

(資料 2) National Pregnancy Registry for Atypical Antipsychotics

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(1) Reproductive safety of aripiprazole: data from the Massachusetts General Hospital National Pregnancy Registry for Atypical Antipsychotics

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Aripiprazole has become one of the most commonly prescribed psychotropics, making a more comprehensive understanding of its reproductive safety profile a priority. The goal of the current analysis was to determine the risk of major malformations in infants exposed during the first trimester of pregnancy to aripiprazole compared to infants whose mothers had psychiatric diagnoses but did not use an atypical antipsychotic during pregnancy. The National Pregnancy Registry for Atypical Antipsychotics is a prospective pharmacovigilance program in which pregnant women are enrolled and interviewed during pregnancy and the postpartum period. Medical records are assessed to confirm presence or absence of major malformations. Pregnant women ages 18-45 with psychiatric diagnoses are enrolled. As of April 2020, N = 848 women who had delivered infants were eligible for analyses. A total of 158 women with first trimester exposure to aripiprazole were compared to 690 controls. For 163 infants born to women in the exposed group, seven major malformations were confirmed (4.29%), compared to fourteen of the 690 unexposed infants (1.99%). The unadjusted odds ratio for major malformations between aripiprazole-exposed and unexposed infants was 2.21 (95% confidence interval [CI] = (0.88, 5.57) The adjusted odds ratio for major malformations was 1.35 (95% confidence interval [CI] = (0.43, 4.20). After adjustment for confounding variables, the risk of major malformations after first trimester exposure to aripiprazole was not significant compared to controls. While these results are reassuring, they are limited by relatively small numbers of participants. Future analyses with larger numbers are expected to provide more of a complete and precise reproductive safety profile regarding aripiprazole use during pregnancy.

(2) Reproductive Safety of Second-Generation Antipsychotics: Updated Data From the Massachusetts General Hospital National Pregnancy Registry for Atypical Antipsychotics

J Clin Psychiatry. 2021 Aug 3;82(4):20m13745. doi: 10.4088/JCP.20m13745.

Objective: Second-generation antipsychotics (SGAs) are prescribed for a wide range of indications in women of reproductive age. The National Pregnancy Registry for Atypical Antipsychotics (NPRAA) was established to determine the risk of major malformations among infants exposed to these medications during the first trimester relative to a comparison group of unexposed infants of mothers with histories of psychiatric morbidity.

Methods: Women, aged 18-45 years, with histories of psychiatric illness were prospectively followed through pregnancy and during the postpartum period. Pediatric and maternal medical records were obtained and screened for evidence of major malformations. Potential cases were adjudicated by a dysmorphologist who was blinded to drug exposure.. Recruitment to the Registry, which is based at the Ammon-Pinizzotto Center for Women's Mental Health at Massachusetts General Hospital (MGH), includes nationwide provider referral, self-referral, and advertisement through the MGH Center for Women's Mental Health website.

Results: As of April 9, 2020, 1,906 women had enrolled, including 889 in the exposure group and 1,017 controls. A total of 1,311 women completed the study and were eligible for inclusion in the analysis. Medical records were obtained for 81.3% of participants. Among 640 live births in the exposure group, 16 (2.50%) had confirmed major malformations reported, and among 704 live births in the control group, 14 (1.99%) had confirmed major malformations reported. The estimated odds ratio for major malformations comparing exposed and unexposed infants was 1.48 (95% CI, 0.625-3.517).

Conclusions: Data from the Registry assessing SGAs as a class indicate that they are unlikely to have a major teratogenic effect. These findings provide pertinent information for women and their health care providers regarding decisions about atypical antipsychotic use during pregnancy.

(3) Establishment of the National Pregnancy Registry for Atypical Antipsychotics

J Clin Psychiatry. 2015 Jul;76(7):986-9. doi: 10.4088/JCP.14br09418.

Objective: Atypical antipsychotics are widely used by reproductive-age women to treat a spectrum of psychiatric illnesses. Despite widespread use of this class of agents in women of childbearing potential, reproductive safety data across these medicines remain limited. The National Pregnancy Registry for Atypical Antipsychotics (NPRAA) at

Massachusetts General Hospital was established in 2008 to address this knowledge gap. Method: Data are prospectively collected from pregnant women, ages 18-45 years, using 3 phone interviews conducted at the following times: (1) proximate to the time of enrollment, (2) 7 months' gestation, and (3) 2-3 months postpartum. Subjects include pregnant women with histories of fetal exposure to second-generation antipsychotics and a comparison group of nonexposed pregnant women. Medical record release authorization is obtained for obstetric, labor and delivery, and newborn pediatric (up to 6 months of age) records. Information regarding the presence of major malformations is abstracted from the medical records along with other data regarding neonatal and maternal health outcomes. Identified cases of congenital malformations are sent to a dysmorphologist blinded to drug exposure for final adjudication.

Results: As of May 2014, 428 subjects have enrolled in the NPRAA. Efforts continue to increase enrollment for the purpose of enhancing the capacity to define risk estimates of in utero exposure to atypical antipsychotics.

Conclusions: The NPRAA gathers prospective data regarding risk for critical outcomes following use of atypical antipsychotics during pregnancy. The NPRAA offers a systematic way to collect reproductive safety information that informs the care of women who use these agents to sustain psychiatric well-being.

(4) Correction to: Reproductive safety of aripiprazole: data from the Massachusetts General Hospital National Pregnancy Registry for Atypical Antipsychotics

Arch Womens Ment Health. 2021 Aug;24(4):669-670. doi: 10.1007/s00737-021-01133-4.

No abstract available

(5) Correction. Reproductive Safety of Second-Generation Antipsychotics: Updated Data From the Massachusetts General Hospital National Pregnancy Registry for Atypical Antipsychotics

J Clin Psychiatry. 2021 Oct 5;5(82):211cx14254. doi: 10.4088/JCP.211cx14254.

No abstract available

(6) Use of atypical antipsychotics in pregnancy and maternal gestational diabetes

J Psychiatr Res. 2017 Dec;95:84-90. doi: 10.1016/j.jpsychires.2017.07.025. Epub 2017 Jul 29.

Background: Second generation antipsychotic medications (SGAs) are widely used by reproductive-age women to treat a number of psychiatric illnesses. Some SGAs have been associated with an increased risk of developing diabetes, although information regarding their diabetogenic effect in pregnant women is scarce.

Objective: To evaluate the risk of gestational diabetes (GDM) among women treated with SGA.

Method: The Massachusetts General Hospital (MGH) National Pregnancy Registry for Atypical Antipsychotics (NPRAA) collects data on drug use, pregnancy outcomes, and other characteristics from pregnant women, ages 18-45 years, using 3 phone interviews conducted at (1) enrollment during pregnancy, (2) 7 months' gestation, and (3) 2-3 months postpartum. Information on GDM was abstracted from obstetric and delivery medical records. The study population was restricted to women without pre-gestational diabetes. Pregnancies exposed to SGAs during the first trimester were compared with a reference group of women with psychiatric conditions but not treated with SGAs during pregnancy. Generalized linear models were used to estimate adjusted odds ratios (OR) and 95% confidence intervals (CI) for GDM.

Results: Of 303 women exposed to SGAs, 33 (10.9%) had GDM compared to 16 (10.7%) in the 149 non-exposed women. The crude OR of GDM for SGA was 1.02 (95% CI, 0.54-1.91). After adjustment for maternal age, race, marital status, employment status, level of education, smoking, and primary psychiatric diagnosis, the OR moved to 0.79 (0.40-1.56).

Conclusions: Findings did not suggest an increased risk of GDM associated with exposure to SGAs during pregnancy in women who had used SGA before pregnancy without developing diabetes, compared to psychiatrically ill women who were not exposed to SGA.

(7) Reproductive Safety of Second-Generation Antipsychotics: Current Data From the Massachusetts General Hospital National Pregnancy Registry for Atypical Antipsychotics

Am J Psychiatry. 2016 Mar 1;173(3):263-70. doi: 10.1176/appi.ajp.2015.15040506. Epub

2015 Oct 6.

Objective: Second-generation antipsychotics are used to treat a spectrum of psychiatric illnesses in reproductive-age women. The National Pregnancy Registry for Atypical Antipsychotics was established to determine the risk of major malformations among infants exposed to second-generation antipsychotics during pregnancy relative to a comparison group of unexposed infants of mothers with histories of psychiatric morbidity.

Method: Women were prospectively followed during pregnancy and the postpartum period; obstetric, labor, delivery, and pediatric medical records were obtained. Eligible enrollees were pregnant women ages 18-45. The Registry is based at the Center for Women's Mental Health at Massachusetts General Hospital. Women were recruited through provider referral, self-referral, and the Center's web site.

Results: As of December 2014, 487 women were enrolled: 353 who used second-generation antipsychotics and 134 comparison women. Medical records were obtained for 82% of participants. A total of 303 women had completed the study and were eligible for inclusion in the analysis. Of 214 live births with first-trimester exposure to second-generation antipsychotics, three major malformations were confirmed. In the control group (N=89), one major malformation was confirmed. The absolute risk of major malformations was 1.4% for exposed infants and 1.1% for unexposed infants. The odds ratio for major malformations comparing exposed infants with unexposed infants was 1.25 (95% CI=0.13-12.19).

Conclusions: The results suggest that it would be unlikely for second-generation antipsychotics to raise the risk of major malformations more than 10-fold beyond that observed in the general population or among control groups using other psychotropic medications. If the estimate stabilizes around the null with ongoing data collection, findings may be reassuring for both clinicians and women trying to make risk-benefit treatment decisions about using atypical antipsychotics during pregnancy. These findings are timely given the renewed focus of regulatory agencies on reproductive safety.

(8) Supplement use by women during pregnancy: data from the Massachusetts General Hospital National Pregnancy Registry for Atypical Antipsychotics

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Women of reproductive age commonly use integrative treatments. However, the

reproductive safety for most complementary products lacks systematic study. We aimed to study the use of supplements by women in a prospective pregnancy registry. The Massachusetts General Hospital National Pregnancy Registry for Atypical Antipsychotics was established to evaluate the reproductive safety of atypical antipsychotics. Exposed and control participants were systematically queried about the use of vitamins and supplements. Slightly greater than half (53.2 %) of the participants eligible for analysis (N = 534) were using at least one vitamin or supplement at the time of enrollment, not including prenatal vitamins or folic acid. The most common supplements used were omega-3 fatty acids (38.0 %), vitamin D (11.0 %), calcium (8.2 %), and iron (4.7 %). Probiotics and melatonin were used by 2.6 and 0.9 %, respectively. In this prospective pregnancy registry, we found that over half of the participants were taking supplements or vitamins other than prenatal vitamins and folic acid. These findings underscore the need for active query on the part of health care providers about the use of supplements during pregnancy, and the need to obtain rigorous reproductive safety and efficacy data for supplements used by pregnant women and reproductive aged women.