Approaches to the Enhancement of Patient Adherence to Antidepressant Medication Treatment

Pedro L. Delgado, M.D.

The number of safe and effective medication treatments for depression has increased significantly over the past 10 years. Relative to the older tricyclic antidepressants and monoamine oxidase inhibitors, the newer medications offer comparable efficacy with fewer side effects and a markedly reduced risk for serious adverse effects. In spite of these benefits, and in spite of the extensive and successful efforts that have been made to inform the general population about the diagnosis and treatment of depression, many patients do not comply with treatment recommendations. Although specific factors such as side effects lead to high rates of noncompliance with medication treatment, noncompliance is a multifactorial phenomenon. The reasons for noncompliance can include rational and intentional decisions based on beliefs about the illness, concerns over side effects, ineffectiveness of treatment, costs of the medication, decisions influenced by the symptoms of the disorder, and many other cultural and attitudinal factors. Some of the important concepts that should be addressed with depressed patients are reviewed. Strategies aimed at informing patients about depression and its treatment and providing a collaborative treatment environment have the potential to significantly improve treatment outcome and treatment adherence.

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The field of clinical psychiatry has matured considerably over the past 50 years. Nowhere is this maturation more evident than in the gradual emergence of principles guiding the treatment of major depression. While far from being complete, our understanding of the phenomenology, prevalence, course, and treatment of major depression has dramatically increased. We now have many safe, well-tolerated, and effective treatments, and we know much more about how, when, and in whom to use them.

In the past 10 years, 8 new compounds have been approved by the U.S. Food and Drug Administration (FDA) for the treatment of major depression: bupropion, fluoxetine, sertraline, paroxetine, venlafaxine, nefazodone, mirtazapine, and citalopram. Reboxetine is expected to be approved by early 2000. Additionally, several new medications are currently in phase 2 or 3 clinical trials, and while not FDA-approved for treatment of depression, fluvoxamine appears to be an effective antidepressant.[1]

These newer drugs are structurally distinct from older antidepressants and were designed with specific pharmacologic actions in mind. Compared with the older drugs, the new antidepressants were intended to selectively enhance noradrenergic and/or serotonergic neurotransmission and have fewer side effects and/or greater efficacy and faster onset of action. By developing drugs without anticholinergic, antihistaminergic, or antiadrenergic properties, the pharmaceutical companies planned to reduce the side effects associated with the tricyclic antidepressants.

By and large, this strategy has been successful. The new medications have dramatically simplified the treatment of depression and led to a large increase in the percentage of depressed patients who are receiving treatment. However, in spite of the improved safety and tolerability of the newer drugs, they only work as long as the patient continues to take them. Currently available medications may restore function, but the disease itself is not "cured." These facts reinforce the need to pay close attention to strategies that enhance treatment adherence.

This article reviews the reasons why enhancement of treatment adherence is an essential part of providing antidepressant treatment and discusses strategies for accomplishing this.

DEPRESSION AS A CHRONIC CONDITION

One important realization that has emerged (or perhaps reemerged) in the recent past is that depression is a

From the Department of Psychiatry, University of Arizona College of Medicine, Tucson, Ariz.

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Reprint requests to: Pedro L. Delgado, M.D., Department of Psychiatry, University of Arizona College of Medicine, 7303 AHSC, 1501 N. Campbell Ave., Tucson, AZ 85724.

chronic condition. The majority of patients with a mood disorder will have more than one episode. Recurrence rates for depression are estimated to be at least 50% for patients with one episode of major depression and 80% to 90% if the person has had 2 episodes.[2,3] Seventy percent to 90% of patients with a successfully treated depressive episode experience a recurrence of illness when placebo is substituted for active medication during a 3-year maintenance phase, as opposed to only 15% to 20% taking full-dose imipramine.[4] In a prospective 10-year epidemiologic follow-up study of young depressed patients, 78% relapsed during the follow-up period.[2]

It is generally accepted that patients who show significant improvement during the acute treatment phase should be continued on treatment with antidepressant drugs for at least 6 months.[5,6] Drugs that are effective in acute treatment of a major depressive episode have generally been found to be efficacious in continuation treatment. Fortunately, the same appears to be true for maintenance treatment. These consistent findings, in the face of the relative safety of the majority of antidepressant drugs, underscore the importance of continuation and maintenance treatment.

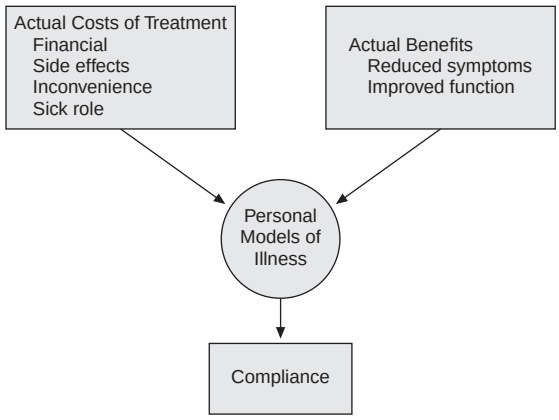
Patients with 2 or more prior episodes of major depression, those with more severe or psychotic episodes, those with incomplete response to treatment, and those with a risk of suicide should be strongly encouraged to consider long-term, if not lifelong treatment.[7] Although specific practice parameters do and should vary, in general, patients should be seen every 4 to 12 weeks for the first year of maintenance treatment and at 6-month to yearly intervals thereafter. The frequency of visits during this phase should be individualized based on psychosocial factors, compliance, and presence of symptoms and side effects. Rates of depressive relapse appear to be higher when antidepressant drugs are discontinued rapidly compared with a slow (3- to 4-week) taper.[3,8] Therefore, if medication is discontinued, it should be tapered over a 4-week period.

MANY PATIENTS STOP TREATMENT PREMATURELY

While the parameters described above for the treatment of major depression are relatively clear-cut, most depressed patients will discontinue medication within the first 180 days of their first prescription.[9] In fact, following "usual care" in a primary care clinic, only 44% of patients prescribed an antidepressant for treatment of depression have taken the drug more than 25 of the prior 30 days by 4 months after the initial prescription.[10] The high rates of recurrence and relapse on antidepressant medication discontinuation have highlighted the need for consideration of the factors that lead patients to discontinue medication prematurely.

In particular, the potential for adverse consequences during a depressive episode makes preventing premature treatment discontinuation imperative. Untreated depression is associated with increased disability[11,12] and excess use of medical services.[12,13] The risk of suicide is one of the most serious consequences associated with depressive episodes. This is especially so when the patient has a comorbid anxiety or medical disorder, where the risk of suicide doubles relative to those without such comorbidity.[14,15]

Figure 1. Role of Personal Models of Illness in Patient Compliance With Medication



WHY DO PATIENTS PREMATURELY DISCONTINUE TREATMENT?

The reasons for premature discontinuation of antidepressant medication treatment are many and often complex and have more than likely changed over time as social and cultural changes have occurred and medical practice has evolved. A considerable body of literature has been written regarding compliance.[16] Compliance occurs in a social context, including the taking on of a "sick role," with all of the benefits and expectations associated with it.[17,18] Patients must weigh the literal and figurative "cost" of treatment with the benefits of treatment. The relative balance between these forces has been suggested to determine the likelihood of treatment compliance.[19]

Perhaps more importantly, their particular "personal model of illness" determines how patients interpret and weigh the costs and benefits of treatment. Figure 1 depicts the way in which patients filter the actual costs and benefits of treatment through their individual attitudes and knowledge of the illness and its treatment. The concept of "personal models of illness" includes the specific attitudes, beliefs, and expectations that a person has about an illness and its treatment.[20,21] Five attributes have been described as common to most illness models.[20,22] These are listed in Table 1.

The impact of these factors is seen in studies that have addressed premature antidepressant drug discontinuation

Table 1. Components of Personal Models of Illness[a]

Beliefs about the symptoms that define an illness
Beliefs about the consequences of having the illness
Beliefs about the causes of the illness
Beliefs about how long it took for the illness to develop and how long it will last
Beliefs about what treatments are most likely to be effective

[a]Based on Leventhal and Nerenz[20] and Hampson et al.[22]

Table 2. General Factors to Consider in Optimizing Adherence

Education
Communication
Collaboration
Respect

Table 3. Common Misconceptions About Depression

"Depression is a natural reaction"
"I am depressed because I am weak and/or defective"
"I am depressed because I don't try hard enough"
"I will never be able to lead a normal life"
"My depression cannot be helped by medication"

Table 4. Common Misconceptions About Antidepressants

"Antidepressants are addictive—I will become dependent on them"
"Antidepressants are mind-altering drugs"
"Antidepressants are 'uppers'"
"Once I get better, I won't need medication any more"

Table 5. Patient and Family Education[a]

Depression is a medical illness, not a character defect or weakness
Recovery is the rule, not the exception
Treatments are effective, and many options are available
Aim of treatment is complete remission and staying well, not just masking symptoms
Risk of recurrence on medication discontinuation is high:
50% after 1 episode
70% after 2 episodes
90% after 3 episodes
Patient and family should be alert for early signs and symptoms of recurrence, seeking help early

[a]Based on Nierenberg.[24]

in primary care settings. Lin et al.[23] administered a questionnaire to patients who had prematurely discontinued antidepressants. Patients could endorse more than one response. When asked why they discontinued treatment, 62% said that they did not like the side effects, 56% said it was because they did not need medication, 50% felt better, 32% felt it was not working, and 11% ran out of medication. These data suggest that better education about depression and medication treatment will make an important difference to outcome.

OPTIMIZING ADHERENCE

Given the above, it is clear that one important aspect of enhancing adherence to treatment involves attempts to understand and better inform the "personal models of illness" that a patient might have. Insufficient research has been conducted on the exact factors that should be targeted for optimal adherence enhancement, but Table 2 lists 4 components that are important to any doctor-patient relationship. These concepts have been articulated in what Nierenberg[24] has described as "thoughtful antidepressant management" negotiated with "collaborative empiricism." The essence of this strategy is to encourage clinicians to take an egalitarian rather than an authoritarian stance toward patients.[24]

One essential aspect of the clinician-patient relationship in regard to treatment adherence is to understand the "personal models of illness" a person has developed; in particular, to explore the beliefs listed in Table 1. It is common for depressed patients to have misconceptions about depression. The most common of these, in the authors' experience, are listed in Table 3. In spite of considerable efforts at public education in regard to depression and its treatment, patients also frequently describe many misconceptions about antidepressant medications. These are listed in Table 4.

To the extent that these misconceptions exist, it is incumbent on the clinician to address them within the first few visits. Unfortunately, most psychiatrists are not trained to do this, and the ability to engage a patient in this process is not commonly assessed in trainees. Most frequently, psychiatric residents are expected to perform an initial evaluation and formulate a treatment plan within a 1-hour time frame. What information is actually conveyed to patients and how this is conveyed are often overlooked in the training process. In the initial visit, patients should be told their diagnosis, prognosis, treatment options, costs, likely duration of treatment, and possible side effects.

Efforts should be made to educate both the patient and relevant family members or appropriate significant others. Some of the concepts that should be conveyed and reiterated many times throughout the treatment course are listed in Table 5. Lin et al.[23] have assessed the educational messages that were associated with better compliance during the first month of antidepressant treatment. These are listed in Table 6. These messages are aimed at correcting the misconceptions that will most likely adversely impact compliance.

Katon and colleagues[25] have pioneered structured approaches to the enhancement of compliance in primary care settings. They have developed a multifaceted intervention designed to increase the overall effectiveness of depression treatment. The intervention includes an intensive patient and provider education program along with surveillance of continued refills of prescribed medication.[25] Using this approach, the investigators have shown that, compared with "usual care," this intervention leads to

Table 6. Educational Messages Associated With Better Compliance During the First Month of Antidepressant Treatment[a]

Patients should take antidepressants daily
Antidepressants must be taken for 2–4 weeks before noticeable effects
Patients should continue to take medication even if feeling better
Patients should not stop taking antidepressants without checking with physician
Patients should be given specific instructions on what to do to resolve questions regarding their treatment

[a]Based on Lin et al.[23]

Table 7. Issues to Be Negotiated

What medication will be used?
Dose titration: what intervals?
When should medication be dosed?
How aggressive should we be in seeking remission?
How long to take the medication and when and how to stop?

higher rates of treatment response (74% vs. 44%), greater decrease in depression severity over time, greater treatment adherence, enhanced satisfaction with treatment, and enhanced perception of antidepressants as being helpful.[25]

One theme that consistently emerges from research that has been done on improving treatment adherence is that of open-mindedness and flexibility on the part of the provider. It is our responsibility to understand the perspective of the person seeking assistance. The patient is the one who is taking the medication and should therefore be an active participant and have the deciding "vote" in the decision-making process. Most treatment issues can and should be negotiated. Some examples are listed in Table 7.

In summary, more than 80% of patients with 2 or more prior episodes of depression will have a third episode after treatment discontinuation.[26,27] Continued antidepressant treatment dramatically reduces the risk of relapse.[4,5] More than 50% of depressed patients will discontinue antidepressant medications prematurely.[10] Spending the time to give support and education and providing a collaborative setting will improve adherence and outcome.[25]

Drug names: bupropion (Wellbutrin), citalopram (Celexa), fluoxetine (Prozac), fluvoxamine (Luvox), mirtazapine (Remeron), nefazodone (Serzone), paroxetine (Paxil), reboxetine (Vestra), sertraline (Zoloft), venlafaxine (Effexor).

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