4

In utero and Peripartum Antiretroviral Exposure as Determinant of Change in Neurocognitive Function among 6 – 12 years old HIV exposed Ugandan Children - A prospective Cohort Study

Ezeamama A[1], *Zalwango S[2], Sikorskii A[1], Tuke R[1], Musoke P[3], Giordani B[4], Boivin M[1]*
[1]Michigan State University, East Lansing, United States, [2]Kampala Capital City Authority, Kampala, Uganda, [3]Makerere University, Kampala, Uganda, [4]Michigan State University, Ann Arbor, Michigan

Background: The long-term effect of in utero/peripartum antiretroviral (IPA) drug exposure during critical developmental windows in HIV-exposed newborns is unclear. Hence, IPA is examined as a predictor of executive function (EF) and socio-emotional adjustment (SEA) over a 12-month period among 203 perinatally HIV-exposed children enrolled at 6-10 years of age.

Methods: IPA exposure was established via medical records and defined as: combination ART (cART), suboptimal IPA (i.e. single dose nevirapine (sdNVP± AZT±3TC) and no IPA. Informant reported neurocognitive assessments were conducted at intake, 6th and 12th months follow-up. Age and sex standardized z-scores for EF and four SEA composites– externalizing problems, internalizing problems, behavioral symptoms index (BSI) and adaptive skills index (ASI)-were calculated via caregiver response to questions on the Behavior Rated Inventory of EF and Behavioral Assessment System for Children respectively. Separate linear mixed effects models were implemented in statistical analysis software (v.9.4) to estimate IPA-related differences in cognitive indices for HIV-exposed uninfected (HEU) and perinatally HIV-infected (PHIV) children.

Results: Among HEU, sub-optimal IPA regimen – particularly sdNVP+AZT+3TC, predicted lower ASI (β=-0.47, 95%CI:-0.81 to -0.13), elevated BSI (β=0.65, 95%CI:0.26 to 1.04), internalizing/externalizing problems (β=0.51, 95% CI:0.11–0.89) and EF dysfunction (β=0.73, 95% CI:0.33 to 1.14), whereas cART predicted higher ASI (β=-0.46, 95%CI:0.04 to 0.88) and lower internalizing problems (β= -0.30, 95%CI: -0.84–0.25) over 12 months relative to HEU without IPA. Adjusted for current ART regimen, early life cART vs. no IPA predicted lower BSI, internalizing and externalizing problems (β=-0.65 to -0.31, all P<0.05) whereas sub-optimal IPA regimen was inconsistently associated with SEA and EF dysfunction over 12 months among PHIV.

Conclusion(s): The protective association of early life cART with long-term change in SEA and EF in this vulnerable population is reassuring. We emphasize the need for prognostic tools to identify HIV-exposed children at high risk of neurocognitive impairment and the need for empirically informed interventions to mitigate sub-optimal IPA-associated long-term neurocognitive risks in this vulnerable population.