INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com
ISSN 2230 – 8407

Research Article

EVALUATION OF CO-TRIMOXAZOLE AS PREVENTIVE THERAPY FOR PEOPLE LIVING WITH HIV/AIDS IN JIMMA HEALTH CENTER, SOUTHWEST ETHIOPIA

Gizat Molla Kassie*[1], Alemayehu Lelisa Duga[2], Paulos Jemaneh Nebi[3]
[1]Clinical Pharmacist and Lecturer, Department of Pharmacy, College of Public Health and Medical Sciences, Jimma University, Ethiopia
[2]Responsible pharmacist, Health quest Pharmaceutical Company, Manzini, Swaziland
[3]Jimma University Libraries
*Corresponding Author Email: geez99@gmail.com

Article Received on: 29/03/14 Revised on: 23/04/14 Approved for publication: 07/05/14

DOI: 10.7897/2230-8407.050584

ABSTRACT
Co-trimoxazole is used as preventing therapy for many opportunistic infections in people living with HIV/AIDS. The main purpose of this study was to evaluate co-trimoxazole as preventive therapy in Jimma health center. A retrospective Cross-sectional method was used and data was collected from June 28 to July 08 2013. Form the total 320 patients, 185 (57.8 %) were females, 142 (98.4 %) were in the child bearing age. Most (90.3 %) of the patients were world health organization clinical stage I. There were not any cases in which co-timoxazole was used against contraindication; co-trimoxazole was used as per the recommended prophylactic dosage in 320 (100 %) of the patients. The treatment was discontinued in 11 patients, eight (2.5 %) of the discontinuations were due to $CD4^+$ count greater than 350 cell/mm^3. Co-trimoxazole preventive therapy was started prior to antiretroviral therapy in 260 (81.3 %), concurrently with Antiretroviral Therapy in 46 (14.4 %) and after Antiretroviral Therapy in 1 (0.3 %) of the patients. Only 29 (9.06 %) patients were monitored regularly and monitoring schedule or data was not recorded for 122 (38.13 %) patients. The evaluation of Co-trimoxazole as preventive therapy among people living with HIV/AIDS was in line with the WHO guideline for indication in all of the patients'. Dosage and observance of contraindication was also consistent with the guideline in most of the cases studied. Problems regarding patient monitoring and initiations of CPT relative to ART were identified in most of the patients.
Keywords: Co-trimoxazole, $CD4^+$, HIV, Antiretroviral therapy, Evaluation

INTRODUCTION

Drugs are among the most expensive inputs of the health service[1]. Moreover, investing on genuine use of drug is fruitful in that possible changes can be made in the clinical safety, efficacy, suitability and cost effectiveness of drugs[2,3]. For Ministries of Health of different developing countries drugs make one third to two third of the total public and private expenditure and in the developed countries drugs expenditures reach as high as 10-20 % of the total health expenditures[4]. Co-trimoxazole is a fixed dose combination of Sulfamethoxazole, a para-amino benzoic acid (PABA) analog that inhibits bacterial dihydropteroate synthase, and trimethoprim a primethamine which selectively inhibits bacterial dihydrofolate reductase. It is a broad spectrum antimicrobial agent active against several aerobics gram-negative and gram-positive bacteria, fungi and protozoa species[5]. It is active against *Pneumococcus,* Non-typhoid *salmonella, Isospora, Cyclospora, norcardia, Toxoplasma, Pneumocystis* (now called *Pneumocystis Jiroveci pneumonia*) and *Falciparum plasmodium* all of which are causes of common opportunistic infections in people living with HIV/AIDS (PLWHA)[6]. Several clinical trials, cohorts and program analysis in several Africa countries have shown that Co-trimoxazole preventive therapy is effective in reducing early mortality and morbidity among PLWHA, A clinical trial in Lusaka, Zambia showed that despite the high prevalence of resistance (60-80 %), Co-trimoxazole preventive therapy (CPT) reduced mortality by 43 % and hospitalization by 23 %[7]. A study in Mali showed that CPT reduced the prevalence of malaria in HIV uninfected patients[8]. It is proven that CPT is helpful and effective for people of all ages whose $CD4^+$ T-cell count is < 200 cell/mm^3 of blood and / or those with WHO stage 2, 3 or 4 for HIV and TB infection[10-12]. Antibiotic therapy has been done simply by traditional principles regardless of the identity of the potential infecting organism and also without a clear concern about the drug sensitivity and potential resistance to drug[13]. PLWHA and or Co-infected by TB, whether or not they have access to ART, they will develop HIV related opportunistic infections due to their compromised immune system[6]. WHO has developed guidelines on Co-trimoxazole Preventive Therapy (CPT) for HIV related infection among children, adolescents and adults in resource limited areas. The guidelines specify recommendations that should be followed during selecting patient candidate for CPT, issues to be considered during therapy; condition on how to manage side effects of CPT, discontinuation of CPT when necessary and how to monitor patient on CPT[5]. Co-trimoxazole has widely used as a treatment for common infections in many resources limited areas and as a result resistance among these pathogens has increased dramatically. Resistance of non-typhoid *salmonella* and *Pneumoccous* isolate to Co-trimoxazole has been reported to 44 % and 52 % respectively in Uganda and approximately 80 % and 90 % respectively in Miami[14].

MATERIALS AND METHODS

The study was conducted in Jimma health center in Jimma town, Jimma health center from May 15-Spetember 30, 2013. It gives service to 42,164 populations. The health center has three health officers, one B.Sc. Nurse, three B.Sc. Lab, ten Nurses, three B.Sc. Lab Technologist, one Pharmacist, one Druggist, and forty two Supportive Stuffs. Retrospective cross-sectional study design has been conducted based on patient information. The source population of the study was all patient of PLWHA in ART office at JHC. The study populations for this study were all patient of PLWHA who

started taking co-trmoxazole preventive therapy during the year 2012. There were 320 patients who were taking co-trimoxazole in Jimma Health Center. All patients were included in the study so as to increase representativeness of the data. Independent variables were patient characteristics (age, sex, pregnant, and breast feeding), Laboratory result, and Patient clinical conditions. Dependent variables were Indication, contraindication, Drug –drug interaction, Dosage, Monitoring of CPT, Discontinuation of CPT and Timing of CPT. Data collection format containing the above variables to be measured has been developed and used to collect the necessary data. Data was extracted from the patient follow up card using pre-tested data collection format. Before data collection on official letter has been written by Jimma university school of pharmacy to Jimma health center, in addition, the patents information was not identified, it were kept secretly. The data collectors has been trained and daily supervised during data collection period, after data collection, processing and analysis were closely controlled by the researchers. The collected data was filtered, categorized and the results were analyzed by tallying and using calculator then interpreted and presented according to the 2012 WHO guidelines.

RESULTS

A total of 320 patients follow up card were reviewed to evaluation of co-trmoxazole (CTX) for preventive therapy in people living with HIV /AIDS. Two hundred fifty eight patients were adults (including the age between 15 years to 49 years and greater than 50 years) and sixty two (19.25 %) were children. Two hundred forty eight (77.4 %) of the patients were in the age of between 15 years and 49 years old, the above fifty years were 10 (3.35 %) patients, from the total population 57.8 % were female, 62 (19.25 %) of the children were in the age between 6 years-14 years old (Table 1).

One hundred forty two (98.4 %) of female in the child bearing age (15-49 years) were neither pregnant nor breast feeding. Two hundred eighty nine (90.3 %) of the PLWHA were presented with WHO clinical stage I HIV infection and all 320 patients of PLWHA were with $CD4^+$ count of less than 350 cell /mm^3 at the start of CPT. Thirty four (10.6 %) were TB infected and there were not laboratory results of the patients hemoglobin < 7 g/dl, neutrophil < 750 cell/dl and platelets < 50,000.Cell/dl as well as the patients were not tested liver function or not attached the report with the follow up card (Table 2).

All 320 patients under the study fulfilled the criteria to be candidate for CPT. During patients taking CTX were not shown any contraindication. CTP was prescribed as per the standard prophylactic dosage specified in the guidelines in 320 (100 %) of the patients (Table 3).

Isoniazid (INH) was another drug prophylactic for TB infection of PLWHA, which was prescribed as per guideline 300 mg/day. CPT was discontinued in 11 patients of which 8 (2.5 %) were withdrawn from CPT due to the $CD4^+$ count were greater than 350 cell/mm^3 and others were unknown the reason discontinuation of CPT (Table 4).

Monitoring of patient on CPT was done regularly only 29 (9.06 %) of the patients. Irregular monitory was done for 169 (52.8 %) of the patients and 122 (38.13 %) patients were not monitored that mean monitoring recorded data were not available. (Table 5)

The majority of CPT was initiated before ART in 260 (81.3 %) of the patient from which CPT was started more than 2 weeks ago 229 (71.6 %), two weeks ago in 31 (9.7 %) and less than 2 weeks before ART in 13 (4 %) moreover it was found that CPT and ART were concurrently started in 46 (14.4 %) of the patients and ART was started before CPT in 1 (0.3 %) of the patients (Table 6)

Following table shows the summary of finding that in accordance with the criteria in the CPT guideline as percentage of the total number of cases (Table 7)

Table 1: Age and sex distribution of PLWHA taking CTP in JHC, 2012

Age	Sex		Total No (%)
	Male No (%)	Female No (%)	
6 years - 14 years	25 (18.50 %)	37 (20.0 %)	62 (19.25 %)
15 years - 49 years	104 (77.0 %)	144 (77.80 %)	248 (77.40 %)
> 50 years	6 (4.50 %)	4 (2.20 %)	10 (3.35 %)
Total	135 (42.2 %)	185 (57.8 %)	320 (100 %)

Table 2: Condition of PLWHA the start of CPT in JHC, 2012

Variables	No (%)
HIV infection clinical; stage I	289 (90.3 %)
II	26 (8.10 %)
III	5 (1.6 %)
TB Co-morbidity	34 (10.63 %)
Laboratory result	
- $CD4^+$ count < 350 cell/mm^3	320 (100 %)
- Hemoglobin < 7 g/dl	0
- Neutrophils count < 750 cell mm^3	0
- platelets count < 50,000 cell/dl	0
- S-GPT>11$\frac{ml}{L}$ for female	0
- >90$\frac{ml}{L}$ *for female*	0

Table 3: CTX dosage prescribed for PLWHA on JHC in, 2012

Age distribution	No of cases		Total No (%)
	Appropriate dosage	In appropriate dosage	
6 years - 14 years	62 (19.25 %)	0	62 (19.25 %)
15 years - 49 years	248 (77.4 %)	0	248 (77.40 %)
> 50 years	10 (3.35 %)	0	10 (3.35 %)
Total	320 (100 %)	0	320 (100 %)

Table 4: Common reason for discontinuation of CPT among PLWHA on JHC in, 2012

Reason for discontinuation	No (%)
The $CD4^+$ count > 350cell/mm^3	8 (2.5 %)
Unknown reason	3 (0.95 %)
Total	11 (3.45 %)

Table 5: Monitoring schedule of PLWHA taking CPT on JHC in, 2012

Monitoring Schedule	No (%)
Regular Monitoring	29 (9.06 %)
Irregular Monitoring	169 (52.8 %)
Monitoring not recorded	122 (38.13 %)
Total	320 (100 %)

Table 6: Timing of CPT initiation relative to ART initiation in JIIMA health center, 2012

Timing of initiation	No (%)
> 2 weeks before ART	229 (71.6 %)
2 weeks before ART	31 (9.7 %)
< 2 weeks before ART	13 (4.0 %)
CPT and ART Started concurrently	46 (14.4 %)
ART before CPT	1 (0.3 %)
Total	320 (100 %)

Table 7: Summary of finding that is in accordance the guideline in JHC, 2012

Criteria	Case in which the finding were in line with the guideline	
	No	Percentage
Dosage	320	100 %
Drug-Drug interaction	0	0 %
Time of initiation CPT	260	81.3 %
Patient Monitoring	29	9.06 %
Discontinuation	11	3.45 %

DISCUSSION

In this evaluation of co-trimoxazole study, 320 patients of PLWHA on CPT reviewed. All (100 %) of the patients fulfilled the criteria in laboratory monitoring were $CD4^+$ count less than 350 cell per mm^3 of all patients started CPT according to WHO guideline, Practitioners fully adhered to the 2005 national CPT guideline with regard to indication to start CTX preventive therapy[15]. Based on WHO clinical staging and $CD4^+$ cell count criteria, Moreover, majority (90.3 %) of the patients were with WHO clinical stage I which is asymptomatic and generalized lymphadenopathy, CTX prophylaxis is initiated based on WHO clinical staging criteria only. CTX prophylaxis is recommended for all symptomatic people with mild, advanced and several HIV disease (WHO clinical stage 2, 3 or 4) for every one with $CD4^+$ cell count less than 350 cell mm^3[16]. Adult and adolescents with a history of severe adverse reaction to CTX or other sulfa drug should not be prescribed CTX prophylaxis. Concerning Contraindication in the use of CPT were not cause any contraindication on the patients during studying, WHO guideline is setting some CPT contraindications (Bone marrow suppression, Hepatic insufficiency and server reaction) In this studying pregnant living with HIV widely use CTX but there is no evidence of an increases in CTX related adverse event among pregnant women versus no-pregnant women. In Jimma hospital studying on CTX preventive therapy, there were 3 (5.0 %) patients in which skin manifestations of ADR were documented in relation to CTX use[17]. Discontinuation should be based on clinical judgment, including both clinical and laboratory parameters. The safety of co-trimoxazole in long-term use has been established. Drug-related adverse events are uncommon and typically occur within the first few weeks of starting prophylaxis. Clinical monitoring should be carried out regularly, ideally at a minimum of three monthly intervals, with individuals encouraged to report adverse symptoms as soon as they are noted[16]. In this studying Clinical monitoring of PLWHA was taken CPT 169 (52.8 %) were irregular monitoring, which was in every three months in the beginning of CPT, 29 (9.06 %) which was taken every month. The rest of the patients 122 (38.13 %) were not available recorded data. About clinical monitoring WHO guideline is should be done each monthly for first 2 months, and 3 monthly then after otherwise deterioration of disease condition and adverse drug reaction should be documented. Co-trimoxazole prophylaxis is prescribed by health workers at the health centre or regional hospital. You are not expected to prescribe the drug, but once these patients are referred back to the community you should make sure they are taking their drugs correctly. As a standard, you will need to follow-up patients on Co-trimoxazole prophylaxis every month for the first three months. Later, if no problems occur and if the patient takes the drugs correctly, the follow-up can be done every three months[17]. CPT was found to be discontinued 11

(3.45 %) of patients. The most common reason for CTX discontinuation was found the $CD4^+$ count of the patients greater than 350 cell/mm^3 which accounts 8 (2.5 %) which was tested the $CD4^+$ T cell count for every 3 months two times before discontinuation and the unknown reason of discontinuation was 3 (0.95 %). WHO recommends discontinuation of CTX among adult and children with a high incidence of bacterial infection and malaria. Also discontinuation of CTX prophylaxis among PLWHA with evidence of immune recovery related to antiretroviral therapy ($CD4^+ \geq$ 350 cell/mm^3) after at least six month of antiretroviral therapy. The national CPT guideline recommends discontinuation of CTX when the CD4 count is greater than 500 cells/mm^3. Only two patients (12.5 %) stopped CPT according to the guideline[15]. The WHO guideline recommended daily dose of CTX for the age between 6 years to 14 years is single strength adult tablet (400 mg SMX with 80 g TMP) or 10 ml suspension and for greater than 14 years old, double strength adult tablet (800 mg SMX with 160 mg TMP). Thus CTX dosage prescribed for PLWHA in JHC were appropriate dosage in age distribution, the studying of CPT Jimma hospital which has similar result of appropriate dosage in age distribution[15]. And also the 2005 national CPT guideline recommended similar dosage. Two hundred twenty nine (71.6 %) of the patient CPT was started before more than ART 2 weeks ago, two weeks ago in 31 (9.7 %) and less two weeks before ART in 13 (4 %) of the patient Moreover it was found that CPT and ART were concurrently started in 46 (14.4 %) of the patients and ART was started after CPT in 1 (0.3 %) of the patients. In this study the problem identified regarding initiation of CPT, 13 (4 %) of the patient were starting less than two weeks before ART. Moreover it was found that CPT and ART 46 (14.4 %) of the patients were concurrently started and regarding CPT 1 (0.3 %) of the patients was started after ART. According to the guideline of WHO and this finding it will be advisable if CPT is started more than two weeks before ART.

CONCLUSION

In this study the evaluation of co-trmoxazole as preventive therapy among people living with HIV/AIDS was in line with the WHO guideline for indication in all of the patients' studies. Dosage and observance of contraindication also consistent with the guideline in most of the cases studied. Problems were regarding patient monitoring and initiations of CPT relative to ART were identified in most of the patient. From the total population the majority of the patients that are taking CPT were found to be female (15-49 years old) which accounts as 57.8 %. According to result of clinical condition of the patients that start CPT, the majority is at stage I which is 90.30 % of the total population. The laboratory result of all patients regarding $CD4^+$ count < 350cell/mm^3 to start CPT, the rest result shows that the patients are not examined with the other laboratory tests. The majority of the patients that are about 2.5 % have discontinued the therapy because their result shows that the $CD4^+$ count > 350 cell /mm^3. In this study the minority patients that are found to be (9.06 %) are following monitoring schedule but the majority which is (52.8 %) follow irregularly. From the timing of CPT initiation relative to ART point of view, the majority accounts to be (71.6 %) are starting CPT more than two weeks before ART but the minority (0.3 %) start ART after CPT.

ACKNOWLEDGEMENTS

We are grateful to the Jimma University for financing this study. Special thanks to the workers of Jimma health centre for allowing us to collect data. Finally we glorify God for a successful completion of this study.

REFERENCES

1. MSH, WHO. Managing drug supply. 2nd edition, USA kumarian press; 1997.
2. Alfonso RG. Riming ton: The science and practice of pharmacy 20th ed. USA, Loppicot Williams; 2001. p. 1625-30.
3. Federal ministry of Health. Guideline for use of cotrmoxazole as preventive therapy among people living with HIV/AIDS in Ethiopia, Addis Ababa, Ethiopia; 2006.
4. WHO/EDM. Medicines strategy: framework for action in essential drugs and medicines policy, 2000-2003, Geneva; 2000.
5. Chambers F. Sulfonamides, Trimethoprim and Quinonnes. In Katzung B. Basic and clinical pharmacology, 10th edition, USA, MCGRAW Hill publishers; 2006.
6. Henry F, Marie A. Chemotherapy of microbial diseases. In: Goodman and Gilman's, The pharmacological basis of therapeutics, 10th edition, USA, McGraw-Hill; 2000. p. 1029-1057.
7. WHO, TB/HIV. A clinical manual 2nd edition, Switzerland; 2004. p. 1157-58.
8. Thera MA, *et al.* Impact and cotrimoxazole prophylaxis on *falciparum* malaria infection. Journal of infectious Diseases 2005; 192: 1823-1829. http://dx.doi.org/10.1086/498249
9. Graham SM. Co-trimoxazole prophylaxis for infants exposed to HIV infection Bulletin of the world Health organization 2004; 82: 297-298.
10. Graham SM. *et al* Clinical presentations and outcomes of PCP in Malawian children. Lancet 2000; 355: 369-373. http://dx.doi.org/10.1016/S0140-6736(98)11074-7
11. Kapalan J. *et al* Guidelines for preventing opportunistic infections among HIV-infected persons-2002 recommendations of the US. Public Health service and the infections Dieses society of America. /WWWR/recommendations and reports 2002; 5/RR08): 1-46.
12. Vano M, *et al*. A community based study of the incidence of Co-trimoxazole use for preventable infections in Malawian adults living with HIV. Journal of AIDS 2005; 39: 626-631.
13. John Hopkins Bloomberg School of public health. Public health news center. http://www.Jhsh.edu.org; 2013.
14. Erbay A. *et al*. Evaluation of antibiotic use intensive care units of tertiary care hospital in Turkey. Journal of Hospital Infection 2005; 59(1): 53-61. http://dx.doi.org/10.1016/j.jhin.2004.07.026
15. Dirba L, Worku F, Girma T. Evaluation of prophylactic use of cotrimoxazole for people living with HIV/AIDS in Jimma University specialized hospital, South West Ethiopia. Ethio J Health Sci 2008; 18(3): 59-64.
16. Guidelines on co-trimoxazole prophylaxis for HIV-related infections among children, adolescents and adults; 2006.
17. Monitoring co-trimoxazole prophylaxis http://labspace. open.ac.uk/mod/oucontent/view.php ?id=452603andsection=1.8.4; 2013.

Cite this article as:

Gizat Molla Kassie, Alemayehu Lelisa Duga, Paulos Jemaneh Nebi. Evaluation of Co-trimoxazole as preventive therapy for people living with HIV/AIDS in Jimma health center, Southwest Ethiopia. Int. Res. J. Pharm. 2014; 5(5):403-406 http://dx.doi.org/10.7897/2230-8407.050584

Source of support: Nil, Conflict of interest: None Declared