Dolutegravir and the fetus

Potent combination anti-HIV therapy (commonly called ART) together with other measures has greatly reduced the risk of HIV-positive mothers giving birth to infected babies, particularly in high-income countries where care and treatment is widely available. By driving the amount of HIV in the mother down to very low levels, ART plays a key role in protecting the fetus from infection.

Anti-HIV drugs move from the mother’s circulation to that of the fetus via a physical connection during pregnancy called the placenta. It is therefore important to study the movement of these drugs across the placenta so that researchers can assess the potential of medicines to protect the fetus from HIV.

Integrase inhibitors

The most potent class of anti-HIV drugs is called integrase inhibitors. Examples of these drugs include the following:

- dolutegravir (Tivicay and in Triumeq)
- elvitegravir (in Genvoya and Stribild)
- raltegravir (Isentress)

When used as part of ART, integrase inhibitor–based regimens quickly reduce viral load. These drugs are generally well tolerated, and raltegravir and dolutegravir have relatively few interactions with other medicines. For both of these reasons integrase inhibitor–based regimens, particularly those that include raltegravir, have been, in some cases, prescribed by doctors for pregnant women who have recently been diagnosed with HIV.

Enter dolutegravir

Dolutegravir is the newest integrase inhibitor and it is increasingly being prescribed in high-income countries. As some HIV-positive women who use dolutegravir-containing ART can become pregnant, it is important to begin to investigate how this drug can affect the fetus. To begin to explore this possibility, researchers in Nijmegen, the Netherlands, have developed a system in their lab, using donated placentas, to simulate the blood circulation between fetus and mother.

Key findings

Dolutegravir can cross the placenta and enter the blood supply of the fetus.

The concentration of dolutegravir in the fetus’ blood supply was considered “moderate to high” by the researchers. Based on their results, the Dutch researchers expect that in pregnant mothers who use dolutegravir, the concentration of this drug in the fetus’ blood supply is likely to be between “five to 10 times higher” than in adults who take dolutegravir.

This relatively high concentration of dolutegravir in the circulation of the fetus means that it is likely that the drug can protect the fetus from HIV. However, the Dutch researchers also note that the high concentration of dolutegravir raises the potential issue of side effects for the fetus. In studies with pregnant mice and rats, other researchers have not found “direct evidence” that exposure to dolutegravir resulted in birth defects or affected the development of the fetus.

A need to report pregnancy outcomes

Most anti-HIV drugs are not formally tested in large randomized clinical trials of pregnant women. The vast majority of information about the safety of ART in pregnancy, both for the mother and fetus, comes from observational studies and databases that collect information on pregnancy in HIV-positive women. Therefore, the Dutch researchers strongly encourage doctors to continue to submit reports to databases on the results of pregnancy in HIV-positive pregnant women. Given that dolutegravir is a relatively new drug in the history of HIV treatment, this is particularly important.

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