Adherence to Antipsychotic Medications

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Taking antipsychotic medication as prescribed is one of the best means patients have of managing psychotic symptoms and preventing relapse. Yet, for various reasons, patients may discontinue taking their medication or skip doses, either occasionally or frequently. Among patients treated with conventional neuroleptics, approximately 40% stop taking their antipsychotic medication within 1 year, and about 75% stop taking the medication within 2 years. Although adverse effects play a large role in a patient's decision to discontinue antipsychotic therapy, other factors also have an effect. Using the health belief model, clinicians can assess the relative impact of various factors on medication adherence. This model posits that adherence to treatment is determined by the patient's assessment of the perceived benefits of treatment and risks of illness versus the costs of treatment (including adverse effects such as weight gain). Other factors in the decision are barriers to adherence and cues to act (i.e., reminders to take medication). Patients who believe the risks of treatment outweigh the benefits are likely to discontinue their medication and are candidates for intervention to increase adherence.

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No medication is effective unless taken, and patient adherence to prescribed antipsychotic medication is often dismal. Studies of the older typical antipsychotics suggest that approximately 40% of patients stop taking their prescribed antipsychotic medication within 1 year[1] and about 75% of patients discontinue their medication within 2 years.[2] Even with depot medication, about 25% of patients stop keeping scheduled appointments and no longer receive depot injections within 1 year after starting treatment.[1]

Adherence to a medication regimen requires that the patient obtain the medication and take the medication as prescribed. Adherence is seldom perfect, with most patients skipping doses occasionally or frequently (occasional missed doses are usually not considered nonadherence in clinical studies). Some patients may take an incorrect dose or take the correct dose at the incorrect time. Any number of obstacles might prevent a patient from adhering to a prescribed regimen.

The most serious potential consequence of discontinuing a prescribed antipsychotic medication is that psychotic symptoms will emerge or worsen. As many as 75% of patients who stop taking their antipsychotic medication experience significant symptom exacerbation over the course of a year, compared with only 25% of those who consistently take their medication.[3] The consequences of symptom exacerbation can be serious. Of particular concern is the increased risk of potentially dangerous behaviors, including aggression toward oneself and others and damage to property.[4] In addition, numerous studies suggest that repeated symptom exacerbations, especially early in the course of a psychotic illness, can worsen the course and prognosis of the disease.[5] Symptom exacerbations can also lead to antipsychotic treatment resistance and development of chronic psychosis.[6] Worsening symptoms increase the health care costs associated with the illness, because of the greater need for hospitalization and use of emergency services. Given the high rates of medication nonadherence, together with the high risk of symptom exacerbation and its resulting consequences, the reasons for lack of adherence to antipsychotic medications clearly need to be identified and addressed.

Patient adherence to a medication regimen is usually influenced by a number of competing factors, with some increasing and others decreasing the likelihood that a patient will take the medication as prescribed. Adverse effects are a commonly cited reason for nonadherence.[7] Because of their improved adverse effect profile, including a decreased risk of extrapyramidal symptoms, the atypical antipsychotic medications, including risperidone, olanzapine, quetiapine, and clozapine, offer important advantages over conventional neuroleptics.[8–13] Weight gain, however, has emerged as a troublesome and potentially serious adverse effect of some newer antipsychotics, particularly clozapine and olanzapine.

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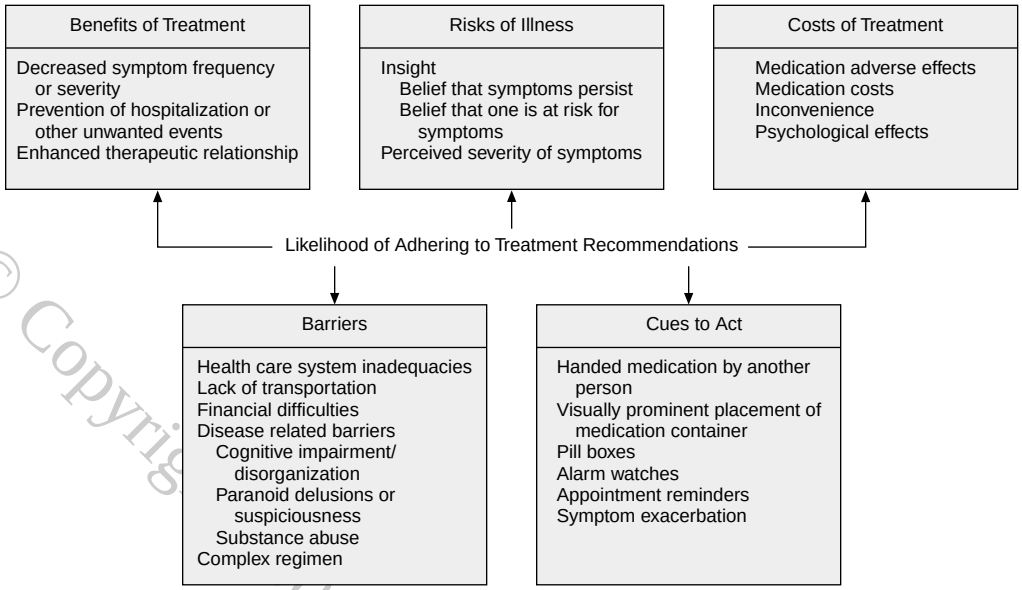
Figure 1. Modified Health Belief Model



HEALTH BELIEF MODEL

The health belief model,[14] originally proposed to explain adherence to vaccinations and other types of preventive health care, may be helpful in examining treatment adherence in patients with psychotic illness and can be used by clinicians to enhance treatment adherence in specific patients.[15] A modified version of the health belief model is shown in Figure 1. At the center of the model is the likelihood that a patient will adhere to treatment recommendations. Factors that positively or negatively affect adherence, including the benefits of treatment, risks of illness, costs of treatment, barriers, and cues to act, make up the rest of the model.

The health belief model posits that patients weigh the perceived benefits of treatment against the perceived risks of illness and costs of treatment. Because the treating clinician and the patient may not define the potential benefits of treatment and risks of illness in the same way, the clinician must try to understand the patient's treatment goals. For example, the clinician may target reduction in paranoid delusions, while the patient seeks decreased anxiety as a benefit of medication. For some patients, symptom reduction may not be considered a potential benefit of treatment. Lack of insight is characteristic of schizophrenia and similar psychotic illnesses, and patients may be unaware of their symptoms, the risk of relapse, and illness-related impairment of functioning. For these patients, the benefits of treatment may be pleasing a family member or health care provider or staying out of the hospital rather than symptom reduction.

Most patients believe there are certain costs or risks of taking medications chronically. These potential costs include adverse effects, inconvenience, and financial expense. Chronic medication use is also a daily reminder of an unwanted illness, which has psychological costs for some patients.

Certain barriers can decrease the likelihood of medication adherence even if patients are willing to take antipsychotic medication. These barriers include lack of transportation to clinical appointments or to the pharmacy and lack of funds to pay for the medication. Another barrier is an inability to remember to take the medication consistently, which is a particular problem for patients with severe cognitive deficits and those with complicated medication regimens.

Many patients require cues to remember to consistently take the right dose at the right time. These cues can be simple, such as placing the medication in an easily visible spot (next to their toothbrush or in front of the kitchen sink, for example) or using pillboxes to help ensure correct dosing.

For patients who must take medication chronically, most at least occasionally miss a dose or 2 of medication. For some, intermittent nonadherence is accidental, such as forgetting to take along medications when away from home. For others, especially those who are ambivalent about taking medication, adherence is unlikely unless the circumstances are optimal, such as having a family member offer the medication. Some patients may be willing to take their medication, but lack the organizational skills required to take medication consistently because of cogni-

Table 1. Health Belief Model and Medication Adherence

Perceived benefits of treatment
Belief that medication does or does not help in some way[16–22]
Perceived costs of treatment
Adverse effects
Weight gain[23,24]
Dysphoric subjective response[17,21,25–29]
Akathisia[21]
Parkinsonian symptoms[16,25,30,31]
Dystonic reaction[21]
Somnolence[21,23,32]
Impaired cognition[21,24]
Overall severity of adverse effects[20,30,33,34]
Dislike idea of taking medication[20,35]
Perceived risks of illness
Rehospitalization[32]
Insight[25,36]
Barriers
Costs[37]
Substance abuse[22,38,39]
Complexity (decanoate injections versus oral administration)[40]
Disorganization, cognitive deficits, psychosis[41–43]
Difficulty getting to appointments or having prescription filled[22,37]
Social isolation[30]
Cues to act
Family support[44,45]
Reminders (to prevent forgetting)[22]
Increased symptoms[32]

tive or other illness-related deficits. Other patients may stop taking medications for brief periods to determine whether there is a relationship between the medication and adverse effects or treatment effects. Stopping medications to test efficacy is especially common among patients whose symptoms are not active, because they seek to determine whether continued use of the medication is necessary to suppress symptoms. Unfortunately, patients may wait for symptoms to recur before starting to take their medication again, an ineffective strategy in psychotic illness.

ANTIPSYCHOTIC MEDICATION ADHERENCE

Most studies examining medication adherence in patients with psychotic illness assume that adherence and factors affecting adherence are fairly stable. However, clinical experience suggests that medication adherence is a dynamic process that is likely to change over time and varies substantially from patient to patient. For example, a patient who is not experiencing any adverse effects will not consider side effects a risk of their prescribed medication. In contrast, a patient experiencing an unpleasant adverse effect, such as akathisia, will understandably weigh the impact of this adverse effect on his or her quality of life compared with the impact of the symptoms that the medication is treating. This in part explains why no one factor can predict adherence in a group of patients.

Factors that may affect a patient's decision to adhere to a medication regimen can be considered in the context of the health belief model, as shown in Table 1.[16–45] Studies indicate that the perceived costs of treatment, especially adverse effects, play a considerable role in medication adherence.[32] In addition to the severity of adverse effects, insight into illness[25,36] and perceived benefits of treatment[16–22] influence some patients' decisions to take medication. Having cues to act, especially family member support with medication administration,[44,45] may increase adherence. Many patients appear to weigh the risks and benefits of continued adherence to an antipsychotic medication regimen. For patients who see a marginal potential benefit from the medication or a low risk of symptom exacerbation, unpleasant adverse effects may tip the balance toward nonadherence. However, patients' evaluation of these risks and benefits is likely to change over time, as the patients become more familiar with their illness or as the severity of adverse effects changes. For example, early in the course of an illness, patients may believe they are at low risk for symptom exacerbation if they discontinue their medication. Patients may reconsider their risk of relapse if they experience repeated symptom exacerbations when they stop taking their medication. Similarly, a small amount of drug-induced weight gain early in the course of illness may be acceptable, but continued weight gain and development of obesity is likely to be unacceptable.

Newer antipsychotic medications are less likely to cause several of the adverse effects associated with conventional neuroleptics, which may increase medication adherence. For example, early evidence suggests that atypical antipsychotics may be less likely to cause a subjective dysphoric response, which has been shown to be a cause of medication nonadherence. However, no published studies have examined adherence with newer antipsychotics or have compared adherence with newer antipsychotics versus conventional neuroleptics. Some indirect evidence indicates that outpatient adherence may be higher with atypical antipsychotics than with conventional neuroleptics, as suggested by studies that have found decreased health service utilization and decreased hospitalization in patients treated with risperidone or olanzapine compared with haloperidol.[46,47]

Although several studies suggest that adverse effects significantly affect a patients' adherence to a medication regimen,[16,17,20,21,23–35] fewer studies have considered the impact of specific adverse effects (other than extrapyramidal symptoms and subjective dysphoric response) on medication adherence. As an adverse effect, weight gain has been included in only a few studies examining adverse effects and medication adherence. In one investigation,[23] 44 patients receiving depot antipsychotics were asked to rate which adverse effects caused the most subjective distress. Of 16 adverse effects listed, weight gain was rated the third most distressing adverse effect, with only sedation and asthenia rated more severe. In a study of 51 patients with bipolar disorder receiving maintenance lithium and other psychotropic medications,[24] weight gain was rated as the most distressing of 27 adverse effects listed and the most

likely to contribute to poor adherence in the future. Self-reports of poor adherence to prescribed medication regimens have been significantly associated with the overall severity of adverse effects,[20,30,33,34] but most studies have not addressed severity of weight gain specifically. One study found that obesity was related to medication nonadherence. In this study of 76 patients with bipolar disorder,[48] 24% stopped taking maintenance lithium because of adverse effects, most commonly obesity and impaired cognition, even though most of these patients believed that lithium was helpful in preventing symptom recurrence. Thus, studies that have specifically examined the impact of weight gain on medication adherence suggest that weight gain may increase the risk of treatment nonadherence.

Therapeutic interventions that address specific components of treatment adherence can increase the likelihood that patients will take their medication as prescribed[14,25,49–51] and may encourage patients to discuss their concerns about adverse effects with their physician.[52] Successful interventions focus on patients' beliefs about treatment efficacy, treatment risks, and risks of illness and seek to identify and address barriers to medication adherence. A growing body of empirical evidence suggests that clinicians can use psychoeducational and cognitive behaviorally oriented psychotherapeutic strategies to improve medication adherence.

A CASE EXAMPLE

Ms. A, a 29-year-old woman, began experiencing psychotic symptoms at age 27 while in graduate school. Her symptoms included bizarre and religious delusions, disorganized speech, and disorganized behavior, and she met the criteria for schizophreniform disorder. The patient was initially hospitalized. During the first few days of her hospitalization, she demonstrated poor insight into her illness and required encouragement from staff and family members to take her prescribed antipsychotic medication (olanzapine, 10 mg/day). Ms. A was discharged from the hospital after 2 weeks. After 10 weeks of antipsychotic treatment, her psychotic symptoms remitted. Initial adverse effects of olanzapine included mild sedation that resolved after 3 weeks and transient elevations in liver function test results that subsequently returned to normal. At the initial hospitalization, her weight was low normal (body mass index [BMI]* = 19 kg/m^2). After starting olanzapine therapy, she gained 3 to 7 lb a month, and after 6 months of treatment had gained 35 lb (BMI = 24 kg/m^2).

Ms. A and her psychiatrist met every 1 to 2 weeks for outpatient therapy and pharmacologic management. Two family meetings were held that focused on education about psychosis and its treatment. Individual therapy initially focused on insight and compliance and included education about symptoms and treatment. As Ms. A's symptoms resolved, she began to understand that she had experienced a psychotic episode and needed medication to control her symptoms. Initially, a family member gave her the antipsychotic medication each night, but as she developed good insight about her psychotic disorder, she began taking the medication on her own. She stated she had no trouble remembering to take her medication and kept the bottle next to her bed to remind her to take her pill just before going to sleep. In therapy, she also explored the impact the psychotic illness had on her life and voiced a desire to "forget that this had ever happened." She began to express doubts that she was at ongoing risk of relapse, and her confidence that her symptoms would not return increased as the length of symptom remission increased. She was told that she had a 70% chance that her symptoms would return if treatment was discontinued[15,53] and that antipsychotic medication was her best protection against symptom recurrence.[3] Aside from weight gain, she reported no other adverse effects from olanzapine. She was mildly distressed about her increasing weight and attempted to control her food intake and exercise more, but without success. She declined to participate in a physician-recommended diet and exercise program, stating she hoped to "lose weight on my own." Her health care insurance covered most costs of treatment, but the 20% copayment for patient visits and medication costs was moderately difficult for her to budget. Her family supported her continued use of medication to prevent re-emergence of symptoms.

Approximately 6 months after her initial hospitalization and 3 months after symptom remission, Ms. A unilaterally discontinued taking olanzapine because she believed she was no longer at risk of relapse. Within 1 week after stopping treatment, her psychotic symptoms, including delusions and disorganized speech and behavior, returned, and Ms. A was hospitalized. She began taking olanzapine again in the hospital and was discharged after 3 weeks. Her symptoms were in remission within 3 months after hospital discharge. Outpatient therapy continued to focus on her understanding of the illness. At this point, the patient believed she had a psychotic illness and that she was at high risk for symptom re-emergence if she stopped taking olanzapine.

Ms. A continued to experience gradual weight gain, with her BMI increasing from 24 to 26 kg/m^2 over the next 2 months. She was becoming concerned about the continued increase in weight despite her attempts to control food intake, and this adverse effect was addressed as part of her treatment. In particular, the health risks of continued weight gain, such as heart disease and diabetes, and potential interventions to stabilize or decrease her weight were

*Optimal BMI is 19 to 25 kg/m^2. Health risks related to weight increase as BMI increases. Health risks secondary to obesity emerge with a BMI greater than 25 and become significant when the BMI is 27 or greater.

emphasized. Potential interventions included switching to another antipsychotic medication with less propensity for weight gain, participating in a formal diet or exercise program, and continuing attempts to decrease food intake and increase exercise on her own. Ms. A agreed to keep a food diary and to try again to decrease her food intake, but this had no effect on her continued gradual weight gain. She decided to try a new antipsychotic with the hope that another medication would be less likely to cause weight gain. She was started on risperidone therapy, and olanzapine was tapered off and discontinued.

While taking risperidone 3 mg/day, Ms. A gradually lost weight, and her weight stabilized at about 7 lb over her initial weight (BMI = 20 kg/m^2). Her psychotic symptoms have remained in remission and have not recurred over the past 6 months. The patient continues to believe she is at some risk for symptom re-emergence because of her experience with relapse. Ms. A has reported no adverse effects with risperidone. The financial costs of her medication and therapy are mildly burdensome, but her family supports her treatment.

Comment

The health belief model provides a helpful framework for understanding Ms. A's initial adherence, nonadherence, and return to adherence with her prescribed medication and the interventions required to maintain adherence. Initially, Ms. A did not perceive that she had an illness and thus did not see any potential benefits to treatment. She took her medication at the urging of family members, with the belief that taking the medication would hasten hospital discharge and please her family. A cost of treatment was that it could be construed by others as a tacit acknowledgment on her part that her recent "revelations" and other experiences were part of an illness. Barriers to adherence were her significant cognitive disorganization, which would have made it difficult for her to adhere, even if she was willing to take medication. She required substantial cues to take her medication; during hospitalization, a staff member had to hand her the pill and watch her ingest the medication.

With time, symptom remission, and psychotherapy, the patient gained insight into her illness and believed she had an illness and that medication controlled the symptoms. She was concerned about the psychological costs of treatment (a reminder that the disturbing symptoms had occurred in the past) and financial costs of treatment. No barriers to treatment were identified. She prominently placed the medication bottle next to her bed as a reminder to take her pill.

Over time, the relative balance between her belief in the need for treatment and the costs of treatment began to change. As her symptoms continued in remission, she believed symptom re-emergence was less likely, and the financial and psychological consequences of treatment first equaled and then surpassed her perception of the potential benefits of treatment. At this point, she chose to discontinue her medication, despite recommendations to continue the treatment.

When her symptoms recurred after she stopped the medication, her perception of the need for treatment and the costs of treatment again changed. She acknowledged her need for medication to control acute symptoms and to prevent symptom re-emergence. With therapy, she saw fewer psychological costs of treatment. Continued weight gain was a new cost of treatment, however, and one that posed health risks. Ms. A and her psychiatrist were able to address this adverse effect by switching her medication from olanzapine to risperidone.

CONCLUSION

A patient's beliefs about the relative risks and benefits of treatment determine his or her willingness to take medication. For this reason, clinicians should attempt to understand a patient's beliefs about the need for and risks of antipsychotic treatment. This is especially true for chronic illnesses such as schizophrenia and other psychotic disorders, where the goal of long-term treatment is usually to prevent symptom re-emergence.[54] To enhance medication adherence, patients should become actively involved in setting treatment goals, and clinicians should identify the possible costs of treatment (including weight gain and other adverse events) and barriers to adherence and help patients develop reminders for taking their medication as prescribed.[14,25,49–51] Long-term adherence to an antipsychotic medication regimen typically results from active collaboration between the patient and psychiatrist, a relationship that allows treatment to be modified over time to meet the patient's changing needs.

Drug names: clozapine (Clozaril and others), haloperidol (Haldol and others), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal).

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