Neurodevelopmental effects of type of ante- & postpartum PMTCT ARV exposure on Ugandan and Malawian PROMISE HIV-exposed children at age 12, 24, and 48 months

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BACKGROUND

• Despite WHO guidelines recommending antepartum and postpartum (if breast feeding) Triple-ARV for the prevention of mother-to-child transmission (PMTCT) of HIV, neurodevelopmental risk to infants for such exposure is unknown.

• Children in the clinical trial Promoting Maternal and Infant Survival Everywhere (PROMISE) Blantyre Malawi (N=188) and Kampala Uganda (N=208) sites were evaluated on the basis of ARV pre- and post-natal treatment arm.

OBJECTIVE: To determine if the developmental (MSEL) and cognitive (KABC-II) performance of HIV/ARV-exposed uninfected African children from Malawi and Uganda differed on the basis of ante-natal and post-natal mono- versus triple-ARV treatment arms within the PROMISE clinical trial of PMTCT.

DESIGN/METHODS

At 12, 24, and 48 months of age, the Mullen Scales of Early Learning (MSEL) was used for developmental assessment. The Kaufman Assessment Battery for Children (KABC-II) was also used at the 48 month assessment.

During pregnancy, HIV-infected mothers were randomized to:

1) Triple-ARV prophylaxis (3TC-ZDV/LPV-RTV; N=178) or FTC-TDF/LPV-RTV; N=37) or
2) Zidovudine (ZDV: N=178).

Postpartum: mother/newborn dyads were then randomized to either:

1) Maternal Triple-ARV (MSEL available for N=186) or
2) Infant Nevirapine (NVP; N=186), continuing on their trial arm regimen throughout breast feeding.

RESULTS

• Antepartum ARV regimen did not differ significantly on MSEL composite cognitive ability at age 12 months (p=0.89), but did at 24 months (p=0.02), with FTC-TDF/LPV-RTV exposed children doing significantly more poorly than Zidovudine (Table 1).

• MSEL expressive language differences were not significantly different among treatment arms at 12 (p=0.84) or 24 (p=0.27) months, but were at 48 months (p=0.03), with antepartum 3TC-ZDV/LPV-RTV doing more poorly than Zidovudine.

• For antepartum by postpartum treatment-arm interaction effects, antepartum FTC-TDF/LPV-RTV, followed by postpartum maternal triple ARV, produced the worst, and ZDV followed by infant Nevirapine produced the best mean MSEL composite cognitive performance scores at 24 months (p<0.01).

• KABC-II: best outcomes for triple ARV followed by maternal triple ARV (Table 2).

CONCLUSIONS

• The combination of ante-partum followed by post-partum triple-ARV exposure did not consistently result in significantly poorer developmental outcomes with the MSEL at age 12, 24, 48 months.

• The combination of ante-partum followed by post-partum triple-ARV exposure did not result in significantly poorer cognitive ability outcomes with the KABC-II at 48 months of age.

• Despite these encouraging preliminary results as to the neurodevelopmental safety of prolonged triple-ARV exposure in African children, we are continuing to monitor cognitive performance of HEU treatment arms at 54/60 months of age with the KABC-II test battery.

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