Plasma Nevirapine Concentrations Predict Virological and Adherence Failure in Kenyan HIV-1 Infected Patients with Extensive Antiretroviral Treatment Exposure

Maureen J. Kimulwo[1], Javan Okendo[1], Rashid A. Aman[1], Bernhards R. Ogutu[1], Gilbert O. Kokwaro[1], Dorothy J. Ochieng[2], Anne W. T. Muigai[3], **Florence A. Oloo[4]***, Washingtone Ochieng[1]

[1]Strathmore University, [2] MCPHS University [3]Jomo Kenyatta University of Science and Technology**, [4]*Department of Chemical Science and Technology Technical University of Kenya**

Abstract

Treatment failure is a key challenge in the management of HIV-1 infection. We conducted a mixed-model survey of plasma nevirapine (NVP) concentrations (cNVP) and viral load in order to examine associations with treatment and adherence outcomes among Kenyan patients on prolonged antiretroviral therapy (ART). Blood plasma was collected at 1, 4 and 24 hours post-ART dosing from 58 subjects receiving NVP-containing ART and used to determine cNVP and viral load (VL). Median duration of treatment was 42 (range, 12–156) months, and 25 (43.1%) of the patients had virologic failure (VF). cNVP was significantly lower for VF than non- VF at 1hr (mean, 2,111ng/ml vs. 3,432ng/ml, p = 0.003) and at 4hr (mean 1,625ng/ml vs. 3,999ng/ml, p = 0.001) but not at 24hr post-ART dosing. Up to 53.4%, 24.1% and 22.4% of the subjects had good, fair and poor adherence respectively. cNVP levels peaked and were > = 3μg.ml at 4 hours in a majority of patients with good adherence and those without VF. Using a threshold of 3μg/ml for optimal therapeutic nevirapine level, 74% (43/58), 65.5% (38/58) and 86% (50/58) of all patients had sub-therapeutic cNVP at 1, 4 and 24 hours respectively. cNVP at 4 hours was associated with adherence (p = 0.05) and virologic VF (p = 0.002) in a chi-square test. These mean cNVP levels differed significantly in non-parametric tests between adherence categories at 1hr (p = 0.005) and 4hrs (p = 0.01) and between ART regimen categories at 1hr (p = 0.004) and 4hrs (p<0.0001). Moreover, cNVP levels correlated inversely with VL (p< = 0.006) and positively with adherence behavior. In multivariate tests, increased early peak NVP (cNVP4) was independently predictive of lower VL (p = 0.002), while delayed high NVP peak (cNVP24) was consistent with increased VL (p = 0.033). These data strongly assert the need to integrate plasma concentrations of NVP and that of other ART drugs into routine ART management of HIV-1 patients.

PLOS ONE| DOI:10.1371/journal.pone.0172960pp.1-14 (2017)
See more at:
https://journals.plos.org/plosone/article/file?id=10.1371/journal.pone.0172960&type=printable