Factors Associated with Dropout and Noncompliance in Patients with Schizophrenia: Results of a One-Year Follow-Up

Alp Üçok,[1] Kazim Yazici,[2] Levent Mete,[3] Savaş Kültür,[3] A. Kemal Göğüş,[4] Şahap Erkoç,[5] Köksal Alptekin [6]

Abstract

The aim of this study was to investigate the dropout predictors for patients with schizophrenia in a naturalistic follow-up study design. After a baseline evaluation with the Brief Psychiatric Rating Scale (BPRS), Clinical Global Impression (CGI), and the UKU Side Effects Rating Scale (UKU), 382 patients with schizophrenia were scheduled for follow-up in monthly visits for one year. However, the majority of the patients (64%) dropped out prior to completion of the one-year follow-up. Patients who were less educated, had no national healthcare social security system coverage, and suffered from later onset of the illness dropped out with greater frequency. There were no differences in baseline BPRS total and subscale scores between patients who completed the one-year follow-up or dropped out; dropout patients had higher BPRS suspiciousness scores. Compliance to medication was also higher in patients who completed the one-year follow-up. We found no differences in compliance among the patients who took atypical antipsychotics, typical antipsychotics, or a combination of the two. Age of onset and BPRS suspiciousness scores were inversely correlated with the duration of follow-up. The patients who took haloperidol dropped out earlier than those who took risperidone, clozapine, or olanzapine. There were no differences between patients taking depot antipsychotic medications versus those taking oral antipsychotics in terms of treatment compliance, duration of follow-up, and dropout rates. Our findings suggest that dropout and compliance remain severe problems in the treatment of patients with schizophrenia, and that these problems are multifaceted, involving patient-related, treatment setting-related, and treatment-related factors.

Key Words: Schizophrenia, Dropout, Compliance, Antipsychotics

[1]İstanbul University, İstanbul School of Medicine, Department of Psychiatry, İstanbul
[2]Hacettepe University School of Medicine, Department of Psychiatry, Ankara
[3]İzmir Atatürk State Hospital, Department of Psychiatry, İzmir
[4]Ankara University School of Medicine, Department of Psychiatry, Ankara
[5]Bakırköy State Hospital of Mental Disorders, İstanbul
[6]Dokuz Eylül University School of Medicine, Department of Psychiatry, İzmir

Address for correspondence: Dr. Alp Üçok, İstanbul University, İstanbul Faculty of Medicine, Department of Psychiatry, Millet Street, Capa 34390, İstanbul, Turkey
Phone: +90 212 4142000 (extension: 31328); Fax: +90 212 5310309; E-mail: alpucok@superonline.com

Submitted: Feb 16, 2007; Revised: June 11, 2007; Accepted: June 15, 2007

Introduction

The findings of studies concerned with the course of schizophrenia are largely based on data obtained from patients who complete an entire follow-up period. Typically, however, substantial numbers of patients do not complete the entire follow-up period in either randomized-controlled or naturalistic studies. As a clinician, it is important to understand which patients are at an increased risk for dropping out and the characteristics of dropout patients. In a recent meta-analysis, it was reported that patients taking atypical antipsychotic medications in flexible and not fixed doses had dropped out later than those who took typical antipsychotic medications (1). Similar to other chronic disorders, compliance is one of the major issues when treating patients

with schizophrenia. Results of the recently published CATIE study showed that high antipsychotic medication discontinuation rates are one of the major obstacles in the treatment of schizophrenia (2). Poor treatment compliance was found to be one of the strongest predictors of relapse in patients with both first-episode and chronic schizophrenia (3, 4).

Compliance is, of course, much broader than just taking medications. Compliance also includes keeping clinical appointments and participating in other treatment-related activities (5). Non-adherence to treatment can be linked to disease features (e.g. suspiciousness), the treatment system (e.g. the use of appointment reminders, availability of specialized outpatient units), the treatment itself (e.g. medication side effects), and patient characteristics (6, 7).

Wahlbeck et al. reported that schizophrenia treatment dropout rates have significantly increased over the years since the mid-1950s, reaching approximately 60% at the beginning of the twenty-first century (8). These findings are from randomized antipsychotic drug trials. A significant cause of dropout was length of trial; type of antipsychotic medication (atypical versus typical) had no influence after clozapine trials had been excluded. Discontinuation of treatment is also a problem, even after the first episode. In three recent studies (3, 9-10), dropout rates were reported as 53%, 60%, and 14%, respectively, within the first year after the first episode. In the second study it was reported that, despite the high dropout rates, compliance, on average, was also high. More pronounced psychopathology at baseline, neurological side effects, and absence of psychosocial treatments seemed to increase the risk for dropping out (10).

In recent studies, the type of antipsychotic medication has been reported as being related to treatment compliance. While Menzin et al. reported that, compared with patients who received typical antipsychotics, patients receiving atypical antipsychotics were significantly less likely to have a switch in medication (11), other authors have found no differences between these two groups (12). In a recent study, it has been reported that the dropout rate for risperidone was higher than olanzapine in randomized studies (13).

The aim of this study is to investigate the predictors of dropout for patients with schizophrenia in a naturalistic, follow-up study design. The study sample is representative of the entire patient population in Turkey in terms of sociodemographic features, duration of illness, treatment facilities, and geographic location.

Methods

Sample Selection

This study is part of the Schizophrenia Follow-up Project of the Schizophrenia Section of the Psychiatric Association of Turkey. The sample consisted of 382 Turkish patients (62% males, 38% females) with a *Diagnostic and Statistical Manual of Mental Disorders-IV* diagnosis of schizophrenia. The investigators selected patients who were being treated in participating clinical settings and were older than eighteen years of age. Fifty-one investigators from twenty-five clinical centers, consisting of psychiatry departments of university and state mental hospitals located in seven geographical areas of Turkey with different cultures, participated in the study. At the beginning of the study, a start-up meeting was arranged in order to introduce the study design and provide education on measurement scales including the Brief Psychiatric Rating Scale (BPRS) (14), the Clinical Global Impression scale (CGI) (15), and the UKU Side Effects Rating Scale (UKU) (16). Reliability within and between centers was at a satisfactory level, with kappas ≥0.79 for BPRS. Each center used a standardized procedure to track patients. The patients agreed to take medications, regularly attend prescheduled visits, and signed an agreement before entering the study. Patients were evaluated monthly. Most of the patients were chronically ill; only 5% of all patients received a diagnosis of first-episode schizophrenia when selected. The sample selection period of the study was four months, and patients were followed-up for one year. Neither patients nor investigators were reimbursed for the study. All of the patients gave informed consent.

The study was designed as a naturalistic one. At initial evaluation all 382 patients were taking various antipsychotic medications: 127 patients (36%) were taking typical antipsychotic medications; 166 patients (46%) were taking atypical antipsychotic medications; and 64 patients (18%) were taking a combination of typical and atypical antipsychotics. The participating investigators were allowed to select their choice of particular antipsychotic medication without any intervention.

Measures

Each patient was seen in prescheduled monthly visits. The one-year follow-up involved a total of thirteen visits, including the initial visit. BPRS and CGI were used to evaluate the severity of symptoms in schizophrenia. CGI was used monthly; whereas BPRS was rated every three months. In addition to the total BPRS score, positive symptom subscales (items for hallucinations, unusual thought content, and conceptual disorganization) and negative symptom subscales (emotional withdrawal, motor retardation, and affective bluntness) were used in statistical analyses.

Since this is an observational follow-up study, patients received adequate antipsychotic medication treatment as scheduled by the treating physician, following the baseline procedures. Compliance to prescribed medication was inquired about at each visit with the patient and his/her relatives. If a patient had used less medication than prescribed

or completely skipped his/her medication for ten consecutive days, then that patient was regarded as "noncompliant." At the end of the follow-up (or at the last visit if the patient dropped out before completing the one-year follow-up) each patient's clinician rated his/her overall medication compliance as "good," "moderate" or "bad" based on the patient's monthly compliance ratings. When a patient had missed two consecutive prescheduled visits, he/she was regarded as a "dropout" and excluded from the follow-up.

Statistical Analysis

Statistical analysis was performed using the SPSS 12 computer program. Group differences between completed follow-up and dropped out patients were analyzed by t-test and chi-square test. Correlation between clinical variables of 382 patients and the duration of follow-up period were studied using the Pearson's correlation test. We investigated the relationship between the different types of the most frequently used antipsychotic medications and duration of follow-up with ANOVA. Logistic regression analysis was used to find the variables that independently contribute to follow-up status. The Mann-Whitney U test was used for not normally distributed variables. Statistical significance was tested using p-value (5% level) and 95% confidence intervals.

Results

Table 1 summarizes demographic and clinical variables for the 382 patients in our sample. The mean age of the patients was 34.5 years±9.5 years. Two hundred and fifty-one patients (66%) were single and never married; 86 patients (22%) were married; 11 (3%) were widowed; 25 (7%) were separated; and 6 (2%) were divorced. The number of patients living with their families was 343 (91%); only 31 patients (8%) were living independently. The number of employed patients, including those who worked on a volunteer basis, was 143 (37%). The mean number of hospitalizations was 3.7±4.4 and the mean years in treatment was 11.50 years±8.25. The mean number of past suicide attempts was 2.1±1.6.

Two hundred and forty-four out of the initial 382 patients (64%) dropped out before completing the one-year follow-up. The dropout rate was 44.2% after the first three months. There were no differences between those who completed one-year follow-up and dropouts in terms of age, gender, employment status, and functionality at baseline.

Table 2 summarizes the differences between the patients who completed the follow-up versus patients who dropped out. Overall, the patients who were followed by general outpatient units dropped out more than patients who were followed by specialized schizophrenia outpatient units (50.8% vs. 33.4%, respectively, x^2=8.43, df=1, p=0.004).

Table 1 Sample Demographics (n=382)

Age, years; mean (SD)	34.5 (9.5)
n single, never married (%)	251 (66%)
n married (%)	86 (22%)
n widowed (%)	11 (3%)
n separated (%)	25 (7%)
n divorced (%)	6 (2%)
n living with their families (%)	343 (91%)
n living independently (%)	31 (8%)
n employed (including as volunteers) (%)	143 (37%)
n hospitalizations; mean (SD)	3.7 (4.4)
n years in treatment; mean (SD)	11.5 (8.25)
n past suicide attempts; mean (SD)	2.1 (1.6)

SD=standard deviation; n=number

In comparing patients who completed the follow-up versus patients who dropped out, patients who were less educated (9.3±3.4 vs. 10.9±4.1 years, t=3.71, p=0.001), had no national healthcare social security system coverage (18.1% vs. 40.7%, x^2=12.9, p=0.001), and experienced later onset of the illness (23.4±7.2 vs. 21.2±5.8, t=-2.93, p=0.003) dropped out more. Although we have not found any differences in both baseline BPRS total and subscale scores between patients who completed the one-year follow-up or not, dropout patients had higher BPRS suspiciousness scores (3.53±1.81 vs. 3.1±1.85, p=0.03).

Compliance to medication also was found to be higher in patients who completed the one-year follow-up (84.8% vs. 73.9%, x^2=5.81, p=0.01). We found no differences in compliance among the patients who took atypical antipsychotics, typical antipsychotics, or a combination of the two. We compared the follow-up duration of the patients who took the most frequently prescribed four antipsychotics (risperidone, n=62; clozapine, n=59; haloperidol, n=40; and olanzapine, n=34) and found differences among these four groups of patients (9.4±3.5, 9.4±3.7, 7.3±4.3, and 9.1±3.7 months, respectively, F=2.89, p=0.03). Post hoc analysis showed that patients who took haloperidol dropped out earlier than the three other medication groups (p=0.009 for risperidone, p=0.01 for clozapine, and p=0.05 for olanzapine).

The mean duration of the follow-up period for the entire sample was 8.9±3.8 months. The age of onset (r=-0.197, p=0.001) and BPRS suspiciousness scores (r=-0.127, p=0.03) were inversely correlated with follow-up duration.

Seventeen patients used depot antipsychotics alone or in combination with an oral antipsychotic. There was no difference between patients taking depot antipsychotics versus

Table 2 Differences between Followed-Up and Dropout Patients

Variable	Followed-Up (n=138) Mean	SD	Dropout (n=244) Mean	SD	t	p
Age (years)	33.9	9.2	34.8	8.7	0.86	ns
Education (years)	10.9	3.4	9.3	4.0	3.71	0.001
Age at onset of illness (years)	21.2	5.8	23.4	7.2	-2.96	0.003
CGI-baseline	4.3	1.2	4.5	1.1	-1.74	ns
BPRS-baseline	51.6	15.4	53.9	16.2	-1.39	ns
	%		%		x^2	p
Have national healthcare social security coverage	40.7		18.1		12.91	0.001
Good or moderate compliance to medication	84.8		73.9		5.81	0.01
Treated in specialized schizophrenia unit	50.8		33.4		8.43	0.004
Employed	43.1		33.7		2.08	ns

ns=not significant; CGI=Clinical Global Impression; BPRS=Brief Psychiatric Rating Scale

Table 3 Variables that Independently Contribute to Follow-Up Status in Logistic Regression Analysis

Variable	Wald	df	Exp(B)	p
Age of onset	9.25	1	1.06	0.004
Education (years)	5.85	1	0.9	0.01
National health-care social security coverage	4.03	1	2.35	0.04
Compliance to medication	2.93	1	1.87	0.08
Type of outpatient unit	1.28	1	1.53	0.2
BPRS-suspiciousness	0.73	1	1.07	0.3
BPRS-total score	0.58	1	1.05	0.7
Type of antipsychotic	0.01	1	0.99	0.9

df=degrees of freedom; Exp(B)=estimated odds ratio; BPRS=Brief Psychiatric Rating Scale

oral antipsychotics in terms of treatment compliance, duration of follow-up, and dropout rates (72.2% and 65.8%, respectively, p>0.05).

Patients taking atypical antipsychotics had lower UKU-mental (6.18±5.09 vs. 7.55±4.06, Z=2.27, p=0.02) and UKU-neurologic side effect (0.84±1.69 vs. 1.79±2.69, Z=3.63, p=0.001) subscales when compared with patients taking conventional antipsychotics. There was no difference on UKU-autonomic and sexual side effect subscales. We found no differences in terms of baseline UKU subscales between groups except that there were more male patients who reported severe levels of decreased sexual desire in the dropped-out group than in males who completed the follow-up (9.6% vs. 2.6%, x^2 =11.3, df=2, p=0.003).

The follow-up status of a patient was taken as a dependent variable, and clinical variables that were found related to the follow-up status in t-test and chi-square tests were explained as variables in logistic regression analysis. The age of onset, education level, and national healthcare social security system insurance coverage were determined to be as important (Table 3).

When we ascertained that a patient had dropped out from our study, we tried to contact that patient and his/her family by calling the home and inviting them to the clinic to discuss why the patient had ceased monthly visits. We could only reach approximately 50% of the dropped-out patients. Patients' unwillingness to continue hospital visits without giving a clear reason was the most common cause of dropping out. Other common explanations included the decision of the patient or family to go to another psychiatrist, stopping the antipsychotic medication because of side effects, or believing that the medications were not helpful.

Discussion

In this study we investigated the predictors of dropout in patients with schizophrenia in a naturalistic follow-up study design. We found that almost two-thirds of the patients dropped out before completing the one-year follow-up, and, although the dropout rate of 64% was higher than we expected, it does approximate other recently reported rates (1).

Logistic regression analysis showed that the patients who were less educated, had no national healthcare social security insurance system coverage and, contrary to our expectations, had experienced disease onset at a later age, were at increased risk for dropping out. It is noteworthy that none of these predictors are related to the clinical features or severity of the illness.

In Turkey, people typically need to be currently or previously employed to be covered by the national social security healthcare insurance system which covers all medical expenses including hospital visits, medications, and diagnostic

investigations. Most patients suffering from schizophrenia have some difficulties in finding and keeping a regular job so they are often not covered by this national healthcare social security system. Our finding that patients without coverage tend to drop out more frequently than patients with coverage is compatible with two previous studies reporting a negative relationship between medication compliance and insurance coverage and financial problems (17-18). This suggests at least two possibilities: 1) these patients might be more disabled than typical patients and are, therefore, less employable (and dropping out may also have an indirect effect on their low functionality); or 2) since these patients are not covered by the national healthcare social security system, they have a real economic hardship in terms of getting their medications and adhering to treatment. As we found no relationship between disability and dropout in our previous report (19), the second possibility seems more plausible.

Similarly, the relationship between a lower level of education and dropout rates may be explained in two ways: 1) either these patients' illness (and its impact on cognitive functionality) has a more severe trend affecting their ability to stay in school (although we found no relationship between measures of clinical severity [BPRS score] and dropping out); or 2) a higher level of education might be related to better disease insight which leads to increased treatment compliance.

The only clinical variable found related to duration of follow-up is the baseline suspiciousness score. The fact that baseline suspiciousness scores of dropout patients were higher is consistent with the findings of Marder et al. (20). In addition, Kamali et al. (21) and Novak-Grubic and Tavcar (3) reported that insight is lower in noncompliant patients upon leaving the hospital. Although our study did not measure insight, a high suspiciousness score may also have a negative effect on insight and thus on treatment compliance. As reported by most of the previous studies, lack of medication compliance was found to be related to dropping out.

Among the patients who have taken one of the four most frequently prescribed antipsychotics, we found that patients receiving haloperidol stayed on their medication for a shorter period of time than patients receiving atypical antipsychotics. There were no differences among patients receiving the different atypical antipsychotics in terms of the time periods that patients stayed on their medications. This finding is consistent with previous reports about time-to-medication discontinuation (22, 23). Since this is a naturalistic study, and we did not control variables such as daily antipsychotic doses nor found any differences between patients who dropped out or followed-up in terms of atypical/typical antipsychotic medication use, general application of this data is limited.

Long-acting depot antipsychotics are often recommended to reduce treatment noncompliance (24, 25), but we found no differences between patients taking depot antipsychotics versus oral antipsychotics. In fact, dropout rates in those patients taking depot antipsychotics were even higher than the rates observed in patients receiving oral antipsychotics. One can speculate that if the reason for prescribing depot antipsychotics to patients is due to past noncompliance with oral antipsychotics, then this pattern of noncompliance might well continue with depot treatment.

Unlike previous reports (6, 9), we found no relationship between medication side effects and dropout. Although we found that male patients who complained about severe reduction in their sexual desire dropped out more frequently, this finding is far from conclusive as the number of patients is relatively small.

Our findings also suggest that treatment conditions contribute to compliance. We found that the patients treated in specialized schizophrenia outpatient units dropped out less frequently than those patients treated by general outpatient settings. In specialized units, patients are seen by the same psychiatrists on each visit, and the duration of the session is generally longer. It appears that there is a better patient-psychiatrist relationship in specialized units, and that this improves compliance.

Gaebel et al. (9) reported that the lack of psychosocial treatments seemed to increase the risk for dropping out. As the treatment of schizophrenia in our study is limited only to pharmacologic therapies in Turkey, the absence of psychoscocial treatments may be one of the reasons for the high dropout rates we experienced.

A sizeable portion of the dropouts occurred in the first three months of the follow-up. In addition to the possible reasons discussed above, the lack of family intervention to increase treatment adherence at the beginning of the follow-up may be a contributing factor. Particularly in traditional societies such as Turkey's, the attitudes of the family to treatment have an important role. If the family hesitates to bring an ill relative to the outpatient clinic for monthly appointments, or does not support the medication compliance, it will increase the dropout rate. Although we did not measure the attitudes of the families in this study, it appears that psychoeducative interventions are necessary to keep the patients in contact with psychiatric clinics.

This study is limited by a number of methodological problems. For example, we have only taken into account the types of antipsychotic medications in use at the time of baseline assessment in looking at the relationship between antipsychotics and dropout/duration of follow-up. As mentioned above, there were also dosing issues. Even among the patients using the same antipsychotic medication, there might be differences in daily doses. These differences are at least partially independent from the severity of the illness

and may be due, in part, to the preferences of the treating physician. Finally, although the number and geographical distribution of the patients in our study is a representative Turkish patient sample, there is a heterogeneity among the treating physicians and centers in terms of patient load, availability of mental health professionals other than psychiatrists, and even the duration of a standard psychiatric examination. Although we tried to minimize these differences in a comprehensive start-up meeting in which we trained all the psychiatrists on the relevant rating scales, we believe that all of the above mentioned deficiencies of our mental health system might have contributed to our higher dropout rate.

In conclusion, our findings suggest that dropout is still a severe problem in the treatment of patients with schizophrenia, and that this problem is multifaceted, including patient-related, treatment setting-related, and treatment-related factors. Our findings emphasize the necessity of psychoeducation programs to improve compliance in patients with schizophrenia.

Acknowledgment

This study was supported by Pfizer, Turkey. The authors wish to thank all the participating psychiatrists and patients.

References

1. Martin JL, Perez V, Sacristan M, Rodriguez-Artalejo F, Martinez C, Alvarez E. Meta-analysis of dropout rates in randomised clinical trials, comparing typical and atypical antipsychotics in the treatment of schizophrenia. Eur Psychiatry 2006;21:11-20.
2. Lieberman JA, Stroup TS, McEvoy JP, Swartz MS, Rosenheck RA, Perkins DO, et al; Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Investigators. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. N Engl J Med 2005;353:1209-1223.
3. Novak-Grubic V, Tavcar R. Predictors of noncompliance in males with first-episode schizophrenia, schizophreniform and schizoaffective disorder. Eur Psychiatry 2002;17:148-154.
4. Robinson D, Woerner MG, Alvir JM, Bilder R, Goldman R, Geisler S, et al. Predictors of relapse following response from a first episode of schizophrenia or schizoaffective disorder. Arch Gen Psychiatry 1999;56:241-247.
5. Marder SR. Overview of partial compliance. J Clin Psychiatry 2003;63(Suppl 16):3-9.
6. Weiden P, Rapkin B, Mott T, Zygmunt A, Goldman D, Horvitz-Lennon M, et al. Rating of medication influences (ROMI) scale in schizophrenia. Schizophr Bull 1994;20:297-310.
7. Fleischhacker WW, Oehl MA, Hummer M. Factors influencing compliance in schizophrenia patients. J Clin Psychiatry 2003;64(Suppl 16):10-13.
8. Wahlbeck K, Tuunainen A, Ahokas A, Leucht S. Dropout rates in randomised antipsychotic drug trials. Psychopharmacology (Berl) 2001;155:230-233.
9. Gaebel W, Moller HJ, Buchkremer G, Ohmann C, Riesbeck M, Wolwer W, et al. Pharmacological long-term treatment strategies in first episode schizophrenia--study design and preliminary results of an ongoing RCT within the German Research Network on Schizophrenia. Eur Arch Psychiatry Clin Neurosci 2004; 254:129-140.
10. Ucok A, Polat A, Cakir S, Genc A. One year outcome in first episode schizophrenia. Predictors of relapse. Eur Arch Psychiatry Clin Neurosci 2006; 256:37-43.
11. Menzin J, Boulanger L, Friedman M, Mackell J, Lloyd JR. Treatment adherence associated with conventional and atypical antipsychotics in a large state Medicaid program. Psychiatr Serv 2003;54:719-723.
12. Velligan DI, Lam F, Ereshefsky L, Miller AL. Psychopharmacology: Perspectives on medication adherence and atypical antipsychotic medications. Psychiatr Serv 2003;54:665-667.
13. Santariasci B, Messori A. Clinical trial response and dropout rates with olanzapine versus risperidone. Ann Pharmacother 2003;37:556-563.
14. Lukoff D, Nuechterlein KH, Ventura J. Manual for the expanded Brief Psychiatric Rating Scale (BPRS). Schizophr Bull 1986;13:261-276.
15. Guy W. ECDEU assessment manual for psychopharmacology. Rockville (MD): U.S. Dept. Of Health, Education, and Welfare, Public Health Service, Alcohol, Drug Abuse, and Mental Health Administration, National Institute of Mental Health, Psychopharmacology Research Branch, Division of Extramural Research Programs; 1976.
16. Lingjaerde O, Ahlfors UG, Bech P, Dencker SJ, Elgen K. The UKU side effect rating scale. A new comprehensive rating scale for psychotropic drugs and a cross-sectional study of side effects in neuroleptic-treated patients. Acta Psychiatr Scand Suppl 1987;334:1-100.
17. Balkrishnan R. Predictors of medication adherence in the elderly. Clin Ther 1998;20:764-771.
18. Ellis AE, Gogel RP, Roman BR, Watson JB, Indyk D, Rosenberg G. The STARK study: a cross-sectional study of adherence to short-term drug regiments in urban Kenya. Soc Work Health Care 2006;42:237-250.
19. Alptekin K, Erkoc S, Gogus AK, Kultur S, Mete L, Ucok A,

et al. Disability in schizophrenia : clinical correlates and prediction over 1-year follow-up. Psychiatry Res 2005;135:103-111.

20. Marder SR, Mebane A, Chien CP, Winslade WJ, Swann E, Van Putten T. A comparison of patients who refuse and consent to neuroleptic treatment. Am J Psychiatry 1983;140:470-472.

21. Kamali M, Kelly BD, Clarke M, Browne S, Gervin M, Kinsella A, et al. A prospective evaluation of adherence to medication in first episode schizophrenia. Eur Psychiatry 2006;21:29-33.

22. Glick ID, Berg PH. Time to study discontinuation, relapse, and compliance with atypical or conventional antipsychotics in schizophrenia and related disorders. Int Clin Psychopharmacol 2002;17:65-68.

23. Tran PV, Hamilton SH, Kuntz AJ, Potvin JH, Andersen SW, Beasley C, et al. Double-blind comparison of olanzapine versus risperidone in the treatment of schizophrenia and other psychotic disorders. J Clin Psychopharmacol 1997;17:407-418.

24. Kane JM. Strategies for improving compliance in treatment of schizophrenia by using a long-acting formulation of an antipsychotic: clinical studies. J Clin Psychiatry 2003;64(Suppl 16):34-40.

25. Davis JM, Chen N. Choice of maintenance medication for schizophrenia. J Clin Psychiatry 2003;64(Suppl 16):24-33.