

# Effect of a clinical pharmacist's interventions on duration of antiretroviral-related errors in hospitalized patients

MARK HEELON, DANIEL SKIEST, GARY TERESO, LAUREN MEADE, JULIA WEEKS, PENELOPE PEKOW, AND MICHAEL B. ROTHBERG

Patients receiving long-term medications are at risk for medication errors at the time of hospital admission.<sup>1-5</sup> Patients infected with human immunodeficiency virus (HIV) are at particular risk for prescribing errors related to highly active antiretroviral therapy (HAART), as these individuals take numerous drugs, have multiple comorbidities, and undergo frequent medication changes and because inpatient providers may not be familiar with increasingly complex HAART regimens.<sup>6-11</sup> Even though adherence to HAART is crucial to prevent HIV resistance, in a recent study, medication errors occurred in 25% of patients with HIV at the time of hospital admission.<sup>6</sup> The purpose of this study was to describe antiretroviral prescribing errors and evaluate the effects of an inpatient HIV clinical pharmacist's interventions on reducing the duration of these errors.

**Purpose.** The effect of a clinical pharmacist's interventions on the duration of antiretroviral-related errors in hospitalized patients was studied.

**Methods.** Between August 4, 2005, and February 4, 2006, all patients at least 18 years of age who were admitted to a 651-bed tertiary care teaching hospital and prescribed highly active antiretroviral therapy (HAART) were identified by one clinical pharmacist. If a HAART error was suspected, the pharmacist intervened with the house staff or outpatient physician to discuss and resolve the problem. The pharmacist also retrospectively identified potential HAART errors among patients with human immunodeficiency virus (HIV) admitted between January 2 and June 30, 2005. HAART errors included the following: incomplete regimen, incorrect dosage, incorrect schedule, medication-disease interaction, incorrect formulation, incorrect antiretroviral, duplication of therapy, and drug-drug interaction. The duration of each error was measured from the time of the initial incorrect order until a correct order was placed or until the patient was discharged.

**Results.** A total of 199 admissions for patients with an order for HAART were identified during the study periods. A total of 73 HAART errors were confirmed in 41 patients. The most common type of error was incomplete regimen. There was no significant difference in the frequency or type of prescribing when comparing the preintervention and intervention phases. The median length of time until an error was corrected, however, was significantly shorter during the intervention phase (15.5 hours) than the preintervention phase (84 hours) ( $p < 0.0001$ ).

**Conclusion.** The duration of prescribing errors was decreased when a clinical pharmacist monitoring patients receiving HAART intervened to resolve errors.

**Index terms:** Antiretroviral agents; Clinical pharmacists; Dosage; Drug interactions; Errors, medication; Formulations; HIV infections; Hospitals; Interventions; Rational therapy

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**Methods**

This study was conducted in a 651-bed tertiary care teaching hospital in Springfield, Massachusetts. Between August 4, 2005, and February 4, 2006 (the intervention phase), all patients at least 18 years of age who were admitted to the hospital and prescribed HAART were identified by one HIV clinical pharmacist using a form in the hospital computerized provider-order-entry (CPOE) system.

The form used by the pharmacist was adapted from a drug-use evaluation (Figure 1). The computer could not detect patients receiving HAART at the time of admission if it was entered into the CPOE system as "patient's own medications." Reports of patients receiving HAART were generated daily Monday through Friday. Weekend admissions were captured the next Monday morning. If an error was suspected, the pharmacist intervened

with the house staff or the outpatient HIV physician to discuss and resolve the problem. The pharmacist recorded all interventions. The same form was then applied retrospectively to the electronic records to identify potential errors among HIV patients admitted between January 2 and June 30, 2005. During this preintervention phase, no special pharmacy services were available for HIV inpatients. Some patients who were followed in the outpatient HIV clinic had their medications reviewed after admission if the care team notified the outpatient HIV pharmacist, but this was not systematic. The following data were recorded for all patients: age, sex, race, medication regimen, categories of HAART used, number and types of potential errors, duration of error, discharge regimen, primary diagnosis, and length of stay. We then reviewed the medical records of all admissions that contained a potential error to determine whether an error had actually occurred. Definitions of medication prescribing errors were based on those used in previous studies.<sup>6-12</sup> Outpatient records were also reviewed. If the inpatient regimen matched the outpatient record, we considered the regimen correct, even if it differed from published guidelines. Finally, hospital discharge summaries were reviewed to assess whether HAART errors continued after discharge.

HAART errors were classified as follows: incomplete regimen (e.g., use of two antiretroviral agents), incorrect dosage, incorrect schedule, medication-disease interaction (e.g., failure to adjust for renal failure), incorrect formulation (e.g., didanosine buffered tablets prescribed in place of enteric-coated tablets), incorrect antiretroviral, duplication of therapy, or drug-drug interaction. The duration of each error was measured from the time of the initial incorrect order until a correct order was placed or until the patient was discharged. For patients with two or more errors, we selected the error with the longest

**Figure 1.** Form completed by clinical pharmacist during review of prescribing orders for patients receiving antiretroviral therapy.

Reviewing Patients on Antiretrovirals		
Name _____	R.Ph. Code _____	
Medical Record # _____	M.D. _____	
Date _____		
Yes ___ No ___	Patient receiving more than three antiretroviral medications	
Yes ___ No ___	Nucleoside inhibitors adjusted for renal failure	
Yes ___ No ___	Antiretrovirals are appropriately dosed	
Yes ___ No ___	Antiretrovirals are appropriately scheduled	
Yes ___ No ___	Appropriate antiretroviral formulation used	
Yes ___ No ___	Atazanavir is not given with proton pump inhibitor or H <sub>2</sub> blocker	
Yes ___ No ___	Didanosine dosing adjusted if given with tenofovir	
Yes ___ No ___	Didanosine is not given with stavudine	
Yes ___ No ___	Stavudine is not given with didanosine or zidovudine	
Yes ___ No ___	Amprenavir or fosamprenavir is not given with sulfa allergy	
Yes ___ No ___	Patient on medications that do not interact with antiretroviral agents	
Yes ___ No ___	HIV patient is on trimethoprim-sulfamethoxazole, dapsone, or atovaquone and CD4+ cell count <200 cells/mm <sup>3</sup>	
Yes ___ No ___	HIV patient is on azithromycin and CD4+ cell count <75 cells/mm <sup>3</sup>	
Yes ___ No ___	Patient is not on contraindicated medications	
See antiretroviral card on pharmacy website for dosing, contraindicated medications, and drug interactions.		
If no, contact patient's HIV care provider.		
Intervention		
Yes ___ No ___		
Comment: _____		
_____		
_____		
_____		

duration. The subset of patients cared for by the HIV pharmacist in the outpatient clinic was excluded from the duration-of-error calculations, because the pharmacist often communicated the antiretroviral regimen to the treating physician during both the preintervention and intervention phases. Association of occurrence of any error, number of errors per patient, and type of error with study period was evaluated using chi-square analysis. Differences in length of stay and duration of error for the preintervention and intervention periods were compared using Wilcoxon rank-sum test. This study was approved by the institutional review board of Baystate Medical Center, Springfield, Massachusetts.

### Results

A total of 199 admissions for patients with an order for HAART were identified during the study periods (Table 1). Most patients were admitted for non-HIV-related diagnoses. No significant differences were noted in baseline characteristics between the patients in the preintervention and intervention periods, except that length of stay was longer during the intervention period. Each admission required 10–30 minutes of a pharmacist's time. The mean  $\pm$  S.D. number of antiretrovirals prescribed was  $3.5 \pm 0.8$  medications in the preintervention period and  $3.7 \pm 0.7$  in the intervention phase.

Seventy-three HAART errors were confirmed in 41 patients. The percentages of patients with HAART errors before and during the intervention were similar (17% versus 24%, respectively). The most common type of error was incomplete regimen (45%), followed by incorrect dosage (30%), incorrect schedule (8%), incorrect formulation (7%), incorrect antiretroviral (3%), and medication–disease interaction (3%). Most patients had more than one error, and some had as many as four (Figure 2). Examples of specific error types appear in Table 2.

Table 1.

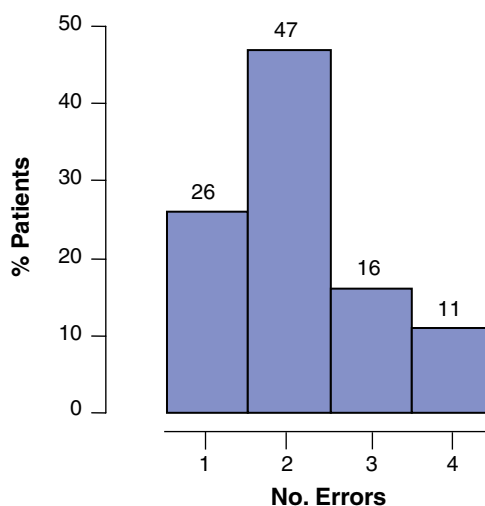
#### Demographic Characteristics of Patients with Orders for Highly Active Antiretroviral Therapy Admitted during the Study Periods<sup>a</sup>

Characteristic	Preintervention Phase (n = 99)	Intervention Phase (n = 100)
Male, no. (%) pts	50 (51)	48 (48)
Median age (range), yr	45 (30–69)	45 (26–69)
Race or ethnicity, no. (%) pts		
Hispanic	52 (53)	48 (48)
Black	29 (29)	27 (27)
White	18 (18)	22 (22)
Asian or Pacific Islander	0	1 (1)
Unknown	0	2 (2)
HIV-related diagnosis, no. (%) pts	13 (13)	17 (17)
Median length of stay (range), days <sup>b</sup>	5 (1–210)	6 (1–206)

<sup>a</sup>Differences between preintervention and intervention periods not significant unless otherwise noted.

<sup>b</sup> $p = 0.005$ , Wilcoxon rank-sum test.

Figure 2. Distribution of errors per patient. A total of 73 errors were confirmed in 41 patients.



There was no significant difference in the frequency or type of prescribing error when comparing the preintervention and intervention phases. The length of time until an error was corrected, however, was significantly shorter during the intervention phase (Figure 3). The median duration of errors was 84 hours (range, 24–7584 hours) in the preintervention phase versus 15.5 hours (range, 1–216 hours) in the intervention phase ( $p < 0.0001$ ). Six patients had antiretroviral prescribing errors in

the preintervention phase that were propagated in the hospital discharge summary, compared with none in the intervention phase ( $p = 0.01$ ).

### Discussion

In this observational study, we found that 21% of HIV patients admitted during a one-year period had errors in their HAART prescribed while in the hospital, with almost half of the errors due to incomplete regimens. We also found that a simple intervention by a clinical pharmacist,

requiring only a few hours per week, detected those errors and decreased the median duration of the errors from 3.5 days to less than 1 day.

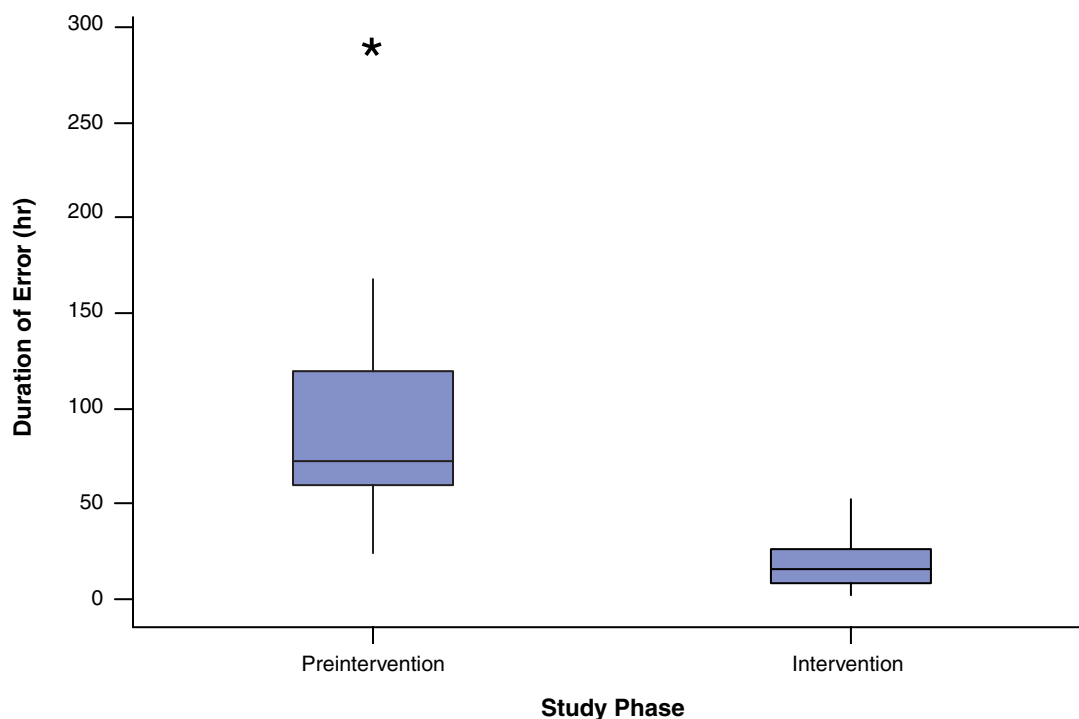
Assuring that patients consistently receive the correct HAART is critical, as incomplete regimens, such as we observed in hospitalized patients,

may result in de facto monotherapy. In such cases, resistance can potentially develop in a matter of days, especially with nonnucleoside reverse

Table 2. Examples of Errors Identified during the Study Periods

Error Classification	Prescription as Ordered	Specific Error Identified
Incomplete regimen	Combivir (lamivudine–zidovudine), one tablet twice daily	Efavirenz 600 mg at bedtime was missing from the regimen.
Incorrect dosage	Abacavir 600 mg twice a day, lamivudine 150 mg twice daily, efavirenz 600 mg at bedtime	Abacavir should have been ordered at a dosage of 300 mg twice daily.
Incorrect formulation	Didanosine, five chewable 25-mg tablets daily; lamivudine 150 mg twice daily; efavirenz 600 mg at bedtime	Didanosine should have been ordered as enteric-coated (EC) tablets 400 mg daily.
Incorrect schedule	Combivir (lamivudine–zidovudine), one tablet daily; efavirenz 600 mg at bedtime	Combivir (lamivudine–zidovudine) should have been ordered to be taken twice daily.
Medication–disease interaction (renal insufficiency)	Didanosine EC 400 mg daily, lamivudine 150 mg twice daily, efavirenz 600 mg at bedtime for a patient with a creatinine clearance of 22 mL/min	Correct dosing for renal insufficiency should be didanosine EC 125 mg daily and lamivudine 150 mg once and then 100 mg daily.

**Figure 3.** Box plot of medication-error duration in the preintervention and intervention phases. The lower and upper vertical lines represent the 10th and 90th percentiles, respectively; the lower ends and upper ends of the boxes represent the 25th and 75th percentiles, respectively; the line in the boxes represents the median duration of error. The asterisk represents an outlier. Outlier of 5040 hours in preintervention phase not pictured.



transcriptase inhibitors and nucleoside cytosine analogues, attributable to the low genetic barrier to resistance associated with these medications. These errors may limit future treatment options, as resistance to one medication can confer resistance to the entire class.<sup>13-16</sup>

Studies of hospitalized patients with HIV infection have shown that prescribing errors involving HAART are common and have increased as the complexity of the regimens has increased.<sup>6-11</sup> Four classes of antiretrovirals are available, with 6 combination products and 21 individual agents to choose from. A recent study at a single institution found that 26% of HIV patients admitted to the hospital had an error in their HAART regimens.<sup>6</sup> Our study found a similar percentage of errors and supports previous findings that incomplete regimens, incorrect dosages, and incorrect schedules are common errors that occur during hospital admission.<sup>6-11</sup> Potential reasons for the errors observed in our study include the patient's lack of knowledge of HAART regimens and lack of familiarity of antiretroviral medications by the admitting physician.

Studies have shown that hospital pharmacists are effective in reducing medication errors, improving patient health outcomes, and decreasing both costs and length of stay.<sup>17-21</sup> This is the first study we are aware of that demonstrates a reduction in the duration of HAART errors in a hospital as a result of a clinical pharmacist's interventions.

This study had several limitations. First, we lacked the ability to detect errors of complete HAART omission at admission, since we reviewed the records only of patients for whom HAART was prescribed. In addition, we did not review the records of patients who used their own HAART medications from home. We believe this is a small percentage of our patients, but including these patients

could have caused our estimates to be higher or lower. Second, since the study was limited to a single pharmacist at one institution, the results may not be generalizable. A number of other studies, however, indicated that these types of errors occur at a similar frequency in other institutions,<sup>6-11</sup> and the algorithm we developed can be easily reproduced. Third, we did not measure the duration of HAART error after discharge nor do we know whether the errors we documented actually led to any demonstrable harm through selection of resistant virus.

This study supports the use of an HIV clinical pharmacist to detect HAART prescribing errors and intervene to decrease the duration of such errors. Future research should focus on improving communication of accurate antiviral regimens among HIV care providers, attending physicians, and ambulatory pharmacies and designing order-entry systems to assist in the ordering of complicated HAART regimens.

### Conclusion

The duration of prescribing errors was decreased when a clinical pharmacist monitoring patients receiving HAART intervened to resolve errors.

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