

Adherence with Outpatient Appointments and Medication: A Two-Year Prospective Study of Patients with Schizophrenia

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ÖZET:

Randevu ve tedaviye uyum: Şizofreni olgularıyla iki yıllık ileriye dönük çalışma

Amaç: Kronik hastalıklarda randevulara katılma ve tedaviye uyum sorunu tedavinin başarısını engelleyen önemli etmenlerdir. Şizofreni gibi belirli tanısal gruplarda randevu ve tedavi uyumunu araştıran az sayıda çalışma vardır. Bu çalışmada, taburcu olduktan sonra "şizofreni ayaktan takip programına" katılan olguların randevularına katılımı ve ilaç uyumu ile ilişkili etkenlerin araştırılması amaçlanmıştır.

Yöntem: Çalışmaya DSM-IV-R ölçütlerine göre şizofreni tanısı konan 132 olgu dahil edilmiştir. Poliklinik randevuları hastanın klinik durumu dikkate alınarak 1 ila 8 hafta aralığında planlanmıştır. Randevuya uyma davranışı ve ilaç uyumunu değerlendirmek için hastalar 2 yıl süreyle takip edilmiştir. Bu 2 yıllık süre içinde, randevularının %20'den fazlasına katılmayan hastalar "uyumsuz grup" olarak değerlendirilmiştir.

Bulgular: Seçilen dönemde randevuya katılmama oranı %44.7 olarak bulunmuştur. Uyumsuzluk düşük eğitim düzeyi ve yalnız başına yaşama ile ilişkili görülmüştür. Taburcu edilmeleri öncesi, Pozitif Belirtileri Değerlendirme Ölçeği (SAPS) ve Kısa Psikiyatrik Değerlendirme Ölçeği (BPRS) toplam puanlarının uyumsuz grupta daha yüksek olduğu saptanmıştır. Ayrıca, randevularına katılmayan hastaların istemsiz psikiyatrik yatış ve hastaneye yatış sayısının daha fazla olduğu ve ilaç uyumsuzluğu oranlarının daha yüksek olduğu bulunmuştur.

Sonuç: Sosyodemografik ve klinik özellikler şizofreni olgularının randevulara katılımını etkilemektedir. Ek olarak, randevulara katılmama özellikle ilaç uyumsuzluğu ile yakından ilişkilidir.

Anahtar sözcükler: Şizofreni, sosyodemografik özellikler, klinik özellikler, randevu, ilaç, uyum

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ABSTRACT:

Adherence with outpatient appointments and medication: a two-year prospective study of patients with schizophrenia

Objective: Especially for patients with chronic diseases, adherence is an important factor that interferes with the success of treatment. There are few reports examining adherence to appointments and medication in diagnostically specific groups such as individuals with schizophrenia. This study aimed to examine the correlates of missed appointments and medication adherence in a sample of persons attending an outpatient schizophrenia follow-up program after hospital discharge.

Methods: The study included 132 patients with schizophrenia. Outpatient appointments were planned to occur in the range of every 1 to 8 weeks by taking into consideration the patient's clinical status. Patients were followed up for a period of two years to assess appointment-keeping behavior and medication adherence. Within this period, patients who did not attend more than 20% of their appointments were evaluated as the "non-attender group."

Results: The rate of patients, who have missed a scheduled appointment, was 44.7% during the chosen period. Non-attendance was related to low educational level and living alone. Before discharge of the patient, the Brief Psychiatric Rating Scale (BPRS) and the Scale for the Assessment of Positive Symptoms (SAPS) total scores were higher in the non-attender group compared to attender patients. Non-attender patients also had higher numbers of psychiatric hospitalizations and involuntary psychiatric hospitalizations and greater medication non-adherence rates.

Conclusion: Sociodemographic factors and clinical features affect patient participation in the appointments. In addition, non-attendance at appointments in particular is closely linked with medication non-adherence.

Key words: Schizophrenia, sociodemographic factors, clinical features, appointment, medication, adherence

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INTRODUCTION

Adherence is an essential condition for successful outpatient treatment. Outpatient non-attendance is a serious problem in clinical and economic terms. However, the rate of non-attendance at psychiatric clinics is twice that of most other specialties (1). Empirical studies indicate a wide range of base rates of missed appointments in psychiatry from 12 to 60% (2). Similar percentages have also been reported in studies on schizophrenia (3,4). As many as one-third to one-half of hospitalized patients with schizophrenia and related disorders miss their scheduled outpatient appointments after hospital discharge (5). A failure of follow up with outpatient care after leaving the hospital greatly increases the risk of relapse and rehospitalization (6).

Failure to participate scheduled appointments may be related to many different factors. Previous research on missed appointments in both medical and mental health settings has provided conflicting findings, with some, but not all, researchers finding an association between missed appointments and low socioeconomic status, younger age, low level of education, a history of missed appointments, drug or alcohol abuse, poor social functioning, having severe psychiatric problems and having a poor relationship with the physician (7-9).

Missed appointments are also one of the important indicators of medication non-adherence (10). Pang et al. identified that at least 50% of patients who did not attend regular appointments did not use their drugs (11). Understanding the predictors of a missed outpatient appointment is crucial. To prevent non-attendance, its determinants should be well understood. However, as mentioned above, factors associated with non-attendance are numerous, and the results of research in this area are somewhat inconsistent (12,13). In particular, there are only a few reports examining such diagnostically specific groups as persons with schizophrenia. Moreover, previous studies of non-attenders have been retrospective and have been initiated in hospital clinics and in general practice. The retrospective nature of these studies has limited the amount of information

available. We have investigated adherence with appointments and medication at an outpatient psychiatric clinic among patients with schizophrenia and have explored the reasons for missed appointments by asking patients and/or their families directly.

METHODS

The study was carried out at the schizophrenia outpatient-unit of the Department of Psychiatry, Gulhane School of Medicine, Ankara, Turkey. In this study, the participants consisted of 132 individuals, who were hospitalized and treated for schizophrenia between December 2007 and December 2009. Cases with a history of cranial trauma, other medical conditions, organic mental disorder and alcohol/drug dependency were excluded from the study. The subjects were fully informed about the nature of the study procedure, and consent was obtained from each subject before entering the study.

Information about the course of disease (the first age of diagnosis, disease duration, number of hospitalizations, hospital length of stay, voluntary hospitalization information, etc.) was recorded. The diagnosis of schizophrenia was confirmed by means of the Turkish Version of the Structured Clinical Interview Form for the DSM-IV (SCID-I) (14,15). The symptoms of schizophrenia were assessed by using the Brief Psychiatric Rating Scale (BPRS), the Scale for the Assessment of Positive Symptoms (SAPS), and the Scale for the Assessment of Negative Symptoms (SANS) (16-18). The scales were performed at regular intervals according to clinical patient monitoring protocols.

Patients presenting with a stable clinical condition were discharged. Before discharge, the patients were also evaluated for a follow-up program, which was carried out by the schizophrenia outpatient-unit and the Social Service Unit of the Psychiatry Department. The sociodemographic characteristics of the participants were obtained by gathering information from their health insurance cards and, when necessary, by interviewing their family members. Their addresses and contact

information were also noted and the time of the first appointment and the frequency of appointments were recorded. The frequency of appointments was individualized within the range of 1 to 8 weeks according to the patient's medication regime, level of symptom control, present level of functioning and current rehabilitative needs.

Patients in this study have been followed for two years. The Social Service Unit of Psychiatry has followed-up these patients after discharge. According to the collected records, patients and their families were contacted by phone when they did not come to their scheduled appointments. For these cases, an appointment was rescheduled. In this conversation or at the subsequent appointments, reasons for not coming to appointments and medication adherence were questioned. Within the planned two-year period, patients, who missed more than 20% of their appointments were classified as "non-attenders." This grouping nomenclature was also used in other studies (1,4).

We assessed differences between the groups with the chi-square test for categorical variables and the independent groups t-test for scaled variables. We used 2-tailed tests throughout and applied the Bonferroni correction to control for multiple comparisons.

RESULTS

Of the patients, who participated in the study, the ratio of patients, who missed more than 20% of their planned appointments (non-attender group) was 44.7% (n= 73/132). In terms of gender, age, marital status, income level and employment status, no significant differences existed between patients, who participated in their appointments and patients, who did not participate ($p>0.05$). However, among patients with a low educational level ($t=3.498$, $p=0.001$) and those who were living alone (Fisher's exact test, $p=0.034$) high rates of failure of participation in appointments were found (see Table 1).

No difference was observed between the attender and non-attender groups with regard to the age at onset, alcohol-substance use disorder, antipsychotic drug group (typical or atypical antipsychotics), route of drug administration (oral, parenteral long-acting) and the total symptom severity, negative symptom severity or positive symptom severity on the first day of hospitalization ($p>0.05$). However, the BPRS and SAPS scores of the non-attender group were higher at discharge [BPRS (26.7±5.9 vs. 30.3±10.5, $t=-2.248$, $p=0.028$), SAPS (24.5±8.7 vs. 33.1±16.9, $t=-2.728$, $p=0.008$),

Table 1: The socio-demographic characteristics of patients

Variable	Attenders (n= 73)	Non-attenders (n= 59)	Statistics
Age; mean±SD (year)	35.0 ± 9.1	36.6 ± 10.5	$t=-0.928$, $df=130$, $p=0.355$
Gender; n (%)			Fisher's exact test, $p=0.647$
Female	14 (19.2)	9 (15.3)	
Male	59 (80.8)	50 (84.7)	
Marital status; n (%)			$\chi^2=0.034$, $p=0.983$
Married	19 (26.0)	15 (25.4)	
Single	46 (63.0)	38 (64.4)	
Widowed/divorced	8 (11.0)	6 (10.2)	
Education; mean±SD (year)	11.7±2.8	9.8±3.3	$t=3.498$, $df=130$, $p=0.001$
Living with whom; n (%)			Fisher's exact test, $p=0.034$
Family	68 (93.2)	47 (79.7)	
Alone	5 (6.8)	12 (20.3)	
Income; n (%)			Fisher's exact test, $p=0.904$
Low	46 (63.0)	38 (64.4)	
Medium/high	27 (37.0)	21 (35.6)	
Employment status; n (%)			Fisher's exact test, $p=0.965$
Yes	15 (21.9)	14 (23.7)	
No	59 (78.1)	45 (76.3)	

SD, standard deviation

Table 2: Comparison of the clinical characteristics of attender and non-attender patients with schizophrenia

Variable	Attenders (n= 73)	Non-attenders (n= 59)	Statistics
Age at onset; mean±SD (years)	25.3±5.8	23.7±4.7	t=1.284, df=130, p=0.202
Number of hospitalizations; mean±SD	1.2±0.6	2.1±1.3	t=-4.881, df=130, p=0.000
Last hospitalization; n (%)			Fisher's exact test= 0.000
Voluntary	52 (71.2)	23 (39.0)	
Involuntary	21 (28.8)	36 (61.0)	
Severity of symptoms; mean±SD			
BPRS (T0)	38.8±8.0	39.9±7.9	t=-0.665, df=130, p= 0.508
BPRS (T1)	26.7±5.9	30.3±10.5	t=-2.248, df=130, p= 0.028
SAPS (T0)	40.6±16.7	45.6±19.8	t=-1.180, df=130, p= 0.242
SAPS (T1)	24.5±8.7	33.1±16.9	t=-2.728, df=130, p= 0.008
SANS (T0)	60.9±16.3	56.1±18.6	t=1.212, df=130, p= 0.229
SANS(T1)	40.1±11.7	43.2±16.2	t=-0.951, df=130, p= 0.345
Drug adherence; n (%)			$\chi^2= 25.75$, p= 0.000
Regular	63 (86.3)	33 (55.9)	
Poor	10 (13.7)	26 (44.1)	
Antipsychotic group; n (%)			Fisher's exact test= 0.527
Conventional	18 (24.7)	11 (18.6)	
Atypical	55 (75.3)	48 (81.4)	
Drug route of administration; n (%)			Fisher's exact test= 0.657
Oral	60 (82.2)	47 (79.7)	
Long-acting injectable	13 (17.8)	12 (20.3)	
Substance use disorder; n (%)			$\chi^2= 0.054$, p= 0.971
No	65 (89.0)	43 (89.8)	
Alcohol	8 (11.0)	6 (10.2)	
Other substances	0	0	

(T0), score at first hospitalization day; (T1), score before discharge

respectively]. Additionally, the involuntary hospitalization rate (61% versus 28.8%, Fisher's exact test, $p= 0.000$), the number of hospitalizations (mean 1.2 ± 0.6 vs. 2.1 ± 1.3 ; $t= -4.881$, $p= 0.000$), and medication non-adherence (13.7% vs. 44.1%, Fisher's exact test, $p= 0.000$) rates were higher in the patients who did not participate in the appointments.

In addition, both patients who participated in appointments and those who did not were compared for their medication adherence. Sociodemographic characteristics (gender, marital status, education, employment status, income level, and living alone) were found to be similar among patients with and without good medication adherence ($p>0.05$). Likewise, no significant differences were found in terms of the clinical features (age at onset, number of hospitalizations, voluntary hospitalization, clinical symptom scores, antipsychotic group, drug route of administration) between the groups ($p>0.05$).

DISCUSSION

The extent of non-attendance in psychiatry is significantly greater than in other medical specialties (1,19). Killaspy et al. found a 40% nonattendance rate for psychiatric patients within a 12-month follow-up period (20). In this area, the most problematic group is patients with schizophrenia and different results have been reported with regard to non-adherence rates (21). Unal et al. followed 401 psychotic patients and reported that 55.1% participated in regular appointments, 29.4% never again came to an appointment, and the remainder participated irregularly in their appointments (22). In our study, the rate of participation in appointments, which was identified in a two-year period, was 44.7%, which is similar to the findings presented in the literature.

Several studies have examined the predictors of non-attendance systematically in mental health settings (23). In the psychiatric population, the most

important predictors for participation in an appointment were reported to be young age, low social-family support, lack of health insurance, male gender, a low educational level, living alone, and unemployment (4,24,25). In a study conducted in Turkey, Unal et al. examined non-attendance in the spectrum of psychotic disorders (22). Predictors of non-adherence were younger age, male gender, lower educational levels, unemployment and poor social functioning. We found that non-attender cases had a lower educational level, and they were more likely to be living alone when compared with attenders. Other demographic variables were not found to be significantly associated with non-adherence.

On the other hand, psychiatric illness factors such as frequent hospitalizations, involuntary hospitalization, age at onset and duration of illness, severity of psychotic symptoms, medication type and route of drug administration were not found to be consistent predictors of non-adherence (4,26). Patients with frequent hospitalizations were more likely to have poor adherence. However, data relating the number of prior hospitalizations to adherence are contradictory; some studies indicated more prior hospitalizations (27,28), while two other studies indicated fewer prior hospitalizations (29,30) and one study indicated no difference in prior hospitalizations (31) among patients judged to be noncompliant at an index assessment. We have shown that frequent hospitalizations were significantly associated with non-adherence. Commonly, frequent hospitalization is considered to be roughly equivalent to chronicity or treatment resistance. In addition, hospitalizations might distort treatment adherence, leading to ideas that the disease could not be treated and treatments, therefore, would not be effective.

Schizophrenia is the most common diagnosis among patients who are involuntarily admitted to psychiatric hospitals and treated against their will (32). We found that involuntary hospitalization was another significant variable related with non-attendance. Steinert and Schmid found a significant correlation between voluntary participation at discharge and agreement to continue treatment

after discharge (33). Similarly, Janssen et al. found a significant correlation between poor medication adherence and involuntary hospital admission (34).

Both inpatient drug refusal and outpatient non-adherence are consistently associated with more severe ratings of psychopathology. Investigations have reported a positive association between positive symptom severity at or after discharge and poor outpatient adherence (27,35,36) or poor attitude toward adherence (37). However, negative symptoms have been shown to be predictors of good adherence (5). In our study, severity of psychopathology (symptom severity, as measured by the BPRS; positive symptoms, as measured by the SAPS; and negative symptoms, as measured by SANS) were similar in patients at the first assessment during hospitalization. However, patients who showed greater clinical improvement of overall psychopathology and positive symptom scores were more compliant with appointments. Similarly, Janssen et al. found that individuals with good adherence showed more improvement of the PANSS score during their inpatient stay (34). These results suggest that participation in the appointments could be seen as a positive influencing factor for better recovery.

Medication adherence is an important part of this study. Non-attendance is particularly closely linked with medication non-adherence (10). Killaspy et al. shown that follow-up patients who miss an appointment were at a higher risk of dropout and admission within a 12-month period (20). Patients who discontinue medication of their own accord may be reluctant to disclose this to medical staff, and indeed cannot disclose it if not seen again. Conversely, patients who miss appointments will not receive the full benefit of medical advice and hence are less likely to make an informed choice about their care and are more likely to act autonomously in a self-directed manner (38). In the psychiatric population, it has been reported that 30%-60% of patients who did not participate in their appointments stopped taking their drugs (23). For patients with schizophrenia, the percentage of patients who have stopped taking their medication has been reported to be as high as 88% (13). In our

study, phone calls to patients, who were not participating in their planned appointments, showed that 44.1% were not using the recommended drug.

When compared for level of medication adherence, schizophrenic patients treated with typical antipsychotics were often (39,40), but not always (41-43), found to have poorer adherence compared to patients treated with atypicals. Dolder et al. found that adherence rates at 6 and 12 months were moderately higher in patients who received atypical antipsychotics than in those who received typical agents (44). However, compliant fill rates were 50.1% for typical and 54.9% for atypical antipsychotics at 12 months. Statistically significant differences in adherence between those groups were not present at 12 months. We also did not find significant differences in antipsychotic adherence among patients prescribed typical vs. atypical agents at the two year follow-up period. These results demonstrate the importance of longer adherence assessments. In addition, several studies have reported that drug route of administration may also be associated with the medication adherence. The use of depot medication has been shown to be effective in preventing non-adherence in studies with a follow-up of 1-7 years (45). Nevertheless, some studies have shown that even with depot medication, non-adherence rates remain relatively high (35,46). In our study, the rates of drug use between oral and depot antipsychotics were similar.

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This study has some limitations. First, the study was conducted with patients, who had social security covering institutional healthcare services, so the results do not completely reflect schizophrenic patients in the wider population. However, patients with no possibility of being admitted to treatment institutions are the most high-risk group with regard to not participating in scheduled appointments. Second, this study relied on information regarding the patient's use of antipsychotic drugs determined during a phone conversation with members of the patient's family (except in the case of patients who lived alone). This information may not fully reflect the patient's actual experience or behavior. Finally, the attitudes of health personnel, including physicians, are among the factors that affect adherence. This area has not been assessed in our study.

Non-adherence to appointments has a major impact on the effectiveness of therapeutic interventions and presents many problems in clinical practice. Clinic attendance adherence might be affected by sociodemographic factors and clinical features. In patients with schizophrenia, participating in appointments after discharge is also an important factor affecting medication adherence.

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