Drug Monitor

ONLINE EDITION

Selective Serotonin Reuptake Inhibitors in Pregnancy: What Are the Real Risks?

According to research, about 3% to 6% of women take selective serotonin reuptake inhibitors (SSRIs) for depression during pregnancy. But, does that put them at risk of giving birth to babies with congenital anomalies, such as septal heart defects, anencephaly, and limb reduction defects? Study findings have been inconsistent, the researchers say. Although current available information points to a "marginally increased" risk of congenital cardiovascular anomalies with fluoxetine and paroxetine, no direct teratogenicity for any of the SSRIs has been established.

Based on those concerns, researchers from Helsinki University, Helsinki University Central Hospital and HUSLAB, and the National Institute for Health and Welfare, all in Finland; and the Nordic School of Public Health, in Göteborg, Sweden, performed a retrospective cohort study using data from national registers between 1996 and 2006 on 635,583 births, congenital anomalies, and terminations of pregnancy because of severe fetal anomalies. Offspring exposed to SSRIs (n = 6,976) during the first trimester were compared with unexposed offspring.

At first, it seemed that major congenital anomalies were indeed more common among offspring exposed to SSRIs, but that difference did not remain statistically significant after adjusting for confounders. The variables independently associated with birth defects were maternal age, year of pregnancy ending (2006 compared with 1996), maternal diabetes, and purchases of other psychiatric drugs.

Nonetheless, the researchers found an increased risk of isolated ventricular septal defects after exposure to fluoxetine (adjusted odds ratio [OR], 2.47), even when excluding neonates requiring neonatal care unit treatment from the analysis. The risk of right ventricular outflow tract defects was increased after exposure to paroxetine (adjusted OR, 4.68). Citalopram was associated with neural tube defects (adjusted OR, 2.46). The researchers also observed a 10-fold jump in fetal alcohol spectrum disorders in offspring of mothers using SSRIs when compared with unexposed offspring.

Women taking SSRIs were 20 times more likely to have purchased other psychiatric medications compared with women who did not purchase SSRIs during pregnancy. When the researchers considered only "other psychiatric drugs," the association between SSRIs and major congenital anomalies became statistically insignificant. When they categorized polytherapy to consist of first-trimester use of both SSRIs and other psychiatric drugs, exposure was statistically significantly associated with overall major congenital anomalies.

The researchers thus conclude that exposure to fluoxetine and paroxetine in early pregnancy is associated with a "small but established risk" of specific cardiovascular anomalies. These findings should guide clinicians, they suggest, to avoid those drugs as first options for women planning pregnancy. Further, they advise special attention for women who drink alcohol, smoke, and use other psychiatric drugs when also using SSRIs while pregnant.

Source. *Obstet Gynecol.* 2011;118(1):111-120. doi: 10.1097/AOG.06013e318220edcc.

Help for Deciding Who Should Get Herceptin

About 20% of women diagnosed with breast cancer are HER2-positive and may be candidates for trastuzumab (Herceptin). Now, deciding who's a good fit is a bit easier, with FDA approval of a new genetic screening test.

The test, Inform Dual ISH, permits measurement of the number of copies of the HER2 gene in tumor tissue. Before now, fluorescence microscopes have been needed. With the new test, clinicians can see the HER2 and chromosome 17 (where the gene is located) signals directly under a microscope for longer periods of time.

The FDA's approval was based on a study involving tumor samples from 510 patients with breast cancer. The test confirmed a greater than normal number of copies of the HER2 gene in 96% of the HER2-positive tumor samples. The test also effectively excluded the possibility that more than the normal number of copies of the gene were present in 92% of the HER2-negative samples. Patients who do not have more than the normal number of copies of the HER2 gene are generally not considered candidates for Herceptin therapy.

Source: FDA news release; June 14, 2011.