

Medication Adherence in HIV Patients: Improvement Is Needed

Paterson DL, Swindells S, Mohr J, Brester M, Vergis EN, Squier C, et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Ann Intern Med* 2000;133:21-30.

Study Overview

Objective. To determine the relationship between adherence to prescribed protease inhibitors (PIs) and virologic, immunologic, and clinical outcomes; to identify variables associated with adherence; and to determine how well clinicians predict adherence in HIV patients.

Design. Prospective, observational study.

Setting and participants. Two HIV clinics, one in a Veterans Affairs medical center and one in a university facility, recruited 99 consecutive patients who were currently taking or beginning a regimen of PIs. Patients were excluded if they were unable to give informed written consent, planned to use a medication organizer with their PI, or were living in a nursing home, jail, or hospice.

Main exposure. Adherence was measured using a micro-electronic system that recorded the time, date, and duration of opening a medication bottle. The adherence rate was defined as the ratio of doses taken to doses prescribed.

Main outcome measures. HIV RNA levels and CD4 lymphocyte subpopulation assays, performed at baseline and every 3 months. Virologic failure was defined as an HIV RNA level > 400 copies/mL. Clinical variables included hospital days per 1000 days of follow-up, number of opportunistic infections, and deaths.

Main results. Patients had a median age of 40 years. 62% were white and 19% were African American. A broad range of educational and income levels was represented. Few patients were using drugs or alcohol or became infected through intravenous drug use. 21% had a history of depression, and 24 patients had an HIV RNA level < 400 copies/mL at baseline. 81 patients had a mean follow-up of 6 months, while 33% had a follow-up of 3 months and 18% did not return any follow-up data.

Virologic failure demonstrated a dose-response relationship with adherence: patients with > 95% adherence to dosing schedules had a failure rate of 21.7%, compared with a failure rate of 66.7% for patients with 80% to 89.9% adherence and a failure rate of 82.1% for patients with < 70%

adherence. Compared with adherence rates < 95%, higher adherence rates were associated with significant increases in CD4 cell counts (83 versus 6; $P = 0.045$) and fewer hospital days per 1000 days of follow-up (2.6 versus 12.9; $P < 0.001$). There were 5 new opportunistic infections and 2 deaths among patients who adhered to < 95% of their doses and none in those with > 95% adherence (not significant). Only low psychiatric morbidity (measured with the General Health Questionnaire) and older age were associated with > 95% adherence on multivariate analyses.

Physicians involved in the study predicted adherence incorrectly for 41% of patients. Clinic nurses predicted it incorrectly for 31% of patients. The difference between physicians' and nurses' prediction rates was not significant.

Conclusion

This study suggests that optimal virologic, immunologic, and clinical outcomes for HIV patients require adherence rates > 95%.

Commentary

Paterson et al documented a small observational trial with mediocre follow-up. The authors examined a large number of potential confounders (probably too many for their total n), but only adherence and baseline viral load were found to predict virologic failure. These results need to be confirmed in a larger, more diverse population. Despite its size limitations, this study provides important evidence that the generally accepted threshold of 80% adherence to medication dosing is inadequate. Given the high prevalence of drug resistance and clinical failure among patients with HIV, Paterson et al's findings should be accepted unless or until they are proven wrong.

Applications for Clinical Practice

Providers caring for HIV patients need to emphasize the goal of 100% adherence to drug regimens. Toward that end, administrators at HIV clinics and other health care facilities should devote resources to creating programs designed to maximize medication adherence. Further, physicians should remember not to base their efforts to improve adherence on their predictions of adherence.