

Original Research

Pattern of drug therapy problems and interventions in ambulatory patients receiving antiretroviral therapy in Nigeria

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ABSTRACT*

Objectives: We describe the frequency and types of drug therapy problems (DTPs), and interventions carried out to resolve them, among a cohort of HIV- infected patients on ART in Jos, Nigeria.

Methods: A prospective pharmacists' intervention study was conducted between January and August 2012 at the outpatient HIV clinic of the Jos University Teaching Hospital (JUTH). Pharmacists identified DTPs and made recommendations to resolve them. The main outcome measures were number of DTPs encountered, interventions proposed and acceptance rate of recommendations.

Results: A total of 42,416 prescriptions were dispensed to 9339 patients during the eight months study. A total of 420 interventions (Intervention rate of 1 per 100 prescriptions) were made to resolve DTPs in 401 (4.3%) patients with a mean age of 41 (SD=10) years, and made up of 73% females. DTPs encountered were drug omission (n=89, 21.2%), unnecessary drug (n=55, 13.1%) and wrong drug indication (n=55, 13.1%). Recommendations offered included; Addition of another drug to the therapy (n=87, 20.7%), rectification of incomplete prescriptions (n=85, 20.2%), change of drug or dosage (n=67, 16.0%), and discontinuation of the offending drug (n=59, 14.0%). A total of 389 (93%) out of 420 of the recommendations were accepted. In all, 50.4% (212) of the problematic prescriptions were changed and dispensed, 22.2% (89) were clarified and dispensed, while wrong identities were corrected in 11.7% (49). However, 7.5% (30) prescriptions

were dispensed as prescribed, 5.2% (21) were not dispensed, and 3% (12) were unresolved.

Conclusion: Our findings suggest that pharmacists-initiated interventions can ameliorate DTPs in patients receiving ART given the high intervention acceptance rate recorded. The implication of this finding is that pharmacists with requisite training in HIV pharmacotherapy are an excellent resource in detecting and minimizing the effect of antiretroviral drug-related errors.

Keywords: Pharmaceutical Services; Pharmacists; Medication Errors; Anti-HIV Agents; Nigeria

INTRODUCTION

Drug therapy problems (DTPs) are harmful clinical events directly related to the use of medicines and may include under or overtreatment, inappropriate dosing, choice of formulation, drug interactions, poor adherence, and harm caused by adverse drug events.^{1,2} The burden of DTP on population health is enormous. As many as one in 10 patients are harmed while receiving hospital care in developed countries.³ In the United States for instance, the Center for Disease Control (CDC) estimates that every day 44 people die from overdose of prescription painkillers.⁴ Although data is limited, the burden of DTP is likely to be much worse in low- and middle-income countries due to weak health systems and shortages of trained health care workers. The potential for DTP in HIV pharmacotherapy is high as a result of the chronic nature of the therapy and the use of combination therapy which increases the potential for drug interactions and adverse drug reactions. Other factors which contribute to DTP in HIV therapy are; the rapidly evolving therapeutic options and treatment guidelines, the need for additional counseling; and near perfect lifelong adherence requirement for ART.⁵

Several studies have characterized the nature of DTP and associated pharmacists' intervention in both hospitalized and ambulatory patients. A review of 25 studies conducted in 2014 revealed a high incidence of 86% medications errors involving both antiretroviral (ARV) and opportunistic infection (OI) prophylaxis medications.⁶ Commonly identified errors include omission of an ARV, inaccurate dosing frequency, or drug-drug interactions.⁷⁻¹⁰

A recent multicenter prospective cohort study conducted in Nigeria, involving 6882 HIV positive patients on ART, followed for 9172.5 person-years

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reported a medication error of rate of 40.5 per 100 person-years. The principal errors reported were wrong ARV regimen prescribed (26.4%). This was followed by potential drug-drug interaction or contraindication (19.8%) and inappropriate duration and/or frequency of medication (16.6%). Pharmacists' intervention resulted in the resolution of 97.4% of potential/actual medication error(s) in the study.¹¹ In another Nigerian study involving 9320 ambulatory HIV positive patients on ART, identification and resolution of DTP by pharmacists resulted in clinically significant improvements in patients HIV virological and immunological outcomes.¹²

With the growing number of HIV-infected individuals worldwide and the ever-increasing intricacies of HIV treatment options, understanding the nature and trend of DTP within a practice context is useful in guiding intervention strategies to reduce drug therapy problems. The present study aims to describe the frequency and types of drug therapy problems, and interventions carried out to resolve them, among a cohort of HIV-infected patients on ART in Jos, Nigeria.

METHODS

Study design and population

This was a prospective descriptive study. Study participants included all HIV infected adults (>15 years of age) that presented at the pharmacy with prescription for routine ARV drug pick up or ART initiation between January and August 2012.

Study Setting

The study was conducted at the HIV clinic of Jos University Teaching Hospital (JUTH), which has enjoyed PEPFAR support since 2004. The clinic provides ambulatory treatment, care and support to over 13000 HIV-infected individuals, with over 9000 currently on ART. The clinic runs from Monday to Friday with an average of 220 patients being attended to on a daily basis.

Drug Dispensing Protocol

Eight clinical Pharmacists trained in HIV pharmacotherapy with a work experience of between 4 and 12 years currently provide pharmaceutical care services at the JUTH HIV centre. Pharmacists were trained in various aspects of HIV care such as pharmacology and pharmacokinetics of ARVs, side effects and management of ARV toxicities, opportunistic infections management, as well as how to identify and resolve drug therapy problems. At every fill/refill visit, pharmacists engaged in face to face interaction with the patient in order to verify the accuracy of prescription with consideration to clinical (Past medication history, drug allergies, co-morbid conditions) and laboratory parameters like Viral load, CD4 cell counts, hemoglobin, serum creatinine and liver function tests. This was done in a bid to ensure regimen appropriateness. Adherence education and monitoring were an integral part of pharmaceutical care in the clinic. Patients encounter; including record of drug

dispensed and interventions carried out were documented in an electronic pharmacy data base (FileMaker Pro, FileMaker Inc. USA, version 10.5) which was developed as part of the Harvard PEPFAR/APIN Plus program.

Data Collection

The main outcome measures were number of DTPs encountered, interventions proposed, acceptance rate of recommendations and the perceived benefits as well as the time taken on intervention. For the purpose of this study, intervention was defined as any action undertaken by the pharmacist that led to an alteration of the patient's prescription before the medication was dispensed. Interventions (mainly drug related) were broadly classified into therapeutic, prescription and adherence/patient education.

Therapeutic DTPs included; inappropriate ARV dose, contraindication, drug allergy, and potential for adverse drug reactions (ADR) or drug-drug interactions. Prescription DTPs included; wrong drug prescribed, unnecessary drug, incompletely filled prescription, identity problems. Adherence/Patient related DTPs included; missed appointment, improper drug use, missed doses, unscheduled drug pick up, and alcohol use. Interventions were further grouped into significant and minor errors based on a previous study.¹³ Adherence and therapeutic related DTPs were classified as significant errors considering its potential to cause harm to the patient, while prescription related DTPs were classified as minor errors due to its tendency to cause little or no injury to the patient. Adherence was determined from the consistency of drug refill using the pharmacy database. Patients who were less than 95% consistent in their drug refill were considered non adherent to therapy, while those who were 95% and above consistent in drug refill were classified as adherent.¹⁴ A research specific pharmacy intervention documentation form adapted from literature¹⁵ was used for documentation of intervention carried out at each patient pharmacy visit. The form also captured information on patient demographics, actions taken, recommendations made, acceptance rate of recommendations, time taken for intervention and perceived patient benefits.

Statistical Analysis

SPSS statistical package version 20 (IBM Corp, Armonk, New York, USA) was used for statistical analysis. Categorical variables were expressed as frequencies and percentages; while continuous variables were described using means and standard deviation.

RESULTS

A total of 42,416 prescriptions were dispensed to 9339 patients during the study period. In all, 420 interventions (intervention rate of 1 per 100 prescriptions) were made to resolve DTP in 401 patients; with a mean age of 41 (SD=10) years, and made up of 73% females. The pattern of drug

Table 1. Pattern of drug therapy problems among patients on antiretroviral therapy in Jos, Nigeria.

Drug therapy problems	Frequency	%
Prescription		
Drug omission	89	21.2
Unnecessary drug	55	13.1
Incomplete prescription	54	12.9
Identity problems	49	11.7
Duplication	1	0.2
Sub-group Total	248	59.1
Therapeutic		
Wrong drug indicated	55	13.1
Prior ADR	18	4.3
High dose	12	2.9
Drug Interaction	6	1.4
Low dose	4	1.0
Contraindication	2	0.5
Sub-group Total	97	23.1
Adherence		
Improper use	34	8.1
Missed appointments	20	4.8
Unscheduled Drug Pick-up	12	2.9
Missed doses	8	1.9
Alcohol use	1	0.2
Sub-group Total	75	17.9
Sum Total	420	100.0

related problems (DRP) encountered during the study are summarized in Table 1. Prescription related errors were the most frequently (59.1%) DTP encountered, with drug omission being the most common prescription related error (21.2%). Example of drug omission included; antiretroviral drugs not indicated and/or omission of cotrimoxazole prophylaxis for patients with CD4 less than 350 cells/ml are recommended by the Nigerian national as guideline.¹⁰ Significant errors such as therapeutic problems (23.1%) and adherence (17.9%) related errors accounted for 41% of the total errors. Wrong drug indication (13.1%) ranked highest among the therapeutic problems while improper use of the drug (8.1%) was the most common adherence problem.

Recommendations made to resolve DTP are summarized in Table 2. The most frequent (n=87, 20.7%) type of recommendation was addition of drug to the therapy, followed closely by complete prescriptions (n=85, 20.2%). Change of drug was recommended to resolve 16.0% of the DTPs while drug discontinuation and dosage modification accounted for 14.0% and 7.6% of the recommendation respectively. Others such as resolve identity problems, counseling and referrals represent 17.1%, while 4.3% of the recommendations were not documented.

Overall, 389 out of 420 (93%) recommendations made to resolve DTP were accepted. However, 11 (3.0%) were rejected, while 20(5%) were unresolved. Most of the interventions (50.4%) took between 5-10 minutes while 26.2% and 8.2% of the interventions took between 10-15 minutes and more than 15 minutes respectively. Interventions which took less than five minutes accounted for 15.2%.

Pharmacist intervention resulted in the modification of about half of the problematic prescription (212 out of the 420 (50.4%)), while 93 (22.2%) prescriptions were clarified and dispensed, and 49 (11.7%) that had no/wrong identity were resolved. In addition, 32 (7.5%) of the prescriptions that received

pharmacists interventions were dispensed as written, 22 (5.2%) were not dispensed as the drug was removed from the prescription, while 3% (12) were unresolved as it was not documented.

The actual or potential benefit of pharmacists intervention included prevention of potential adverse drug reactions in 268 (40.5%) of the interventions; through the prevention of drug allergy, contraindication and drug interaction. Other interventions such as resolution of identity problems and modification of unnecessary drug prescriptions potentially resulted in increased therapeutic effectiveness in 252 (38.1%) of the interventions, while improved adherence monitoring through identification of missed appointment, excessive duration, improper drug use, missed doses, fill too soon, alcohol use followed by appropriate counseling, accounted for 127 (19.2%) of the intervention benefits. In 8 (1.2%) of the intervention, the benefits were not documented, and it was unclear in 6 (0.9%) of the interventions.

DISCUSSION

Identification, prevention and resolution of potential/actual DTP are critical pharmacists interventions that can improve the outcome of therapy and reduce harm associated with medicine use. In this study, pharmacists' intervention prevented medication errors with the potential to cause adverse drug reactions from reaching the patient and identified patients with additional therapy needs. Intervention by pharmacists lead to modification of prescriptions for improved therapeutic effectiveness, and improved adherence monitoring. Over 90% of the recommendations made by the pharmacist to resolve DTP were accepted.

Unlike previous studies reporting a high rate of DTP.^{6,11,16} This study observed a low rate (1 per 100 prescriptions) of DTP requiring pharmacist intervention. The DTP rate in this study is similar to a Saudi Arabian study.¹⁷ The low rate of DTP observed in this study might be a reflection of the quality of prescription practice in the study setting. Strategies to improve rational prescribing in the clinic included regular training of all persons involved in medication therapy management, use of structured prescription order forms, availability of electronic medical record system to validated patients previous medications and regimen simplification using fixed dose combinations (FDC). Notwithstanding the good prescription practice, under-reporting which has been shown to be a common practice as found in another study which

Table 2. Types of recommendations made by pharmacists to resolve drug therapy problems.

Recommendation Type	Frequency	%
Add drug	87	20.7
Complete/Clarify	85	20.2
Change Drug	67	16.0
Stop offending drug	59	14.0
Change Dosage	32	7.6
Not indicated	18	4.3
Others	72	17.1
Total	420	100.0

reported that less than 30% of interventions carried out in the ward were not documented¹⁸ may have contributed to the low prevalence of interventions observed in the study. The primary reason for this attitude was lack of time. Other grounds for the low intervention rate included inadequate pharmacotherapy skills and perception of the significance of prescription error.¹³

Over 40% of DTPs identified and resolved in this study were major prescription errors with potential to impact negatively on patients' health outcomes. The results of our study correlate with several other studies involving patients on ART. A Nigerian study reported major and minor prescription errors of 45.5% and 54.5% respectively¹³, while Pottergard *et al.*¹⁹ also reported similar results of 32% and 68% major and minor prescription problems respectively. Drug omission was the major prescription related error encountered in the study. This type of error is common in HIV therapy as a result of the intricacies in the management of HIV and changing guidelines.⁵ In response to the complex nature of HIV therapy, recent guidelines like the WHO 2013 guideline for prevention and management of HIV in adults and adolescents have adopted treatment simplification as one of the core strategies to improve HIV management.²⁰ Synonymous with previous studies¹¹, prescription of wrong drug was common in this study. Prescriptions of wrong drugs are major errors with potential to cause medical harm if not corrected. The frequency of this type of error in the management of HIV is a cause for serious concern. There is an overarching need to strengthen the prescription process through standardization of the prescription process, creation of independent checks for crucial steps in the process and learning from mistakes when they occur. Feedback control systems, immediate and regular review of prescription will help in reducing medical mishaps resulting from prescribing wrong drugs. In addition, training and retraining of prescribers and peer group discussions should be employed as strategies to promote rational prescribing.²¹

About half of the interventions carried out took between 5-10 minutes per intervention; this is in tandem with other studies that reported an average time per intervention ranging from 7 minutes to 10 minutes.^{22,23} Time spent on intervention can be useful in estimating the amount of work the clinical pharmacist does with a view to improving the standard of pharmaceutical care provided to patients.²²

Consistent with other studies^{13,17}, the acceptance rate of the recommendations in this study was quite high. The high acceptance rate of recommendations is an opportunity for the pharmacists to make meaningful contribution to optimize patients' drug therapy and reduce harm related to medicine in a multidisciplinary health care team. Pharmacist should therefore consider their roles as critical in the medication use process and proactively contribute to rational drug use.

The potential benefits of pharmacists' intervention in this study are in agreement with other literature

reports that have it that 46% of the interventions prevented morbidity, complications and rationalized therapy.⁶ In this study, prevention of ADRs resulting from ARV drug-drug, drug-disease or drug-food interaction ranked highest among the perceived benefits. Other perceived benefits which have also been reported by other studies²⁴, included increased therapeutic effectiveness achieved through improved adherence to medication and selection of the right combination and dose of ARVs.

Our study had some limitations. The low intervention rate observed in this study could be due to under reporting. Several reasons could be attributed to this; some prescriptions with problems may have been dispensed with some assumptions, and thus was not documented. Also, poor documentation could be as a result of high patient load. Finally, it is more acceptable to grade DTP into minor and major through a multidisciplinary approach to avoid bias, but this was not done in this study as a result of resource constraint. However, the rating of DTP by independent clinical pharmacists was to minimize bias.

CONCLUSIONS

The high acceptance rate in our study clearly shows that clinical pharmacists make significant contributions towards achieving optimal therapeutic outcome. It also demonstrates the need for active scrutiny of prescriptions and interventions by clinical pharmacists; particularly in an antiretroviral setting before such prescriptions are filled. Documentation of interventions carried out by pharmacists should be emphasized and encouraged especially in resource-constrained settings where such activities are scarce.

CONFLICT OF INTEREST

There are no conflicts of interest to be declared

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PATRÓN DE PROBLEMAS RELACIONADOS CON MEDICAMENTOS E INTERVENCIONES EN PACIENTES AMBULATORIOS QUE RECIBEN TRATAMIENTO ANTIRRETROVIRAL EN NIGERIA

RESUMEN

Objetivos: Describimos la frecuencia y los tipos de problemas relacionados con medicamentos (DTP) y las intervenciones realizadas para resolverlos en una cohorte de pacientes infectados con HIV a tratamiento con antirretrovirales (ART).

Métodos: Se realizó un estudio prospectivo de intervención farmacéutica entre enero y agosto de 2012 en la consulta ambulatoria de HIV del Hospital Universitario de Jos (JUTH). Los farmacéuticos

identificaban DTP e hicieron las recomendaciones para resolverlos. Los *outcomes* principales fueron el número de DTP encontrados, las intervenciones propuestas y la tasa de aceptación de las recomendaciones.

Resultados: Se dispensó un total de 42.416 recetas a 9.339 pacientes durante los 8 meses del estudio. Se realizaron un total de 420 intervenciones (tasa de intervención de 1 por 100 recetas) para resolver los DTP de 401 (4,3%) pacientes con una media de edad de 41 (DE=10) años, de los que el 73% eran mujeres. Los DTP encontrados fueron omisión de medicamento (n=89; 21,2%), seguido de medicamento innecesario (n=55; 13,1%) e indicación terapéutica errónea (n=55; 13,1%). Las recomendaciones ofrecidas incluyeron: Adición de otro medicamento al tratamiento (n=87; 20,7%), rectificación de receta incompleta (n=85; 20,2%), cambio de medicamento o dosis (n=67; 16,0%), y discontinuación de medicamento problemático (n=59; 14,0%). Un total e 389 (93%) de las 420 recomendaciones fueron aceptadas. En total, el 50,4% (212) de los

medicamentos problemáticos fueron cambiados y dispensados, el 22,2% (89) fueron aclarados y dispensados, mientras que se corrigieron identidades erróneas en el 11,7% (49). Sin embargo, el 7,5% de las recetas fueron dispensadas como fueron prescritas, el 5,2% (21) no fue dispensada, y el 3% (12) quedó sin resolver.

Conclusión: Nuestros resultados sugieren que las intervenciones farmacéuticas pueden mejorar los DTP en pacientes que reciben ART, dada la alta aceptación registrada. La implicación de este hallazgo es que los farmacéuticos con entrenamiento en terapéutica para HIV son un recurso excelente para detectar y minimizar el efecto de los errores de los antirretrovirales.

Palabras clave: Servicios farmacéuticos; Farmacéuticos; Errores de medicación; Fármacos Anti-VIH; Nigeria

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