A STUDY OF PHARMACOKINETICS OF ANTITUBERCULOSIS DRUGS IN ZAMBIAN PTB PATIENTS CO-INFECTED WITH THE HUMAN IMMUNO-DEFICIENCY VIRUS.

By

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DEDICATION

To ROKAYA and SALIM
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AIDS  Acquired Immune Deficiency Syndrome
ATT  Anti-Tuberculosis Treatment
ANOVA  Analysis of Variance
AUC  Area under the concentration versus time curve
CD4  Cluster Differentiation: T-helper/inducer lymphocytes
CD8  Cluster Differentiation: T-helper/inducer lymphocytes (Comprises 2/3 circulating T cells)
Cmax  Maximum measured Drug Concentration
CN  Cyanide
CSF  Cerebral Spinal Fluid
DOTS  Directly Observed Treatment Short Course
FBC  Full Blood Count
GIT  Gastro-intestinal Tract
HIV-1  Human Immune Deficiency Virus type 1
HIV-2  Human Immune Deficiency Virus type 2
HPLC  High Performance Liquid Chromatography
LFTs  Liver Function Tests
MDR-TB  Multi-Drug Resistance Tuberculosis
MIC  Minimum Inhibitory Concentration
PAS  Sodium para-aminosalicylate
PTB  Pulmonary Tuberculosis
RNA  Ribonucleic Acid
TB  Tuberculosis
TDM  Therapeutic Drug Monitoring RNA
UK  United Kingdom
USA  United States of America
UTH  University Teaching Hospital, Lusaka, Zambia
UV  Ultra Violet
WHO  World Health Organization
ZDHS  Zambia Demographic and Health Survey
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ABSTRACT

SETTING:
The present study assesses the pharmacokinetic parameters for rifampicin, isoniazid and pyrazinamide in Zambian PTB patients with HIV at the University Teaching Hospital, Lusaka, Zambia. The assaying of the drugs was done at the University College London Medical School.

OBJECTIVE:
To determine whether the pharmacokinetics of anti-tuberculosis drugs at steady-state are altered in HIV infected patients especially those with chronic diarrhoea.

METHOD:
60 pulmonary tuberculosis patients, (20 HIV negative, 20 HIV positive without diarrhoea and 20 HIV positive patients with diarrhoea) were entered into a pharmacokinetic trial. Following supervised administration of standard doses of isoniazid, rifampicin and pyrazinamide, the plasma concentrations were measured over 24 hours to obtain the pharmacological parameters of the drugs. The following were then compared in the three groups for any significant difference: maximum measured drug concentration ($C_{\text{max}}$) and area-under-the-concentration-time curve to 24 hours ($\text{AUC}$).

RESULTS:
No notable differences emanated between the three groups i.e. HIV negative, HIV positive without and with chronic diarrhoea, on comparing the $C_{\text{max}}$ and $\text{AUC}$ ($P>0.05$). 20% of the participants were found to be fast acetylators (extrapolated using $t_{1/2}$ for isoniazid).

CONCLUSION:
This study could find no conclusive evidence that HIV infection, especially associated chronic diarrhoea affected the pharmacokinetics of the anti-tuberculosis drugs.