Correspondence

Patient Self-Report as a Marker of Adherence to Antiretroviral Therapy

Sir—Duong et al. [1] have shown that patient self-report, together with determination of plasma drug levels and biological markers, has positive value in the assessment of adherence to antiretroviral therapy and its relationship to the attainment of virologic response. We have also studied the usefulness of patient self-report for first-line measurement of adherence to treatment in a group of Chinese patients with HIV/AIDS.

In acknowledgment of the importance of adherence to highly active antiretroviral therapy (HAART) for the attainment of its benefits, we commenced a drug-adherence counseling program at our clinic in 1997. In this program, nurse counsellors see patients who receive antiretroviral treatment at each clinic visit, often at an interval of 4–6 weeks. Patients are asked questions regarding their knowledge about their drug regimens, their drug-taking behaviors, and the barriers to adherence, and they also receive counseling. In addition, the patients’ drug adherence is assessed via a self-report method. Patients are asked to recall and report the number of doses that they have missed since the most recent visit; this question is similar to that posed by Duong et al. [1] about long-term adherence (i.e., the proportion of drugs taken in the previous 4 weeks). We consider each drug in the regimen important for control of the virus; thus, 1 drug is counted as 1 dose. Drug adherence level (expressed as a percentage) is defined as follows: \([(\text{total doses of the drug that were actually taken between the 2 visits}) / (\text{total doses of the drug that should have been taken between the 2 visits})]\) × 100%. Four levels of grading are assigned according to the adher-

<table>
<thead>
<tr>
<th>Grade</th>
<th>Number of missed doses in 2 weeks</th>
<th>Number of missed doses in 4 weeks</th>
<th>Number of missed doses in 6 weeks</th>
<th>X &amp; Y index</th>
<th>Number of missed doses in Z weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>zero ([0])</td>
</tr>
<tr>
<td>B</td>
<td>1-2</td>
<td>1-5</td>
<td>1-8</td>
<td>X</td>
<td>1.4</td>
</tr>
<tr>
<td>C</td>
<td>3-5</td>
<td>6-11</td>
<td>9-16</td>
<td>Y</td>
<td>2.8</td>
</tr>
<tr>
<td>D</td>
<td>&gt;5</td>
<td>&gt;11</td>
<td>&gt;16</td>
<td></td>
<td>greater than y ([&gt;y])</td>
</tr>
</tbody>
</table>

Percentage of drug adherence = \(\frac{\text{Total no. doses have been taken} \times 100\%}{\text{Total no. doses should be taken}}\)

Calculation of X & Y index:

If a client takes 4 doses of HAART per day (i.e., 28 doses per week), then the X & Y index are:

\[
\frac{28 - X}{28} = 0.95 \quad (95\%)
\]

\[
X = 1.4
\]

\[
\frac{28 - Y}{28} = 0.90 \quad (90\%)
\]

\[
Y = 2.8
\]

Finding x & y

\[
x = X \times Z
\]

\[
y = Y \times Z
\]

Figure 1. Table for grading adherence to antiretroviral therapy

Remarks:

Grade A = 100% adherence
Grade B = 99%-95% adherence
Grade C = 94%-90% adherence
Grade D = <90% adherence
ence rate: grade A, 100% adherence; grade B, 95%–99% adherence; grade C, 90%–94% adherence; and grade D, <90% adherence.

To speed up the grading process, we developed a “grading table” (figure 1). Information obtained regarding total number of doses of antiretrovirals that should be taken per day, the total number of missed doses, and the time lapse since the last visit can be easily checked against the grading table to determine the adherence grade. For example, let us suppose that a patient who is receiving combivir (1 tablet b.i.d.) and indinavir (800 mg q8h), for a total of 5 doses of antiretrovirals per day, reported having missed a total of 6 doses in the past 4 weeks. According to the grading table, the patient has a grade B adherence level.

To evaluate the reliability of our assessment method, we examined the relationship of the adherence grade to virologic response in Chinese patients, who constituted >80% of our total patient population. Patients who had received HAART consecutively for >1 year (as of the end of 2000) were studied. Of the 161 eligible patients, 142 (88.2%) were male, 88 (54.7%) were >40 years of age, 82 (50.9%) had symptomatic HIV disease, and 138 (85.7%) were receiving regimens that contained ≥1 protease inhibitor. The mean number of doses and pills taken per day were 6 and 10, respectively. With the aid of the grading table, 130 patients (80.7%) were found to have grade A adherence at their most recent visit, whereas the remaining 31 patients had grade B–D adherence. The concurrent virus load was undetectable (i.e., <500 copies/mL) in 135 patients (83.9%). One hundred fifteen (88.5%) of the 130 patients with grade A adherence and 20 (64.5%) of the 31 patients with grade B–D adherence had undetectable virus loads. Performance of this self-reported assessment method in the prediction of virologic response was as follows: sensitivity, 85%; specificity, 42%; positive predictive value, 89%; and negative predictive value, 36%.

Multivariate analysis by logistic regression revealed that sex, age, and duration of treatment were not significant factors influencing plasma virus load. Only disease stage and drug adherence level were found to be significant factors (P < .005 and P < .003, respectively). We found that patients with partial adherence (i.e., grades B to D) were 4 times more likely to have a detectable virus load than were patients with grade A adherence (adjusted OR, 4.22; 95% CI, 1.75–12.33).

Like Duong et al. [1], we found that self-reported adherence was independently associated with antiretroviral efficacy, in terms of good virus suppression. However, instead of using a score derived from 4 questions [1], we used an adherence level that was calculated from the absolute number of missed doses and checked by use of the grading table. The sensitivity and positive predictive value of our method were slightly higher than those of the adherence score used by Duong et al. [1], and the specificity and negative predictive value were lower. The high positive predictive value of our method suggests that a single assessment of longer-term adherence (i.e., 4–6 weeks) worked.

Continual monitoring and reinforcement of patients’ adherence to therapy has clearly become one of the most crucial elements in the success of HIV management [2]. To date, all methods that have been developed to measure levels of drug adherence have had limitations [3]. The self-report approach has significantly predicted virological treatment failure in HIV-infected patients [4]. Conceivably, assessment of drug adherence using methods other than self-report may not be feasible in most clinical settings. This would definitely be true for developing countries, where access to combination antiretroviral treatment has been increasingly necessary [5]. We have developed a user-friendly tool to assess and grade self-reported antiretroviral drug adherence among HIV-infected patients. The grading table that we have designed is simple, standardized, fast, and cost-free. Its application may aid the use of antiretroviral therapy in developing countries.

**References**


Interleukin-1 Receptor Antagonist Gene Polymorphism and Cancer

Sr—We read with great interest the review article by Witkin et al. [1] about the influence of IL-1 receptor antagonist (IL-1RA) gene polymorphism on disease. IL-1RA is an anti-inflammatory cytokine that binds specifically to the IL-1 receptor [2]. Its expression has been found in association with several types of tumors, such as endometrial cancer [3], bronchogenic carcinoma [4], glioblastoma [5], and gastric...