A Pilot Study of Barriers to Medication Adherence in Schizophrenia

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Background: Interventions to improve adherence to antipsychotic medication are needed. The aims of the current study were to identify the most common barriers to medication adherence in a cohort of patients receiving outpatient and inpatient treatment for an acute exacerbation of schizophrenia, compare clinical and demographic characteristics of patients with lower versus higher numbers of barriers, and characterize patients most likely to be nonadherent to antipsychotic medication.

Method: The present study analyzed data collected during the Schizophrenia Guidelines Project (SGP), a multisite study of strategies to implement practice guidelines that was funded by the U.S. Department of Veterans Affairs and conducted from March 1999 to October 2000. Nurse coordinators had conducted clinical assessments and performed an intervention designed to improve medication adherence by addressing barriers to adherence. Data on patient symptoms, functioning, and side effects had been obtained using the Positive and Negative Syndrome Scale (PANSS), the Schizophrenia Outcomes Module, the Medical Outcomes Study 36-item Short-Form Health Survey, and the Barnes Akathisia Scale (BAS). Administrative data were used to identify patients with an ICD-9 code for schizophrenia. A total of 153 patients who met this criterion and participated in the intervention arm of the SGP had complete data available for analysis in the current study.

Results: The most common patient-reported barriers were related to the stigma of taking medications, adverse drug reactions, forgetfulness, and lack of social support. Bivariate analysis showed that patients with high barriers were significantly more likely to be nonadherent ($p \le .02$), to have problems with alcohol or drug use ($p = .02$), to have higher PANSS total scores ($p = .03$), and to have higher mean BAS scores ($p = .02$). Logistic regression showed that lower patient education level (odds ratio [OR] = 3.95, $p = .02$), substance abuse (OR = 3.24, $p = .01$), high PANSS total scores (OR = 1.02, $p = .05$), and high barriers (OR = 2.3, $p = .05$) were significantly associated with the probability of nonadherence.

Conclusions: It may be possible to identify patients most likely to benefit from adherence intervention. The data presented here will help to inform future research of clinical interventions to improve medication adherence in schizophrenia and help to stimulate further work in this area.

(J Clin Psychiatry 2004;65:211–216)

Antipsychotic medication is a critical component of successful treatment for schizophrenia,[1–4] yet nonadherence to these medications continues to be a major problem for 40% to 50% of patients with schizophrenia.[5,6] With the introduction of novel antipsychotic medications in the 1990s, many clinicians and researchers were hopeful that adherence rates would improve as patients experienced fewer disturbing side effects from these medications.[7–9] Current research, however, is mixed regarding rates of adherence to the newer antipsychotic medications.[10–15] Medication nonadherence is also associated with poor outcomes, more hospital readmissions, and increased costs of care.[16,17] For these reasons, developing and testing strategies to improve medication adherence remains an important topic for both clinicians and researchers.

Some of the most promising strategies for improving medication adherence are based on assertive community treatment models and the use of motivational interviewing techniques.[18] Interventions that help patients learn to use behavioral techniques such as self-monitoring, reminders/cues, and reinforcement also appear to be useful.[18–20] Unfortunately, as recently noted by others,[6,18,21] more research is needed to develop adequate theory-driven interventions and methods for identifying patients most likely to benefit from a particular type of medication

adherence intervention. The present study used data collected for the Schizophrenia Guidelines Project (SGP), a multisite study funded by the U.S. Department of Veterans Affairs (VA) designed to examine how standard and enhanced strategies to implement clinical practice guidelines for schizophrenia affect patient care and the outcomes of that care. The aims of the current study were to identify the most common barriers to medication adherence in a cohort of patients receiving outpatient and inpatient treatment for an acute exacerbation of schizophrenia, compare clinical and demographic characteristics of patients with lower versus higher numbers of barriers, and characterize patients most likely to be nonadherent to antipsychotic medication.

METHOD

Schizophrenia Guidelines Project

Required human subjects approval was obtained from the designated institutional review board at each VA Medical Center (VAMC) that participated in the SGP, conducted March 1999 to October 2000. The SGP compared the usual strategy for implementing clinical practice guidelines (4 sites) with an intervention (3 sites) that promoted guideline-concordant prescribing by physicians and medication adherence by patients. Personnel at standard sites included a site principal investigator and research assistant. In addition to the principal investigator and research assistant, personnel for the intervention sites included a nurse coordinator who was responsible for conducting the intervention.

A total of 399 patients with schizophrenia were enrolled in the SGP: 226 patients at standard sites and 173 patients at intervention sites. The intervention arm was conducted at 3 VAMCs; 2 were located in the midsouthern and 1 in the northeastern United States. The intervention consisted of using designated nurse coordinators at each intervention site to promote guideline concordant prescribing by physicians and to perform a clinical intervention with patients to improve medication adherence. Patients were considered eligible for the SGP if they (1) were identified by inpatient or outpatient providers as experiencing exacerbation of schizophrenia and had an ICD-9 code for schizophrenia (295.1–295.3, 295.6, and 295.9), (2) were 18 to 65 years of age, (3) were planning to receive follow-up outpatient care at the VAMC of study enrollment, and (4) were able to give informed consent.

Clinical and Demographic Data

The site principal investigator and research assistant were responsible for identifying eligible subjects. The site principal investigator was specifically responsible for verifying that patients met the diagnostic criteria for the SGP. Once informed consent was obtained, the research assistant interviewed each patient at baseline and 6 months later using a battery of valid and reliable instruments. Study participants received $20.00 as compensation for each completed research interview.

Instruments used for the research interview included the Positive and Negative Syndrome Scale (PANSS),[22] the Barnes Akathisia Scale (BAS),[23] and the Schizophrenia Outcomes Module (SCHIZOM). The SCHIZOM was developed by researchers at the Center for Mental Health and Outcomes Research with support from the National Institute of Mental Health and the VA. It is a brief, yet comprehensive, set of instruments that assesses duration of illness, premorbid adjustment,[24] alcohol and drug use,[25] medication adherence,[26–27] and health-related functioning as measured by the Medical Outcomes Study 36-item Short-Form Health Survey (SF-36).[28] The reliability and validity of the SCHIZOM have been demonstrated,[29,30] and it has been utilized in longitudinal outcome studies in the VA and in state mental health systems. Current alcohol or drug use was measured according to responses to the CAGE questionnaire[25] and questions about quantity and frequency of use. Medication adherence was assessed via patient self-report for the 30 days prior to the interview and rated on a 5-point scale. Ratings of 1 or 2 were considered adherent (never missed medication or missed a couple of times but basically took all, respectively), and ratings of 3 through 5 were classified as nonadherent (missed several times but took at least half of it, took less than half, stopped taking medication altogether, respectively).

In addition, research assistants used medical record chart review instruments specifically designed for this study (available from T.J.H. on request) to obtain provider documentation of medication adherence from patients' medical records for all inpatient and outpatient encounters during the 6-month study period. For the chart abstraction adherence variable, patients were classified as nonadherent if the chart review instrument noted the patient had not been taking prescribed antipsychotic medication prior to the encounter.

Nurse Coordinator Intervention and Assessment of Barriers

The medical director and chief of psychiatry or nursing services at each intervention VAMC selected a nurse coordinator to conduct the intervention. At 2 sites, the nurse was selected from among existing nurses working in the mental health service, and 1 site hired a nurse with extensive mental health experience specifically for the SGP. Nurse coordinators completed $1\frac{1}{2}$ days of training with the research team, based in Little Rock, Ark., to learn how to deliver the enhanced intervention. Nurse coordinators were given a detailed manual of the intervention protocol, which included flexible scripts and suggestions to use when conducting clinical patient interviews and assessing

barriers. Forms prepared by the study principal investigator were used to document specific elements of the intervention and the barrier assessment. The nurses also received instructions for maintaining contact with patients during the study period and for providing feedback to the physicians for each patient. Feedback to physicians included patient preferences for treatment, barriers to medication adherence, and information about VA clinical practice guidelines. Role-play was used to ensure that nurses understood the intervention and how to conduct it. Fidelity to the study protocol was monitored by research staff in Little Rock who received copies of all project forms and logs of activities conducted for each enrolled patient and maintained regular phone contact with the personnel at each study site.

After patients completed research interviews with the research assistants, nurse coordinators followed the written protocol for the intervention and conducted a clinical interview lasting 20 to 60 minutes. During this interview, the nurse completed a checklist of 9 domains of barriers to medication adherence including (1) memory problems, (2) problems with the medication regimen, (3) patient fear of medications, (4) adverse drug reactions, (5) denial of illness, (6) stigma of taking medication, (7) lack of trust in the provider, (8) lack of social support, and (9) other issues (responses that were reported but not listed in the previous 8 domains). Based on the barriers identified, the nurse coordinator worked with the patient to select and tailor strategies that could be used to overcome that particular barrier. For example, if a patient had difficulty remembering to take the medication, the nurse could offer the patient a pill organizer, use behavioral tailoring techniques[19,20] to help the patient remember to take medication when performing routine tasks such as brushing teeth, or work with a family member to help the patient remember to take the medication. The patients could use 1 or all of the strategies suggested in the study protocol depending on which strategies they felt were most likely to be effective for their particular situation. The nurses conducted barrier assessments with enrolled patients at baseline entry into the study and approximately every 6 weeks throughout the 6-month study period or as often as the patient utilized mental health–related treatment services at the VAMC.

Procedures and Analyses for Current Study

Of 399 subjects enrolled in the SGP, 173 patients were enrolled at intervention VAMCs, and 153 of those patients had complete data available for analysis in the current study. All demographic information; PANSS, BAS, and SF-36 scores; and information from the SCHIZOM (education level, duration of illness, premorbid adjustment, alcohol and drug use, and medication adherence) were obtained during the baseline research interview. Barrier information for this study was based on information col-

Figure 1. Frequency of Barriers to Medication Adherence in Patients With Schizophrenic Disorders
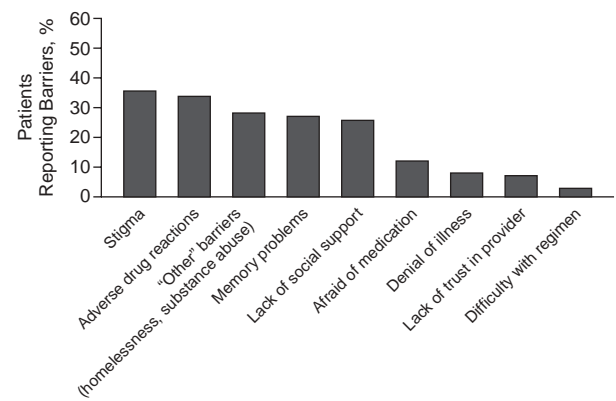
lected during the nurses' first clinical interviews with each patient. Patients were considered nonadherent if either patient self-report or medical record data reported nonadherence. Drug or alcohol abuse problems were defined as a positive response to 1 or more CAGE questions (for alcohol or drugs) and a report of recent or current use. Descriptive statistics, including the mean number of barriers per patient and the frequency of individual barriers, were calculated. A median split was used to divide the sample into 2 groups: those with a low number of barriers (< 2) and those with a high number of barriers (≥ 2). Chi-square and t test statistics were used to compare the high- and low-barrier groups in terms of demographics, duration of illness, premorbid adjustment, medication adherence, alcohol or drug use, and scores from the PANSS, BAS, and SF-36. Logistic regression was used to explore the association between high/low number of barriers and nonadherence, while controlling for demographic and clinical characteristics of patients. We also ran a regression using the stepwise option to explore the relationship between specific barrier domains and adherence.

RESULTS

Of the 153 patients included in this study, 94% (N = 144) were male, 20% (N = 30) were married, 22% (N = 34) were white, and 87% (N = 133) had completed high school or less. At the time of barrier assessment, 43% (N = 66) of the study population were inpatients and 57% (N = 87) were outpatients. Inpatients were significantly less adherent to antipsychotic medication (p < .05). Only 6% (N = 4) of inpatients were adherent compared with 45% (N = 39) of outpatients.

Frequency of Barriers

The mean number of barriers per subject was 1.8 (range, 0–6). As shown in Figure 1, the most commonly reported barriers to medication adherence were stigma,

Table 1. Comparison of Demographic and Baseline Clinical Characteristics of Schizophrenic Disorder Patients With High Versus Low Barriers to Medication Adherence

Characteristic	High Barriers ($\geq$ 2) (N = 84)	Low Barriers (< 2) (N = 69)	Significance
Age, mean, y	45.7	44.6	NS
Gender, male, %	95.2	92.8	NS
Race, white, %	23.8	20.3	NS
Marital status, married, %	17.9	21.7	NS
Education level, college or above, %	8.3	18.8	NS
Duration of illness, mean, y	22.3	20.8	NS
Premorbid adjustment problems, %	49.4	51.5	NS
Medication adherence, %			
Patient interview	56.6	79.7	$\chi^2 = 9.095$, df = 1, p = .003
Chart abstraction	28.6	49.3	$\chi^2 = 5.272$, df = 1, p = .02
Alcohol or drug problems, %	53.6	34.8	$\chi^2 = 5.40$, df = 1, p = .02
PANSS total score, mean	89.8	82.3	t = −2.20, df = 151, p = .03
BAS score, mean	3.8	2.7	$\chi^2 = 2.46$, df = 151, p = .02
SF-36 scores, mean			
Mental health subscale	50.6	54.6	NS
Physical health subscale	72.6	74.5	NS

Abbreviations: BAS = Barnes Akathisia Scale, PANSS = Positive and Negative Syndrome Scale, SF-36 = Medical Outcomes Study 36-item Short Form Health Survey.

Table 2. Results of Logistic Regression Analysis Predicting Medication Nonadherence in Patients With Schizophrenic Disorders

Parameter	Odds Ratio	95% Confidence Interval	p Value
Gender, male	2.627	(0.485 to 14.243)	.26
Marital status, married	1.348	(0.438 to 4.154)	.60
Race, white	1.517	(0.556 to 4.143)	.42
Education, $\leq$ high school	3.950	(1.282 to 12.179)	.02
Age	1.022	(0.963 to 1.085)	.47
Alcohol or drug problem	3.240	(1.320 to 7.955)	.01
Premorbid functioning	1.501	(0.648 to 3.479)	.34
SF-36 score			
Mental health subscale	1.004	(0.984 to 1.025)	.69
Physical health subscale	0.993	(0.975 to 1.012)	.48
Barnes Akathisia Scale score	0.997	(0.850 to 1.170)	.98
PANSS total score	1.023	(1.0 to 1.047)	.05
High barriers	2.330	(1.0 to 5.430)	.05

Abbreviations: PANSS = Positive and Negative Syndrome Scale, SF-36 = Medical Outcomes Study 36-item Short Form Health Survey.

adverse drug reactions, memory problems (i.e., forgetting to take medications), and lack of social support. Approximately 28% of patients had barriers in the "other" category; the most common were substance abuse (N = 28) and homelessness (N = 14).

Comparison of High Versus Low Barriers

Patient demographics and baseline clinical characteristics for the 84 patients with high barriers and 69 patients with low barriers are presented in Table 1. There were no significant differences in age, race, gender, marital status, education level, or duration of illness among patients with high barriers compared with patients with low barriers. Patients with high barriers were significantly less adherent to antipsychotic medication than were those with low barriers according to both self-report (56.6% vs. 79.7%, p = .003) and medical record data (28.6% vs. 49.3%,

p = .02). Patients with high barriers were significantly more likely to have problems with alcohol or drug use compared with patients with low barriers (53.6% vs. 34.8%, p = .02). The PANSS total score was significantly higher for patients with high barriers compared with that for patients with low barriers (mean score 89.8 vs. 82.3, p = .03), and patients with high barriers had significantly higher BAS scores compared with patients with low barriers (mean score 3.8 vs. 2.7, p = .02). There were no differences in the SF-36 mental or physical health summary scale scores for patients with high barriers compared with those for patients with low barriers.

Factors Associated With Medication Nonadherence

Results for the logistic regression model explored the association between high barriers and nonadherence, controlling for some demographics and clinical characteristics (Table 2). Patient education level, substance abuse, PANSS total score, and high barriers were strongly associated with the probability of nonadherence. Specifically, patients with lower education level, defined as having completed $\leq$ 12 years of school (odds ratio [OR] = 3.95, p = .02), who screened positive for substance abuse on the CAGE questionnaire (OR = 3.24, p = .01) had an increased probability of nonadherence. Patients with higher mean PANSS total score (OR = 1.02, p = .05) and high barriers (OR = 2.33, p = .05) were also significantly more likely to be nonadherent. In order to determine if a specific barrier was associated with medication nonadherence, we also ran a regression using the stepwise option with nonadherence (yes/no) as the dependent variable and the barrier domains as independent variables (controlling for age, gender, race, marital status, education level, and substance abuse). None of the specific barrier domains alone were significantly associated with the probability of nonadherence.

DISCUSSION

The results of our study found that, based on patient report, the most common barriers to patient adherence to antipsychotic medication were related to the stigma of taking medications, adverse drug reactions, forgetting to take medications, and lack of social support. Our study is an initial step to examine patient-reported barriers to adherence to antipsychotic medication as experienced by patients with schizophrenia and to understand the relationship between number of barriers and adherence.

The types of barriers identified in our study are consistent with emerging research on medication adherence for other psychiatric and chronic medical disorders (e.g., depression, acquired immunodeficiency syndrome, asthma, chronic heart failure). For example, Sirey et al.[31] found that perceived stigma associated with mental illness was an important factor related to nonadherence to antidepressant medication for recently diagnosed depressed outpatients. Two qualitative studies[32–34] of patients infected with the human immunodeficiency virus reported that the main barriers to medication adherence were related to forgetfulness, complexity of medication regimens, medication side effects, inadequate patient knowledge, social relationships, and the social/physical environment. In a study of patients with chronic heart failure, Simpson et al.[35] found that poor social support and previous adverse reactions were the most common barriers to medication adherence and that good medication adherence was associated with fewer patient barriers to medication use. In our study, comparisons between patients with high versus low barriers found that patients with high barriers were significantly more likely to be nonadherent, to have problems with alcohol or drug use, to have higher PANSS total scores, and to experience more akathisia.

In exploring the effect of barriers on risk for nonadherence, we found that lower patient education, substance abuse, high barriers, and symptom severity were associated with nonadherence to antipsychotic medication. In general, our findings are consistent with other studies of risk factors for nonadherence in schizophrenia. Previous work has identified factors such as patient education level, substance abuse, and higher symptom severity to be associated with nonadherence.[36] To our knowledge, however, the present study is the first report of the association between number of barriers and nonadherence in schizophrenia. Although individual barriers did not predict medication nonadherence, the number of barriers experienced by patients was an important factor that influenced medication adherence.

Implications

Our pilot study identified several strategies that warrant further research. As seen in the results presented here, it may be possible to identify patients at risk for nonad-

herence by assessing the number of barriers to medication adherence, presence of substance abuse, and symptom severity. If it is possible to identify patients most likely to benefit from an adherence intervention, it will be necessary to study the cost-effectiveness of such an approach.[37]

Although the results of this study can inform future work, the limitations of this study must be recognized. Although the barrier assessment was developed on the basis of existing literature at the time of our study, it is not a standardized, validated instrument. Rather, the type and number of barriers experienced by patients were collected for this study primarily to facilitate the clinical interview and intervention and to ensure fidelity to the study protocol as delivered by nurse coordinators. Nevertheless, the associations seen in these data are clinically relevant and are strong enough to warrant further research.

We acknowledge that our study may only address a fraction of the potential barriers that could be associated with medication nonadherence among patients with schizophrenia, including cost of medications. For example, patients receiving treatment from the Veterans Health Administration (VHA) usually have either no co-pay or a very small co-pay for their prescriptions. It was not possible, therefore, to assess the potential impact of cost of antipsychotic medication as a barrier, especially for the newer antipsychotics, which tend to be very expensive. Recent research from a national sample of adults with disabilities suggests that cost may be a very prevalent barrier to medication adherence.[38] Our study, as with other studies using patients treated in the VHA, comprised primarily male subjects; we recognize the limits this factor places on generalizability. Future research, therefore, should include assessment of adherence barriers in both male and female subjects.

Finally, we recognize that there is no single "gold-standard" for adherence measurement and that using patient self-assessment may overestimate adherence. We addressed this issue by using 2 measures of adherence: patient self-report and medical record documentation. Future studies may consider an additional measure, such as medication refills.

Despite the limitations of our study, we believe that the data presented here will help to inform future research of clinical interventions to improve medication adherence in schizophrenia and help to stimulate further work in this area. Much more work is needed to further refine barrier assessments for schizophrenia and to develop strategies to identify patients likely to be nonadherent who would benefit from an adherence intervention.

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