ORIGINAL ARTICLE

EVALUATION OF PROPHYLACTIC USE OF COTRIMOXAZOLE FOR PEOPLE LIVING WITH HIV/AIDS IN JIMMA UNIVERSITY SPECIALIZED HOSPITAL, SOUTHWEST ETHIOPIA.

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ABSTRACT

BACKGROUND: ***Drug use evaluation is a performance improvement method that focuses on evaluation and improvement of drug use processes to achieve optimal patient outcomes. The objective of this study was to evaluate the use of cotrimoxazole for prophylaxis among people living with HIV/AIDS in Jimma University Specialized Hospital.***

METHODS: ***Drug use evaluation criteria were set along with threshold based on the national guidelines for cotrimoxazole preventive therapy. The study was done by a cohort design with retrospective review of medical records of r sixty people with HIV/AIDS who have been on cotrimoxazole prophylaxis in the hospital from January 19, 2006 to January 18, 2007. A systematic sampling method was used to select records of the study participants. Data were collected from January 19 to February 3, 2007 using structured format and evaluated against the set criteria and thresholds.***

RESULTS: ***Fifty one (85.0%) patients were in the age range of 15 to 49 years and 33 (55.0%) were females. In all cases, the indication to start, dose and frequency of administration of cotrimoxazole were according to the national guidelines for Cotrimoxazole Preventive Therapy. Forty-six (76.6%) cases were consistent with guidelines for indications to discontinue the drug; however, CD4 count was done only for 28 (46.7%) of patients during follow-up. Fifty-eight (96.7%) and 59(98.3%) of the cases were in accordance with the guidelines for contraindication and drug interactions, respectively***.

CONCLUSION*: The use of cotrimoxazole for preventive therapy for people living with HIV/AIDS was found to be good in Jimma University Specialized Hospital with regard to initiation and dosage. However, the practice of discontinuation of cotrimoxazole and follow-up for drug adverse effects should be improved by proper implementation of the guideline*.

KEY WORDS*: drug use evaluation, cotrimoxazole, HIV/AIDS, Jimma, Ethiopia*

INTRODUCTION

One of the most pressing problems facing public health providers and administrators in many countries is ensuring rational drug use. The Conference of Experts on the Rational Use of Drugs, convened by the World Health Organization (WHO) in Nairobi in 1985, defined rational drug use as: "*The rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community".* Rational drug use implies an individual approach to patient treatment. 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 mechanism to ensure correct prescribing and use is drug use evaluation (DUE) (1).

DUE is a performance improvement method that focuses on evaluating and improving drug use processes to achieve optimal patient outcomes. DUE may be applied to a drug or therapeutic class, or diagnosis. Through its focus on the system of drug use, DUE helps to identify actual and potential drug-related problems, resolve actual drug-related problems, and prevent potential drug-related problems that could interfere with achieving optimum outcomes from drug therapy (23).

Antibiotics represent approximately 30% of acute care hospitals' drug expenditure and they are prescribed for 20-50% of inpatients. The development of bacterial resistance to antibiotics has become a major problem throughout the world. Resistant organisms may emerge as a result of many factors, including irrational use of drugs. Studies have shown that 22-65% of antibiotic prescriptions are inappropriate. In several situations, the rational use of antibiotics has been reported to reduce the emergence of resistant strains (4-6). DUE is one of the increasingly used methods in combating the development of bacterial resistance to antimicrobial agents (5).

Pneumocystis carini pneumonia (PCP) is the most common AIDS-defining illness. Cotrimoxazole (CTX) prophylaxis was shown to effectively prevent PCP in

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patients with clinical evidence of immune suppression (7-9). WHO and the Joint United Nations Program on HIV/AIDS (UNAIDS) have recommended CTX preventive therapy (CPT) for PLWHA in Africa with symptomatic HIV disease (WHO stage 2, 3 or 4) and asymptomatic individuals who have a CD_4 count of less than or equal to 500 cells/mm^3. Wide-scale use of prophylactic CTX may increase the spread of antimicrobial resistance in communities to other pathogens. It would therefore be prudent to confine the use of CPT only to those patients who will benefit from it (10).

Ethiopia has adopted the WHO recommendation and the first TB/HIV and antiretroviral guidelines were issued by Ministry of Health in 2005. So far, there are no published reports in the country aimed at evaluating whether the actual use of CTX for prophylaxis is inline with the guidelines or not. This study evaluated the use of CTX prophylaxis among people living with HIV/AIDS on follow-up at Jimma University Specialized Hospital.

METHODS AND MATERIALS

The study was conducted in Jimma University Specialized Hospital (JUSH) which is found in Jimma Town, South-West Ethiopia. A total of 2155 PLWHA were registered for follow-up care in the hospital until January 19, 2007. Among these, 1293(60%) were taking CTX for preventive therapy. The Number of patients to be included in the study was determined based on DUE guideline recommendation that a DUE report should include data from 30 to 50 cases for commonly prescribed drugs (1). Accordingly, sixty records were selected using systematic sampling method from sequentially arranged medical records (by date of CTX initiation) of PLWHA that were on CPT in the hospital during the period of January 19, 2006 to January 18, 2007. Medical records of patients who have been on CTX for less than three months were excluded from the study since they have inadequate follow-up data for evaluation.

Drug use evaluation criteria with thresholds were set based on the 2005 national guidelines (11,12). The criteria included were; indications to start and discontinue CTX, dose and frequency of administration, contraindications, adverse drug reactions (ADR), and some laboratory tests conducted for monitoring patient conditions. For each criterion a threshold limit was set to measure the extent of practitioner's adherence to the national CPT guidelines (Table 1).

One nurse working in the antiretroviral therapy (ART) clinic collected the data using a pre-tested data collection format. The collected data were analyzed using Excel spreadsheet and interpreted and the results were evaluated against the set criteria and thresholds, and presented in tables and figures.

RESULTS

Sixty patients' records were evaluated for CPT appropriateness. Fifty one (85.0%) patients were in the age group of 15 to 49 years whereas 7 (11.7%) and 2 (3.3%) were under 15 and above 50 years of age, respectively. Thirty-three (55.0%) patients were females and 31(51.7%) were in the age group of 15-49 years. One female was pregnant but the pregnancy history of 11 (35.5%) females was not documented (Table 2).

Table 2. Age and sex distribution of PLWHA on CPT in JUSH, January 19, 2006 to January 18, 2007.

Variable		Number	Percent
Age	< 15 years	7	11.7
	15-49 years	51	85.0
	Above 50 years	2	3.3
	Total	60	100
Sex	Male	27	45.0
	Female	33	55.0
	Total	60	100

Table 1. Drug use evaluation criteria for CPT for PLWHA

Criteria	Threshold (%)
Indications to start Adults • HIV–positive patient with active TB • Symptomatic HIV disease (Stages 2, 3 or 4 of WHO HIV clinical staging) • Asymptomatic patient, CD4 < 500cells/mm^3 Children > 15months • Have event of PCP • Have symptomatic infection • AIDS defining illness • CD4 Percent < 15% Infants > 6 weeks Born to HIV positive mother	100
Indications to discontinue Adults • CD4>500cells/mm^3 • Severe anemia (Hgb<7g/dl) at least for 3 months • Severe thrombocytopenia (platelet < 50,000cells/ml) • Severe Neutropenia (Neutrophil <750cells/ml) • 1st trimester of pregnancy Children CD4 percentage persistently greater than 20% for more than 6 months	100
Dose Adults: • 960 mg/day Children • < 6 months: 120 mg/day • 6 months-5 years: 240 mg/day 6-14 years: 480 mg/day	100
Contraindications • Sulfa allergy • First trimester of pregnancy Breast feeding mothers during the 1st 6 weeks • Renal insufficiency (Creatinine >1.5 mg/dl) • Hepatic diseases (SGPT>115 UI/L for males, 90 UI/L for females) • Bone marrow suppression - Severe anemia (Hgb < 7g/dl) - Severe Neutropenia (Neutrophil < 750 cells/mm^3) Severe thrombocytopenia (platelet < 50,000cells/ mm^3)	95
Drug interactions • Zidovudine • Phenytoin Digoxin	95
Patient monitoring • CD4 count every 3 months • CBC every 3 months Creatinine every 3 months	80

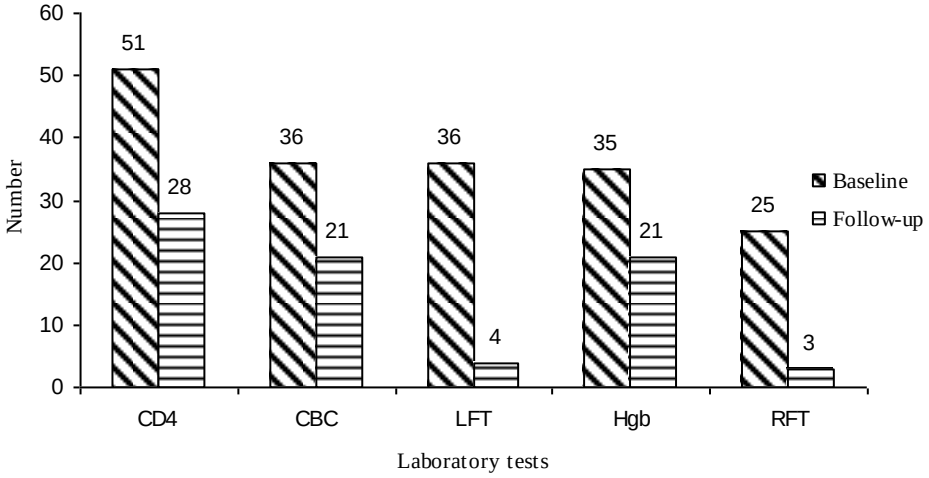

Figure 2: Laboratory tests for monitoring of CPT for PLWHA in JUSH, January 19, 2006 to January 18, 2007.

Table 3: Actual performance versus set criteria and thresholds for CPT for PLWHA in JUSH, January 19, 2006 to January 18, 2007.

Criteria	Expectation/Threshold No. (%)	Actual performance No. (%)
Indication to star CTX	60 (100)	60 (100)
Indication to discontinue CTX	60 (100)	45 (76.6)
Dose	60 (100)	60 (100)
Contraindication	54 (95)	58 (96.7)
Drug Interactions	54 (95)	59 (98.3)
Monitoring	48 (80)	28 (46.7)

The average duration of CPT was 306.8 days (range 135-729 days). Forty-five (75.0%) patients have been taking CTX for a duration of six months to one year. CPT was started for majority of the patients 31(51.7%) while they were in WHO clinical disease stage 3 (Figure 1). All adults were taking 960 mg daily and children were taking depending on their age: 120 mg/day for under 6 months, 240 mg/day for 6 months to 5 years and 480 mg/day for 6-15 years of age.

CTX was discontinued in 17 (28.3%) patients of which the CD_4 count was between 200 and 500 cells/mm^3 with a mean count of 339 cells/ mm^3 in 11 (64.7%) of them. Only two patients (12.5%) stopped CPT according to the guideline. One patient (5.9%) was put off CTX due to severe allergic reaction. The reason for discontinuation of CPT was not recorded in 3 (17.6%) of the patients.

Two(3.3%) patients received CTX despite the presence of contraindication. A pregnant lady was taking CTX throughout her gestation. CTX was concurrently used with Zidovudine (ZDV) at the time of the study in 18 cases. Hemoglobin was checked only for eleven of these concurrent users of CTX and ZDV. Severe anemia was documented in 1 (5.6%) case for whom ZDV was discontinued but CTX was not.

ADR was recorded in 4 (6.7%) patients which included persistent pruritic eruption 2(50.0%) and severe anemia and allergic reactions, 1(25.0%) each. Monitoring of patient conditions during initiation and use of CTX was based on laboratory tests. Initially, CD_4 count, Complete Blood Count (CBC), Liver Function Test (LFT), Hgb and Renal Function Test (RFT) were performed for 51(85.0%), 36(60.0%), 36 (60.0%), 35 (58.3%) and 25(41.7%) of the patients, respectively. During follow-up, the same tests were performed for 28(46.7%), 21(35%), 4(6.7%), 21(35%), and 3(5%) patients, respectively (Figure 2).

Only one of the 18 patients (5.6%) that were taking CTX with ZDV experienced severe anemia. In seven (38.9%) of the 18 patients the level of Hgb or CBC were not documented. Other drug interactions with CTX were not documented. Therefore, the threshold set for drug interaction with CTX (95.0%) was achieved though the Hgb level was not assessed in 7 (38.9%) of the patients

who were taking CTX and ZDV concurrently. Table 3 summarizes the finding of this study in relation to the set criteria and thresholds. The thresholds set for most of the criteria were met.

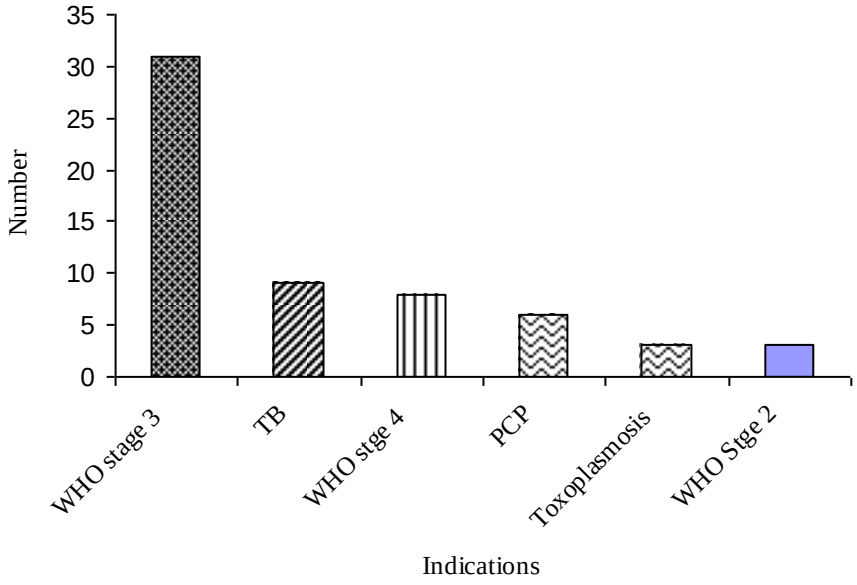

Figure 1: Indications to start CPT for PLWHA in JUSH, January 19, 2006 to January 18, 2007.

DISCUSSION

Practitioners fully adhered to the 2005 national CPT guideline with regard to indication to start CTX preventive therapy though there was a problem in discontinuing the drug. The national CPT guideline recommends discontinuation of CTX when the CD_4 count is greater than 500cells/mm^3. Only two patients (12.5%) stopped CPT according to the guideline. Patients on CPT should be monitored appropriately in order to assess their progresses as a result of prophylaxis to look ADRs and initiate appropriate management. Monitoring of patients on CPT also enables practitioners to assess patients' adherence to their medication and discontinue the drug when the CD_4 count is restored to the recommended level.

All adults were taking 960mg of CTX daily which is consistent with the guideline(11, 12). Children were taking CTX daily on the basis of their age. For pediatrics, the guideline recommends to follow the WHO Guidelines on CTX Prophylaxis (9). Intermittent dosing of CTX was reported to be more acceptable to patients, reduces health service cost and the risk of neutropenia (13). Nevertheless, the 2006 national guideline recommends the daily use of CTX and the hospital practice was inline with it (14). Therefore, the threshold set for dose and frequency of use of CTX was achieved 100% for both adult and pediatric patients.

There were 3(5.0%) patients in which skin manifestations of ADR were documented in relation to CTX use. Two patients developed persistent pruritic eruption (PPE) which was managed by antihistamines and topical anti-inflammatory agents. In one case, the patient was said to be allergic to CTX but whether the patient was initially allergic to sulfa drugs or developed allergy for the first time on the course of therapy was not documented.

CTX was used despite contraindications in two cases; patient with hemoglobin 4.9g/dl and pregnant woman during the whole period of pregnancy. The first case was managed by changing the ZDV. Guidelines recommend monitoring of ZDV toxicity when ZDV and CTX are used concurrently (15). The CD_4 count of the pregnant woman was 218/mm^3, which was adequate to discontinue the drug according to the current practice in the hospital. The pregnancy history of one third of female patients who were in the fertile age group was not documented. This might imply that CXT may have been used in other pregnant women during the first trimester of pregnancy.

According to the national guidelines during follow-up, routine laboratory tests are not required but investigations should be done for patients with clinical

indications for CBC and RFT every three months. Inline with this, CBC and Hgb levels were determined for 21 (35.0%) patients at least once during their course of CPT. LFT and RFT were performed in 4(6.7%) and 3(5.0%) patients, respectively. Even though the average stay of patients on CPT in this study was 306 days, the CD_4 count and the CBC or Hgb level of all patients should have been measured at least once during the course of CPT for better care.

In this hospital, follow-up of pediatric patients was appropriately done and documented as compared to adults where only some laboratory tests were conducted to assess the development of certain ADRs and the level of CD_4 count of the patients. CD_4 count was performed in 28 (46.7%) of the patients at least once during the course of CPT and this enabled to withdraw CPT in those patients with improved CD_4 counts to the recommended level. This helps to reduce the pill burden of patients on ART thereby to improve their adherence and treatment outcome.

To date, there are no published studies conducted on evaluation of cotrimoxazole use for prophylaxis in PLWHA and hence it was not possible to compare the practice of this hospital with practices of other clinical settings. The findings were discussed in relation to the 2005 CPT guideline of Ethiopia.

In conclusion, the overall use of CTX in PLWHA in JUSH was inline with the national guidelines and met the thresholds set for most of the criteria. But, discontinuation of CPT for those patients showing improvements in their CD_4 count was not according to the national guidelines. Moreover, monitoring for adverse reactions during follow-up visits was not consistently done for all patients. Therefore, the practice of discontinuation of cotrimoxazole and follow-up for adverse drug effects should be improved by proper implementation of the guideline.

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