International Journal of Pharmacy Teaching & Practices 2015, Vol.6, Issue 1, 1598-1602.

Evaluation of Prophylactic Use of Cotrimoxazole for People Living with HIV/AIDS

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Research Article

Please cite this paper as Dagmawi Mekonnin, Fanta Gashe. Evaluation of Prophylactic Use of Cotrimoxazole for People Living with HIV/AIDS. IJPTP, 2015, 6(1), 1598-1602.

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ABSTRACT

Background: Co-trimoxazole prophylaxis prolongs the survival and prevents opportunistic infections in persons infected with human immunodeficiency virus (HIV).The aim this study was to evaluate the use of co-trimoxazole prophylaxis in people living with HIV/AIDS in Shenan Gibe Hospital, Ethiopia.

Methods: A retrospective cross sectional design was used to evaluate the use of co-trimoxazole for prophylaxis using patient medical records. The study included all the patients who were on co-trimoxazole during one year period starting from December 2012 to January, 2013.

Results: The majority of study patients (70.99%) were females, and most of them were in the agegroup of more than 14 years (86.45%). A total of 243 (96.83%) patients appropriately initiated co-trimoxazole of which almost half of them (47.52%) were in clinical stage three. Among patients who took inappropriate dose (3.59%), most of them (2.79%) were subjected to under dose drugs. Moreover, co-trimoxazole was used by 6.14% patients in spite of its contraindication, and drug interaction was documented in four patients who had been taking co-trimoxazole with zidovudine. The results also showed that seventy patients discontinued co-trimoxazole and the main reason stated for discontinuation was CD4count greater than 350 cells/mm^3(57.33%). However, nine of these patients discontinued the therapy inappropriately.

Conclusion: The initiation and dose of co-trimoxazole therapy was almost found to be consistent with national guide line. However, co-trimoxazole was used in many patients even if it was contraindicated in these cases. Therefore, both the prescribers and pharmacists should strictly adhere to the guideline for co-trimoxazole prophylaxis in HIV/AIDS patients to promote rational drug use.

Keywords: *Cotrimoxazole, HIV/AIDS, prophylaxis, drug use evaluation, Ethiopia*

Introduction

Drug use evaluation is a systematic process designed to maintain the appropriate and effective use of medications [1].It involves a comprehensive review of patients' prescription and medication data before, during, and after dispensing in order to assure appropriate therapeutic decision making and positive patient outcomes [2].In appropriate use of drugs adversely affects the quality of health care systems in general and patients in particular. It is a common public health problem in developing countries[3].

Cotrimoxazole (CTX) is a broad spectrum antimicrobial agent that targets a variety of aerobic Gram-positive and Gram-negative organisms and protozoa [4]. Therefore, it is of particular interest for prophylactic treatment as it has a wide range of action against common bacteria, parasites including toxoplasmosis and those causing chronic diarrhea, and fungi and yeasts such as Pneumocystics carinii pneumonia (PCP)[5].

Prophylactic treatment with CTX can potentially enhance essential HIV care programs in Africa by preventing several secondary bacterial and parasitic infections in people living with HIV/AIDS (PLWHA) [6]. But, there has beenconcern over the limited evidence base on CTX prophylaxis. However, over the past few years, more data from resource-limited settings have become available on the feasibility and the positive impact of CTX prophylaxis on morbidity and mortality among adults and children infected with HIV [7].

It was reported that CTX is associated with a 25–46% reduction in mortality among individuals infected with HIV in sub-Saharan Africa, even in areas with high bacterial resistance to the antibiotic. These improvements in survival have been accompanied by substantial reductions in severe disease events [8].

Wide scale use of prophylactic CTX may increase the spread of antimicrobial resistance in communities to other pathogens. It is therefore be prudent to confine the use of CTX prophylaxis therapy (CPT)

only to those patients who will benefit from it (9). Accordingly,WHO and joint united nation program on HIV/AIDS (UN AIDS) have recommended CPT for people living with HIV/ADIS (PLWHA) in Africa with symptomatic HIV diseases (WHO stage 2, 3, 4) and asymptomatic individuals who have a CD4 cell count of less than or equal to 350 cells/mm^3[10,8].

The presence of standard treatment guidelines and drug formularies for selected drugs in a health facility does not ensure that they are prescribed and used correctly. One of themechanisms used to ensure correct prescribing and use is drug use evaluation. It is an important tool to improve patients out comes by promoting the rational use of drugs [11]. Therefore, the aim of this study was to evaluate the use of CTX prophylaxis in people living with HIV/AIDS in Shenan Gibe Hospital and Health Center, Ethiopia.

Methodology

The study was conducted in Shenen Gibe Hospital and health center which are located at about 347 Km away from the capital city of Ethiopia, Addis Ababa in south west of the country. The heath institutions provide different services such as outpatient services, inpatient services, mother and child health care and ART services.

A retrospective drug use evaluation was conducted using patient medical record cards based on drug use evaluationguide line of the country. The health center and the hospital together had a total of 2435 people living with HIV /AIDS. The study included all the patients who were on CTX therapy during one year period starting from September 2012 to August 2013. There were 251 patients who were taking CTX during the stated period as prophylaxis, and all these patients were included in study.Independent variableswerelaboratory results, clinical conditions, diagnosis, patent conditions (like age, sex, pregnancy, breast feeding) while the dependent variables were contraindications, indication of CTX, drug-drug interaction, reasons of CTX discontinuation and dose of the drug used.

Data was collected by using data collecting formats which was constructed based on the variables to achieve the objective of the study. The data was collected from patient medical records of PLWHA who took CTX. The collected data was thenanalyzed by using SPSS version 16 and presented using tables, graphs and charts.

Ethical clearance was obtained from Jimma University student research program (SRP). Then, formal letter was written to Shenan Gibe Hospital and health center to get permission for data collection; the confidentiality of the patients was also maintained.

Results & Findings

From the study subjects (251), 178 (70.99%) patients were females and the majority of them werein the age group of more than 14 years (86.45%). Most patients in the age group of more than 14 years were females (62.15%). Patients in age group of less than one year accounted for 2.79% (Table 1).

Table 1: Age and sex distribution of PLWHA on CTX prophylaxis therapy

Age	Sex		Total No (%)
	Male	Female	
< six month	2 (0.89%)	2 (0.69%)	4 (1.58)
six month-1year	1 (0.38%)	2 (0.99%)	3 (1.37)
1-5 years	2 (0.76%)	5 (1.98%)	7 (2.74)
5-14 years	7(2.79)	13(5.18)	20 (7.98)
>14 years	61 (24.30%)	156 (62.15)	237 (86.45)
Total	73 (29.08%)	178 (70.99)	251 (100)

Among the study population, 243 (96.83%) patients appropriately initiated co-trimoxazole according to the national guideline.Almost half of the patients (47.52%) were inclinical stage III when they started CTX prophylactic therapy. The prevalence of Pneumocystics carinii pneumonia, tuberculosis (TB) and fungal infections were 17.84%, 11.92% and 14.35%, respectively. According to the national guideline, it is recommended to measure the laboratory profile of the patient before commencing CPT. Among the study population, CD4 count and hemoglobin level were determined for 207 (82.47%) and 11 (4.38%) of cases, respectively. However, Neutrophil count were performed only in 3 (1.20%) cases (Table 2)

Table2: Indications for initiation of cotromoxazole among PLWHA

Variables		Number (%)
Clinical stage	I	9 (3.47%)
	II	83 (33.17%)
	III	119 (47.52%)
	IV	40 (15.84%)
Concomitant illness	Fungal infection	36 (14.35%)
	Active TB	30 (11.92%)
	PCP	45 (17.84%)
	Toxoplasmosis	9 (3.47%)
	Chronic diarrhea	86 (34.23%)
	Chronic cough	62 (24.76%)
	Oral ulceration	39 (15.62%)
	Fever and GIT symptoms	58 (23.16%)
Laboratory results	CD4 count <350 cells/mm3	207 (82.47)
	Hemoglobin <7m/dl	11(4.38)
	Neutrophil count <750 cells/dl	3 (1.20)

About 96.41% of patients took an appropriate dose of CTX. Among those who took an inappropriate dose, most of the patients (2.79%) were subjected to under dose drugs while two of them took overdose drugs. Three patients and one patient in age group of 5-14 years took under dose and overdose drugs, respectively (Table 3).

Table3: Prescribed dose of co-trimoxazole for prophylaxis among PLWHA

Age	Appropriate dose No (%)	Inappropriate dose No (%)	
		Under dose	Over dose
< six months	2 (0.80%)	1 (0.40%)	0 (0.00)
six month-1year	3 (1.20%)	0(0.00)	0 (0.00)
1-5 year	5 (1.99%)	2 (0.80%)	1 (0.40)
5-14 years	16 (6.37)	3 (1.20)	1 (0.40)
>14 years	216 (86.06%)	1 (0.40%)	0 (0.00)
Total	242 (96.41%)	7 (2.79%)	2 (0.80)

Co-trimoxazole was used by 6.14% patientsin spite of its contraindication in these individuals. The majority of these patients were anemic patients (2.53%) whose hemoglobin level was less than 7gm/dl followed by patients with sever neutropenia (<750 cell/dl)(1.28%)(Table 4).

Table 4: Co-trimoxazole use against contraindication among PLWHA

Contraindication with CTX	**No (%)**
Severe anemia (Hgb<7 g/dl)	6 (2.53%)
Sever neutropenia (<750 cell/dl)	3 (1.28%)
Pregnancy (1st trimester)	2 (0.83%)
Sulpha dry allergy (ADR)	2 (0.99%)
Brest feeding (in 1st four weeks)	1 (0.51%)
Total	14 (6.14%)

Out of 77 patients who took CTX with zidovudine, only four patients experienced severe side effects like anemia (Hgb<7g/dl). The results also showed that seventy five patients discontinued CPT and the main reason stated for discontinuation was CD4count greater than 350 cells/mm^3 (57.33%). Other reasons such as anemia (17.33%), 1st trimester pregnancy (8%), breast feeding (8%) and skin rash (5.33%) were also documented, but in three patients the reason for cessation was not written (Table 5). Nine of these patients discontinued the therapy inappropriately.

Nine of these patients discontinued the therapy inappropriately.

Table 5: Reasons for the discontinuation of CTX prophylaxis therapyin PLWHA

Reason for discontinuation	**Frequency (%)**
CD4>350 cells/mm3	43 (57.33%)
Anemia	13 (17.33%)
Pregnancy(1st trimester)	6 (8%)
Breast feeding	6 (8%)
Skin rash	4 (5.33%)
Not documented	3 (4%)
Total	75 (100%)

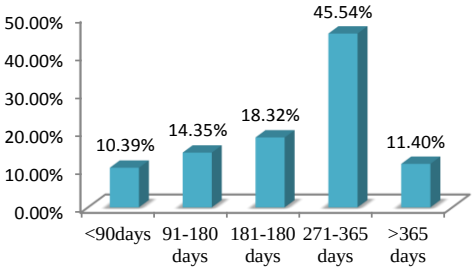

Figure 1: Length of stay of patients on CTX prophylaxis therapy

The duration of CTX prophylaxis therapywas assessed among the study population. Accordingly, the majority of patients (45.54%) stayed on the prophylaxis therapy for 271-365 days followed by 181-270 days (18.32%)(Figure 1).The results also indicated that regular monitoring was done and recorded for 218 patients (86.74%) whereas monitoring results was not documented for 9.53% patients (Figure 2).

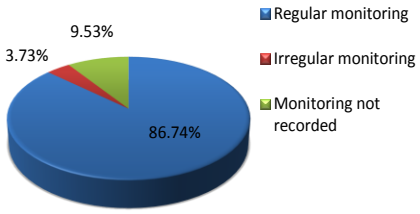

Figure2:Monitoring schedule for PLWHA on CTX prophylaxis therapy

Discussion

The majority of patients (70.99%) on CTX therapies were females. This indicates that the prevalence of HIV/AIDS was higher in females than males in the study area. This finding is almost similar with the observation reported in Hawasa referral hospital [12] and Jimma teaching specialized hospital [13].

Consistent evidence supports the effectiveness of primary co-trimoxazole prophylaxis in those with CD4 counts <350 cell/mm^3 and those with WHO stages 2,3,4 in the absence of CD4 count, patients with WHO HIV clinical stages 3or 4 irrespective of the level of CD4 count[8,10]. In line with this, the majority of patients (96.83%) started CTX for the prevention of opportunistic infections such as Pneumocystics carinii pneumonia, toxoplasma and TB. However, some WHO stage Ipatients (3.17%)whose CD4 level >350 cells/ml initiated CTX

without any symptomatic disease which is not consistent with national guide line. This might result in an increase the risk of CTX side effect to the patients, and increase antibiotic resistance as the patients' immunity is strong enough to defend[14].

In the present study all adults took 960mg of CTX which is consistent with the 2006 WHO CPT guidelines[7]. In HIV exposed or infected children the recommended daily dosage should be accordingly with their age. Those less than six months take 120mg CTX(2.5ml of 240mg/5ml syrup), six months to five years take 240mg/5ml (i.e. 5ml syrup), 6-14 years take 480mg tablet of CTX [7]. However, in this study six patient whose ages less than 14 years took under dose drugs. This could contribute to patient morbidity and mortality as under therapeutic dose of the drug was used. Pharmacists can play a key role in preventing underdoing of medications by ensuring that patient-specific pharmacotherapy is prescribed and administered, and by providing patient and provider education regarding appropriate use of medications [15]. Moreover, two patients from age groups of 1-5 years and 6-14 years received over dose drugs which might cause toxicity even though it was not recorded.

Despite its contraindication, CTX was used in 14 (6.14%) patients. Most of these patients (2.53%) were with severe anemia whose hemoglobin was less than 7mg/dl. The use of CTX in patients with Neutropenia (1.28%), 1st trimester pregnancy (0.83%) sulpha drug reaction (0.99%) and breast feeding (0.51%) were also observed. Compared to the previous study done in Jimma University Specialized Hospital the number of patients used CTX against its contraindication is high [13]. This shows that there was a problem of taking attention about contraindication in the study areas.

In this study only four patients who were taking CTX with Zidozudine experienced severe side effects because of drug-drug interaction. This value is inconsistent with the study done in Boru Meda Hospital wherein almost half of the patients subjected to drug- drug interactions [16]. On the contrary, there were only one patient encountered drug-drug interactions in other study [17].

The national guide line recommend to stop CTX if the patient develops hematological abnormalities, severe skin rash, in pregnancy (1st trimester) if no opportunistic infection and CD4 count >350 cells/mm^3 [18], but in this study nine patients who developed mild anemia, mild skin rash and breast feeding discontinued CPT inappropriately which is not consistent with the national guideline.

Co-trimoxazole prophylaxis for PLWHA should be used where regular follow - up of patients is possible and should be initially every month and then every three months, if the medication is well tolerated children should be evaluated on a monthly basis [18]. In this study regular monitoring was made for 218 (86.74%) patients while 9 (3.73%) patients were monitored irregularly, but in 24 (9.53%) patients monitoring was not recorded. Monitoring in adults should include measurements of hemoglobin and WBC every six months as well as clinically indicated.But, in this study during follow up CD4 count and hemoglobin level were determined for only 82.47% and 4.38% patients, respectively.

Conclusion

The initiation and dose of CTX for preventive therapy for people living with HIV/AIDS was found to be good and consistent with national guide line. However, CTX used in patients with severe anemia, sulpha allergic reaction, severe neutropenia, pregnant mothers (1st trimester) and breast feeding mothers which actually be contraindicated in such situations. Moreover, the discontinuation of CTX for those patients with mild anemia, mild skin rash and breast feeding were not according to the national and WHO CTX guide line. Therefore, both the prescribers and pharmacists who work in the ART clinic should strictly adhere to the guideline for CTX prophylaxis in HIV/AIDS care and treatment to promote rational drug use.

ACKNOWLEDGEMENT

The authors would like to acknowledge the Research Project of Jimma University for funding this research.

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AUTHORS' CONTRIBUTIONS

Authors contributed equally to all aspects of the study.

PEER REVIEW

Not commissioned; externally peer reviewed.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.