Assessment of an Antiretroviral Adherence Sensitivity Training Exercise in the Doctor Of Pharmacy Curriculum

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The degree of HIV viral suppression is closely linked to the patient's ability to adhere to complex antiretroviral medication regimens. Unfortunately, numerous reports indicate that healthcare professionals have difficulty understanding the adherence problems that patients who are HIV-positive may encounter. The purpose of this project was to assess the value of performing an antiretroviral adherence sensitivity training exercise in the Doctor of Pharmacy curriculum. Sixty-five pharmacy students were prescribed seven days of a placebo antiretroviral regimen. Each student was given a placebo representing zidovudine/lamivudine (Combivir®), and indinavir (Crixivan®). They were instructed to take indinavir on an empty stomach, and advised to drink at least six glasses of water a day to reduce the risk of renal complications. The student's adherence with these regimens and restrictions were measured and compared with that of real HIV-positive patients. The median adherence rate with Combivir® was 92.8 percent (range 43-100 percent), and 85.7 percent (range 29-100 percent) with indinavir. Reasons for non-adherence were very similar to those quoted by HIV-positive patients, suggesting a sympathetic link to a "real-life" experience. An anonymous survey found that more than 90 percent of the students believed that the exercise was beneficial. The antiretroviral adherence exercise is a valuable tool for educating pharmacy students regarding real-life restrictions that HIV-positive patients have with antiretroviral adherence.

BACKGROUND

Highly active antiretroviral therapy (HAART) consisting of combinations of potent antiretroviral agents has made a dramatic impact on the natural progression of HIV disease(1). Strict adherence to HAART therapy is essential in order to suppress viral growth in the body and to limit therapeutic failure(2,3). Additionally, decreased oral absorption of antiretroviral agents has lead to subtherapeutic concentrations (4). Poor adherence to therapy has been attributed to a number of patient-related factors as well as many medication-related factors(2). Patient-related factors are usually associated with psy-chosocial traits. Medication-related problems are typically related to pharmacologic issues *(i.e.,* side-effects and drug interactions), or administration-related issues such as complex dosing schedules and dietary restrictions(2).

Difficulty in following complex regimens with specific timing and dietary restrictions has even been reported to outweigh the burden of side effects as a cause of nonadherence in some reports(5). A trusting relationship between HIV-positive patients and health care providers is essential for optimal adherence to antiretroviral therapy(6,7).

Unfortunately, perceptions about HAART therapy often differ substantially between health care providers and HIV-positive patients(5,8). In one particular study, HIV-positive patients stated that the need to take medications "with or without food" was the number one reason for difficulty in adhering to HAART regimens. Conversely, their treating physicians remarked that they believed that the "number of doses per day" was the most important reason(5). This discrepancy in opinion suggests that healthcare professionals may need to be more empathetic to the barriers that HIV-positive patients face with antiretroviral therapy. Empathy is vital in establishing a trusting relationship with patients.

Pharmacists, who are generally the most accessible health care professionals, are in a unique position to help HIV-positive patients understand and adhere to their medication regimens. Unfortunately, their knowledge about antiretroviral therapy and HIV disease is often limited(9). Therefore, pharmacy curricula should better prepare students to handle HIV medication-related issues to help patients optimize therapeutic outcomes.

Sensitivity or empathy training has been successfully incorporated in the training of other health care professionals for other chronic diseases that require strict patient adherence such as diabetes(10). For that reason, it seems logical to explore the use of similar training methods to help pharmacy students understand some of the medication-related issues that HIV-positive patients must face on a daily basis. Therefore, the purpose of this project was to assess the value of performing an antiretroviral adherence sensitivity training exercise in the Doctor of Pharmacy curriculum.

METHODS

Sixty-five third year Doctor of Pharmacy students, 42 females and 23 males, were prescribed seven days of a placebo antiretroviral regimen in the Pharmaceutical Care Lab-V course. Each student was asked to take a simulated HAART regimen consisting of candy placebos for one week. The placebo anti-

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retroviral agents represented the common regimen of zidovudine 300 mg/lamivudine 150mg (Combivir®), one tablet every 12 hours and indinavir (Crixivan®) 400mg, two tablets every eight hours. This regimen was selected because it was one of the most well established initial HAART regimens at the time of the exercise. Licorice and cinnamon flavored candy were chosen as the placebo agents because they were believed to have unpleasant aftertastes. This was by design, as taking medicine should not be an enjoyable experience and some medications often have bad tastes. Pseudonyms of "Doublevir" and "Mountainavir" were placed on the prescription vials in place of Combivir® and Crixivan® respectively, to protect the students' privacy if the vials were discovered. Sugar-free candy placebos were available to any student who wanted to avoid a sugar containing food. Students also had the option not to participate. This project was exempt from Institutional review board approval.

Each student was instructed to take the indinavir placebo on an empty stomach (one hour before a meal or two hours after a meal) in order to maximize oral absorption(11). In addition, each student was instructed to drink at least six glasses of water or acceptable liquids a day to reduce the risk of renal complications associated with indinavir. The students were also told to keep indinavir placebo in its original (oversized) vial with desiccant as per the manufacturer's recommendations. Alternatively, they were permitted to carry a one day supply of indinavir placebo in a pill box to avoid carrying the large manufacturer's vial.

The students' adherence with these regimens and dietary restrictions were recorded on daily log sheets (see Appendix). The students recorded doses taken, time of doses, times of meals, number of glasses of fluids (non alcoholic), reasons for missed doses, as well as any additional comments. The students had to return their log sheets and medication bottles at the end of the exercise to facilitate a pill count. The students were not graded on their rate of adherence with the regimen, but rather on completion of the exercise and the log sheet. Any dishonest students would be found in violation of the school's honor code.

Upon return to the Pharmaceutical Care Lab the following week, the students shared their experiences of the exercise in a facilitated class discussion. The instructor then led the class in a discussion about antiretroviral medications, resistance, adherence, and salvage regimens. In the last part of the exercise, the students were asked to recommend alternative salvage regimens in case of failure to the current regimen or if the patient had experienced an adverse event or drug interaction.

Since pharmacy students without HIV infection cannot have the same perspective as actual patients, the faculty investigators realized that it would be very difficult to assess the value of such an exercise. The students' rates of adherence to dietary restrictions and drug regimens and reasons for non-adherence were compared to those of actual HIV-positive patients reported in the published literature.[1] Additionally, students were anonymously asked to complete a laboratory satisfaction survey.

This laboratory exercise was positioned to occur two weeks prior to the HIV lectures in the therapeutics course. This was done for two reasons. First, so that the students had limited knowledge of antiretrovirals and related adherence data before the exercise, and second, to give them a brief but active introduction to a complex disease state.

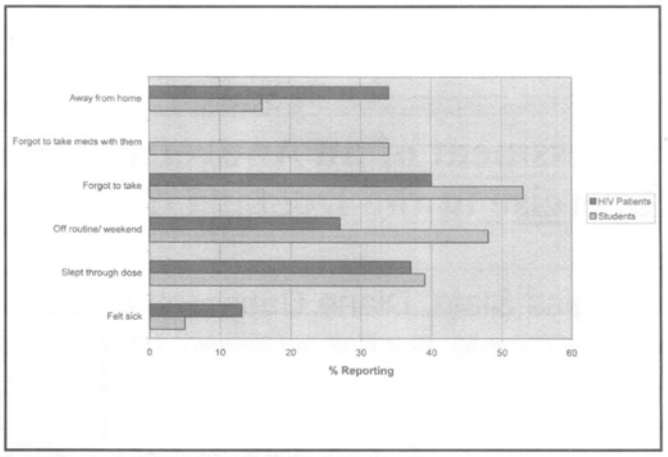

Fig. I. Stated reasons for missed closes by pharmacy students and HIV-positive patients. HIV patient data comes from reference #6.

RESULTS

Student Adherence Rate. The median adherence rate with the zidovudine/lamivudine (Combivir®) placebo tablets was 92.8 percent (range 43-100 percent), and 85.7 percent (range 29-100 percent) with indinavir placebo. The pharmacy students' overall rate of adherence was higher than that of HIV-positive patients, which has been estimated to average as low as 50 percent by some accounts(2). It is difficult to make this comparison between a group that was taking placebos for one week and real patients taking potentially toxic medications indefinitely. The higher rate of non-adherence with the thrice daily indinavir placebo regimen over the twice daily Combivir " placebo regimen appears to be consistent with other reports in HIV-positive patients(12).

When asked to list the reasons for missing doses, the students cited "just simply forgetting to take the medication" as the most common reason (53 percent), followed by change in routine/weekend (48 percent), sleeping through the dose (39 percent), forgetting to bring medications with them (34 percent), being away from home (16 percent) feeling too ill (from " the flu") to take anything (five percent). The students' reasons for non-adherence were very similar to those quoted by HIV-positive patients(6), suggesting an empathetic link to a "real-life" experience. Responses from the pharmacy students and published responses from actual HIV-positive patients are presented in Figure 1.

Dietary Restrictions Adherence Rate. Full adherence with indinavir's meal restriction was achieved by only 44 percent of students. Dietary adherence rates of about 50 percent in HIV-positive patients have been previously reported(13). The median number of glasses of water-based drinks consumed was 5.2 (0.5-15) per day. Twenty-four of 62 students averaged a daily intake of at least six glasses of water-based drinks. Five students (seven percent) said that the water requirement actually made them miss doses of indinavir placebo. The students made more comments about the fluid intake requirement than the meal restriction.

Student Evaluation of Exercise. An anonymous survey found that 60 of the students (92 percent) believed that the exercise was beneficial. Most students (85 percent) recommended keeping the exercise in the Pharmaceutical Care Lab curriculum, while three students (4.6 percent) recommended dropping it

'H1V patient data comes from reference # 6.

because they did not see the value of the exercise. Three students (4.6 percent) suggested shortening the length of the exercise.

DISCUSSION

Obviously, non-HIV-infected students cannot experience the effects of HIV disease or adverse effects from antiretroviral medications. A commitment to a one-week simulation of candy will clearly be quite different from a lifetime of antiretroviral medications. Additionally, there may be psychosocial issues that cannot be experienced by the students. They may not empathize with many of the issues that HIV-positive patients face. However, the sensitivity training exercise may alert pharmacy students to certain medication-related "real-life" barriers to adherence. The students appeared to report many of the same challenges to adherence as did HIV-positive patients. The similarities of reasons for non-adherence were striking, albeit not identical. The students saw the difficulty in adhering to a thrice daily drug versus a twice daily drug. As with real patients, the students also saw how a change in daily routine impacted adherence. Rates of adherence dropped during the weekend for most students either because their routine was changed *of* because they left town without their medications. The effect of just simply forgetting to take a dose appears to be the major reason for missed doses in both students and patients. It was also interesting that even a small number of students could not tolerate taking anything by mouth when they felt nauseated from the flu. When the students were developing alternative second-line antiretroviral regimens, it was apparent that they tried to choose agents that required less frequent dosing and minimal dietary restrictions.

Because the students' responses were not selected from predetermined choices, they were subject to interpretation by the investigators. Fortunately, most of the responses required little interpretation. By keeping the process open-ended, there was less of a chance of introducing suggestion bias. Conversely, not using standardized answers may have caused the formation of different but related responses. For example, if students or patients listed "being away from home" as a reason for non-adherence, others may have responded more specifically "forgot to take medications with them." The reason for non-adherence could have been the same, but the way they responded may have resulted in different answers. As such, the investigators could not use rigorous statistical analyses to compare the responses of the students to those of HIV-positive patients. The fact that substantial numbers of both students and patients listed the same reasons for non-adherence leads us to believe that the students had similar experiences. The sensitivity training exercise was well accepted by the pharmacy students.

Empathetic learning experiences may have an added benefit of reducing negative attitudes of pharmacy and other healthcare students towards HIV-infected patients(14). Negative attitudes and fear about caring for HIV-positive patients can be seen as an additional barrier to establishing a trusting relationship(15,16).

HIV-positive patients often take several other medications, such as prophylactic agents that prevent various opportunistic infections. Our students were only asked to take antiretroviral placebos. The addition of other drugs or scenarios may also be considered for future exercises. Based on this initial experience, the investigators believe that the antiretroviral adherence sensitivity-training exercise was a valuable tool for exposing Doctor of Pharmacy students to real-life medication-related restrictions that HIV-positive patients have with anti-retro virals.

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APPENDIX. ADHERENCE EXERCISE LOG SHEET

Exercise Log Sheet Pharmaceutical Care Lab 5

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday	Monday
Doublevir Dose								
Doublevir Dose								
Mountainavir Dose								
Mountainavir Dose								
Mountainavir Dose								
Meal times:								
Glasses of water								

Reasons for misssed doses:

Comments: