

Use of oral antifungal medication during pregnancy, risk of spontaneous abortion

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In an analysis of approximately 1.4 million pregnancies in Denmark, use of the oral antifungal medication fluconazole during pregnancy was associated with an increased risk of spontaneous abortion compared with risk among unexposed women and women who used a topical antifungal during pregnancy, according to a study in the January 5 issue of *JAMA*.

Pregnant women are at increased risk of vaginal candidiasis (yeast infection); the prevalence of vaginal candidiasis among pregnant women is estimated to be 10 percent in the United States. Although intravaginal formulations of topical azole antifungals are first-line treatment for pregnant women, oral fluconazole is often used despite limited safety information. Ditte Molgaard-Nielsen, M.Sc., of the Statens Serum Institut, Copenhagen, Denmark, and colleagues evaluated the association between oral fluconazole exposure during pregnancy and the risk of spontaneous abortion and stillbirth. The study included 1,405,663 pregnancies in Denmark from 1997-2013. From this group, oral fluconazoleexposed pregnancies were compared with up to 4 unexposed pregnancies, matched on maternal age, calendar year, and gestational age. Filled prescriptions for oral fluconazole were obtained from the National Prescription Register.

Among 3,315 women exposed to oral fluconazole from 7 through 22 weeks' gestation, 147 experienced a spontaneous abortion, compared with 563 among 13,246 unexposed matched women (women not exposed to antifungals). There was a significantly increased risk of spontaneous abortion associated with fluconazole exposure. Among 5,382 women exposed to fluconazole from gestational week 7 to birth, 21 experienced a stillbirth, compared with 77 among 21,506 unexposed matched women. There was no significant association between fluconazole exposure and stillbirth. Using topical azole exposure as a comparison, 130 of 2,823 women

exposed to fluconazole vs 118 of 2,823 exposed to topical azoles had a spontaneous abortion; 20 of 4,301 women exposed to fluconazole vs 22 of 4,301 exposed to topical azoles had a stillbirth.

"In this nationwide cohort in Denmark, oral fluconazole use in pregnancy was associated with a significantly increased risk of spontaneous abortion," the authors write. "Until more data on the association are available, cautious prescribing of fluconazole in pregnancy may be advisable. Although the risk of stillbirth was not significantly increased, this outcome should be investigated further."

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