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Drug Interactions

Altered plasma levels of nevirapine after commencing rifampicin containing TB regimens in Malawi

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Introduction: The reduction in nevirapine exposure by rifampicin is well characterised in patients commencing antiretroviral therapy (ART). Conversely there are limited data on the impact of rifampicin on patients stable on nevirapine containing ART who develop TB. In such patients, the national treatment protocol for Malawi stipulates continuation of ART (without dose-modification) in addition to rifampicin-containing TB treatment for 6 months. A major concern is that rifampicin induces CYP450 enzymes leading to a reduction in nevirapine plasma levels.

Materials & Methods: We conducted a prospective cohort study in HIV positive patients stable on NVP containing ART (200mg twice daily, for at least 2 weeks) and who started rifampicin-based TB treatment. To determine the effect of rifampicin on plasma nevirapine levels, a truncated nevirapine PK profile (2ml of blood taken at 0, 1, 2, 4, 8 hours post dose) was performed in 10 male and 10 female patients on day 0 and day 14 after commencing TB treatment. In addition, a single trough level was measured on day 3 and 7 to determine how rapidly nevirapine levels declined. Nevirapine levels were measured by LC-MS at the University of Liverpool.

Results: Of the 20 patients, 2 had sub-therapeutic levels on day 0. Overall By day 14, there was a 22% reduction in the geometric mean AUC of nevirapine. Six (30%) patients had sub therapeutic nevirapine levels at day 14. This reduction occurred as early as day 3 with a progressive drop in geometric mean concentration.

Conclusions: Our data show that there is a moderate decrease in plasma nevirapine levels when rifampicin is commenced in a patient stable on ART. More research is required to determine the consequences on ART outcome and the value of changing nevirapine to efavirenz during TB treatment or increasing the nevirapine dosage temporarily.

No conflict of interest

11th International Workshop on Clinical Pharmacology of HIV Therapy - 7-9 April 2010, Sorrento, Italy