New Antiretroviral Therapies: Adherence Challenges and Strategies

At the April International AIDS Society–USA course in Chicago, Margaret A. Chesney, PhD, from the University of California San Francisco, reviewed the available data on adherence and suggested some strategies that can be used to enhance adherence in the clinical setting.

Nonadherence to prescribed medication is not a new issue in medicine, nor is it one that is unique to HIV disease. Much of the research available on adherence is from the field of hypertension. In general, studies have estimated that only 50% of individuals take more than 80% of their anti-hypertension medications. Two early studies of subjects infected with HIV indicated that 63% and 67% of the subjects were taking more than 80% of prescribed zidovudine monotherapy. As Dr Chesney noted, the 80% figure has been quoted historically as a cutoff for "adequate" adherence, but there is no evidence that "80%" is specifically related to a satisfactory effect (ie, appropriate viral suppression) with any particular drug regimen.

Adherence decreases as the number of medications, doses, and side effects increase, as well as when the frequency of interference with daily routines increases. The complexity and duration of potent antiretroviral therapy is unprecedented in the ambulatory care setting. Dr Chesney noted that a variety of leading experts in HIV are underscoring the importance of adherence; for example, recommendations for antiretroviral therapy published by the International AIDS Society–USA and ones developed by the Department of Health and Human Services both stress that excellent and consistent adherence is necessary to prevent viral breakthrough and the evolution of drug-resistant strains of HIV.

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Prevalence of Nonadherence Among Patients Taking Combination HIV Therapy

To date, there have been two surveys conducted on adherence to combination HIV therapy. The first study, conducted by the Recruitment, Adherence, and Retention Subcommittee of the AIDS Clinical Trials Group (ACTG), included 76 patients from 10 sites who were enrolled in a clinical trial and were taking a protease inhibitor. In the study, almost 20% of patients reported missing at least one dose in the 2 days prior to the interview.

A study of patients at San Francisco General Hospital found very similar results and also showed a significant association between the patients' plasma HIV RNA levels and the reported degrees of adherence. These and other data suggest that at least 25% of patients are at risk for viral breakthrough as a result of nonadherence.

Among the commonly reported reasons for missing medications are that patients just forgot, fell asleep, were too busy, or were depressed. Ironically, many of the reasons, such as being away from home or changes in routine, involve returning to an active lifestyle that is due in part to the success of the combination antiretroviral drug therapy. A significant percentage of patients reported feeling sick as the reason for missing medication. This finding underscores the need to proactively discuss and manage side effects. It also points to an important research question: what are the effects of vomiting on drug levels in the blood? Few data are available, and the issue of whether to take another pill after vomiting is a commonly asked question from patients.

Predictors of Nonadherence

In adherence studies, stress/depression is the only variable that predicts nonadherence across disease categories. Gender, age, ethnic, or educational differences have not been identified as consistent predictors of nonadherence.

In a recent study, patients were categorized as having reported taking all of their medications in the past 2 weeks and having reported skipping at least one dose. Nonadherent patients had statistically higher monthly rates of alcohol consumption than adherent patients. In addition, a higher percentage of nonadherent patients were working outside the home.

The Role of the Clinician in Improving Adherence

In order to ensure optimal adherence, it is essential for clinicians to (1) give patients a clear rationale for the need for strict adherence; (2) provide clear instructions, including the exact timing of doses, the number of pills, and specific dietary restrictions; (3) proactively manage side effects; and (4) create a partnership with patients based on honesty and trust. Selected strategies for working with patients on these issues are listed in the Table 1.

From the initial interaction, the goals of treatment should be discussed with patients to ensure that they understand that decreasing and maintaining viral load to below detectable levels is the primary objective of therapy. In addition to remembering to take each dose, patients need to understand the specific instructions asso-

Table 1. Improving Adherence: Strategies for the Clinician

- **Manage side effects proactively.**
  - Educate patient about the potential for different side effects.
  - Provide patients with the medications they may need to relieve potential side effects.
  - Ask patients to contact you (by phoning the office) if they experience any side effects so you have a record of it.

- **Call the drug whatever the patient calls the drug, unless the name is wrong.**
  - If a patient refers to a drug as "the little white capsule," ask how many little white capsules he or she is taking and when he or she is taking them.

- **Ask patients about daily routine activities that can serve as cues to take the pills. Use reminder cards or other tools to plan an individual schedule.**
  - Establish cues for the first and subsequent pills of the day (examples of cues may be going to the bathroom first thing in the morning, watching a specific TV show, or feeding a pet, etc). Emphasize that the medications should be taken before the routine activity. Continue to identify activities throughout the day. If the second dose of a drug is scheduled for 3:00 PM, ask what he or she does everyday at 3:00 PM.
  - Think of activities in patients' lives rather than meals, since many of us skip or are irregular about eating meals.
  - Suggest using an inexpensive watch with a timer that can be set for a given time of day.

- **Use nonjudgmental questions to ask how patients are doing.**
  - Avoid saying, "Are you taking your medications the way you are supposed to?"
  - Create an environment in which the patient feels comfortable talking candidly. Use language such as, "Taking these medications regularly can be a real challenge. A lot of people are having trouble remembering. What I need you to tell me is how you are really doing. Don't tell me what you think I want to hear. Let's look at yesterday. Did you miss any of your doses? How many?"

- **Anticipate problems.**
  - Every time medication is changed, adherence is likely to be problematic. Reemphasize the adherence issues and make sure patients understand the new regimen.
  - Plan for schedule changes such as holidays, weekends, and vacations. At holidays, send patients a holiday card reminding them to take their medications.

- **Troubleshoot problems and involve patients in problem-solving.**
  - Ask patients:

    What is the reason they missed taking the medication?

    What would have worked instead?

    How might they have remembered to carry the medications with them?

    Do they need extra vials so that they can keep medications at their desk or other places?
  - Keep a supply of snack-size baggies at the clinic. Show patients how to open one up, reach in, and remove the drugs from a pocket. Ask them to demonstrate how they will do the same.

- **Reinforce patients' efforts to adhere to medications, even if they are having trouble.**
  - If a patient tells you that he or she missed taking the medication yesterday, respond: "I am so glad that you told me that. Always tell me what is really going on." Reinforce whatever it is that a patient is doing right and build from there.

ciated with each drug. Thus, it is important to avoid the use of confusing names for the drugs (eg, using trade names and generic names for the drugs interchangeably) or confusing medical abbreviations (eg, "bid" and "tid"). If a physician's schedule does not allow sufficient time for explanations, the patient should be referred to a designated person on the health care team for follow-up and additional questions.

Patients must also be prepared for potential side effects and their management. Discussing side effects will not create the effects. In fact, patients who are not prepared for side effects frequently discontinue the medication, or they may try to self-manage the side effects (such as diarrhea) on their own by experimenting with different dosage schedules.

It is essential to help patients tailor the medication to their lifestyle rather than tailoring their lives to the drugs. Identifying regular activities to serve as cues can help patients remember to take their drugs. Generally, they will already have consistent daily activities that can direct the medication intervals. Patients with symptoms of stress or depression should be referred for services or treatment. Similarly, it is necessary to help patients manage drug and alcohol use through appropriate referrals, as increased alcohol or substance use may indicate depression. Such measures focus on the whole patient and address issues of adherence on a realistic basis.

By acknowledging from the beginning that adherence will be a challenge, but that the clinical team will work with the patient, clinicians can establish a trusting relationship that increases the likelihood that the patient will report honestly about his or her adherence. Nonjudgmental questions, a willingness to problem-solve with patients, and accessibility of a staff member for questions and follow-up are key factors in building a trusting relationship.

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