.481, r=-0.402, r=-0.413, respectively, p< 0.01). The correlation of the insight level with clinical characteristics of the patients is shown in Table 2.

Logistic regression analysis was carried out to determine which clinical variables were more predictive on the treatment adherence. The logistic regression analysis including the SANS, SAPS, SAI, and GAF scales revealed that functionality level (Odds ratio=4.158, p=0.041, B=0.065) was more predictive on poor adherence. The logistic regression analysis is demonstrated in Table 3.

Discussion

Nearly one-fourth of the patients with schizophrenia showed poor medication adherence. Sociodemographic variables did not show a significant difference between the poor and good adherence groups. Severity of clinical symptoms was related with poor treatment adherence and other variables associated with poor adherence were low functionality level and male gender. The patients with good medication adherence had higher insight level compared to those with poor adherence. Insight level was also not associated with the sociodemographic variables.

Table 1. Comparison of the sociodemographic and clinical characteristics between the patients with good and poor treatment adherence.

	Patients with good adherence (n= 174)	Patients with poor adherence (n= 55)	p	
Age (year) [a]	39.30±10.11	37.89±11.15	0.177	F=1.832
Gender [b]			0.011*	x^2= 6.517
Female	60 (34.5)	9 (16.4)		
Male	114 (65.5)	46 (83.6)		
Marital Status[b]			0.245	x^2=1.350
Single or Seperated	122 (70.1)	43 (78.2)		
Married	52 (29.9)	12 (21.8)		
Education level[b]			0.527	x^2= 2.227
Primary school or lower	53 (30.5)	12 (21.8)		
Middle school	45 (23)	19 (34.5)		
High school	57 (32.8)	18 (32.7)		
University	19 (10.9)	6 (10.9)		
Onset age[a]	23.50±6.41	21.91±5.09	0.094	F= 1.768
Duration of schizophrenia[a]	15.49±6.41	15.73±8.49	0.850	F=0.084
Number of hospitalizations[a]	2.75±1.86	3.44±2.25	0.057	F=2.271
SANS[a]	28.50±7.06	32.51±6.28	0.000*	F=0.743
SAPS[a]	28.16±7.85	32.82±6.85	0.000*	F= 2.606
BPRS[a]	21.97±8.27	26.45±5.86	0.000*	F=8.908
GAF[a]	57.24±7.06	52.36±5.92	0.000*	F=1.459
CDSS[a]	1.76±1.90	1.71±1.23	0.906	F=0.143
SAI[a]	10.03±1.72	9.11±1.44	0.000*	F=2.087

Data; number of cases (percentage). # Mean±S.D. a Independent sample t-test, b Chi-square test for independence, p < 0.05 * Scale for the Assessment of Positive and Negative Symptoms (SAPS/SANS), Brief Psychiatric Rating Scale (BPRS), Calgary Depression Scale for Schizophrenia (CDSS), Schedule for Assessing the three components of insight (SAI), and Global Assessment of Functioning Scale (GAF).

Although onset age of schizophrenia and duration of the disorder were not related with treatment adherence, lower insight level was associated with earlier age of onset and longer duration of schizophrenia. Severity of positive, negative, and general psychiatric symptoms showed a moderate negative correlation with insight level. Functionality level demonstrated the highest correlation with insight level, and it was found to be more predictive on poor treatment adherence.

Table 2. Correlation of the insight level with clinical characteristics of the patients.

Variables	p	r
Age	0.402	-0.056
Onset age	0.017	0.157
Duration of schizophrenia	0.009	-0.172
Number of hospitalizations	0.223	-0.095
SANS	<0.000	-0.413
SAPS	<0.000	-0.402
BPRS	<0.000	-0.481
CDSS	0.305	0.109
GAF	<0.000	0.541

Pearson Correlation Analysis, p < 0.05* SAPS: Scale for the Assessment of Positive Symptoms, SANS: Scale for the Assessment of Negative Symptoms, BPRS: Brief Psychiatric Rating Scale, CDSS: Calgary Depression Scale for Schizophrenia, SAI: Schedule for Assessing the three components of insight, GAF: Global Assessment of Functioning Scale.

The rate of poor treatment adherence was 24 % in patients with schizophrenia, and there is a great need to plan more preventive strategies on poor adherence. Treatment adherence consists of adherence to medical treatment and compliance to suggestions of the medical team. Our study assessed medication adherence and it is the most researched issue of treatment adherence. As known, maintenance of recovery can be provided with good adherence to medical therapy in all chronic disorders, however, poor adherence is common in chronic disorders [26,27]. Medication adherence is the core of the schizophrenia treatment

and poor treatment adherence in nearly one-fourth of the patients demonstrated a substantial problem in the present study [5]. On the other hand, our study did not assess compatibility with suggestions of the healthcare staff, which is more complex part of the adherence issue.

Table 3. Logistic regression analysis for variables associated with poor adherence.

Variables	Exp (B)	Standard Error	Wald	p value
SANS	0.011	0.035	0.100	0.752
SAPS	0.035	0.030	1.423	0.233
GAF	-0.065	0.032	4.158	0.041
SAI	-0.146	0.017	1.566	0.211

SAPS: Scale for the Assessment of Positive Symptoms, SANS: Scale for the Assessment of Negative Symptoms, BPRS: Brief Psychiatric Rating Scale, CDSS: Calgary Depression Scale for Schizophrenia, SAI: Schedule for Assessing the three components of insight, GAF: Global Assessment of Functioning Scale.

No significant differences were seen in terms of marital status and education level between the patients with good and poor adherence. It was not surprising as there was no significant relationship between treatment adherence and those variables in most of the previous studies [1,6]. There was no significant relationship between age and treatment adherence in the present study, however, some studies found that nonadherence was significantly associated with younger age [28]. Cultural factors and higher family support in our country might have provided a better medication adherence in younger age. In addition, the poor adherence rate was 13 % in female patients, whereas it was 29 % in male patients. The finding of higher rate of poor adherence in male patients was shown in some previous studies [29]. It was suggested that female patients tend to have more enduring and connected social relationships, and thus, they showed better treatment adherence in those studies [29,30]. In addition, seeking help from others was more common in female patients compared to male patients.

In terms of clinical variables, poor treatment adherence was associated with more severe positive, negative, and general psychiatric symptoms. Lower functionality level was related with poor adherence while onset age of schizophrenia and duration of the disorder did not show a significant association with medication adherence. Those findings of more severe clinical symptoms in the patients with poor medication adherence confirmed the results of previous studies [6,11]. As shown in previous studies, poor treatment adherence is a substantial variable on the clinical course of schizophrenia and causes relapses in many patients with schizophrenia [31]. On the other hand, there was no significant difference in severity of the depressive symptoms between the patients with poor and good treatment adherence. This finding indicated that severity of the depressive symptoms was not associated with psychotic symptom severity, and affective symptoms showed a distinct clinical pattern in patients with schizophrenia [10].

Age, gender, marital status, and education level were not associated with the insight level, and that finding was consistent with most of the previous studies [7,8]. There was a significant difference in insight level between the patients with poor and good adherence, and the good adherence group had higher insight level. In addition, the severity of positive, negative, and general psychiatric symptoms was all negatively correlated with the insight score. Therefore, the present study supported the approval that insight level is a predictive factor on treatment adherence, and closely associated with the severity of clinical symptoms [32]. Many previous studies reported that OCD patients with poor insight show poor treatment adherence, more resistant symptoms, and more severe clinical symptoms [33]. Furthermore, duration of OCD was found to be related with lower insight level in several studies, and the insight level was also negatively correlated with the duration of the disorder in the present study [34]. Therefore, it can be suggested that there is a close similarity between OCD and schizophrenia regarding the relationship between lower insight level and clinical course of the patients.

The insight level was negatively correlated with mean duration of the disorder and mean antipsychotic dose. As schizophrenia causes a gradual cognitive impairment during the clinical course, duration of the disorder and longer antipsychotic use might have affected the insight level [5,35]. Besides that, it can be suggested that low insight is also predictive on mean antipsychotic dose in schizophrenia, considering its predictivity on the clinical severity. The insight level showed a positive correlation between advanced onset age and higher functionality level of the patients. That finding was also similar with previous studies [7,8].

The present study has some limitations. It was designed as a cross-sectional study and the clinical associations cannot be presented in a causal relationship. Additionally, effectiveness of the psychotherapeutic interventions on the treatment adherence and insight were not assessed due to the cross-sectional design. Treatment adherence was not assessed in a particular period and was not confirmed with a blood sample test.

It was noteworthy that medication adherence and insight both showed a high predictivity for functionality of the patients. Furthermore, functionality level was found more predictive on treatment adherence compared to severity of positive and negative symptoms. Therefore, psychotherapeutic interventions should be implemented to increase treatment adherence and insight in schizophrenia even if the psychotic symptoms show resistance [31]. Finally, a complete treatment adherence and full insight level in patients with schizophrenia cannot be achieved, nevertheless, improving treatment adherence and insight might provide better clinical and functional outcomes [36]. Future studies are needed to clarify clinical correlates of the treatment adherence and insight in patients with schizophrenia.

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