Study confirms key therapeutic advance for children living with HIV and tuberculosis

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Superboosting for children living with HIV, mother and son. Credit: Scholars & Gentlemen /DNDi

The non-profit research and development organization Drugs for Neglected Diseases initiative (DNDi) has released results of a study in

South Africa that will make it easier for healthcare workers to treat children living with HIV who are co-infected with tuberculosis (TB). The study, presented as a late-breaker this week at the Conference on Retroviruses and Opportunistic Infections (CROI) in Seattle, provides essential evidence and data to counter the negative interactions between two critical HIV and TB treatments.

"TB is extremely common in children with HIV but until now, when a child has both diseases, we simply did not know for certain if our approach to dosing was correct. This is crucial to ensure long-term control of the HIV virus and keep kids alive," said Dr Helena Rabie from Stellenbosch University and lead investigator of the DNDi study. "These kids are extremely neglected: HIV-positive children have fewer treatment options and in many cases cannot switch to different antiretrovirals when taking concomitant TB treatment."

Protease inhibitors such as lopinavir (LPV) form a key component of HIV treatment, but must be "boosted" with ritonavir (RTV) to ensure they inhibit the virus. But when children are also treated for TB, the drug rifampicin, which forms the backbone of TB treatment, reduces the concentration of RTV and hence the effectiveness of LPV. To counteract this effect, the amount of ritonavir in the lopinavir/ritonavir (LPV/r) combination must be increased, a procedure known as "super-boosting".

An earlier study had suggested that super-boosting LPV/r with ritonavir up to a 1:1 ratio during a child's simultaneous HIV and TB treatment, as opposed to the commonly used 4:1 ratio used during treatment for HIV alone, was effective. But the study included only 15 children. DNDi and partners aimed to consolidate the evidence around the safety and effectiveness of super-boosting through a larger study including 96 children - 30 of whom were under one year of age at enrollment - across five sites in South Africa.

The final results presented this week at CROI show that this approach counteracts the negative interactions between LPV/r and rifampicin, easing the co-administration of HIV and TB treatment for this particularly vulnerable population.

"This study brings the scientific proof needed so that health workers can give children the right dose and ensure that their HIV and TB treatment works," said Dr Marc Lallemant, Head of DNDi's HIV program.

Interim results from the study were presented by DNDi to the World Health Organization (WHO) guidelines review committee, which recommended super-boosting of LPV/r in TB/HIV co-infected children in 2016.

But further uptake by other countries of this therapeutic advance is hampered by the short shelf-life of pediatric RTV, as well as difficulties giving both LPV/r and stand-alone RTV to children, linked to their high alcohol content and extremely bitter taste. In Kenya and Uganda, DNDi and partners are piloting a more child-friendly formulation of LPV/r that comes in the form of pellets. In a separate study due to start in South Africa, DNDi and partners will pilot super-boosting in children co-infected with TB and HIV using a new solid RTV formulation.

"DNDi's ultimate goal is to deliver a simple, first-line antiretroviral regimen that overcomes the many different barriers that stand in the way of giving treatment to infants and young children," said Dr Marc Lallemant. "With our industrial partners we're aiming to develop an easy-to-use '4-in-1' fixed-dose combination that is palatable, does not require refrigeration, and that thanks to super-boosting can address drug-drug interaction with medicines for TB."

Provided by Drugs for Neglected Diseases Initiative