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Poster Sessions – Abstract P053

Low isoniazid and rifampicin concentrations in TB/HIV co-infected patients in Uganda

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Introduction: There is limited data available on exposure to anti-tuberculosis (TB) drugs in this region. Peloquin has described reference ranges [1] however some studies have demonstrated that patients actually achieve concentrations below these ranges [2]. There is limited data about exposure to anti-TB drugs in the HIV/TB co-infected population in Sub-Saharan Africa. Our objective is to describe the concentration of anti-TB drug levels in a well characterized prospective cohort of adult patients starting treatment for pulmonary TB.

Methods: This study is an ongoing study carried out in the TB/HIV integrated clinic at the Infectious Diseases Institute in Kampala, Uganda. Sputum culture and microscopy was done for all patients. We performed pharmacokinetic blood sampling of anti-TB drugs for 1 hour, 2 hours and 4 hours post dose at 2 weeks, 8 weeks and 24 weeks after initiation of anti-TB treatment using ultraviolet high-performance liquid chromatography (UV-HPLC). We described the maximum concentration (Cmax) of isoniazid (H), rifampicin (R), ethambutol (E) and pyrazinamide (Z) and compare them with the values observed by Peloquin et al. referenced in other studies.

Results: We started 113 HIV infected adults on a fixed dose combination of HREZ. The median age of our population was 33 years, of which 52% were male with a median BMI of 19 kg/m^2 and a median CD4 cell count of 142 cells/μL. In 90% of the participants, the diagnosis of TB was based on microscopy and or cultures. The boxplot graph shows the median Cmax and IQR of H and R.

Levels of H were found to be below the reference ranges (3–6 μg/mL) in 54/77(70.1%), 38/59(64.4%) and 15/24(62.5%) participants at weeks 2, 8 and 24. Rif levels were also found to be below the reference ranges (8–24 μg/mL) in 41/66(62.1%), 26/48(54.2%) and 8/10(8%) participants at weeks 2, 8 and 24, respectively. The mean Cmax of E and Z were within the reference range at week 2 and 8; mean Cmax of 3.2 ± SD2.1 μg/mL and 4.0 ± SD3.1 μg/mL for E and 41.6 ± SD13.1 μg/mL and 42.6 ± SD16.4 μg/mL for Z.

Conclusion: We observed lower concentrations of isoniazid and rifampicin in our study population of HIV/TB co-infected patients. The implications of these findings are not yet clear. We therefore need to correlate our findings with the response to TB treatment.

References

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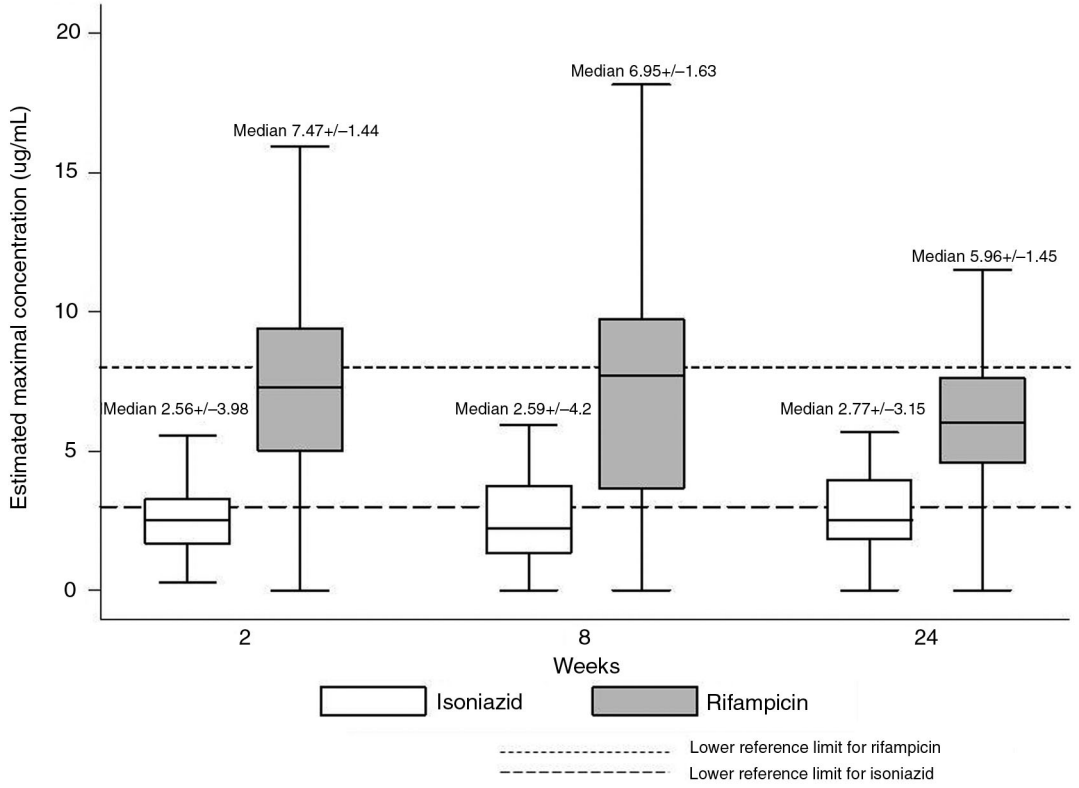

Figure 1. Maximum drug concentrations in comparision to reference ranges.