Effect of Antituberculosis Therapy on the Pharmacokinetics of Efavirenz in Children

Awewura Kwara, 1 Hongmei Yang, 1 Sampson Antwi, 1 Anthony Enimili, 1 Fizza Gillani, 2 Animia M. Sarfo, 2 Antonette Ortsin, 3 Albert Dompere, 4 Lubbe Wiesner, 5 Charles A. Peloquin

1University of Florida, Gainesville, FL, USA; 2University of Rochester, Rochester, NY, USA; 3Komo Anokey Teaching Hospital, Kumasi, Ghana; 4Brown University, Providence, Rhode Island, USA; 5University of Cape Town, Cape Town, South Africa

INTRODUCTION

• Tuberculosis (TB) is one of the most common opportunistic infections (OIs) affecting children with HIV.
• Globally, efavirenz (EFV)-based antiretroviral therapy (ART) is the preferred regimen in HIV-infected children aged 3 to 14 years or adults with TB coinfection who need rifampin-containing therapy.
• As in adults, World Health Organization (WHO) recommend no EFV dose adjustment with concurrent anti-TB therapy.

METHODS

• A two-arm parallel assignment PK study was performed at Komo Anokey Teaching Hospital, Kumasi, Ghana (Fig. 1).
• Eligible HIV-infected children with or without TB were enrolled and initiated on two NRTIs + EFV. Children with OIs other than TB were excluded from the study.
• Participants were seen in follow-up at 2 weeks after starting ART, and then monthly for 8 months or for up to a month after completion of TB therapy.
• Clinical evaluations, CBC, LFTs, renal function were performed at scheduled visits, as well as when indicated by side effects.
• PK sampling was performed after 4 weeks on ART.
• On the day of sampling, blood samples were drawn into EDTA tubes, immediately placed on ice and centrifuged within 30 minutes and plasma stored at -80°C until assay.
• EFV plasma concentrations were determined using gas chromatography with mass spectrometry (LC-MS) at University of Cape Town Pharmacology Laboratory.

RESULTS

• Baseline characteristics are shown in Table 1.
• Children with TB/HIV coinfection children had 53% lower EFV C0-24h, 37% lower C24h, and 28% lower AUC0-24h (Table 1).
• C0-24h and C24h were lower in the TB/HIV co-infected group (Fig. 2).
• The proportion of children with EFV C0-24h < 1 µg/mL was 47.4% in co-infected children and 17.6%, respectively in those with HIV only (P = 0.008).
• EFV-based ART was well tolerated in both groups with no treatment discontinuations due to drug side effects.
• Virologic suppression (VS) rate at 6 months of ART was lower in TB/HIV co-infected children (Fig. 3). However, it should be noted that only 18 children with TB/HIV and 19 with only HIV had viral load data for these analyses.

CONCLUSIONS

• Rifampin-containing anti-TB therapy significantly reduces EFV concentrations in children. This is concerning as low EFV concentrations may lead to poor ART outcomes.
• As EFV-based ART is most compatible with anti-TB therapy, adequately powered studies to examined virologic outcome in TB/ HIV-co-infected children is urgently needed.

Acknowledgements

• We wish the study participants and their parents as well as KAHIV/TB/HIV clinic staff.
• Primary grant support: Eunice Kennedy Shriver National Institute of Child Health and Development (FD: HD021779). Other grant support: P2G K24AI08523, P50 AIDS and U1 AI080832

CONTACT: Awewura Kwara, MD

awewura.kwara@medicina.uf.edu