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Predictors of Noncompliance in Patients With Schizophrenia

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Background: Around 50% of patients with schizophrenia do not fully comply with treatment, and noncompliance is linked to relapse, rehospitalization, poor outcome, and high economic costs. The health belief model views noncompliance as a decision made by the patient, arrived at after weighing the perceived risks and benefits of treatment.

Data sources: A MEDLINE search for the years 1980–2002 using combinations of the keywords *schizophrenia*, *compliance*, *adherence*, *antipsychotics*, *tolerability*, and *side effects* was used to identify articles investigating the factors influencing compliance in schizophrenia.

Results: Many factors influence compliance, including those that affect patients' beliefs about their illness and the benefits of treatment (e.g., insight into illness, belief that medication can ameliorate symptoms), perceived costs of treatment (e.g., medication side effects), and barriers to treatment (e.g., ease of access to treatment, degree of family or social support). Medication side effects that are distressing to patients and linked to noncompliance include extrapyramidal side effects, neuroleptic dysphoria, akathisia, sexual dysfunction, and weight gain. Compliance can be improved by cognitive-behavioral therapies, such as compliance therapy, and other psychosocial interventions associated with improved social functioning and a lower risk of rehospitalization. Treatment adherence may also be improved by use of atypical antipsychotics with few perceived side effects.

Conclusion: By considering the factors leading to noncompliance and adopting a comprehensive strategy for improving compliance, encompassing psychosocial intervention and optimum choice of medication, the management of schizophrenia could be greatly improved.

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Patient compliance may be defined as "the extent to which a person's behaviour coincides with the medical advice he/she has received."[1(p167)] There is some controversy surrounding the term *compliance*, since it implies that the patient should passively obey the advice of the doctor,[2] and more neutral terms such as *adherence* or *concordance* are therefore sometimes used. However, *compliance* is long-established and widely recognized and will be used throughout this review.

Noncompliance with treatment, i.e., anything less than full compliance, can take many forms, such as failure to attend clinics, refusal to enter the hospital, failure to begin a treatment program, premature cessation of treatment, and incomplete performance of instructions.[1] With specific reference to medication, noncompliance encompasses failure to fill a prescription, refusal to take medication, stopping medication prematurely, and taking the wrong amount of medication at the wrong times.

At least half of patients prescribed long-term medication for chronic diseases do not fully comply with treatment,[3] and the proportion is remarkably consistent across diseases as disparate as epilepsy, arthritis, diabetes, hypertension, and asthma.[4,5] Noncompliance is particularly likely when the treatment goal is to prevent symptom recurrence or illness relapse. Schizophrenia is no exception to this pattern of treatment compliance (Table 1).

Improving compliance with treatment is a major challenge in the management of schizophrenia and has been recognized as an important issue for more than a quarter of a century.[8] This article reviews the factors affecting compliance and discusses possible strategies for improving medication compliance in the treatment of schizophrenia.

Relevant data relating to treatment compliance in schizophrenia were identified through an online (MEDLINE) search for the years 1980–2002 using combinations of the keywords *schizophrenia*, *compliance*, *adherence*, *antipsychotics*, *tolerability*, and *side effects*.

CONSEQUENCES OF NONCOMPLIANCE

It has been argued that the rate of poor outcome in schizophrenia is substantially higher than could be achieved if all patients received optimal treatment.[9] For

Table 1. Prevalence of Noncompliance in Patients With Schizophrenia

Reference	Noncompliance, %
Young et al, 1986[3]	41 (median rate in 21 published studies)
Curson et al, 1985[6]	40
Corrigan et al, 1990[7]	48 (first year of treatment), 74 (first 2 years of treatment)

example, the 1-year relapse rate of patients with schizophrenia on maintenance treatment is about 20% to 30%,[10] whereas relapse rates of 10% to 15% can be achieved in patients receiving optimal treatment.[9,10] This compares with the very high risk of relapse (up to 70%) in patients not receiving treatment.[10]

Many factors affect outcome in schizophrenia treatment, and they have been reviewed comprehensively.[11–13] Poor compliance or noncompliance with treatment is considered to be one of the most important factors,[2] being strongly associated with an increased risk of relapse,[6,11,14,15] greater likelihood of hospital admission,[16,17] and a longer duration of hospitalization once admitted.[18] Such negative impact of noncompliance on long-term outcome was demonstrated convincingly by Helgason[19] in a 20-year follow-up study of patients with schizophrenia in Iceland. In addition, poor compliance may negatively impact prognosis, especially in patients who are in the early stages of schizophrenia.[15,20]

A high proportion of hospital admissions may be attributable to noncompliance. In a 7-year follow-up study of patients receiving depot antipsychotic medication, all the noncompliant patients were admitted to the hospital during the study, compared with 50% of the compliant patients.[6] A study of "revolving door" schizophrenic patients in the United States found that medication noncompliance was the most common reason for hospital admission, cited as the cause for 50% of patients.[21] Similar results were reported by Jeffreys et al.[22] in a United Kingdom survey, who found that the reason for the most recent hospital admission was medication noncompliance for 55% of patients.

The economic cost of noncompliance has not been calculated, but some estimates suggest that it could account for up to one quarter of the health service expenditure on treating schizophrenia, largely because of the high cost of hospital care.[2] As the total annual cost of schizophrenia treatment has been calculated at almost £400 million in the United Kingdom,[23] and over $10 billion in the United States,[24] the worldwide cost of poor compliance could amount to billions of dollars per year.[9]

MODELS OF COMPLIANCE

One model of compliance is derived from the "sick role" concept. As described by Bebbington,[2] sick persons partially or wholly abandon their normal social role (e.g., by taking time off work, staying in bed, or not performing tasks of household management or child care) and move into the sick role, in which they are looked after by other people. The doctor is viewed as an expert who sanctions the patient's entry into the sick role and prescribes behavior that will help the patient recover from illness and return to his or her normal social role.[25] While this model allows for patient input regarding subjective experiences with illness or with treatment, failure to follow the advice of the physician is most often ultimately seen as a failure on the part of the patient, for example, as due to making self-defeating choices (as when patients do not comply with prescribed diets in diabetes or hypertension), to unreasonable beliefs about the illness or treatment, or to some other failing on the part of the patient, such as lack of insight or cognitive impairment.[26]

An alternative view is proposed by the "health belief" model. The health belief model proposes that patients weigh the perceived benefits of the treatment against its perceived costs and will comply with the instructions if they believe the benefits to exceed the costs, assuming that barriers to compliance do not overwhelm the patient.[2] Originally developed to explain compliance with preventive treatments such as vaccines, the health belief model has been modified to explain compliance with treatment in chronic diseases, including schizophrenia, and may offer guidelines to improving compliance in schizophrenia.[11,27] Within the health belief model, beliefs about potential benefits of treatment in part depend on the patient's beliefs about his or her illness, as well as beliefs that the treatment may impact the severity of symptoms or affect risk of future symptoms or illness. Patients, especially those with reduced insight into illness, often will consider other, non–illness-related benefits of treatment in their decision to comply, for example, pleasing a trusted family member or avoiding an unwanted event (e.g., hospitalization or an injection), or compliance as a means to an end (e.g., if compliance is rewarded with something else the patient wants). Thus, the perceived benefits of treatment include both the potential impact on illness as well as other non–illness-related benefits. Similarly, the costs of treatment may include unwanted side effects, but also may include other costs related to taking a medication, such as how the medication may remind the patient of his or her chronic disease or embarrass the patient if other people observe the pill-taking, and the use of limited financial resources. The health belief model may offer guidelines to improving compliance in schizophrenia. Within this model, the clinician's therapeutic stance emphasizes collaboration in treatment decision making.[2] Important treatment goals include development of an understanding of the patients' beliefs about the illness, and the patients' perception of the impact of illness and treatment on their lives. The clinician's therapeutic stance emphasizes collaboration in treatment decision making.[2]

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The health belief model thus emphasizes the patient's rather than the physician's understanding of illness and of treatment options as pivotal in the patient's decision to adhere to treatment.

FACTORS AFFECTING COMPLIANCE IN SCHIZOPHRENIA

Research studies indicate that several factors may influence the likelihood of treatment compliance in patients with chronic psychotic disorders. Within the health belief model, these factors can be defined as those concerning patients' belief that they have a psychotic disorder and/or that treatment may offer benefits, the perceived cost of treatment, barriers to treatment, and the availability of reminders or cues to comply with treatment (see Figure 1 in reference 13, p. 26).

Perceived Risk of Illness and Benefits of Treatment

The belief that treatment may reduce the severity of symptoms or prevent relapse often influences compliance in some patients. For example, studies have shown better compliance in patients who believed that medication helped prevent relapse or that they were personally susceptible to rehospitalization. Poor compliance has been reported in patients with a lack of insight and awareness of their illness[1,11,28] and in those who believed that medicine should be taken only when they were feeling ill, that medication would cause physical harm, or that taking medicine is unnatural.[11] However, although awareness of illness increases likelihood of treatment compliance, other factors may critically influence treatment compliance, and thus insight into illness or belief in the potential benefit of treatment is not required and is not necessarily found in all patients who comply with treatment.[29]

In particular, patients may regard the relationship with their health care provider as a major benefit of treatment and take medication due to the recommendation of a trusted health professional. Several studies have reported that improved medication compliance is associated with a better relationship between the physician and the patient.[11] In one study, the rate of noncompliance was 74% in patients whose relationship with their therapist was fair or poor, compared with only 26% in patients who had a good relationship.[30] Patient satisfaction and understanding of need for treatment may be related to the effectiveness of communication between doctor and patient and are in turn linked to a greater willingness to follow the doctor's advice.[26]

The health belief model predicts that compliance should also be influenced by the patient's perception of the beneficial effects of medication. This aspect has received less research attention than the study of side effects, but it has been reported that perceived benefits of medication have a greater impact on compliance than side effects.[1] One problem in the treatment of schizophrenia is that relapses often do not occur for several months after the patient stops taking medication.[31] Patients may therefore fail to associate noncompliance with the loss of the drug's beneficial effects.

Perceived Costs of Treatment

Side effects. Part of a collaborative clinician-patient interaction involves providing education about and monitoring of side effects. There is a growing awareness of the potential health risks associated with atypical antipsychotics, especially weight gain (and related risks of cardiovascular disease, osteoarthritis, diabetes, and social consequences), endocrine abnormalities (e.g., hyperglycemia, hyperlipidemia, diabetes, hyperprolactinemia), and cardiovascular side effects. It is important to remember that patients would have no reason to know about some of these potential medication risks unless explicitly informed by their health care provider (e.g., elevated prolactin, hyperglycemia, corrected QT interval prolongation) or may not recognize a medical complication, such as weight gain, as a side effect.

A side effect may be clinically innocuous but nonetheless embarrassing or distressing and have a major impact on quality of life (e.g., galactorrhea, sexual dysfunction). From the viewpoint of understanding compliance, those side effects that cause subjective distress to the patient are likely to be the most influential on willingness to take medication, and there may be considerable individual differences in the subjective tolerability of an antipsychotic.

Antipsychotic side effects are consistently associated with noncompliance or reluctance to accept treatment in patients with schizophrenia. High scores on side effect rating scales have been reported to predict noncompliance in several studies, and the proportion of patients citing side effects as their primary reason for noncompliance ranges between one quarter and two thirds (reviewed by Fenton et al.[11]). Eleven of 12 studies reviewed by Young et al.[3] reported a direct association between side effects and noncompliance. For example, in a survey of 346 noncompliant schizophrenic patients who were asked to state their main reason for stopping medication,[26] the most common reason given was medication side effects, followed by a belief that the medication was unnecessary. Only about 10% of patients said they forgot to take the medication. Available research suggests that extrapyramidal side effects (EPS) and the related phenomena of neuroleptic dysphoria, sedation, weight gain, and sexual dysfunction are the side effects most likely to have negative effects on compliance with antipsychotic medication.[31–33]

Negative subjective response. The subjective response to antipsychotics could be defined as the effect of the drug on the patient's perception of well-being. It is recog-

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Table 2. Association Between Neuroleptic Dysphoria and Noncompliance in Schizophrenic Inpatients[a]

Type of Noncompliance	Dysphoric Group (%)	Nondysphoric Group (%)
Refused treatment and left hospital against medical advice	31	6
Planned not to comply with outpatient medication after discharge	92	11

[a]Data from Weiden et al.[33]

Table 3. Percentage of Dysphoric and Nondysphoric Patients Treated With Haloperidol or Thiothixene Who Refused to Continue Medication Beyond 14 Days[a]

Drug	Dysphoric	Nondysphoric
Haloperidol	67	20
Thiothixene	62	11

[a]Data from Van Putten et al.[36]

nized that standard antipsychotics can produce a negative subjective response (also called "neuroleptic dysphoria").[11,34] This response is variable but clearly perceived as unpleasant, and the patient may feel that the medication is worsening his or her condition.[34] It appears to be a common reaction to acute antipsychotic treatment. For example, in a sample of 55 patients in acute schizophrenic relapse, 45% had a negative subjective response during the first 24 hours of treatment with either haloperidol or chlorpromazine.[34]

This negative subjective response is strongly correlated with poor compliance.[28,29,35,36] In a study of 50 schizophrenic inpatients, neuroleptic dysphoria predicted both a reluctance to comply with treatment and an intention to discontinue therapy on discharge (Table 2).[33]

A negative subjective response early in treatment also appears to be predictive of a poor outcome. Only 23% of patients with a negative subjective response in the first 24 hours of treatment showed marked improvement in Brief Psychiatric Rating Scale score 3 weeks later, compared with 82% of those without a negative subjective response.[34]

Extrapyramidal side effects. EPS can be divided into 4 groups: akinesia or rigidity (parkinsonism), akathisia (an intense subjective feeling of restlessness, often manifested as relentless physical activity such as pacing or marching on the spot), dystonia (abnormal muscle tone or muscle spasms), and dyskinesia (abnormal involuntary movements). The appearance of EPS is a frequent reason for noncompliance, being cited as the reason for discontinuing treatment in 28% to 52% of patients receiving depot injections,[3] and present in 89% of patients with varying degrees of reluctance to accept medication.[8]

Akathisia is highly distressing, and some patients describe it as "more difficult to endure than any of the symptoms for which they had been originally treated."[3(p111)] It is not surprising that it is also closely associated with both neuroleptic dysphoria (discussed in the preceding section) and noncompliance. A study of 105 patients with relapsed acute schizophrenia found that all the patients with a dysphoric response to haloperidol experienced akathisia within the first 4 hours, whereas 84% of the nondysphoric patients did not.[36] In turn, dysphoria was strongly correlated with noncompliance, as shown in Table 3.[36] A similar relationship was reported by a more recent study,[37] which found that outpatients with schizophrenia who experienced a dysphoric response to antipsychotic therapy also had a higher incidence of EPS.

Akinesia is also a source of significant distress to patients and was associated with poor compliance in a 2-year outpatient follow-up study.[38] These 2 types of EPS appear to be the most important in terms of patient distress and therefore, probably, noncompliance. In a study of 92 inpatients, the subjective distress due to akathisia and akinesia outweighed all other forms of EPS combined.[39] Perhaps surprisingly, tardive dyskinesia (including fear of developing tardive dyskinesia in the future) was reported as a source of distress by only 11.6% of patients, compared with 20.2% for akathisia and 24.7% for akinesia.[39]

Other side effects. Sexual dysfunction and weight gain are frequently cited as major causes of noncompliance, although there have been few systematic studies in this area.[31] Antipsychotic-treated male schizophrenic patients report low sexual satisfaction,[40] and in a study of 41 patients who were asked to rate the "bothersomeness" of a list of schizophrenic symptoms and drug side effects, "impotence" was rated as worse than any of the psychotic symptoms.[41]

This is consistent with the findings of Buis,[42] who interviewed 44 patients receiving depot antipsychotics and asked them to rank the side effects they experienced in descending order of subjective discomfort. Sedation, weight gain, diminished sexual function, and akathisia were in the top 10, ranked as worse than akinesia, tremor, rigidity, or dystonia.[42]

Like EPS, sexual dysfunction and weight gain occur frequently in patients treated with standard antipsychotics. The prevalence of obesity in patients receiving depot antipsychotics is 31% to 50%, more than 4 times the population average,[43] and in a separate study, 54% of men receiving antipsychotics reported some form of sexual dysfunction.[44] Some atypical antipsychotic drugs are also associated with substantial weight gain, e.g., olanzapine at a dose of 12.5 to 17.5 mg/day was associated with a mean weight gain of over 10 kg per patient in the first year of treatment.[45]

Barriers to Treatment and Cues to Act

Some of the symptoms of schizophrenia, especially cognitive impairments, disorganization, and the presence of paranoia, may negatively impact a patient's ability or

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Table 4. Possible Strategies for Improving Compliance in Patients With Schizophrenia[a]

Type of Compliance Problem	Strategies for Improving Compliance
Patient related	Cognitive therapy
	Education about the illness
	Education about the benefits of treatment
	Memory aids (eg, phone reminders, medication timers)
	Involvement of patient in therapeutic alliance
Physician related	Education on the impact and management of side effects
	Use of a "patient-centered" approach
Social environment related	Education and support for the patient's family
	Improved access to mental health services:
	Assertive case management
	Home visits
	Convenient clinic times and places
	More attractive clinic environment
	Improved coordination between different service providers
Treatment related	Minimizing complexity of regimen
	Titration to optimum dose
	Minimizing impact of side effects on patient's life
	Providing clear instructions on medication use
	Selection of antipsychotic with minimal extrapyramidal side effects, weight gain, or prolactin effects

[a]Based on Fenton et al.[11] and Dencker and Liberman.[25]

willingness to comply with treatment.[1,3] Studies have found that patients with more severe psychopathology are less likely to comply with treatment, suggesting that severity of illness may impact adherence.[11] Severity of paranoid ideation is associated with poor compliance, theoretically related to the impact of paranoia on the ability to trust health care providers and to form a therapeutic alliance. There has been little systematic research into the impact of cognition on compliance, but it is theoretically reasonable that patients with impairments in executive function or aspects of memory may have difficulty regularly taking medication despite a full willingness to comply with treatment. In addition, studies have found that patients with more severe psychopathology are less likely to comply with treatment.[11]

Environmental factors, however, can address these obstacles to treatment compliance. In particular, the simpler the treatment regimen, the higher the likelihood of compliance,[11] e.g., compliance is enhanced by the use of depot regimens.[3] Social isolation, living alone, and poor housing are all associated with noncompliance,[3] whereas patients with the support of relatives, a spouse, or friends are more likely to comply with medication than patients lacking such support.[11] Thus, while there may be practical barriers to treatment compliance, such as cognitive impairments or disorganization that impair ability to remember to take medications, lack of money to buy medication, or lack of transport to reach treatment services, support from outside sources can sometimes be arranged to overcome these barriers, once identified.

POSSIBLE STRATEGIES FOR IMPROVING COMPLIANCE

Compliance in schizophrenia treatment has received relatively little research attention until recently.[46] However, there is growing evidence that psychosocial interventions, such as education for patients and their families, can substantially improve both compliance and outcome.[46] Improvements in compliance can be attained even in challenging subgroups such as homeless patients[47] or patients with poor insight and/or modest intellectual functioning.[48] Since compliance is a multifactorial behavior, there are many possible strategies that could be considered when attempting to improve it.[25] Table 4 lists some examples.

Compliance Therapy

Relatively few strategies for improving compliance have been subjected to systematic investigation. One that has is compliance therapy, in which inpatients are guided through the risks and benefits of accepting antipsychotic treatment using cognitive-behavioral therapy and motivational interviewing. This intervention was compared with nonspecific supportive counseling (in which therapists listened to patients' concerns but did not discuss treatment) in a randomized controlled trial.[49] Compliance was similar in both groups of patients at baseline, but improved significantly more in the group receiving compliance therapy than in the group receiving nonspecific counseling.[49] This improvement was maintained throughout the 6-month follow-up period after discharge from hospital[49] and remained evident after 18 months.[48] Moreover, patients in the compliance therapy group also showed better insight, improved global social function, and lower likelihood of readmission over the 18-month follow-up.[48] Cost-effectiveness analysis demonstrated that compliance therapy was more cost-effective than nonspecific counseling, as it was no more expensive but produced a better outcome.[50]

Other Therapeutic Interventions

Although cognitive-behavioral therapies such as compliance therapy address the important issues of patients' beliefs about illness and the need for treatment, there are other practical issues that may pose specific barriers to consistent compliance with treatment. Therapeutic interventions can be designed to address identified barriers to compliance. For example, some patients may have difficulty remembering to take medication regularly, and the use of various cues, such as pill boxes, placing medication in a visually prominent place, alarm watches, reminder phone calls, or even arranging for another person to administer the medication, can all be discussed with patients as strategies to be used to enhance compliance. In addition, a health care provider can routinely determine if spe-

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cific barriers to treatment (e.g., medication expense) exist and, if so, can develop a strategy to overcome the barrier (e.g., pharmacy-sponsored indigent care programs).

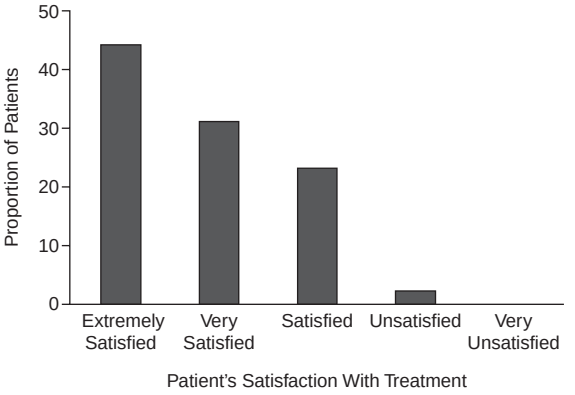
Drug Choice

Given that patients will weigh the benefits of treatment against its costs, careful consideration should also be given to minimizing the negative experiences of drug therapy. Slow dose titration and a low starting dose may help to ameliorate some side effects. Atypical antipsychotics are now considered first-line treatment for schizophrenia, given their reduced risk of EPS, generally improved tolerability, and good efficacy. Atypical antipsychotics, in contrast to typical antipsychotics, show a greater dose separation between efficacy and side effects, particularly EPS and prolactin elevation,[51] although the degree of separation varies between drugs. For example, risperidone is associated with significant prolactin elevation, even at low doses, and EPS at higher doses,[52–54] whereas quetiapine has demonstrated placebo-level incidences of EPS and prolactin elevation across its full clinical dose range and a low incidence of sexual side effects (e.g., breast enlargement, lactation, impaired sexual function) and hormonal side effects.[55,56] Olanzapine shows a less pronounced dose-related increase in EPS and prolactin elevation than risperidone, but akathisia and parkinsonism increase in frequency with higher doses, and modest prolactin elevations may persist during chronic therapy.[57]

Some atypical antipsychotics have side effects, particularly weight gain, that may influence treatment compliance. The atypical antipsychotic drugs differ in their propensity to produce weight gain, with clozapine and olanzapine having particularly pronounced effects.[58] Olanzapine has demonstrated a clear dose-related increase in weight gain, with a mean increase in weight of over 10 kg during 52 weeks of treatment in patients receiving 12.5 to 17.5 mg/day.[45] In contrast, risperidone and quetiapine have lesser effects on weight. Risperidone was associated with a mean weight gain of 2.6 kg in 1200 patients treated for 30 weeks,[59] and in a group of 455 patients treated with quetiapine monotherapy, minimal changes in weight were observed on long-term treatment, and over 18 months a mean weight gain of 1.87 kg was observed.[60]

The improved benefit:risk ratio of atypical antipsychotics for many patients compared with standard agents has the potential to contribute to increased patient acceptance and increased compliance.[61] This hypothesis has not yet been tested in randomized trials, but encouraging results have been reported from a patient acceptability study involving quetiapine.[62] A total of 129 patients enrolled in the open-label extension phase of quetiapine clinical trials for at least 6 months completed a questionnaire survey assessing their satisfaction with quetiapine treatment.

Figure 1. Patient Satisfaction With Long-Term Quetiapine Treatment (N = 128)[a]



[a]Reprinted with permission from Hellewell et al.[62]

Quetiapine was rated as "somewhat helpful," "very helpful," or "extremely helpful" by 99% of patients, and 98% said they were "satisfied," "very satisfied," or "extremely satisfied" with treatment (Figure 1).

Side effects were rated as "mild" or "nonexistent" by 126 (98%) of 129 patients, and, of the 118 patients who expressed a preference, 114 (97%) preferred quetiapine to their previous antipsychotic medication. Beneficial effects were reported on a wide range of domains related to efficacy, quality of life, and activities of daily living, and 98% of patients (all except 2) expressed a readiness to continue taking quetiapine.[62]

This study indicates that patients are aware of improvements in drug efficacy and tolerability and can clearly perceive beneficial effects of treatment. This awareness in turn was reflected in a high level of patient satisfaction and a high proportion of patients who were willing to comply with continuing treatment. While this finding should be confirmed by randomized controlled studies, it provides grounds for optimism that the combination of psychosocial support and optimal drug treatment has great potential for improving compliance with treatment in schizophrenia.

CONCLUSION

Major advances in understanding the biology of schizophrenia have occurred in the half century since the introduction of the first antipsychotic drugs, and recent years have seen the advent of several new atypical antipsychotics with substantially improved efficacy and tolerability profiles. However, there is still a need for improvement in the way that these new drugs are applied in the management of patients with schizophrenia. Noncompliance with therapy remains high and is a major contributor to relapse, poor outcome, and high costs.

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The health belief model views compliance as a decision made by the patient after weighing the perceived costs and benefits of therapy. Compliance is therefore seen to be influenced by a multitude of factors, many of which can be modified by suitable intervention. For example, the patient's beliefs about benefits, costs, and barriers to treatment can be routinely assessed, optimal choice of drug can maximize beneficial effects and minimize unpleasant ones, and psychotherapy can influence the patient's beliefs about illness and the value of medication. Strategies for improving compliance should take a comprehensive and individualized approach, addressing the patients' concerns and identified factors in a coherent program.

Within a broad strategy for compliance improvement, the choice of antipsychotic drug should be given careful consideration. Patient acceptability data indicate that a combination of high effectiveness and a low level of side effects (including those such as EPS, sexual dysfunction, and weight gain, which patients report as most distressing) results in a high degree of patient satisfaction and willingness to continue with treatment. The optimal use of drugs with a high level of patient acceptability is likely to be a valuable component of a strategy for improving compliance in schizophrenia.

Drug names: chlorpromazine (Thorazine, Sonazine, and others), clozapine (Clozaril and others), haloperidol (Haldol and others), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), thiothixene (Navane and others).

Disclosure of off-label usage: The author has determined that, to the best of her knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

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