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Plasma Efavirenz in HIV-Infected Children Treated with Generic Antiretroviral Drugs in India

We measured plasma concentration of efavirenz (EFV) in 16 HIV-infected Indian children receiving antiretroviral treatment at Government ART centres. The mean 12-hour concentration was 2.39 µg/mL (range: 0.72- 7.82 µg/mL). The majority of children treated with generic EFV at currently recommended doses had blood levels within the therapeutic range.

Key words: *Antiretroviral treatment, HIV-infected children, Plasma Efavirenz.*

The National AIDS Control Organisation (NACO) has developed a weight-based dosing card used in antiretroviral treatment (ART) centres, which aims to provide the correct dose of antiretroviral drugs to children(1). We measured the steady state 12-hour plasma concentration of efavirenz (EFV) in HIV-infected Indian children receiving treatment with generic drugs, to determine if this weight-based approach resulted in optimal blood levels.

Sixteen HIV-infected children (6 males) receiving an EFV-containing ART regimen for at least two weeks from Government ART centres at Kilpauk Medical College and Hospital, Chennai; Government Rajaji Hospital, Madurai; and BJ Wadia Hospital, Mumbai; were recruited. The mean age was 101 months, mean CD4 count was 14% and mean body weight was 18.8 kg. None were on concurrent rifampicin-containing anti-TB treatment. The study was cleared by the Institutional Ethics Committee; informed written consent was obtained from parent/guardian. Twelve-hour plasma EFV concentration was determined by HPLC(2).

The mean 12-hour EFV concentration in the 16 children was 2.39 µg/mL (range: 0.72-7.82 µg/mL). The blood levels were within the therapeutic range (1 – 4 µg/mL) of EFV in 12, below 1.0 µg/mL in 1 and above 4.0 µg/mL in 3 children. The only child who had sub-therapeutic EFV concentration had not shown an increase in CD4 cell counts up to 36 months of treatment. Weight gain ranged from 0.3 to 19.5 kg during a treatment period of 1 to 93 months and clinical status showed improvement in all children.

The clinical recommendations for treatment of children with EFV are based on data obtained in adult patients(3). In this small group of children studied, the mean dose of EFV received was 14.6 mg/kg body weight, which is within the recommended dosing range (10.0 to 16.7 mg/kg). Hirt, *et al*.(4) suggested that pediatric dosing guidelines for EFV should be based on both age and body weight, since plasma clearance of EFV decreased significantly with age, due to higher activity of hepatic drug-metabolizing enzymes in younger children.

We found that the majority (15 out of 16 children) receiving EFV doses based on the NACO guidelines had 12-hour EFV concentrations within or above the therapeutic range. Three children with drug levels above the therapeutic limit did not have any obvious adverse effects due to EFV. Although these findings are encouraging, the small sample size limits the

generalizability of the conclusions. Our study findings are consistent with those in Thai HIV-infected children(5), but differ with von Hentig, *et al*.(6) and Ren, *et al*.(7), who reported a higher proportion of children with sub-therapeutic plasma EFV. The difference could be due to ethnic variations and genetic factors which are known to influence EFV pharmacokinetics. Our limitations include the small sample size, lack of information on CYP2B6 516G>T polymorphism and post-ART viral load. However, our data provides some preliminary information that can be used to guide treatment policy for HIV-infected children in India.

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