DETERMINING THE RATE, NATURE AND PREDICTORS OF ADVERSE DRUG REACTIONS ASSOCIATED WITH THE USE OF HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART) IN A RESOURCE LIMITED SETTING (ZIMBABWE).

THESIS

BY

TINASHE MUDZVITI

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SUPERVISOR: DR. C. C. MAPONGA

SCHOOL OF PHARMACY

UNIVERSITY OF ZIMBABWE

P O BOX MP 167

MOUNT PLEASANT

HARARE
ZIMBABWE

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ABSTRACT

Background: Dilemmas exist between balancing cost and toxicity of antiretroviral therapy (ART) in resource limited settings (RLS). Most pharmacovigilance programmes in RLS are unable to monitor adverse drug reactions (ADRs) due to inconsistent support systems. The study was carried out to implement a 3-step approach in identifying ADRs in patients on ART. The study was also designed to determine the rate nature and predictors of toxicities associated with ART in a RLS (Zimbabwe).

Methods: The 3-step approach involved a pharmacist, physician and a drug regulatory agency (Medicines Control Authority of Zimbabwe, MCAZ) at each respective step. The pharmacist (investigator) was responsible for collecting data of suspected ADRs from the patient charts. The physician documented patient information in the patient charts, while the drug regulating body ascertained the causality of the suspected ADRs. The 3-step approach was used in ascertaining causality of cutaneous ADRs in 221 patients. To determine the rates and predictors of ADRs, 388 HIV positive adults stable on first line ART dispensed from Parirenyatwa Hospital, Harare, Zimbabwe were interviewed and their respective patient charts were consulted. Data analysis was carried out using the Statistical Analysis System (Version 9.2, Cary, North Carolina, USA). Three regression models, one multiple linear regression model and two logistic regression models were run to identify predictors of ADRs.

Results: Of the 221 patient case report forms that were reviewed for causality assessment by the MCAZ, 39 patients had cutaneous drug eruptions. The rates of ADRs that were observed in the population included peripheral neuropathy (42%), skin rash (26%), lipodystrophy (3%), abdominal pain (8%), gastro-intestinal symptoms (7%) and headache (3%). Peripheral neuropathy and skin rash were mainly observed with stavudine (93%) and nevirapine (88%) based regimens respectively. Lipodystrophy occurred only in participants on stavudine based therapy. 161(58%) ADRs were grade 1 events (World Health Organization's ADR grading system), 96(34%) were grade 2, 15(7%) were grade 3 and 1(0.3%) was grade 4. One patient on a nevirapine containing regimen had grade 4 Stevens - Johnson syndrome. In a logistic regression model, two indigenous herbal remedies were associated with the occurrence of ADRs in participants. Rates of toxicities were higher in the population receiving stavudine and nevirapine based therapies.

Conclusion: Implementation of the 3-step approach in a RLS can an accurate technique in implementing pharmacovigilance programmes in RLS. The results of this study showed that 3 in every 4 patients initiated on first-line HAART in the government roll-out programme experienced a clinical adverse drug event.

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