

In HIV Therapy Adherence, Almost Isn't Good Enough

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

Being almost compliant with antiretroviral therapy was associated with a sharp increase in the risk that HIV-infected patients would develop resistance to one or more of the drugs, P. Richard Harrigan, Ph.D., reported at an American Medical Association press briefing.

In a prospective cohort study of 1,191 HIV-infected patients, those who picked up 80%-90% of their prescription refills, and those who occasionally had low serum drug levels even if they picked up 95% of their medication, had more than a fourfold increase in the risk of developing drug-resistant mutations, said Dr. Harrigan, director of the British Columbia Center for Excellence in HIV Research Labs, Vancouver, B.C.

He joined other HIV experts in stressing the importance of antiretroviral therapy adherence. Inconsistent drug levels allow viral loads to increase and also put pressure on the virus to adapt. Patients who consistently take all their medication suppress viral reproduction so well that mutations are unlikely, and those with poor adherence don't have enough drugs in their system to stimulate mutations.

"Physicians should get this message to patients: Be fully, completely adherent as much as humanly possible," he said.

In the study of patients in British Columbia, the median age was 37 years, the median CD4 cell count was 280 cells/ μ L, and the median viral load was 120,000 copies/mL. All patients began antiretroviral therapy during 1996-1999; 26 drug combinations were used. Viral load, drug levels, and resistance genotyping were assessed at baseline, after 1 month of therapy, and then quarterly (*J. Infect. Dis.* 2005;191:339-47).

After an average follow-up of 2.5 years, 25% of the cohort had developed resistance to one or more drugs. Among this group, 68.5% were resistant to lamivudine (3TC), 40% to nonnucle-

oside reverse transcriptase inhibitors, 33% to nucleoside reverse transcriptase inhibitors, and 23% to protease inhibitors.

The highest risk of resistance mutations occurred in those who picked up 80%-90% of their prescription refills. This group was 4.15 times more likely to develop resistance mutations than were those who picked up 0%-20% of their refills.

An 80%-90% refill rate is "pretty reasonable for some diseases, but not for this. It's not like in horseshoes, where close is good enough. Here, close is a bad thing," Dr. Harrigan said.

Patients with one or two abnormally low drug concentrations in their first two posttherapy plasma samples were 1.45 times more likely to develop mutations than were those with normal drug levels.

But some patients who picked up more than 95% of their medication still weren't taking it consistently, and they, too, were at a high risk of developing resistance mutations. Among this group, those who had two abnormally low drug plasma levels were 4.57 times more likely to develop mutations than were those with normal drug plasma levels.

As long-term survival increases drug resistance is becoming more of a problem, Dr. Harrigan said. In recent studies, up to 50% of the U.S. population being treated for HIV infection had some degree of resistance.

The 25% resistance rate among the study patients reflects free access to antiretroviral drugs, provided by Canada's nationalized health system. Still, even with free access to medication, only 30% of the study group was fully adherent.

The complexities of antiretroviral dosing interfere significantly with adherence, said Kathleen Squires, M.D., of the University of Southern California, Los Angeles. The risk of nonadherence increases as patients move beyond initially prescribed regimens, which usually are the most manageable. ■

Handheld Computers May Assist in HIV Education

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — Educational videos on handheld computers were a hit with patients learning how to start or switch HIV medications, a preliminary study of 50 patients found.

Handheld computers, also called personal digital assistants (PDAs), could be useful tools in educating patients with low literacy levels, Scott R. Smith, Ph.D., said in a poster presentation at the triennial congress of the International Medical Informatics Association.

Previous data have shown that one in four patients living with HIV or AIDS has a hard time understanding simple medical instructions or medical terms and concepts. A previous assessment of literacy levels in patients at the University of North Carolina Hospitals Infectious Diseases Clinic found reading abilities at the eighth-grade level or lower in 30 of 75 patients, noted Dr. Smith of the university.

In the current study, pharmacists created interactive educational audio and video clips geared toward patients of different ethnicities that explained how to take antiretroviral medications, manage side effects, and adhere to treatment. Patients answered questionnaires before and after using the PDAs.

At the start of the study, 19 patients reported some or a lot of trouble adhering to medication regimens, 14 reported a little trouble, 2 said they had no trouble, and 15 were just starting a new regimen.

After watching the PDA movies, 48 of 49 patients who answered follow-up surveys said they felt very or extremely sure that they would be able to adhere to therapy. Forty-five patients said they believed that the medicine would have a positive effect on their health, and 47 patients agreed that not taking their medications would make the HIV become resistant to the drugs.

Twelve patients in the study were white, and 38 were African American. Nineteen had never used a computer before. The average age of the subjects was 42 years, with a range of 25-70 years. On average, they were supposed to take three antiretroviral drugs, twice per day.

Most patients said the PDA movie was helpful, valuable, easy to follow, and exciting, rather than boring. Nearly all rated the movie as excellent, and said it made the information easier to remember, that they found it easier to learn from movies than from books, and that they liked using a handheld computer to watch the movie.

In general, printed health education materials are written for people with at least a 10th-grade reading ability, Dr. Smith said. Literacy increasingly is being recognized as a contributor to disparities in health outcomes.

"As devices become smaller, more portable, easier to use, and less costly, they hold potential for innovative uses in patient education," he added.

Dr. Smith reported no relationship with the company that makes the PDAs. ■

Pros and Cons to Testing For HIV-Drug Resistance

SAN FRANCISCO — All official guidelines on HIV treatment either make blanket recommendations for drug-resistance testing or at least suggest that the clinician consider such testing depending on the patient's circumstances, Brad Hare, M.D., said at a meeting on HIV management sponsored by the University of California, San Francisco.

But deciding whether to use genotypic or phenotypic assays can be difficult, said Dr. Hare, a physician in the positive health program at the university.

Genotypic drug-resistance assays identify the presence of specific mutations in the HIV genome. Drug resistance is then inferred using an algorithm or a database analysis

Phenotypic assays, on the other hand, use viral isolates or recombinant virus derived directly from the patient's plasma. The analysis derives from a culture-based system, and the concentration of a specific drug needed to inhibit viral replication can be quantified.

In general, genotypic testing holds the edge early in a patient's disease, before the virus has a chance to develop complex patterns of resistance. Phenotypic testing tends to be better late in a patient's infection, when the patient is likely to be experiencing more regimen failure as a result of virus with complex mutations. (See box.)

Both tests may be required in complicated patients to get the optimal information for management.

—Robert Finn

Advantages, Disadvantages of HIV Drug-Resistance Testing

Genotypic Assay

Advantages

- ▶ Results are available in days.
- ▶ Is less technically complex than phenotypic assay.
- ▶ Has proven value in predicting short-term virologic outcome.
- ▶ Mutations may precede phenotypic resistance.
- ▶ Can detect mixtures of resistant and wild-type virus.
- ▶ Is less expensive than phenotypic assay.

Phenotypic Assay

Advantages

- ▶ Is a direct measure of resistance.
- ▶ Results are similar to assays of bacterial resistance.
- ▶ Results are easily understood.
- ▶ Can be used for any drug.
- ▶ Requires no knowledge of genotypic correlates of resistance.
- ▶ Assesses effects of interactions between mutations.
- ▶ Able to test new drugs immediately.

Disadvantages

- ▶ Is an indirect measure of resistance.
- ▶ Requires a viral load $\geq$ 1,000 copies/mL.
- ▶ May not detect viral species with <20% prevalence.
- ▶ Requires interpretation.
- ▶ Cannot assess interactions between mutations.
- ▶ Correlates of resistance are less clear for some (especially new) drugs.
- ▶ Cannot test new drugs immediately.

Disadvantages

- ▶ It takes weeks to get results.
- ▶ Results may oversimplify the situation.
- ▶ Resistance thresholds are not defined for all drugs and are not standardized for different assays.
- ▶ Does not take into account the activity of drugs in combination.
- ▶ Requires a viral load $\geq$ 500-1,000 copies/mL.
- ▶ May not detect minor species.
- ▶ Is more expensive than genotypic assay.

Source: Dr. Hare