Retrospective Study of Antiretroviral Drug Associated Hepato Toxicity among Human Immune Deficiency Virus Infected Pregnant Women in Kisumu, Kenya.

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ABSTRACT

Antiretroviral associated toxicity among pregnant women is a concern in HIV treatment. Among these is viramune® (Nevirapine, Germany) which is known to cause hepatotoxicity among patients with over 250/mm^3 CD4 counts as seen in altered alanine aminotransferase (ALT) and total bilirubin (TBILI) levels. These two were evaluated in women participating in the Kisumu breastfeeding study (KiBS) who received combivir® (lamivudine and zidovudine, England) and either nevirapine or viracept® (nelfinavir, U.S.A).

Alanine transaminase and total bilirubin levels were measured at screening, delivery; 2, 6 and 14 weeks;6, 9, 12, 18 and 24 months postpartum. For inclusion into the study, ALT had to be <2.5 times the upper limit of normal values. Medians and inter-quartile ranges were analyzed, data was stratified by CD4 counts and drug regimen, and toxicities categorized according to the Division of AIDS (DAIDS) toxicity tables. Toxicities were further compared using U.S.A reference ranges against local ranges.

There were 522 HIV infected pregnant women enrolled; 310 on lamivudine/zidovudine/nevirapine and 212 on lamivudine/zidovudine/nelfinavir. Median ALT increased slightly whereas total bilirubin remained unchanged. Among the 522 participants enrolled, 496 (95%) had normal ALT and total bilirubin values throughout the study period. There was no increase in risk for Grade≥2 ALT observed among participants on nevirapine as compared to those on nelfinavir and further there was no increase in risk for Grade≥3 alanine transaminase observed among participants on nevirapine as compared to those on nelfinavir. There was no increase in risk for Grade≥2 and Grade≥3 ALT elevation among participants with

CD4 count >250 as compared to those with CD4<250 observed. Further among participants on nevirapine there was no increase in risk for Grade≥2 and Grade≥3 ALT elevations and no increase in risk for rash in those with CD4 count >250 observed. Finally among participants with CD4 count >250, no increase in risk for Grade≥2 and Grade≥3 ALT elevation in those on nevirapine was observed. One case of hepatitis B infection and two cases of Stevens Johnson Syndrome occurred however all SAEs resolved with substitution or cessation of ARV. Comparing the frequencies of elevated values using U.S.A against local reference ranges, higher frequencies were observed with U.S. ranges for total bilirubin ($P<0.0001$) and ALT ($P<0.0001$). Majority of the participants depicted normal ALT and total bilirubin values and the percentage of adverse events among women on nevirapine were low but similar to other trials utilizing nevirapine regimens. There was no increase in risk among women with CD4 count >250 and who were on NVP, while this data is reassuring, close observation and laboratory monitoring of patients being started on ARVs, particularly nevirapine is prudent. More participants were categorized with elevated chemistry values with U.S.A as compared to local laboratory reference ranges, showing the need to derive local ranges for efficient care and treatment of patients in PMTCT clinical interventions.