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Use of cotrimoxazole prophylaxis in HIV infected in patients at a referral hospital

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Abstract

Objective: To assess the extent of use of cotrimoxazole prophylaxis in the prevention of opportunistic infections in HIV infected patients.
Setting: Parirenyatwa Hospital, a major referral and teaching hospital.
Design: A retrospective study.
Subjects: 234 HIV infected patients admitted between January and June 2004, with a history of symptoms falling into the WHO stage 3 AIDS, were included.
Main Outcome Measures: Cotrimoxazole prophylaxis, PCP prevalence, and mortality.
Results: 234 patients' records were reviewed and 19% of the patients had received cotrimoxazole prophylaxis. PCP prevalence was 36% which was diagnosed mainly by clinical examination and sometimes

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with the additional help of chest X-rays. Of those who were on prophylaxis, 75% were on primary prophylaxis and the rest on secondary prophylaxis. All patients on prophylaxis were using cotrimoxazole, with the 960mg once daily dosing being the most common regimen (96%). Receiving prophylaxis was associated with being female (p=0.0067), widowed (p=0.012), and taking ARV therapy (p=0.0026). Prophylaxis significantly reduced mortality (p=0.0017). The development of PCP was associated with a history of tuberculosis relapse (p=0.022).

***Conclusion*:** Cotrimoxazole prophylaxis is important in reducing hospital admissions due to opportunistic infections and increasing survival especially in areas with limited access to antiretroviral therapy.

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Introduction

The sub-Saharan region is the most affected by the HIV/AIDS pandemic with an average of 8% of the population being infected.[1] Opportunistic infections have a major impact on the health and survival of HIV infected patients. The advent of highly active anti-retroviral therapy has, however, significantly reduced the prevalence of opportunistic infections in HIV infected patients.

Primary prophylaxis of opportunistic infections continues to be one of the most important strategies in the management of patients infected with HIV.[2] In addition, primary prophylaxis against opportunistic infections including *Pneumocystis carinni* pneumonia (PCP) has already been shown to have an independent role in prolonging survival.[3,4] *Pneumocystis carinii* remains an important pathogen for the broad spectrum of immunocompromised individuals, despite significant advances in antimicrobial therapy. Cotrimoxazole is recommended as the drug of choice for the prevention and treatment of PCP.[2,5]

In Zimbabwe, PCP has been reported to be one of the most common life-threatening opportunistic infections, occurring in 33% of HIV positive people.[6] Its significant contribution to the high mortality and morbidity rate makes it very critical to the clinician who is concerned about improving survival in this group of patients. The World Health Organisation (WHO) and the Essential Drugs List of Zimbabwe (EDLIZ) recommends that cotrimoxazole should be given to all patients with symptomatic HIV (and not on antiretroviral therapy), or who have had an attack of PCP, and to all patients who have any AIDS defining condition. The regimen recommended is a life-long, 960mg (sulphamethoxazole 800mg and 160mg trimethoprim) once daily dosing.

In resource-poor settings where accessibility and affordability of ARV therapy are major stumbling blocks to the provision of highly active antiretroviral therapy (HAART), prophylaxis against opportunistic infections may be the next best alternative in the management of HIV and AIDS. The use of cotrimoxazole prophylaxis is associated with a significant decrease in the incidence of opportunistic infections, notably *streptococcus pneumoniae* pneumonia, PCP, non-typhoid salmonelloses, non-specific gastroenteritis, cerebral toxoplasmosis, pneumococcal pneumonia, bacteria dermatoses, acute unexplained fevers, nocardiosis, isosporiasis and malaria.[7] The study seeks to assess the extent of the use of cotrimoxazole prophylaxis in HIV infected patients admitted at a major referral hospital.

Materials and Methods

The study was carried out at Parirenyatwa Hospital, a major referral and teaching hospital in Harare, Zimbabwe. Medical records of HIV infected patients admitted into the medical wards during the period 1 January to 30 June 2004 were reviewed. Patients above the age of 18 with a medical history falling into the WHO stage 3 AIDS category were recruited into the study. The inclusion criteria was having a history of one or more of the following: unexplained fever or diarrhoea of more than four weeks duration, oropharyngeal candidiasis, hairy leukoplakia, more than 10% weight loss, pulmonary TB, PCP, CD4 cell count less than 200/ml, bedridden for more than 50% of a day and a documented positive HIV test. Ethical approval was obtained from the hospital Ethics Review Committee.

A computer print out was used to retrieve patient medical records. A structured collection tool was then used to extract data on socio-demographic characteristics and medical history including a history of prophylaxis. Cotrimoxazole prophylaxis was defined as receiving the drug continuously for at least one month.

Statistical analysis was performed using STATA 7.0, Texas USA. After checking for normality of the data, the variables age and number of admissions were noted to be normally distributed. The mean (SD) and median (Q_1, Q_3) were used to describe normally and non-normally distributed variables respectively. The student's t-test and the Mann-Whitney test were used where appropriate to compare the distribution of variables between groups. The 0.05 level of significance was used.

Results

Four hundred and three medical records were reviewed, of which 234 (58%) had complete information and were therefore included in the study. Table I shows the characteristics of patients grouped according to whether they received prophylaxis or not and history of PCP infection as determined by the medical history. Table I

Table I: Characteristics of study participants. Values are numbers (percentages) unless stated otherwise.

Characteristic	Overall (n=234)	On Prophylaxis (n=51)	Not on Prophylaxis (n=183)	p value
Sex, Males	108 (46)	15 (29)	93 (51)	0.0067
Age (mean, SD) years	37.8 (9.8)	37.2 (10.5)	38.0 (9.7)	0.5993
Employed	99 (42)	17 (33)	82 (45)	0.1415
Marital				
Single	26 (11)	6 (12)	20 (11)	0.012
Divorced	42 (18)	10 (20)	32 (18)	
Windowed	36 (15)	15 (29)	21 (12)	
Married	130 (56)	20 (39)	110 (60)	
Patients on ARV therapy	18 (8)	9 (18)	9 (5)	0.0026
Pneumocystis carinii	85 (36)	18 (35)	67 (37)	0.8644
Mortality	85 (36)	9 (17)	76 (42)	0.0017
Number of admissions (mean SD)	1.4 (0.74)	1.3 (0.17)	1.4 (0.75)	0.5824
Average duration stay per Admission (median; Q_1, Q_3) days	6.0 (3,12)	6.0 (3,12)	6.0 (3,12)	0.7089
Other opportunistic infections	89 (38)	26 (51)	63 (34)	0.3563

Out of 216 patients 42 (19%) who were not on antiretroviral therapy received cotrimoxazole prophylaxis. The commonest regimen was 960mg once a day (96%), and the rest were on 480mg two times a day. A small proportion of patients (8%) were on antiretroviral therapy.

More than half (58%) of the patients were not formally employed and 56% were married. The main qualifying criteria for prophylaxis were a history of tuberculosis (25%), recurrent respiratory infections (16%) and PCP (13%). Others qualified on the following criteria: chronic diarrhoea (14), recurrent candidiasis (8), Kaposis' sarcoma (4), meningitis (8), weight loss greater than 10% (9), unexplained fever for longer than four weeks (2), and cytomegalovirus infection (1). Of the patients not on cotrimoxazole prophylaxis and not on antiretroviral therapy (n=183), 5% were allergic to cotrimoxazole. The prevalence of all the opportunistic infections was 38%, while a 36% prevalence of PCP was also recorded.

Prophylaxis was associated with being female (p=0.0067), widowed (p=0.012) and receiving ARV therapy (p=0.0026). In addition, prophylaxis was found to significantly reduce the risk of mortality (p=0.0017).

A significantly high rate of co-infection was recorded in patients who had PCP with 48% having TB and 12% with other forms of pneumonia. Co-infections were successfully treated in 67% of the patients. Antibiotic treatment for PCP included cotrimoxazole (81%) and clindamycin (19%).

Of patients who developed PCP 39% had a past history of other respiratory infections especially TB (35%). Statistical analysis further revealed a strong association (p=0.022) between PCP infection and a history of TB relapse. However, treatment of the respiratory infections which preceded PCP was successful in almost all the patients (91%). On the other hand, patients who did not get PCP had a 71% prevalence of other respiratory infections. The most common being TB (85%) followed by bacterial pneumonia (15%). Most (72%) of these were successfully treated.

A mortality rate of 36% was recorded with the major cause of death being PCP followed by TB and meningitis respectively.(Table II).

Table II: Major causes of death, n=85.

Causes of death	Frequency	%
PCP	27	32
Tuberculosis	18	21
Meningitis	11	13
Bacterial pneumonia	8	9
TB + bacterial pneumonia	9	11
Kaposi's sarcoma	4	5
Other	8	10

Discussion

The study recorded a low use of cotrimoxazole prophylaxis accompanied with a high mortality rate on patients not on prophylaxis. The PCP prevalence recorded (36%) is in agreement with that reported in an earlier study conducted nearly a decade ago.[6] This possibly suggests that very little has changed in terms of therapeutic strategies in reducing opportunistic infections in HIV infected patients. The low number of patients accessing antiretroviral therapy probably explains this observation.

It is interesting to note that being on prophylaxis was associated with being female, widowed and being on antiretroviral therapy. Generally, females have a different health seeking behaviour in comparison to males. Females are known to be more health conscious, taking more responsibility for their health and that of family members. It is also natural that after the death of a spouse due to an AIDS related disease, the surviving partner will be more health conscious and therefore seek medical advice on preventing opportunistic infections. Even though a small number of patients were on anti-retroviral therapy, it would appear as if constant contact of the patient with the physician promotes the use of prophylaxis. This is probably due to the fact that regular visits to the physician allow continuous and constant monitoring of the patient's condition and hence better management.

A significant benefit of cotrimoxazole prophylaxis in reducing mortality was not surprising, as this has been reported in clinical trials. The benefit in reducing PCP infection was also observed in this study even though this was not statistically significant. This is probably due to the small sample size studied, a low level of compliance in those patients on prophylaxis and the use of hospital subjects who by definition are of ill health in comparison to outpatients. In a meta-analysis of 35 randomised controlled trials involving 6 538 patients, cotrimoxazole prophylaxis was shown to be associated with a significant reduction in the incidence of both PCP and toxoplasmosis.[8]

The strong association observed between the history of TB relapse and the development of PCP is also not surprising. HIV infected patients in WHO stage 3 already have a deteriorating immune system which makes them more likely to have TB relapses and other opportunistic infections. As stated in HIV treatment guidelines, cotrimoxazole prophylaxis is very important in this group of patients for preventing these opportunistic infections.

This was a retrospective study and hence prone to biases inherent in this design. The use of patient medical records is associated with incomplete entries; however patient records that were deemed not to contain adequate information were excluded. In addition, this study was carried out in a hospital and used data collected from in patients. The use of hospital subjects may have introduced bias in estimating the extent of cotrimoxazole prophylaxis. In patients, as earlier alluded to, are different from out patients in many respects. First, by definition in patients are of ill-health, and secondly the extent of cotrimoxazole use could be different. Outpatients who visit the clinics regularly are more likely to be on cotrimoxazole prophylaxis and compliant. These patients are less likely to have opportunistic infections and therefore less likely to be admitted to a hospital. Conversely, as observed in this study in patients are likely not to be on prophylaxis or non-compliant. Therefore, these results cannot be generalised to outpatients and there is need for a follow up study to assess the use of cotrimoxazole prophylaxis in patients seen at the outpatients department.

The study underscores the importance of cotrimoxazole prophylaxis in preventing opportunistic infections and reducing disease burden and mortality. Reduced opportunistic infections will result in a reduction in admissions. Health care resources spent in the treatment of these opportunistic infections can then be redeployed to other departments that would ultimately result in improved health delivery services. The major causes of death in this study were PCP and TB, which can be prevented by prophylaxis with cotrimoxazole and isoniazid respectively. Cotrimoxazole is cheap, widely available and the regimen of once a day dosing means compliance is not likely to be a problem.

Conclusion

Cotrimoxazole prophylaxis is important in reducing hospital admissions due to opportunistic infections and increasing survival especially in areas with limited access to antiretroviral therapy.

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