Quebec study is reassuring about the safety of HIV treatment during pregnancy

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In Canada and other high-income countries much progress has been made in reducing the risk of HIV transmission from mother to child in the past several decades. According to the Canadian Perinatal HIV Surveillance Program, mother-to-child transmission of HIV is extremely rare in Canada today.

A key part of reducing this risk is to significantly reduce the amount of HIV (the viral load) in the mother’s blood as early as possible in the course of pregnancy so that it becomes as low as possible and stays that way. This is why potent combination anti-HIV therapy (ART) plays an essential role in helping to reduce the spread of HIV from mother to child. By following a series of steps outlined below, the risk of mother-to-child HIV transmission can be reduced to less than 1%:

- counselling with a doctor about pregnancy planning followed by referrals to an obstetrician, an infectious disease specialist who treats adults and a visit to an infectious disease specialist who treats children
- the use of ART during pregnancy so that the mother’s viral load is less than 50 copies/ml
- regular visits to a clinic for care and advice during pregnancy
- giving the infant between four and six weeks of HIV medication
- using formula and not breastfeeding, as HIV can be spread via breast milk
- avoid pre-chewing food for the baby when solids are introduced. Adults with HIV who also have an oral infection can inadvertently cause a small amount of blood to leak and be present in the food that they chew. This blood can contain HIV, and if the pre-chewed food is fed to the infant, it could transmit HIV.

One concern that HIV-positive pregnant women and their doctors may have is about the safety of ART for the fetus. This concern arises because the fetus, particularly in the first trimester (the first three months), can be susceptible to a range of harmful effects if exposed to some medicines. However, several studies in high-income countries have reviewed the benefits and risks of the use of ART during pregnancy and have found that, in general, the benefits significantly outweigh any risks.

A study in Quebec

Recently, researchers in Quebec undertook a study to review health-related information collected from pregnant women (both HIV negative and positive) and their infants. The research team was interested in the distribution of major birth defects between 1998 and 2015.

Researchers reviewed data from 214,240 pregnancies, 343 of which were from HIV-positive women. Among the HIV-positive women, 174 took ART during their first trimester of pregnancy and 169 others did not take ART during the first trimester of pregnancy.

The researchers found the following:

- Women who were HIV positive and who did not use ART during their first trimester of pregnancy were significantly more likely to give birth to infants with major birth defects, compared to HIV-negative women.
- Women who were HIV positive and who used ART during their first trimester were not significantly more likely to give birth to infants with major birth defects, compared to HIV-negative women.
The Quebec study underscores the overall beneficial effects of ART during pregnancy. It also has raised a troubling finding—perhaps HIV infection itself may be linked, at least in part, to an increased risk for birth defects and the use of ART seems to reduce this risk. The findings from this study will hopefully spur researchers elsewhere to undertake similar reviews of data from HIV-positive women and their infants.

**Study details**

Researchers have been collecting health-related information from pregnant women and their infants in the Quebec Pregnancy Cohort. The researchers analysed the data that was collected from January 1998 to December 2015 and focused on major birth defects.

The study team was able to find out about the medicines that women in the study were taking because of links to the Quebec Public Prescription Drug Insurance database. Thus, only women who used the public healthcare system in Quebec were studied.

**A note about the first trimester**

The researchers specifically separated the data on women who were taking ART during the first three months of their pregnancy from women who were not taking ART during this time. The importance of the first trimester is that it marks a time of rapid development and growth of the fetus. This rapid development and growth makes the fetus susceptible to the potentially injurious effects of substances and, in some cases, medicines.

**Results—Major birth defects**

Data from a total of 214,240 pregnancies were analysed and researchers found that 18,407 infants had “at least one” major birth defect.

In total, the proportions of HIV-positive women who gave birth to infants with major birth defects were as follows:

- women who used ART during their first trimester of pregnancy - 10%
- women who did not use ART during their first trimester of pregnancy - 15%

For comparison, the proportion of HIV-negative women who gave birth to infants with major birth defects was 9%. This may seem high (the figure from other regions is usually between 3% and 5%) but the researchers stated that it is “what is expected in the province of Quebec, due to high concentration of genetic risk factors…”

Thus, pregnant HIV-positive women who did not use ART during their first trimester were at an increased risk for giving birth to an infant with a major birth defect. The difference in the distribution of major birth defects between HIV-positive women was statistically significant; that is, not likely due to chance alone.

Among HIV-positive women who used ART during their first trimester there was one infant born with a defect in the small intestine and another with a defect of the digestive system. But due to the small number of infants affected, the statistical robustness of any association of these defects with ART use by the mother during pregnancy is weak.

The proportion of major birth defects among HIV-positive women who used ART during the first trimester was not significantly different from the rate of birth defects seen among HIV-negative women.

**Bear in mind**

According to the researchers, their study “showed that the use of ART during the first trimester was not associated with the risk of overall major birth defects, which is reassuring.”

The findings from the Quebec study suggest the possibility that HIV itself may increase the risk for the development of major birth defects. How HIV (or its proteins) could trigger such a process is unclear; the present study was not designed to explore this.

The researchers said there was “a signal” for a possible link between the use of ART during the first trimester and the two infants born with defects of their intestines. However, as there were only two cases of this problem in the present study, this finding needs to be explored in a larger study with more HIV-positive pregnant women.
Large studies from Western Europe have not found that the use of ART is associated with a significant increase in major birth defects among infants born to HIV-positive women who used ART during pregnancy.

Some studies have reported that HIV-positive women who used ART during their first trimester were at increased risk for giving birth prematurely and to infants with less-than-ideal weight. The Quebec researchers were able to compare data among HIV-positive women (those who used ART during the first trimester and those who did not) and between HIV-positive and HIV-negative women. As a result of these comparisons, they found that it is likely that underlying HIV infection may be responsible for the increased risk of premature birth and low birth weight. That HIV infection itself may play a role in premature birth is supported by the results of a study from the pre-ART era in Rwanda where there was an increased risk of premature birth among HIV-positive women vs. HIV-negative women.

The Quebec study did not have data on smoking, intake of the B-vitamin folic acid or alcohol use—all factors that could have affected the risk of birth defects. Despite this, the findings from the Quebec study are generally in line with those from other high-income countries and are reassuring to mothers and their doctors about the general safety of ART during pregnancy.

Acknowledgement

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Resources

Recommendations for Use of Antiretroviral Drugs During Pregnancy from The Recommendations for the Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women and Interventions to Reduce Perinatal HIV Transmission in the United States

La thérapie antirétrovirale pour les adultes infectés par le VIH : Guide pour les professionnels de la santé du Québec - Ministry of Health and Social Services of Quebec

Prevention of vertical HIV transmission and management of the HIV-exposed infant in Canada in 2014 – Canadian Paediatric and Perinatal AIDS Research Group

Canadian HIV pregnancy planning guidelines

Canadian HIV treatment, care and support guidelines – Prevention in Focus, Fall 2017

REFERENCES:


Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

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