Central nervous system toxicity of efavirenz in HIV-infected children in Tanzania

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Background: The World Health Organization recommends efavirenz as part of the first-line combination antiretroviral therapy (cART) for HIV-infected children. Awareness of central nervous system (CNS) side effects in adults is increasing. Reliable data on CNS toxicity in children, however, remain sparse. We compared neuropsychological symptoms, cognitive performance as well as adherence between long-term treated HIV-infected Tanzanian children on efavirenz vs. control regimens.

Methods: Cross-sectional observational study among HIV-infected children (6 to 12 years) on cART for ≥6 months and with viral loads ≤1000 copies/mL in Kilimanjaro, Tanzania. We used the Child Behavior Checklist (CBCL6-18) to evaluate behavioral and emotional problems. Cognitive performance was assessed using the Raven’s Colored Progressive Matrices and the Digit Span test. Non-adherence was defined as any reported missed doses over the previous three days or <100% adherence since the last clinical visit. Our study was powered to show a group difference of 0.5 SD in CBCL6-18 total problem scores. MANCOVA and logistic regression were used to assess differences between groups. Analyses were adjusted for age, sex, being treatment naïve, duration of cART, history of TB treatment, parental loss, and HIV disclosure.

Results: One-hundred-forty-one children were enrolled of whom 72 (51%) used efavirenz. Groups did not differ in age, sex, nadir CD4+ or general demographics. We found no differences in the CBCL6-18 behavioral and emotional problem scores (total/internalizing/externalizing), cognitive performance tests or adherence. Efavirenz-treated children had lower CBCL 6 to 18 competence scores (p = 0.025), which was mainly due to lower scores on school performance with mean (SD) 4.1 (1.4) and 4.7 (0.9) (p = 0.001) for efavirenz and controls respectively.

Conclusions: Overall, we did not see differences in emotional and behavioral problems, cognitive performance scores or adherence between efavirenz-treated children and controls, which is in contrast to earlier studies in adults. The lower school performance scores in efavirenz-treated children, however, warrant further study.