

Abstract

The non-nucleoside reverse transcriptase inhibitor, efavirenz is metabolized primarily by the polymorphic cytochrome P450 2B6 (CYP2B6), and high plasma concentrations of the drug are associated with a single nucleotide substitution at position 516 (516 G>T) of CYP2B6 giving rise to CYP2B6*6 allelic variant with functional or non-functional activities. The pharmacokinetics of efavirenz is associated with a long steady state half-life of 40-55 h, which is suitable for once daily dose regimen [1-3]. The study was carried out to investigate the steady state plasma levels of efavirenz in HIV/AIDS out-patients with a view to recommending a genotype-based dose adjustment on the administration of efavirenz. Following written informed consent, one hundred and six (106) HIV/AIDS sero-positive black African patients of Kenya origin (made up of 40 males and 66 females) undergoing treatment at the Comprehensive Care Center of the Kenyatta National Hospital, Nairobi were enrolled in the study. Plasma concentrations of efavirenz were determined using a high performance liquid chromatographic (HPLC-UV) technique. Out of the 106 HIV/AIDS patients investigated, 4% had efavirenz plasma levels below 1mg/L, predicted to be the minimum effective concentration and 70% had plasma concentrations above the predicted maximum safe concentrations of 4mg/L, whereas, 25% had plasma levels within the predicted lower and upper limit of the safety margin (i.e. >1mg/L<4mg/L). Plasma concentration based on gender differences was identified as covariates of efavirenz disposition. The findings suggest that a possible daily dose reduction in patients with high plasma levels could be effected without any negative impact on the therapeutic efficacy. Furthermore, previous study on CYP2B6*6 (Q172H) polymorphism revealed a poor metaboliser (PM) allele frequency of 35 % in healthy Kenya populations [4]. However, genotyping for the CYP2B6*6 functional and non-functional genotypes on the HIV/AIDS patients will be necessary to corroborate these findings, so that a definite statement on the genotype-base dose adjustment can be inferred. The occurrence of high plasma levels of efavirenz in population of African origin has grave implication on the dosage of efavirenz. Preliminary data in this study suggests that a genotype inspired dose optimization of efavirenz may be necessary in African populations