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ARV PROPHYLAXIS/ART INITIATION AT BIRTH LIMITS THE SIZE OF THE RESERVOIR IN CHILDREN
Clinical: (Q) Pediatrics and Adolescents
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Background: Early antiretroviral therapy (ART) limits the size of the HIV reservoir in adults; however pediatric data are limited. We assessed the impact of age of ARV prophylaxis (proARV)/ART initiation on the size of the HIV reservoir in early-treated vertically infected infants.
Methods: We measured markers of HIV persistence in infants (4-23 weeks of age) who received uninterrupted triple proARV since birth (n=9) and those who did not receive proARV or interrupted either triple or AZT prophylaxis (n=17). In addition, samples from suppressed children (median 2.7 years of age) who initiated continuous ART/proARV at birth (n=12) or later (range 3-26 weeks, n=63) were also studied. Total and integrated HIV DNA in CD4 T-cells were quantified by real-time PCR and we used TILDA to measure the frequency of CD4 T cells producing multiply spliced RNA (msRNA) as a proxy for virus production, with and without stimulation.
Results: Viral loads were significantly lower in infants who received continuous proARV from birth compared to those who interrupted or never received prophylactic treatment ($p<0.001$). Similarly, levels of integrated HIV DNA tended to be lower in infants receiving uninterrupted proARV compared to those in whom proARV was interrupted or not initiated ($p=0.08$). The frequencies of cells producing msRNA spontaneously and after stimulation were significantly lower in infants who received uninterrupted proARV ($p=0.003$ and $p=0.005$, respectively). Importantly, the frequency of latently infected cells was significantly lower in infants who received uninterrupted proARV since birth ($p=0.048$). After ART initiation, children who received proARV/ART since birth had significantly lower total and integrated HIV DNA than children starting treatment later ($p=0.01$ and $p=0.03$, respectively). Although TILDA values were equally low and often below the limit of detection in both treated groups (43% and 47% samples with detectable TILDA, in the immediate and deferred groups, respectively), the size of the inducible reservoir correlated with age at which continuous proARV/ART was initiated for the first time ($r=0.28$, $p=0.04$).
Conclusion: Neonatal proARV without complete viral suppression significantly limits the size of the reservoir. Notably, uninterrupted ART dramatically restricts the pool of cells harboring total and integrated HIV DNA. Importantly, the age at which continuous proARV /ART is initiated for the first time impacts the size of the inducible reservoir.