Risk of birth defects small with HIV drugs

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The risks of birth defects in children exposed to antiretroviral drugs in utero are small when considering the clear benefit of preventing mother-to-child transmission of HIV but where there are safe and effective alternatives, it might be appropriate to avoid use by pregnant women of drugs that may be associated with elevated risks of birth defects, such as zidovudine and efavirenz, according to a study published by French researchers published in this week's *PLOS Medicine*.

The researchers, led by Jeanne Sibiude from the INSERM, Centre for Research in Epidemiology and Population Health, used a large national health database, the French Perinatal Cohort, (ANRS CO1/CO11) which contains information on HIV-infected mothers who delivered infants in 90 centers throughout France. The researchers included 13,124 children who were born between 1994 and 2010 and had been exposed to antiretroviral therapy during pregnancy. Using two birth defect classification systems (EUROCAT and MACDP) the researchers investigated the link between birth defects and exposure to individual antiretroviral drugs.

Although limited by the absence of data on termination of pregnancy, stillbirths, tobacco and alcohol intake, and concomitant medication, the authors found a small increase in the risk for heart defects in children exposed to zidovudine using both classification systems (an absolute risk of +1.2%) and a possible association between efavirenz exposure and neurological defects, but only when using the MACDP classification system (an absolute risk of + 0.7%).

The authors found no association between several other antiretroviral drugs, including nevirapine (a drug in the NNRTI family, like efavirenz); tenofovir, stavudine, and abacavir (drugs in the NRTI family, like zidovudine); and lopinavir and ritonavir (drugs in the protease inhibitor family) and any type of birth defect.

The authors stress: "Whatever the impact that some [antiretroviral] drugs may have on birth defects, it is surpassed by the major role of [antiretroviral therapy] in the successful prevention of mother-to-child transmission of HIV."

In an accompanying Perspective, US experts Lynne Mofenson from the National Institutes of Health and Heather Watts from the Office of the Global AIDS Coordinator say: "While the Sibiude study raises some important questions, given the enormous benefits of maternal antiretroviral drugs, the unclear clinical significance of the heart defects and the lack of a specific pattern of CNS defects with efavirenz, no change in prescribing practices is indicated, but continued surveillance is critical."

More information: Sibiude J, Mandelbrot L, Blanche S, Le Chenadec J, Boullag-Bonnet N, et al. (2014) Association between Prenatal Exposure to Antiretroviral Therapy and Birth Defects: An Analysis of the French Perinatal Cohort Study (ANRS CO1/CO11). *PLoS Med* 11(4): e1001635. DOI: 10.1371/journal.pmed.1001635

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