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Title: Therapeutic drug monitoring of isoniazid, rifampin, and pyrazinamide in HIV-infected patients with tuberculosis

Dr. Shadi 7387 Baniasadi sbaniasadi@yahoo.com [1], Dr. Fanak 7388 Fahimi fanakfahimi@yahoo.com [2], Dr. Payam 7389 Tabarsi tabarsi@nritld.ac.ir [2], Dr. Seyed Alireza 7390 Nadji sarnadji@nritld.ac.ir [1], RN. Shadi 7391 Khabiri shadi.khabiri@yahoo.com [2], Ms. Nahid 17799 Shahsavari nahidshahsavari@yahoo.com [3] and Dr. Farzad 7398 Kobarfard farzadkf@yahoo.com [3]. [1] Virology Research Center, Natonal Research Institute of Tuberculosis and Lung Disease, Tehran, Islamic Republic of Iran ; [2] Chronic Respiratory Disease Research Center, Natonal Research Institute of Tuberculosis and Lung Disease, Tehran, Islamic Republic of Iran and [3] Medicinal Chemistry Department, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Islamic Republic of Iran .

Body: Introduction: Therapeutic drug monitoring (TDM) is the process of adjusting drug dosages based on serum concentration data. Several reports have shown altered pharmacokinetic profiles for the anti-tuberculosis (TB) drugs in HIV patients. Such patients may benefit from TDM and early interventions may prevent the development of further drug resistance. Aims: This study aimed to determine serum isoniazid (INH), rifampin (RIF), and pyrazinamide (PZA) concentrations in a cohort of patients with HIV-related TB who were treated in a referral TB center. Methods: Twenty HIV-infected patients who received 4 first-line anti-TB drugs for active TB were eligible for the study. Venous blood was obtained 2 h after daily dose of INH (5mg/kg), RIF (10 mg/kg), and PZA (25 mg/kg). Serum levels of anti-TB drugs were analyzed using high –pressure liquid chromatography (HPLC) and compared with published normal ranges. Results: Of the 20 patients (mean age 36.25 years, range 30-57 years), 18 (90%) had a very low maximum concentration of INH (<1 µg/mL), and 2 (10%) had a low maximum concentration of INH (<2 µg /mL). All patients had a very low maximum concentration of RIF (<7 µg /mL) and 7 (35%) had a low maximum concentration of PZA (<20 µg /mL). Conclusions: Low serum concentrations of INH, RIF, and PZA, which may be related to malabsorption, are common in HIV-infected TB patients. TDM of anti-TB drugs may helps clinicians to optimize drug therapy and improve TB cure rates.