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.

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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...
carcinoma [6]. We would like to add some interesting details concerning the connection between IL-1RA gene polymorphism and cancer.

Witkin et al. [1] mentioned that the concentration of IL-1RA in the serum of patients with gynecologic cancers is elevated in comparison with that in patients with benign diseases and with that in healthy women. This observation is based on an article by Fujiwaki et al. [7]. It should be noted that only 15 patients with solid tumors were enrolled in that study: 7 patients with cervical cancer, 6 with endometrial cancer, and only 2 with ovarian cancer.

It is known that gene polymorphisms can cause changes in the expression of proteins [8]. Therefore, a polymorphism in the IL-1RA gene may have a substantial impact on the IL-1 cytokine system. For instance, the study of Unfried et al. [9] demonstrated a significant association between the allele 2 polymorphism of the IL-1RA gene and recurrent idiopathic miscarriage. Furthermore, El-Omar et al. [10] and Machado et al. [11] have observed an association between IL-1RA and gastric cancer.

Because few data are available on the connection between IL-1RA and cervical cancer, we conducted a prospective case-control study to investigate the relationship between polymorphisms in the gene encoding for the IL-1RA and the clinical characteristics of patients with cervical cancer. Blood samples were analyzed, and DNA was extracted. The genomic DNA fragments were amplified by PCR.

One hundred thirteen women with cervical cancer and 107 female control subjects with benign disorders were enrolled. Because germline mutations do not fluctuate with age, the age of control subjects was not specified; however, only women >47 years old were included in the control group. The median age of the patients with cervical cancer was 46 years (range, 25–80 years). Of the 220 women included in our study, 58.4% were in stage T1 or T2, and 41.6% were in stage T3 or T4. The frequency of the IL-1RA 1/2 genotype in the study group was statistically significantly different from that in the control group with respect to allele 2 heterozygosity (24.8% vs. 13.1%, respectively; \( P = .04 \)). No statistically significant differences were observed between the frequency of the IL-1RA 1/3 genotype among patients with cervical cancer and the frequency in the control group (4.4% vs. 3.7%) or in the frequencies of the homozygous allele 2. Only 1 woman with cervical cancer was identified as homozygous for allele 3, and an additional 9 patients were identified as homozygous for allele 2. In the control group, 3 women were heterozygous for allele 2/3. No statistically significant correlations were observed between IL-1RA 1/2 polymorphism and tumor stage \( (P = .5) \), grade of tumor differentiation \( (P = .4) \), recurrence status \( (P = .5) \), and age at treatment \( (P = .5) \).

These data support the claim that allele 2 of the gene encoding for IL-1RA plays a role as a genetic determinant of whether an individual will develop cancer with solid tumors. Further prospective studies are warranted to clarify the role of the IL-1RA gene in the pathophysiology of cancer.

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