ABSTRACT

Human Immunodeficiency Virus (HIV) remains the leading cause of morbidity and mortality in Kenya with a prevalence of 6.5%. Highly active antiretroviral therapy (HAART) is used to manage the disease by increasing the CD4 concentration and reducing the viral load. Majority of these HAART based medication contain nevirapine (NVP) that is metabolized through the cytochrome P 450 (CYP450) system. Polymorphisms on CYP2B6 gene may interfere with catalytic activity of the enzyme leading to either an increase or reduction in NVP plasma concentrations. The study aimed to determine the influence of CYP2B6 gene polymorphisms on nevirapine plasma concentration, CD4 T-cell concentration, viral load change among HIV infected individuals on NVP-containing HAART regimen. This was a prospective study among 228 HIV infected adults attending Kenyatta National Hospital. Whole blood samples were collected from the study participants at enrolment and six months post-treatment. The samples were genotyped for CYP2B6 516G>T and 983T>C mutations using real-time polymerase chain reaction (RT-PCR) technique. Pharmacokinetic analysis was done six months post treatment using tandem quadruple mass spectrometer; to determine NVP plasma concentrations. The CD4 cell count and plasma viral load were analyzed at both enrollment and six months post treatment. Descriptive statistics of frequency, mean and standard deviation were used to describe the participants’ socio-demographic and clinical characteristics. Chi square test was conducted to determine if the genotypes were in Hardy-Weinberg equilibrium. A one way analysis of variance (ANOVA) was used to determine the relationship between the changes in CD4 cell count, HIV RNA viral load, biochemical and haematological parameters and CYP2B6 genotypes. The frequency of the T variant allele on the CYP2B6 516G>T polymorphism was 45.2% while the proportion of participants with GG, GT and TT genotypes were 50%, 36%, and 14% respectively. The frequency of the C variant allele on the CYP2B6 983T>C polymorphism was 38.6% while participants with TT genotypes were 61.4%. Nevirapine mean plasma concentrations were higher among homozygous participants with CYP2B6 516TT mutant at 5.335.9 ng/mL compared to those heterozygous 516GT (4.985.5 ng/mL) and 516GG wild type (3725.8 ng/mL). Heterozygous participants with CYP2B6 983T>C genotype had higher mean nevirapine plasma concentration of 47.489 ng/mL compared to the wild-type CYP2B6 TC at 41.615 ng/mL. There was a lower mean CD4+ concentration at six months post treatment among individuals with CYP2B6 516TT and CYP2B6 516GT polymorphisms compared to those with the wild-type CYP2B6 516GG. In the general linear model controlling for baseline CD4+ cell count, HAART regimen and NVP plasma level; GG genotype (wild type) and GT genotype (heterozygous mutant) predicted greater change in CD4 cell count. HIV-1 RNA plasma viral load concentration were found to be higher among those with 516GT and 516TT compared to those with 516GG. There were no significant effect on CD4 and viral load concentration among those with 983T>C polymorphisms. This study indicates that CYP2B6 516G>T polymorphism is associated with a significant reduction in viral load concentration and an increase in CD4 cell count among participants on NVP. CYP2B6 983T>C polymorphism was found not to have a significant effect on NVP plasma concentration, increase in CD4 cell count and reduction in viral load concentration. These findings are similar to the studies by Oluka in Kenya and Ngaimisi, in Tanzania. It can therefore be concluded that a polymorphism on CYP2B6 genotype results in both immunological and virological changes among patients on NVP containing therapy. Further studies need to be conducted among different population groups with specific genetic mutants such as GT and TT to determine the specific immunological and virological changes.