Starting Infants With HIV on Treatment Very Early Limits Viral Reservoir

Continuously providing such infants with antiretrovirals as early as possible limits the size of the reservoir.

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Infants who contract HIV from their mothers wind up with smaller viral reservoirs if they are provided antiretrovirals (ARVs) continuously—meaning there is no break between using the drugs prophylactically and as standard treatment for the virus—and if that treatment is started earlier after birth.

Marta Massanella, PhD, of the Centre de Research du Centre Hospitalier de l'Université de Montreal, presented findings from an analysis of HIV-positive infants at the 2018 Conference on Retroviruses and Opportunistic Infections (CROI) in Boston.

Massanella and her colleagues factored into their analysis two cohorts of Thai pediatric cases. One was the HIVNAT 194 cohort, which included 46 children who were born to HIV-positive mothers and started on ARVs before the age of 6 months. At this study's single point of analysis, the children's median age was 5.1 years. In the second cohort, HIVNAT 209, 76 children born to HIV-positive mothers were followed over time since birth. They were all started on prophylactic ARVs at birth; if tests confirmed they had contracted the virus, they were started on ARVs for treatment of the virus. The investigators conducted annual follow-up visits with these children for up to three years.

The study authors looked at data from the first study visit of 11 infants in the HIVNAT 209 cohort who received uninterrupted triple-ARV treatment (prophylactically starting at birth and as standard treatment upon confirmation of their HIV infection). They also studied data from the first study visit of 20 infants from that cohort who either did not receive prophylactic treatment before their infection was confirmed or had a break between taking prophylactic treatment with either a triple-ARV regimen or Retrovir (zidovudine, or AZT) prophylaxis before starting standard ARV treatment for the virus. Between the two groups, the infants' median age was 2.1 months at this first visit.

Additionally, the researchers studied samples taken from children in both cohorts, 42 children from the HIVNAT 209 cohort and 46 from the HIVNAT 194 cohort, after they started standard ARV treatment for the virus. When it came to the former study, the investigators looked at data from

study visit number three, when the children's median age was 1.2 years; and for the latter study they relied on data collected when the children's median age was 5.1 years. These children began traditional HIV treatment at a respective 2.4 and 3.9 months after birth.

The study team used various means of estimating the size of the viral reservoir in the children, including measuring the total HIV DNA in CD4 cells as well as the total HIV DNA that was integrated into those cells' own genetic code. They also assessed how frequently CD4 cells were productively infected with the virus—this was a measure of the size of the so-called inducible reservoir. Looking at the infants who had not yet started ARV treatment for the virus, the investigators found a strong correlation between viral load at that point and all three of these measures.

Comparing children who received continuous ARV treatment with those who either had an interruption between their prophylactic and treatment phase or never received prophylactic treatment before starting standard treatment, the researchers found that receiving ARVs continuously was associated with a lower viral load, a lower number of CD4 cells carrying both total and integrated HIV DNA, and a smaller inducible reservoir.

In short, the scientists found that prophylactic treatment prior to standard HIV treatment limits the size of the viral reservoir in infants who contract the virus from their mothers. They also found that the sooner after birth that continuous ARV prophylaxis and treatment is begun in these children, the smaller the size of the inducible reservoir.

To view a webcast of the conference presentation, click here.

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