Factors Influencing Compliance in Schizophrenia Patients

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Scientifically, compliance can be expressed as the ratio between an observed treatment behavior and given treatment standards. Although the factors that influence compliance often overlap or influence each other, it is possible to differentiate between factors that are related to the patient, the patient's environment, the treating clinician, and treatment itself. Although this differentiation is in some ways artificial, it may aid the practicing clinician in assessing the various reasons why a particular patient is likely to develop or has already developed compliance problems. The fact that a number of circumstances and parties are involved in the multifaceted issue of compliance makes it evident that patients must never be solely blamed for compliance problems. Despite the fact that compliance behavior is difficult to study from a methodological point of view, the scientific information available to date does provide many important leads for the engaged clinician to prevent and manage compliance problems. *(J Clin Psychiatry 2003;64[suppl 16]:10–13)*

Scientifically, compliance can be expressed as the ratio between an observed treatment behavior and given treatment standards.[1] This definition, if taken at face value, explains most of the difficulties of compliance research: first, we have no truly objective measure for observed treatment behavior and, second, although there are numerous clinical guidelines and recommendations for the treatment of schizophrenia, the field has not yet established definitive treatment standards for these disorders. The fact that we still lack an adequate methodology to study compliance and are forced to rely on indirect evidence, such as subjective reporting by patients or staff, pill counting, and measurements of plasma drug levels, also explains why we have so far been only modestly successful in improving compliance. This lack of direct evidence is in contrast to the enormous amount of scientific effort devoted to the topic: a recent electronic search of the National Library of Medicine online database yielded 52,433 references for the key word *compliance*. In passing, this large number of references indicates that compliance is an issue that is pertinent far beyond the treatment of patients with schizophrenia or other psychiatric disorders. When *schizophrenia* was added as an additional keyword, the list still included an impressive number of 855 publications since 1966.

On a more positive note, all of this work coming from various angles and encompassing a host of different methodologies has provided many pieces that supplement the compliance puzzle. In this article, we attempt to summarize some of the key features of compliance behavior. When reviewing the available literature, it is interesting to note that, although findings stem from different types of studies, some of which investigated predictors of good compliance and some of which investigated indicators of compliance problems, the conclusions from these reports are very similar.

FACTORS INFLUENCING COMPLIANCE

Although the factors that influence compliance (Figure 1) often overlap or influence each other, it is possible to differentiate between factors that are related to the patient, the patient's environment, the treating clinician, and the treatment itself. Although this differentiation is in some ways artificial, it may aid the practicing clinician in assessing the various reasons why a particular patient is likely to develop or has already developed compliance problems.

Patient-Related Factors

Certain demographic characteristics have been linked to compliance behavior. Age is a somewhat controversial

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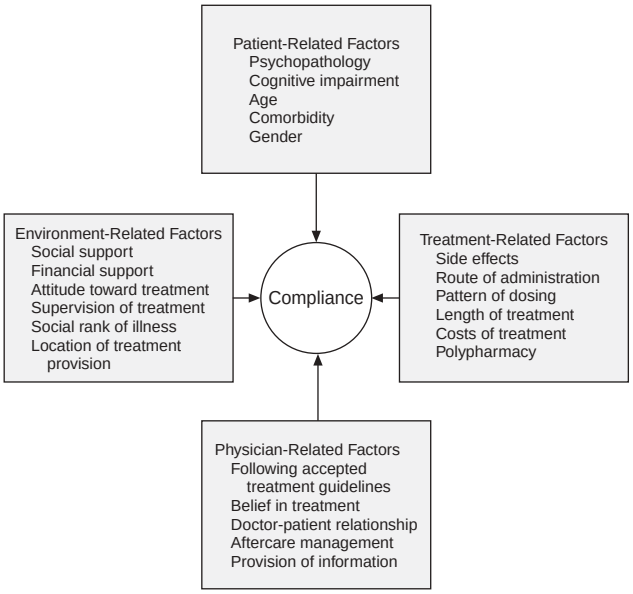
Figure 1. Factors Influencing Compliance



issue: it seems that patients at the extreme ends of the age distribution have more problems adhering to treatment recommendations. Young, especially male, patients have been found to be poor compliers.[2] One reason for this could be that young adults associate any kind of treatment or keeping scheduled appointments as typical features of the generation they are trying to be different from. On the other hand, the elderly may have memory deficits, which can impede compliance.[3] Also, they are more prone to receive multiple medications due to physical comorbidities, which is also a predictor of compliance problems. Women tend to be more compliant than men, and younger women have been found to show better compliance than older women.[4]

The nature of a patient's illness also has a strong impact on the acceptance of treatment. Patients who feel persecuted or are afraid to be poisoned will be reluctant to take medication. On the other hand, it is difficult to convince patients suffering from grandiose delusions or manic symptoms to comply with treatment recommendations.[5] The influence of negative symptoms in schizophrenia patients is controversial: negative symptoms have been shown to be predictors of both good[6] and bad compliance.[7] This apparent paradox is not surprising, considering that motivational deficits may have a negative impact on following a treatment regimen in general, while such a lack of energy can also prevent any sort of active confrontation with a doctor's recommendation, thereby ensuring a quasi-automated, nonreflective continuation of drug treatment. Apart from the primary illness, comorbid alcohol or substance abuse is a strong predictor of noncompliance.[8–10]

Another issue is the individual health belief model, which reflects patients' thoughts about both the causes and the severity of their illness. When patients were asked to relate schizophrenia to other diseases and disorders in a recent study that we performed,[11] most of them judged schizophrenia to be a less important and less serious disorder than some somatic diseases, such as diabetes, epilepsy, or cancer. Clearly, if a patient believes that his or her disorder is not serious or important enough to warrant treatment, compliance will be compromised. The social perception of an illness may also be of fundamental importance for compliance.[12] If the social perception is poor, the patient may try to avoid everything connected with the illness, including its treatment.

Individual attitudes about drug treatment also need to be taken into account. Observing, discussing, and, if necessary, attempting to change patients' attitudes toward treatment are crucial. Among patients suffering from schizophrenia, attitudes concerning treatment with antipsychotic drugs range from the very negative to the very positive. Hofer and colleagues[13] recently found that a negative attitude toward treatment is related to positive symptoms and certain side effects. In this context, it is necessary to appreciate that, over the duration of their illness, patients may change their attitudes toward treatment.

Finally, financial problems may also hinder compliance. Some patients may not be able to afford certain antipsychotics or even afford a bus trip to the pharmacy to buy them.[14]

Environment-Related Factors

Support and assistance are important variables in medication compliance. Patients who live alone generally have lower compliance rates, while patients who live in supportive environments where they have people caring for them—either professionals or significant others—are more likely to be compliant.[15] Alternatively, negative attitudes in patients' social environments toward psychiatric treatment or toward the patients themselves have an adverse effect on compliance. Stressful social interactions may counteract the positive influence on compliance that is usually exerted when patients live with others. An overly emotional, demanding family or significant others who do not share the patient's positive attitudes toward treatment are common examples of this problem.[16]

In addition, one must not underrate the influence of the media in shaping attitudes. On one hand, sensationalist reports about "miracle cures" may give rise to unfounded expectations, while on the other, exaggerated reports of safety concerns with antipsychotics will lead to worries and, consequently, to a reluctance to continue taking such drugs.[12]

When we investigated the influence of patient attitudes on actual compliance, the most important factor we found was the patient's feeling that the drug had a positive effect

on the illness.[13] It is important to reinforce positive attitudes toward treatment that patients and relatives may have. As doctors become content with the fact that their patients are compliant, they forget that these positive attitudes need regular reinforcement.

The therapeutic environment must also be taken into account. An inpatient setting where a fellow patient has only had bad experiences with a specific drug and shares these experiences will shape the attitude of the patient being treated with the same drug.

Treatment by multiprofessional teams can also influence compliance when attitudes differ among members of the team. Medical professionals tend to have a higher likelihood of advocating the use of antipsychotic drugs when treating patients with schizophrenia than nonmedical mental health professionals, such as social workers.[11] Attitudes about the value of antipsychotic treatment must be consolidated within the therapeutic team.

Physician-Related Factors

The therapeutic relationship that a clinician builds with his or her patient is a cornerstone of treatment compliance. Nelson and collaborators[17] reported that the most important factor influencing compliance was the patient's perception of the doctor's interest in him or her, which is clearly reinforced by the amount of time that physicians spend with their patients. Such a relationship is a prerequisite for a working therapeutic alliance, and providing reliable information is a crucial factor in this context. Information can be given to patients and their relatives or significant others, either informally during scheduled visits or in psychoeducational groups. In the latter, patients and relatives, usually separately, are informed about the nature of the illness and possible treatments. Psychoeducation has been shown to enhance compliance and significantly reduce relapse rates.[18,19] Providing information also includes discussing treatment plans regularly with patients and their significant others, which gives both an active part in the treatment planning process. The notion that information about side effects will lead to noncompliance is a common misconception.[20]

The fact that patients usually show better compliance and better treatment response rates in clinical trials than in real-life treatment settings nicely exemplifies the success of the notions discussed above. This is most likely a consequence of the additional effort and the rigidity of structure that are features of clinical studies. Patients receive scheduled appointments that the doctor will keep and that will not be rescheduled even if the doctor's workload indicates otherwise. The structured nature of therapy signals to the patient the importance of the therapeutic measures that are being taken.

Providing adequate information can also improve insight and thereby enhance the likelihood that patients consent to neuroleptic treatment. Marder[21] demonstrated that such patients were more satisfied with ward staff and their physicians.

In addition, clinicians should follow treatment guidelines or recommendations. Following these guidelines will make the usefulness and the rationale of treatment procedures easier for patients to understand, and they will be less disoriented by conflicting treatment recommendations that they may receive when seeking second opinions.

Treatment-Related Factors

Van Putten et al.[22] were the first to show that side effects that occur early in treatment lead to a substantial impairment of compliance later. Even though adverse effects of medication are commonly associated with compliance problems, it is important not to oversimplify this relationship. Some patients are clearly compliant with medication despite substantial side effects, while others who tolerate antipsychotics perfectly may develop poor compliance behavior. It must be understood that side effects are just one of the facets of the complex issue of compliance. In support of this notion, some reports have failed to find significant correlations between the advent of side effects and poor compliance.[1,23] It may even be possible that adverse events are linked to good compliance, since patients who take their medication regularly have a higher likelihood of experiencing side effects than patients who do not take their medication. All of these interactions emphasize the fact that patients need to be monitored regularly for side effects, and, if side effects occur, clinicians need to give them sufficient weight when discussing treatment plans with patients. Since there are considerable interindividual differences with regard to tolerating adverse events, any sort of intervention needs to be tailored according to the specific patient's needs.

An additional problem with treating schizophrenia is that most drugs have a delayed onset of action, so patients do not experience immediate positive effects. To the contrary, patients sometimes experience side effects before intended effects.[22] Also, people with schizophrenia who are in remission usually do not have a relapse immediately upon stopping treatment. Relapse can happen weeks or even months after drug discontinuation, so patients may not relate stopping the drug to the worsening of their condition. Conversely, some patients in full remission have problems realizing that this remission is related to the drug they are taking. These relationships must be reinforced regularly.

Patients may also find that drugs are not as effective (or as "dangerous") as they expected them to be. As discussed in previous sections, such perceptions are shaped by a number of sources of questionable reliability, such as the mass media and the next-door neighbor. It is the responsibility of the treating clinician to provide the patient with a balanced and realistic view of an antipsychotic's risk-benefit profile.

The complexity of prescription also plays a role in compliance.[24] Patients who have complicated treatment regimens—who must take drugs at various different times in the day or take 2 or more different medications—have more problems adhering to their prescriptions than patients who are receiving once-daily treatment with a single drug.

Route of administration has an influence on compliance as well. While a review of 26 studies showed compliance advantages for administering depot neuroleptics compared with oral neuroleptics,[25] other authors have reported that switching noncompliant patients from oral to depot drugs does not seem to be effective.[26,27] It is a common misconception that depot administration in and of itself will improve compliance. On the other hand, treatment with depot neuroleptics does have the advantage that noncompliance will be detected immediately, as soon as patients do not show up for their injections, which makes it much easier to intervene early.

CONCLUSIONS

As outlined in the sections above, a number of circumstances and parties are involved in the multifaceted issue of compliance. This variety of factors makes it evident that patients must never be solely blamed for compliance problems. Clinicians must realize that different factors are involved in assuring compliance and that these factors may change over the course of treatment, for example, sexual dysfunctions may not be a problem for a patient during the acute psychotic stage, while they clearly reduce quality of life during the maintenance and rehabilitation phases. On the other hand, negative attitudes toward drug treatment in a first-episode patient may improve over time based on the patient's experience and the information provided to him or her in psychoeducational groups. Compliance is rarely compromised by a single cause; usually, an array of interrelated factors impeding compliance is encountered. While we state in the introduction that compliance behavior is difficult to study from a methodological point of view, the scientific information available to date does provide many important leads for the engaged clinician to prevent or cope with compliance problems.

Disclosure of off-label usage: The authors of this article have determined that, to the best of their 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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