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Efavirenz-based antiretroviral therapy is a better choice for HIV-positive patients treated with rifampicin-based antituberculous therapy.

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Risk of active tuberculosis increases significantly in people infected with HIV, and tuberculosis contributes substantial morbidity and mortality in this population. Despite the complexities of co-administration of antituberculous and antiretroviral therapy (ART), such as adherence challenge of polypharmacy, overlapping side effects of the two regimens, risk of immune reconstitution inflammatory syndrome (IRIS), and drug-drug interactions, early ART is indicated since recent studies have shown mortality of TB/HIV-coinfected patients caused by delayed ART far exceeds that caused by IRIS or hepatotoxicity resulting from early ART, especially in resource-limited settings. However, rifampicin, the key agent of antituberculous regimen, is a potent inducer of the cytochorome P450, and coadministration results in >90% decrease in trough concentrations of protease inhibitors, 20-55% and 20% decreases in serum concentrations of nevirapine and efavirenz, respectively. Thus, current guidelines recommend standard dose efairenz or nevirapine to be co-administered with rifampicin. As for protease inhibitors, only saquinavir/ritonavir and lopinavir/ritonavir with adjusted doses are recommended with caution for hepatitis. Nevertheless, clinical studies, instead of pharmacokinetic data, regarding use of specific antiretroviral regimens during anti-TB treatment remain sparse.

Boulle A and colleagues prospectively assessed the virological efficacy of standard doses of efavirenz or nevirapine-based ART coadministered with rifampicin in a large population of 2,035 HIV-infected persons in Africa. Compared with patients starting nevirapine without concurrent tuberculosis, patients starting nevirapine with concurrent tuberculosis were at significantly higher risk of failure to suppress viral load, especially at 6 months (adjusted HR 2.1, 95% CI 1.2-3.4), and virological failure (adjusted HR 2.2, 95% CI 1.3-3.7). However, such difference was not observed in patients starting efavirenz-based ART with or without concurrent antituberculous treatment or when patients initiated antituberculous treatment for newly developed tuberculosis while taking established nevirapine- or efavirenz-based ART.

Manosuthi and colleagues conducted the first prospective, open-label, randomized trial to compare standard doses of nevirapine- or efavirenz-based ART in 142 TB/HIV-coinfected Thai patients receiving rifampicin. They found the concentrations of NNRTI at 12 hours after dosing (C_{12}) was significantly less compromised in patients receiving efavirenz than in those receiving nevirapine (3.1% vs. 21.3%) while immunological and virological responses at week 48 were comparable in two groups. In multivariate analysis, low C_{12} values and body weight <55 kg were independently associated with higher risk for all-cause antiretroviral treatment failure.

The two studies demonstrated, when coadministered with rifampicin, efavirenz-based ART is more favorable than nevirapine-based ART. Low drug exposure and low body weight are predictors for treatment failure.

References

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