Original Research

Impact of an HIV-trained clinical pharmacist intervention on error rates of antiretroviral and opportunistic infection medications in the inpatient setting

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Abstract

Background: Based on a retrospective study performed at our institution, 38% of inpatients living with human immunodeficiency virus (HIV) were found to have a medication error involving their anti-retroviral (ARV) and/or opportunistic infection (OI) prophylaxis medications.

Objective: To determine the impact of a dedicated HIV-trained clinical pharmacist on the ARV and OI prophylaxis medication error rates at our institution.

Methods: A prospective quality improvement project was conducted over a six month period to assess the impact of a dedicated HIV-trained clinical pharmacist on the ARV and OI prophylaxis medication error rates. IRB approval received.

Results: There were 144 patients included in this analysis, who experienced a combined 76 medication errors. Compared to historical control study conducted at our institution, the percent of patients who experienced a medication error remained stable (38% vs. 39%, respectively) and the error rate per patient was similar (1.44 vs. 1.36, p=NS). The percent of medication errors that were corrected prior to discharge increased from 24% to 70% and the median time to error correction decreased from 42 hours to 11.5 hours (p<0.0001).

Conclusions: Errors relating to ARV or OI prophylaxis medications remain frequent in inpatient people living with HIV/AIDS. After multiple interventions were implemented, ARV and OI prophylaxis medication errors were corrected faster and with greater frequency prior to discharge, however, similar rates of errors for patients existed. Dedicated HIV clinicians with adequate training and credentialing are necessary to manage this specialized disease state and to reduce the overall number of medication errors associated with HIV/AIDS.

Keywords

Pharmacy Service, Hospital; Pharmacists; Medication Errors; Quality Improvement; Anti-Retroviral Agents; Acquired Immunodeficiency Syndrome; HIV Infections; Inpatients; Historically Controlled Study; Illinois

INTRODUCTION

Adopting recommendations by the U.S. Department of Health and Human Services to initiate antiretroviral therapy (ART) in all people living with the human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) (PLWHA), regardless of CD4 count, increased the number of patients receiving ART for the management of HIV/AIDS.[1] Additionally, advances in treatment have prolonged the expected survival of PLWHA, effectively making HIV infection a chronic disease state. It was estimated that by 2015 half of the PLWHA population would be over the age of 50. While the use of anti-retrovirals (ARVs) have prolonged survival and improved the quality of life of these individuals, medication errors involving ARVs place PLWHA at significant risk for developing adverse events, clinically significant drug-drug interactions, and failure of ART. The incidence of ARV errors reported in the inpatient setting has been as high as 86% with an average of 1.16 - 2.70 medication errors per patient.[2,3] The most commonly identified errors were omission of an ARV, incorrect frequency of dosing, and drug-drug interactions.[2,4-8] Additionally, those with CD4 counts <200 cells/mm^3 and/or AIDS-defining illnesses require additional medications for prophylaxis against opportunistic infections (OIs), creating another potential source for medication errors.

In a retrospective, quality improvement (QI) study completed at our institution errors with ARV and OI prophylaxis medications were found in 38% of patients.[9] The estimated medication error rate was 35% in those receiving ART and 22% in those receiving OI prophylaxis. During this study period, the standard of care at our institution was not to have a dedicated, HIV-trained clinical pharmacist review any ARV or OI prophylaxis order. As a result of that study, a prospective QI project was implemented at our institution to evaluate the impact of having a dedicated HIV-trained clinical pharmacist on the ARV and OI prophylaxis medication error rates at our institution.

METHODS

In this prospective QI project, adult patients were included if they were admitted to the University of Illinois Hospital & Health Sciences System in Chicago, IL over a 6-month intervention period, had a diagnosis of HIV/AIDS, and were taking ARV or OI prophylaxis medications. Exclusion criteria included patients who were co-infected with hepatitis B or C virus (HBV or HCV), not taking ARV or OI prophylaxis

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Table 1. Baseline demographics and exclusion criteria		
	Pre-Data	**Post-Data**
Gender (N)		
Male	192	93
Female	152	51
Age (years [range])	46 [18-85]	50 [18-76]
Race (N)		
Black	259	116
Other	40	12
White	30	11
Hispanic	11	5
Asian/Pacific Islander	4	0
Followed at Institution Clinic (N)		
Yes	226	7
No	118	
CD4 (cells/mm^3)		
Mean	332	363
Median	255	325
(range)	(1-1,680)	(2-1,414)
patients >200	178	85
patients <200	166	43
HIV-RNA (copies/mL)		
Mean	76,541	65,272
Median	73	8,387
(range undetectable)	(4,259,831)	(537,171)
Undetectable (<48 copies/mL)	163	57
HIV-related admission (N)		
Yes	36	21
No	308	123
Length of stay (days)		
Median (range)	5 (1-61)	3 (1-30)
Total Excluded		
HBV, HCV	n/a	32
Not a confirmed HIV diagnosis	108	5
Not taking ARV/OI meds	9	4
<18 yo	24	10
Not admitted	218	4
Pregnant	n/a	6
HIV-Related Admissions		
Kaposi Sarcoma	4	1
HIV-associated B-cell lymphoma	n/a	7
AIDS-related failure to thrive	n/a	4
Suspected cryptococcus	3	1
Suspected toxoplasmosis	4	1
Other	21	7

medications, did not have a confirmed HIV diagnosis, were <18 years old, pregnant, or were not admitted to the hospital. An automated alert, created based on historical data, was generated upon admission of a PLWHA (based on ICD-10 coding) or if an inpatient order for ARV(s) was placed. The alert notified the investigators to review the patient's electronic medical record (EMR). All investigators were HIV-trained, whereas, staff and other clinical pharmacists were not HIV-trained. Specific HIV training included post-graduate residency year 2 education and training in HIV/infectious diseases (ID), ID fellowship training, and also those who have achieved certification as an American Academy of HIV Medicine Trained Pharmacist (AAHIVP). The investigators would evaluate if a medication error occurred and whether it was corrected by the clinical pharmacist, if present, on the admitting service within the first 24 hours of admission. In the event that no clinical pharmacist was present on the admitting service, the investigator would directly contact the medical team to make any recommendations regarding a HIV-related medication error. After 24 hours, the investigators would

contact the clinical pharmacist or medical team managing the patient with any further recommendations.

Baseline demographic data collected included gender, age, race, most recent CD4 count and HIV-RNA viral load, renal and/or hepatic impairment (renal defined as estimated creatinine clearance <50 mL/min and hepatic defined as Child-Pugh Class C), and whether the patient was followed at an outpatient HIV clinic associated with our institution. Collected hospital admission data included whether the admission was HIV-related, admitting medical service, presence of a clinical pharmacist on the admitting service, presence of ID consult service, length of stay, and all ARV and OI prophylaxis medications ordered including dose, frequency, formulation, and formulary status.

All medication errors were documented and classified into one of the following categories: omitted order, missed dose(s), wrong medication, incorrect frequency, incorrect dose, renal adjustment not performed, duplicate order, drug-drug interaction, incorrect formulation, and known drug allergy. This classification and identification of errors was only done by the HIV-trained clinical pharmacist study investigators. At the time of the chart review, Micromedex 2.0® was available through the institution's intranet; therefore, this was used to check drug-drug interactions, which were documented if classified as 'major'.[10] All data was collected from the EMR system, recorded on a data collection form, and organized using REDCap.[11] Also collected was the type of medication error(s) and its associated specific ARV or OI, correction of the error prior to discharge, and how long it took to make the correction. The study received Institutional Review Board (IRB) approval.

For demographic data, the Chi-squared and Wilcoxon Mann-Whitney tests were utilized for categorical and continuous variables, respectively. Descriptive statistics were used to create tables of errors by medication. Statistical significance was set under a p-value of 0.05.

RESULTS

During the 6 month enrollment, 203 patient alerts were sent to the investigators through the EMR system, of which 144 patients were included in the study. Most of the excluded patients were either co-infected with HBV or HCV (N=32), were <18 years old (N=10), or pregnant (N=6). Baseline characteristics (Table 1) included a mean age of 50.6 years, 65% male, and 80.6% African-American. A CD4 count was documented for 128 patients, with a mean of 363 cells/mm^3 (range 1-1,414 cells/mm^3). Approximately 65% of these patients had a CD4 count >200 cells/mm^3. A viral load was documented for 81.3% of patients (N=117), and was detectable (>20 copies/mL) in 51.3% of those patients (N=60). The average daily pill burden was 3.7 tablets (range 1-9). Other baseline information included 53.5% (N=77) of patients following at one of our institution's outpatient HIV clinics. Infectious disease was on consult for 43.1% (N=62) of patients, and a PharmD was on service for 69.4% (N=100) of patients. Compared to the historical data, there were little differences found between pre- and post-data, with the exception of mean CD4 332 cells/mm^3 in pre and 363 cells/mm^3 in post (p = 0.004).

Table 2. Medication errors per patient pre- and post-interventions			
	Pre	Post	p-value
Total number of errors (N)	190	77	0.99
ARV errors (N, %)	151 (79%)	58 (75%)	
OI errors (N, %)	32 (21%)	19 (25%)	
Total number of patients with an error (N, %)	132/344 (38%)	56/144 (39%)	
ARV Error (N, %)	113/320 (35%)	47/144 (33%)	0.99
OI Error (N, %)	37/166 (22%)	17/57 (30%)	0.74
Errors corrected (N, %)	45 (24%)	56 (73%)	
ARV errors corrected (N, %)	40 (26%)	42 (72%)	0.35
OI errors corrected (N, %)	5 (13%)	14 (74%)	0.69
Median time to corrected error (hours)	42	11.5	<0.0001
ARV: anti-retroviral; OI: opportunistic infection			

There were 76 medication errors identified, of these 56 (73.7%) were ARV medications and 20 (26.3%) were OI prophylaxis medications (Table 2). A total of 56 (38.9%) patients had at least one medication error occur during their admission, and 53 (69.7%) of the errors were corrected prior to discharge. Compared to the historical data, the percent of medication errors that were corrected prior to discharge increased from 24% to 70% and the median time to error correction decreased from 42 hours to 11.5 hours (p<0.0001).

The most common reasons a medication error occurred were drug-drug interaction (17.9%), incorrect timing (16.1%), omitted order (14.3%), incorrect dose (14.3%), and missed dose (12.5%). The drugs involved in the drug-drug interactions with ARVs were famotidine (N=5), fluticasone (N=4), and lansoprazole (N=1). A total of 27 non-formulary ARV orders were placed for 25 patients. Of the 56 ARV medication errors that occurred, 6 involved a non-formulary ARV.

We found no stastically significant difference between the pre- and post- medication error rates of either ARV (p=0.99) or OI prophylaxis medications (p=0.74). Likewise, we found no statistically significant difference in the rates of corrected ARV (p=0.35) or OI prophylaxis medication (p=0.69) errors.

DISCUSSION

PLWHA often present to the hospital on multiple medications, including ART and possibly OI prophylaxis medications depending on their CD4 count and past medical history. The combination of multiple medications, unfamiliarity with ARVs, and medications that may or may not be on the hospital formulary can create various avenues for the development of medication errors. This QI project demonstrated that the medication error rate for ARVs and OI prophylaxis medications has unfortunately not improved at our institution since the historical study was performed (38% vs. 39%, respectively), therefore indicating the need for a clinical pharmacist specialized in the area of HIV/AIDS. Medication errors predominantly occurred at the time of order entry by the admitting service. The most common medication errors were incorrect timing, omitted order, incorrect dose, missed dose, and drug-drug interactions. Incorrect timing had a high association with the most common ARV medications associated with an error, ritonavir and darunavir, because their administration was not timed together. Omitted orders mostly involved the omission of the third-most common ARV associated

with an error, tenofovir disoproxil fumarate (TDF), or missing OI prophylaxis medications. In patients with end-stage renal disease, weekly dosing of TDF was often ordered or administered incorrectly. With the newer tenofovir alafenamide fumarate (TAF) formulation being used more often, this may no longer be a significant concern. Although combinations agents including TAF are not approved for hemodialysis, with the exception of elvitegravir/cobicistat/emtricitabine/TAF, these agents may still be used given that TAF itself has been shown to be safe and effective and the other agents appear to be safe as well. Importantly, the rate of medication errors due to incorrect dosing decreased compared to the historical control study performed at our institution (47% vs. 26%). We hypothesize that the addition of single tablet regimens to our hospital formulary was most likely responsible for this decrease.

In the case of drug-drug interactions, the most commonly observed interactions included protease inhibitors and either famotidine or fluticasone. In one case, the fluticasone interaction resulted in symptoms consistent with Cushing's syndrome. It was also observed that after being removed from our hospital formulary, etravirine was still ordered with regularity. As a result, the recommendation was made to add etravirine back to the formulary. The use of non-formulary ARVs resulted in six errors during the course of the study.

Although many previous studies have evaluated the presence of ARV errors in the inpatient setting, fewer have addressed the potential impact that a HIV-trained clinical pharmacist can make on ARV-related error rates. Heelon et al. showed that having a clinical pharmacist review an HIV patient's medication profile upon admission decreased the duration of prescribing errors from 84 hours to 15.5 hours.[12] Daniels et al. found that by implementing targeted interventions such as a small drug reference card, alerts in the pharmacy order-entry system, adding default orders into the computerized physician order entry (CPOE) system, and adding combination ARVs to the formulary, they were able to decrease medication errors from 72% to 15%.[13] Liedtke, et al. involved a dedicated HIV-trained pharmacist and found a 73.9% reduction in errors.[14] Eginger et al. reported 54.7% of patients on ART and/or OI prophylaxis experienced at least 1 medication error at their institution. In that study, the primary investigator was a post-graduate year 2 pharmacy resident, but it appears all incorrect regimens were reviewed by an AAHIVE-certified practitioner. Furthermore, they reported 94.7% of ART errors and 89.9% of combined ART and OI prophylaxis errors were corrected by a HIV-trained pharmacist.[15]

Additionally, Carcelero *et al*. expressed having a clinical HIV-trained pharmacist may reduce errors, which were found in 21.7% of patients with HIV at their institution.[16]

While overall medication error rates remained stable at our institution, the proportion of errors corrected prior to discharge, and the median time to error correction, both drastically improved. This improvement can be contributed to having a designated HIV-trained clinical pharmacist reviewing all inpatients living with HIV/AIDS on a daily basis, who notified the responsible services with recommendations to resolve any medication errors. Similar positive intervention results have been seen in the literature.[13-16] Initially, the intention of the project was to empower the clinical pharmacists on service to better evaluate the PLWHA admitted to their service. However, the investigators found medication error rates slightly rose due to a potential-perceived expectation that the HIV-trained investigators reviewing the patients would recognize any errors and contact the service directly to address any issues. Future directions of this QI data is to demonstrate the need for a dedicated, HIV-trained clinical pharmacist who can monitor these patients to eliminate potential medication errors. Additionally, with HIV guidelines receiving updates frequently, staff education by an HIV-trained clinical pharmacist should be reviewed and provided just as often.

Limitations

Limitations to our study include different investigators performing the historical retrospective study analysis and this prospective QI project. This could potentially create bias and/or the potential to interpret the same error differently. The implementation of multiple types of interventions following the retrospective QI project (in-services for the clinical and staff pharmacists, in-service for the internal medicine residents, a clinical pharmacist checklist for HIV patients based on the most common errors found at our institution, formulary updates, and order sentence changes to the CPOE system) could potentially confound the impact of the HIV-trained investigators each intervention type on ARV and OI prophylaxis medication error rates. However, the similar incidence of error rates between the pre- and post-implementation QI projects suggests these additional interventions had minimal impact on ARV and OI prophylaxis medication error rates at our institution. In some cases, the EMR alerts were sent to the investigators before the patient made it to the floor, in which case the clinical pharmacist on the admitting service may not have had the opportunity to make interventions prior to the investigators.

CONCLUSIONS

With the increased number of patients receiving ART and the growing number of ARVs and combinations on the market, this study helps demonstrate the importance and impact that a HIV-trained clinical pharmacist can have on the timeliness to resolution of medication errors in the inpatient setting. Although the accuracy of medication histories upon admission were not assessed, we believe placing an emphasis on obtaining accurate and complete medication histories at admission may play an important role to decrease ARV and OI medication errors in PLWHA. Additionally, continued and consistent staff pharmacist education may increase the likelihood that medication errors occurring during the ordering process would be identified and resolved prior to order verification. Based on our findings, we believe that a full-time HIV-trained clinical pharmacist should consistently provide review of admission, daily, and discharge medications to reduce errors in PLWHA which also may assist in improving effective transitions of care.

CONFLICT OF INTEREST

No personal connections that could be perceived to bias the work are to report for any authors.

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