Medication Adherence

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Optimizing Adherence to Treatment in Patients With Schizophrenia

Based on an interview with Jonathan Lacro, PharmD

Antipsychotic medications have been shown to be effective in treating patients with schizophrenia. But if these patients do not follow their prescribed medication regimens, their chances of successful treatment are severely diminished. The following article, based on an interview with Jonathan Lacro, PharmD, examines some of the reasons patients with schizophrenia do not adhere to prescribed medication regimens and discusses ways to increase adherence rates. Dr. Lacro is a program manager and clinical pharmacist at the VA San Diego Healthcare System, a research scientist at the Veterans Medical Research Foundation, and an associate clinical professor of psychiatry at the University of California, San Diego.

Long-term adherence to antipsychotic therapy is the cornerstone of contemporary management of psychosis, and patients who stop therapy have a markedly increased risk of exacerbation of disease. Patients with schizophrenia who take their medications as prescribed are much more likely to have positive outcomes, including a decreased likelihood of rehospitalization and better daily functioning and quality of life, compared with those who do not adhere to their prescribed medication regimens. In an analysis of Medicaid refill and medical claims data collected in California between 1999 and 2001 (N=4,325), risk of hospitalization among patients with schizophrenia correlated significantly with gaps in medication adherence (see Figure 1). Further, a review of the literature between 1995 and 2002 found that, for schizophrenia and for mental disorders generally, the most significant direct costs were related to hospitalization. This was true for initial episode costs as well as for subsequent relapses. The authors concluded that poor adherence with medication treatment “is likely to result in an increased frequency of relapse, more intense symptoms, and longer inpatient stays.”

Almost every patient with schizophrenia is at risk for relapse at some point. In a study of individuals who had responded to treatment for their first psychotic episode, up to 82% had at least one psychotic relapse within 5 years, and 78% had a second relapse within that time. Patients who discontinued medication were almost five times more likely to relapse than patients who continued taking medication, whether it was the first or the second relapse. Therefore, in addition to other treatments that have been prescribed for patients with schizophrenia, such as cognitive behavioral therapy and social skills training, it is essential for these patients to take their medications as prescribed.

Unfortunately, like many patients with psychiatric disorders, those with schizophrenia generally do not adhere well to their prescribed medication regimens. While rates of medication nonadherence may reach as high as 40% for patients with chronic medical conditions in general, medication nonadherence rates in patients with schizophrenia can reach 50%. In a recent study of Medicaid beneficiaries with schizophrenia, 24% were found to be nonadherent, 16% were partially adherent, and 19% were “excess fillers”—they received more days of medication than necessary for a given period. Medication nonadherence refers to any deviation from the prescribed regimen. While the more common pattern involves skipping doses or not taking medication for several days or even weeks, some patients may actually take extra doses of medications. Excess medication fills may result from overuse of antipsychotics.
to reduce symptoms or from confusion about the dosing regimen. Excess fills also may occur when a patient receives prescriptions for antipsychotic medications from several healthcare providers who are unaware that the person is seeing other prescribers. Overuse of medications increases the risk of adverse events.

When discussing medication nonadherence among patients with schizophrenia, it is important to understand that there is no such thing as a “typical” patient with schizophrenia. Individuals differ in the type and severity of their symptoms, and in their relative risk of relapse. Some patients with less intense symptoms can maintain meaningful relationships and hold jobs. Others with more severe illness may hope to live successfully in residential communities. Patients with severe schizophrenia, however, often must be hospitalized frequently or, in the worst cases, require lifelong inpatient care.

There is no specific degree of nonadherence that causes negative consequences in every patient. Missing a single dose can put some patients at risk; for others, medical and psychiatric issues may appear after a week or more of nonadherence. Of course, patients in any population, including those with schizophrenia, occasionally will miss a dose. However, when someone with schizophrenia misses several days at a time, a healthcare provider or educator should proactively intervene to stop the cycle before serious clinical consequences arise. This is especially true for patients who don’t recognize that the medication is necessary to their well-being.

**Reasons for Nonadherence**

Patients with schizophrenia may not adhere to their prescribed medication regimens for several reasons, including the following.

**Lack of insight.** Many patients with schizophrenia have poor insight into their medical condition. They do not grasp the severity of their illness, and they may not believe that they need treatment. Some patients with schizophrenia don’t accept that they have a mental illness.

**Lack of tolerance for adverse events.** Like any medication, agents used to treat schizophrenia can be associated with uncomfortable adverse events. The older, first-generation antipsychotics in particular can cause symptoms similar to those in Parkinson’s disease, including obvious tremors and involuntary body movements. Since these symptoms are quite noticeable, they often lead to social stigma for patients, who subsequently do not want to take their medications.

The newer “atypical” antipsychotics are also associated with adverse events. While movement disorders may be less common with this group, the newer agents are sometimes associated with weight gain and metabolic irregularities. Nevertheless, recent research shows that use of the atypical antipsychotics may improve medication adherence rates.

In a study of pharmacy refill records of outpatient veterans receiving antipsychotic medications, the rates of adherence were moderately higher in patients who received atypical antipsychotics compared with those who received conventional antipsychotics (compliant fill rates at 12 months: 50.1% for conventional vs. 54.9% for atypicals). Nonadherence was considerable, however, even among the patients receiving atypical antipsychotic medications.

**Lack of access.** Some patients with schizophrenia do not adhere to their prescribed medication regimens because they are unable to readily access their medications. For some patients, just getting to a pharmacy is costly and difficult, and they may ultimately choose not to fill the prescription at all rather than battling these challenges.

Hospitalized patients with schizophrenia receive medications directly through the hospital’s ordering system. However, when they are discharged, these individuals often have

![Figure 1. In a retrospective analysis of Medicaid data, days of missed medication correlated significantly with hospitalization rates for patients with schizophrenia. (From Weiden et al. Psychiatr Serv 2004.)](image)
immediate difficulty filling their prescriptions. It is likely that patients with schizophrenia who do not keep their outpatient posthospitalization appointments will not adhere to their prescribed medication regimens.

**Lack of early therapeutic response.** Regardless of the diagnosis, any patient may become discouraged and lose faith in the medication if early improvement is not seen. Patients with schizophrenia may be especially likely to discontinue their medications if they perceive that the treatments are not providing results. In a recent study, more than one-third of patients with schizophrenia who discontinued therapy cited “poor response” or “worsening condition” as the reason for stopping their prescribed medication (see Figure 2).

**Substance abuse.** Substance abuse is a clear risk factor for nonadherence, especially among younger patients. The rate of drug abuse among patients with schizophrenia has been estimated at 47%, compared to a lifetime prevalence of about 16% in a community sample.

In addition, patients with schizophrenia and comorbid substance abuse tend to require more hospitalization and have lower adherence with treatment regimens. Alcohol and drug problems clearly contribute to relapse. The rate of drug abuse among patients with schizophrenia experiencing relapse (44%) is significantly higher than the rate in patients who regularly attended outpatient clinics. Finally, studies indicate that substance abuse rates are higher among males (79%) than females (21%).

For these reasons, psychiatric treatment facilities need to get better at identifying these dual-diagnosis patients and integrate addiction treatments with psychotic relapse management to avoid the destabilizing effects of alcohol and drug abuse on patients with underlying mental illness.

**Intervention Strategies**

Fortunately, intervention strategies can help patients with schizophrenia overcome problems with nonadherence.

**Education.** Patients with schizophrenia should be educated on treatment adherence before they receive their first dose of medication. Providers should counsel patients on the importance of taking their medications and the problems that can occur if they stop taking them. This information can be shared one-on-one between the provider and patient or in a group education setting, facilitated by the prescriber or by other treatment team members. Facilitators can furnish information both orally and through printed materials, such as take-home leaflets and brochures.

**Behavior modification.** Healthcare providers and educators can tailor behavior modification programs to fit the specific needs of patients with schizophrenia. For example, they might instruct patients on how to use pillboxes or how to get timely refills.

Using behavior modification techniques, healthcare providers and educators can teach patients specific tactics that will make adherence more likely. For example, they may advise patients to place pillboxes on their sinks before they go to bed so that the medication will be incorporated into their daily morning routines. Patients can also be taught how to communicate more effectively with prescribers, so that they can work together to develop a medication routine the patients can understand and follow. Using role-play activities, patients may practice with educators to effectively describe adverse events or barriers to medication access. These skills can improve communication between the patient and the provider during short follow-up appointments so that any problems can be addressed before they lead to nonadherence. Additionally, a patient may be encouraged to write down questions or concerns to discuss with the prescriber so that these issues are not forgotten during the appointment.

**Affective interventions.** Affective interventions appeal to patients’ emotions. For example, healthcare providers and educators may point out that taking medications as
prescribed increases the possibility that patients can live more independently. Affective interventions also appeal to caregivers and families. When caregivers and family members understand the serious consequences that can occur because of medication nonadherence, they may be more proactive in helping loved ones adhere to their prescribed medication regimens.

Other interventions. Providers can use a variety of other pharmacologic, psychological, social/family, and service tactics to increase adherence to prescribed medication regimens, including:

- simplifying the dosing regimen, including optimizing the dose before adding on multiple medications;
- changing the medication to reduce adverse events (or adding another agent to manage unwanted effects if switching is undesirable);
- encouraging social support networks; and
- ensuring continuity of care when transferring from one healthcare system to another. (For example, providing an adequate supply of medications to last until the initial postdischarge outpatient appointment. Along these lines, the outpatient provider should be forwarded a copy of the inpatient discharge summary whenever possible.)

A Combined Approach
Most importantly, using a combination of the three main strategies—educational, behavioral, and affective interventions—may increase the likelihood of adherence success, with additional secondary gains such as reduced relapse rates, decreased hospitalization rates, decreased psychopathology, and improved social functioning.14,15

In addition, healthcare providers and educators should engage in a combination of these three strategies on a regular basis, regardless of whether patients indicate that they have been adherent with their prescribed medication regimens. Ideally, these strategies should be employed at every interaction between the provider and the patient. But it is imperative that these strategies be used if there is any pattern of nonadherence. And it is equally important for prescribers to continually assess whether an intervention is required because of possible nonadherence.

Providers must be constantly vigilant when it comes to nonadherence because, for most patients, schizophrenia is a lifelong illness. Early intervention is critical to success. If providers wait too long to intervene, the likelihood of success diminishes significantly.

The Importance of the Therapeutic Alliance
The therapeutic alliance between the provider and patient is critical to ensuring adherence to the prescribed medication regimen. If patients feel comfortable with their provider and are confident that the prescriber is working with them to improve their well-being, they will be more likely to adhere to their prescribed medication regimens.10

While the terms “adherence” and “compliance” often are used interchangeably, they each have specific meanings when seen in the context of the therapeutic relationship. “Compliance” implies that patients have no control or say in the provider’s decision to prescribe medications for the treatment of schizophrenia. However, “adherence” connotes patient participation in deciding the treatment, conveying a belief that the patient and the provider are working together to arrive at a consensus on the optimal treatment plan. Of course, this mutually beneficial relationship doesn’t always pan out in practice. For patients with severe schizophrenia, collaboration may not always be possible, and prescribers must exercise more control over the choice of medication regimen.

It is important to understand that patients’ reports of their own treatment adherence are not always reliable. Patients with schizophrenia may declare that they are taking their medications when they are not, misrepresenting their behavior either intentionally or because of confusion and cognitive difficulties. They may make statements about adherence to please their prescribers or because they think that it is the appropriate thing to say. Patients with schizophrenia, like patients in any other population, also tend to overestimate the extent of their adherence. While relying on
patient self-reporting of medication adherence is the quickest way to assess the situation, it is not always the most accurate.\textsuperscript{9,16} Instead, providers also should seek independent assessment, evaluation, and verification of adherence from caregivers, family members, or other sources. For example, healthcare providers and educators should monitor pharmacy refill records to determine if there are delays in picking up or refilling prescriptions. In addition, healthcare providers should look for any “red flags” in the attitudes and actions of patients with schizophrenia, including a reversion to previous patterns of behavior or worsening of residual symptoms, which could indicate nonadherence and suggest the need for immediate intervention.

Concluding Thoughts
The impact of nonadherence is significant, both for patients with schizophrenia and for society as a whole. Nonadherence is clearly one of the most significant barriers to optimal outcomes and can lead to harmful personal, economic, and social consequences. Since psychiatric, behavioral health, and medical care for patients with schizophrenia is largely subsidized by the public sector, nonadherence can result in waste of tax dollars and other public resources as well as continued, needless suffering for patients. Nonadherent patients with schizophrenia often end up in legal custody or in emergency rooms, suffering a serious blow to their recovery and attainment of life goals.

Increasingly, many healthcare systems may be able to use pharmacy data to identify poor medication adherence in their patients with schizophrenia. Based on pharmacy refill records, providers and caregivers can determine which patients with schizophrenia may not be adhering to their prescribed medication regimens and who, therefore, are more likely to be rehospitalized for psychiatric as well as medical reasons.\textsuperscript{11} For schizophrenia and mental disorders in general, the most significant direct costs are due to hospitalization, both for the initial episode of the disease and for subsequent relapses. In fact, several analyses have shown that lower rates of treatment adherence in patients with schizophrenia are a greater risk factor for hospitalization than any other determinant.\textsuperscript{3,8,17}

Every time nonadherent patients with schizophrenia use social and medical services provided by public funding, the risk is high for an unfortunate and theoretically preventable waste of resources. By considering the factors leading to nonadherence and adopting a comprehensive strategy for improving adherence rates, we can significantly improve the management of schizophrenia, to the benefit of patients and society.

References