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Adherence to HIV Drug Therapy

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Adherence to HIV Drug Therapy

Abstract

Antiretroviral therapy has dramatically improved the prognosis for many patients with HIV infection. For many patients who can navigate combinations of drugs and time their doses precisely, these drug regimens typically slow the progression of the disease and lengthen survival. But because these drug regimens are very complex, adherence—the degree to which patients follow medical advice in taking the prescribed drugs—is now a major determinant of HIV treatment success. This Issue Brief summarizes recent work on the effect of adherence on short-term outcomes, and the ability of providers to predict and estimate their patients' adherence to therapy.

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Editor's Note: Antiretroviral therapy has dramatically improved the prognosis for many patients with HIV infection. For many patients who can navigate combinations of drugs and time their doses precisely, these drug regimens typically slow the progression of the disease and lengthen survival. But because these drug regimens are very complex, adherence—the degree to which patients follow medical advice in taking the prescribed drugs—is now a major determinant of HIV treatment success. This Issue Brief summarizes recent work on the effect of adherence on short-term outcomes, and the ability of providers to predict and estimate their patients' adherence to therapy.

Adhering to antiretroviral therapy poses challenges for patients

Since its introduction in 1995, highly active antiretroviral therapy (HAART) has been effective in slowing progression of HIV infection to AIDS. It works by reducing the amount of HIV in the blood (decreasing viral load) and by bolstering the immune system (increasing the number of infection-fighting CD4+ cells).

- HAART combines three or more HIV drugs, and may involve taking large numbers of pills each day for long periods of time. The dosing requirements, duration, and side effects make adherence to therapy particularly difficult.

- Adherence is not only difficult, it is also important for treatment success. Suboptimal adherence to HIV therapy can allow the virus to replicate. Some studies have suggested that greater than 95% adherence is needed for successful treatment.

- In addition, suboptimal adherence likely contributes to the emergence of drug-resistant strains of the virus, and so may threaten our continuing ability to fight this infection.

- Practice guidelines recommend that providers consider each patient's ability and willingness to adhere to the treatment regimen in deciding whether to prescribe HAART to asymptomatic patients. Thus, there are important ramifications if a provider's assessment of adherence is inaccurate, because errors in predicting good adherence may promote resistance, and errors in predicting poor adherence may unnecessarily delay treatment.

Study tracks pill-taking, outcomes over four months

Dr. Gross and colleagues studied patients just starting a HAART regimen that included the protease inhibitor nelfinavir. They determined whether adherence was different between those who did and did not achieve undetectable blood levels of HIV within four months.

- Between 1998 and 1999, 58 patients enrolled in the study, and 41 completed it. Patients were mostly male (73%) and African-American (83%).

- Study visits occurred at enrollment and then again monthly for a total of four months. This endpoint was chosen because most patients who achieve an undetectable viral load—a measure of successful treatment—will have done so by this time.

- Adherence was measured using microelectronic monitors on the nelfinavir bottle. These monitors record the time and date of each bottle opening, and are considered one of the best techniques for tracking adherence. Patients were instructed to open the bottle only when they were scheduled to take a dose.

- Adherence was summarized using a number of different metrics: the percentage of the prescribed doses taken over four months; the percentage of days with the optimal number of doses; the maximal duration of the interval between doses; and number of extended periods between doses (3-day pill-taking gap or 7-day "drug holiday.")

Results confirm link between adherence and response to treatment

Overall, 61% of patients achieved undetectable viral loads after four months of therapy. These "undetectable" patients had adherence levels that differed markedly from those whose viral loads remained "detectable."

- The undetectable group took a median of 93% of prescribed doses, compared to the detectable group, who took a median of 70% of doses.

- Taking more doses was associated with a greater decrease in viral load and a greater increase in CD4+ cell counts. However, the data suggest that the relation between adherence and viral load may be more complex than a simple dose-response relationship. Rather, the data are more suggestive of a threshold effect at 80%, with the proportion of individuals achieving an undetectable viral load steeply dropping off below that level.

- All of the metrics analyzed differed between the detectable and undetectable groups. For example, only 4% of those in the undetectable group had a 7-day drug holiday, compared with 44% of those in the detectable group, some of whom had multiple week-long gaps.

Poor adherence not found until second month of therapy

The investigators explored the timing of adherence problems during the study. They focused especially on the first month of therapy, because guidelines recommend that providers monitor viral loads at the end of one month. Patients with significant decreases in viral load are thought to be adhering and responding to therapy.

- In the first month, adherence was high for all study patients. The percentage of prescribed doses taken did not differ between the detectable and undetectable groups (around 95% for both).

- Nearly all patients achieved significant decreases in viral load over the first month. This measure at an early stage in therapy did not distinguish between patients who ultimately achieved undetectable viral loads at four months and those who did not. This finding is important, because it argues against the current guidelines, which urge that adherence be assessed at one month.

- Group differences in adherence did not emerge until the second month of therapy, and then they persisted into the third month.

Clinicians do not accurately predict or estimate adherence

Within the same group of patients, the investigators studied the ability of physicians and other providers to predict and estimate adherence to HAART. Dr. Gross asked providers within seven days of enrollment whether their patients would have undetectable viral loads after four months of HAART, and to predict the percentage adherence over four months. After four months, each provider was asked to estimate his or her patients' adherence during the study.

- There was no correlation between predicted and actual adherence. Providers erred in their predictions both by overestimating and underestimating adherence levels. Overall, 65% of estimates missed by more than 10%.

- Providers predicted which patients would achieve undetectable viral loads 53% of the time, which could not be said to differ from chance agreement.

- Providers were only slightly more accurate at estimating adherence at the end of the study. Overall, 47% of the estimates missed by more than 10%.

POLICY IMPLICATIONS

These results have important implications for health professionals providing care to HIV-infected patients and for researchers designing interventions to improve adherence to HIV drug therapies.

- Adherence must remain a high priority area for the attention of HIV care community given the strong relation between adherence and virological success demonstrated in this study and others.

- Providers should not assume that their patients will not have adherence problems if the viral load is appropriately suppressed after one month. The end of the first month of antiretroviral therapy is a period of high risk for waning adherence, although it is not clear whether a drop in adherence at that point can be used to predict treatment failure for an individual patient. These findings suggest that providers schedule monthly visits after initiating HAART, to allow time for non-judgmental inquiries about adherence.

- Investigators designing interventions to improve adherence should strongly consider focusing on strategies that extend beyond the first month of therapy. Further research is needed, however, to define the optimal timing and targets for an intervention.

POLICY IMPLICATIONS
Continued

- Patients may not need nearly perfect adherence to achieve successful results with HAART. These findings suggest that there may be a "threshold" effect of 80% rather than 95% adherence. Further studies are needed to more accurately define optimal and achievable levels of adherence.

- In deciding whether to offer antiretroviral therapy, providers should not rely solely on their judgment about a patient's ability to adhere to HAART. Similarly, providers should not rely on their own assessments to determine if patients are adhering to therapy. Other methods of measuring adherence, such as patient self-reports and microelectronic monitors, should be considered in clinical practice to replace providers' clinical judgments.

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