



Date of Search: 30 Dec 2016

Sources Searched: Medline, Embase, NICE Evidence.

Antipsychotics and Metabolic Disorders in Pregnancy

Summary:

Antipsychotic drug use in pregnancy has increased in recent years, but most studies have evaluated the older, “typical” antipsychotic drugs, which are now less commonly used. The few studies that have evaluated atypical antipsychotic drugs in pregnancy suggest that these drugs may be associated with increased risk for maternal metabolic complications in pregnancy (such as gestational diabetes) with resultant consequences (such as altered fetal growth), but these are limited in terms of sample size and in considering important confounding factors. A propensity matched cohort study ([Vigod, S.N et al, 2015](#)) found that compared with non-users (1021), women prescribed an antipsychotic medication in pregnancy (also 1021) were not at higher risk of gestational diabetes. It concluded that antipsychotic drug use in pregnancy appears to have minimal evident impact on important maternal medical and short term perinatal outcomes, but that the rate of adverse outcomes is high enough to warrant careful assessment of maternal and fetal wellbeing among women prescribed an antipsychotic drug in pregnancy.

A retrospective cohort study based on UK primary health care records ([Peterson, I et al 2016](#)) concluded that there was no significant difference in the risk of developing gestational diabetes between women who continued antipsychotics in pregnancy and those who discontinued. However, gestational diabetes appeared to be strongly associated with obesity and after adjustment for health, lifestyle factors and concomitant medication, women who continued antipsychotics in pregnancy were at lower risk of developing gestational diabetes.

Screening Recommendations During Pregnancy:

According to NICE recommendations [Antenatal and postnatal Mental Health: Clinical Management and Service Guidance \(NICE, December 2014\)](#) :

1.4.24 Advise pregnant women taking antipsychotic medication about diet and monitor for excessive weight gain, in line with the [guideline on weight management before, during and after pregnancy](#) (NICE guideline PH27).

1.4.25 Monitor for gestational diabetes in pregnant women taking antipsychotic medication in line with the [NICE guideline on diabetes in pregnancy](#) and offer an oral glucose tolerance test (at 24-28 weeks).

Search Results:

Continuation of atypical antipsychotic medications during pregnancy and the risk of gestational diabetes

Author(s): Park Y.; Bateman B.T.; Patorno E.; Mogun H.; Huybrechts K.F.; Hernandez-Diaz S.; Cohen J.

Source: Pharmacoepidemiology and Drug Safety; Aug 2016; vol. 25 ; p. 235-236

Publication Date: Aug 2016

Publication Type(s): Journal: Conference Abstract

Available in full text at [Pharmacoepidemiology and Drug Safety](#) - from John Wiley and Sons

Abstract: Background: Gestational diabetes mellitus (GDM) is a serious complication of pregnancy that can lead to adverse outcomes. Some atypical antipsychotics (AAP) are associated with weight gain and insulin resistance, which are risk factors for GDM. There is lack of evidence to inform the decision about whether to discontinue AAP during pregnancy due to this concern. Objectives: To examine the risk of GDM associated with continuation of aripiprazole (ARI), olanzapine (OLZ), quetiapine (QTP), risperidone (RSP), or ziprasidone (ZIP) through the first half of pregnancy compared to discontinuation prior to pregnancy. Methods: We conducted a cohort study using Medicaid data (2000-2010) from non-diabetic women with a live-born infant who had > 1 AAP dispensing during the 3-months prior to pregnancy. For each AAP, we compared women with > 2 dispensings (continuers) to women with no dispensing during the first half of pregnancy (discontinuers). GDM was defined using previously validated algorithm in claims data. We used a generalized linear model and propensity score stratification to obtain absolute and relative risks (RR), adjusting for confounders including psychiatric diagnoses and duration of AAP use before pregnancy. Results: Among 1,543,334 pregnancies, the number of baseline AAP users was 1,924 for ARI, 1,425 for OLZ, 4,533 for QTP, 1,824 for RSP, and 673 for ZIP. The proportion of continuers ranged between 20% and 34%, depending on the drug. Continuers generally had higher comorbidity and longer baseline AAP use compared to discontinuers. The crude risk of GDM for continuers vs. discontinuers, respectively, was 4.8% vs. 4.5% for ARI, 12.0% vs. 4.7% for OLZ, 7.1% vs. 4.1% for QTP, 6.4% vs. 4.1% for RSP, and 4.2% vs. 3.8% for ZIP. The adjusted RRs were 0.80 (0.48-1.33) for ARI, 1.86 (1.22-2.83) for OLZ, 1.31 (1.02-1.68) for QTP, 1.37 (0.84-2.25) for RSP, and 0.93 (0.34-2.54) for ZIP. Conclusions: Our results suggest that compared to discontinuation, continued use of OLZ, QTP, and possibly RSP during the first half of pregnancy is associated with an increased risk of GDM. ZIP and ARI, the newer AAPs with less weight gain potential, were not associated with an increased risk.

Database: EMBASE

Risks and benefits of psychotropic medication in pregnancy: Cohort studies based on UK electronic primary care health records

Author(s): Petersen I.; McCrea R.L.; Sammon C.J.; Freemantle N.; Nazareth I.; Osborn D.P.J.; Evans S.J.; Cowen P.J.

Source: Health Technology Assessment; Mar 2016; vol. 20 (no. 23); p. 1-208

Publication Date: Mar 2016

Publication Type(s): Journal: Article

URL: <http://psychiatr.ru/download/2677?view=1&name=FullReport-hta20230.pdf>

Abstract:Background Although many women treated with psychotropic medication become pregnant, no psychotropic medication has been licensed for use in pregnancy. This leaves women and their health-care professionals in a treatment dilemma, as they need to balance the health of the woman with that of the unborn child. The aim of this project was to investigate the risks and benefits of psychotropic medication in women treated for psychosis who become pregnant. Objective(s) (1) To provide a descriptive account of psychotropic medication prescribed before pregnancy, during pregnancy and up to 15 months after delivery in UK primary care from 1995 to 2012; (2) to identify risk factors predictive of discontinuation and restarting of lithium (multiple manufacturers), anticonvulsant mood stabilisers and antipsychotic medication; (3) to examine the extent to which pregnancy is a determinant for discontinuation of psychotropic medication; (4) to examine prevalence of records suggestive of adverse mental health, deterioration or relapse 18 months before and during pregnancy, and up to 15 months after delivery; and (5) to estimate absolute and relative risks of adverse maternal and child outcomes of psychotropic treatment in pregnancy. Design Retrospective cohort studies. Setting Primary care. Participants Women treated for psychosis who became pregnant, and their children. Interventions Treatment with antipsychotics, lithium or anticonvulsant mood stabilisers. Main outcome measures Discontinuation and restarting of treatment; worsening of mental health; acute pre-eclampsia/gestational hypertension; gestational diabetes; caesarean section; perinatal death; major congenital malformations; poor birth outcome (low birthweight, preterm birth, small for gestational age, low Apgar score); transient poor birth outcomes (tremor, agitation, breathing and muscle tone problems); and neurodevelopmental and behavioural disorders. Data sources Clinical Practice Research Datalink database and The Health Improvement Network primary care database. Results Prescribing of psychotropic medication was relatively constant before pregnancy, decreased sharply in early pregnancy and peaked after delivery. Antipsychotic and anticonvulsant treatment increased over the study period. The recording of markers of worsening mental health peaked after delivery. Pregnancy was a strong determinant for discontinuation of psychotropic medication. However, between 40% and 76% of women who discontinued psychotropic medication before or in early pregnancy restarted treatment by 15 months after delivery. The risk of major congenital malformations, and neurodevelopmental and behavioural outcomes in valproate (multiple manufacturers) users was twice that in users of other anticonvulsants. The risks of adverse maternal and child outcomes in women who continued antipsychotic use in pregnancy were not greater than in those who discontinued treatment before pregnancy. Limitations A few women would have received parts of their care outside primary care, which may not be captured in this analysis. Likewise, the analyses were based on prescribing data, which may differ from usage. Conclusions Psychotropic medication is prescribed before, during and after pregnancy. Many women discontinue treatment before or during early pregnancy and then restart again in late pregnancy or after delivery. Our results support previous associations between valproate and adverse child outcomes but we found no evidence of such an association for antipsychotics. Future work Future research should focus on (1) curtailing the use of sodium valproate; (2) estimating the benefits of psychotropic drug use in pregnancy; and (3) investigating the risks associated with lifestyle choices that are more prevalent among women using psychotropic drugs. Copyright © Queens Printer and Controller of HMSO 2016.

Database: EMBASE

Antipsychotic drug use in pregnancy: high dimensional, propensity matched, population based cohort study

Author(s): Vigod S.N.; Gomes T.; Wilton A.S.; Taylor V.H.; Ray J.G.

Source: BMJ (Clinical research ed.); 2015; vol. 350

Publication Date: 2015

Publication Type(s): Journal: Article

Abstract:OBJECTIVE: To evaluate maternal medical and perinatal outcomes associated with antipsychotic drug use in pregnancy. DESIGN: High dimensional propensity score (HDPS) matched cohort study.SETTING: Multiple linked population health administrative databases in the entire province of Ontario, Canada.PARTICIPANTS: Among women who delivered a singleton infant between 2003 and 2012, and who were eligible for provincially funded drug coverage, those with > 2 consecutive prescriptions for an antipsychotic medication during pregnancy, at least one of which was filled in the first or second trimester, were selected. Of these antipsychotic drug users, 1021 were matched 1:1 with 1021 non-users by means of a HDPS algorithm.RESULTS: Compared with non-users, women prescribed an antipsychotic medication in pregnancy did not seem to be at higher risk of gestational diabetes (rate ratio 1.10 (95% CI 0.77 to 1.57)), hypertensive disorders of pregnancy (1.12 (0.70 to 1.78)), or venous thromboembolism (0.95 (0.40 to 2.27)). The preterm birth rate, though high among antipsychotic users (14.5%) and matched non-users (14.3%), was not relatively different (rate ratio 0.99 (0.78 to 1.26)). Neither birth weight 97th centile was associated with antipsychotic drug use in pregnancy (rate ratios 1.21 (0.81 to 1.82) and 1.26 (0.69 to 2.29) respectively).CONCLUSIONS: Antipsychotic drug use in pregnancy had minimal evident impact on important maternal medical and short term perinatal outcomes. However, the rate of adverse outcomes is high enough to warrant careful assessment of maternal and fetal wellbeing among women prescribed an antipsychotic drug in pregnancy.MAIN OUTCOME MEASURES: The main maternal medical outcomes were gestational diabetes, hypertensive disorders of pregnancy, and venous thromboembolism. The main perinatal outcomes were preterm birth (97th centile). Conditional Poisson regression analysis was used to generate rate ratios and 95% confidence intervals, adjusting for additionally prescribed non-antipsychotic psychotropic medications. Copyright © Vigod et al 2015.

Database: EMBASE

Antipsychotic use in pregnancy

Author(s): Kulkarni J.; Storch A.; Baraniuk A.; Gilbert H.; Gavrilidis E.; Worsley R.

Source: Expert Opinion on Pharmacotherapy; Jun 2015; vol. 16 (no. 9); p. 1335-1345

Publication Date: Jun 2015

Publication Type(s): Journal: Review

Abstract:Introduction: Antipsychotic medications are being prescribed for a growing number of women with mental illnesses. However, evidence regarding their safety in pregnancy is still insufficient to provide adequate support for clinical practice, creating increasing concern among pregnant women and clinicians.Areas covered: The aim of this article is to review published data regarding the safety of antipsychotic medications in pregnancy with a focus on the most commonly used atypical antipsychotics.Expert opinion: Given the potential harm of not treating severe psychiatric illnesses during pregnancy, careful administration of antipsychotics is recommended for pregnant women who suffer from severe mental disorders. The most frequently used antipsychotics

in pregnancy are olanzapine, risperidone and quetiapine, and do not appear to cause consistent, congenital harm to the fetus. No specific patterns of fetal limb or organ malformation related to these drugs have been reported. There is some evidence suggesting an association between antipsychotic use in pregnancy and the development of gestational diabetes. Also there appears to be an association between antipsychotic medication use in pregnancy and increased neonatal respiratory distress and withdrawal symptoms. Further studies are needed for clinicians to balance good maternal mental health, healthy pregnancies and good infant health outcomes. Copyright © Informa UK, Ltd.

Database: EMBASE

Antipsychotic use in pregnancy: Maternal and fetal outcomes

Author(s): Stewart M.; Pretlove S.; Downer O.; Ismail K.; Berrisford G.; Whitmore J.; Kapadia H.; Coccia F.

Source: Archives of Women's Mental Health; Apr 2015; vol. 18 (no. 2); p. 303-304

Publication Date: Apr 2015

Publication Type(s): Journal: Conference Abstract

Available in full text at [Archives of Women's Mental Health](#) - from ProQuest

Abstract:Background There are currently a substantial number of women of childbearing age who suffer from a psychotic disorder often treated with atypical antipsychotic medication. The introduction of atypical antipsychotics (since the mid-1990s) and the lack of robust studies evaluating the use of antipsychotic medication during pregnancy, means that further exploration of the effects of these medications is needed to provide pregnant women and clinicians with adequate information to make an informed choice about whether to continue on medication during pregnancy. Objective: To describe the short-term maternal and fetal outcomes of pregnant women on antipsychotic medications, who have a current or past psychotic disorder. Methods Retrospective case-note review of all pregnant women on antipsychotic medication for a psychotic disorder, who were referred to the Perinatal Mental Health Clinic between 1st April 2010 to 31st March 2013 for the unit with the largest birth cohort and from 7th May 2012 to 31st March 2013 for the four remaining units. Results Data was obtained on 53 pregnancies that included exposure to Quetiapine (n=21), Olanzapine (n=11), Aripiprazole (n=14), Risperidone (n=5), Clozapine (n=1), Trifluoperazine (n=1) and Haloperidol (n=1). There was a trend towards variation in some of the maternal and fetal outcomes. Amongst the cohort of women taking Quetiapine, Olanzapine and Aripiprazole, 14.3, 27.3 and 0 % developed gestational diabetes while 14.3, 10 and 21.4 % had small for gestational age babies respectively. There were 5 cases of congenital anomalies recorded in total. Conclusion From the results, there are evident differences between outcomes studied, specifically gestational diabetes and small for gestational age. However, it is clear that additional studies need to be completed to assess whether findings are replicated.

Database: EMBASE

Pregnancy exposure to second-generation antipsychotics and the risk of gestational diabetes

Author(s): Gentile S.

Source: Expert Opinion on Drug Safety; Dec 2014; vol. 13 (no. 12); p. 1583-1590

Publication Date: Dec 2014

Publication Type(s): Journal: Review

Abstract:Introduction: Assessment of the metabolic safety of second-generation antipsychotics (SGAs) is mandatory in pregnant women, where the occurrence of metabolic complications and, especially, gestational diabetes mellitus (GDM) may severely impact on pregnancy and fetal outcomes.Areas covered: The aim of this article is to review published data reporting the occurrence of GDM during SGA treatment, and to establish whether or not this iatrogenic complication is a relevant concern in clinical practice. Medical literature information published in any language since 1996 was identified using MEDLINE/PubMed, EMBASE, Scopus, and The Cochrane Library. All articles reporting metabolic complications in pregnancies exposed to single, specific SGAs were acquired, without methodological or language limitations.Expert opinion: Among studies assessing the metabolic safety of specific SGAs, we have 18 cases of GDM overall: 5 cases involve clozapine (CLO), 9 olanzapine (OLA)-The SGA agent that shows the highest number of reported cases of pregnancy exposure-And 2 each for quetiapine and risperidone. Four of these cases, 2 involving CLO and 2 OLA, were complicated by serious fetal and/or neonatal consequences. Such reports of SGA-Associated GDM, together with preliminary data coming from retrospective and prospective studies, may represent signals of a potential safety issue. Copyright © 2014 Informa UK, Ltd.

Database: EMBASE

Antipsychotic drugs in pregnancy: A review of their maternal and fetal effects

Author(s): Galbally M.; Snellen M.; Power J.

Source: Therapeutic Advances in Drug Safety; Apr 2014; vol. 5 (no. 2); p. 100-109

Publication Date: Apr 2014

Publication Type(s): Journal: Review

Available in full text at [Therapeutic Advances in Drug Safety](#) - from National Library of Medicine

Abstract:Understanding the risks of antipsychotic medication use in pregnancy is becoming an important clinical concern given the evidence of their increasing rate of prescription in the general population for a range of disorders. Despite antipsychotics being amongst the earliest of psychotropic medications to be introduced, the evidence for their effects secondary to pregnancy exposure is extremely limited. While this review does not identify clear evidence for a risk of malformation, there is evidence for risks associated with pregnancy and neonatal outcomes. Studies identified found risks that included prematurity, low and high birth weight, and gestational diabetes. There have also been studies that suggest neonatal withdrawal and abnormal muscles movements. The longer term neurodevelopmental outcomes for children exposed in utero remain unclear with only four studies identified: two of first generation antipsychotics and two of second generation antipsychotics. When considering the risk of these medications in pregnancy, the risk of untreated maternal illness (particularly schizophrenia and bipolar disorder) on both maternal and child outcomes is relevant. Future research needs to focus on prospective, longitudinal studies with adequate measures of key confounding variables including maternal mental illness, other exposures (such as smoking, alcohol and illicit drug use) and adequate length of follow up where accurate child developmental measures are obtained. © The Author(s), 2014.

Database: EMBASE

Safety of atypical antipsychotics in pregnancy

Author(s): Mirdamadi K.; Bozzo P.; Koren G.; Einarson A.

Source: Birth Defects Research Part A - Clinical and Molecular Teratology; May 2013; vol. 97 (no. 5); p. 365

Publication Date: May 2013

Publication Type(s): Journal: Conference Abstract

Available in full text at [Birth Defects Research Part A: Clinical and Molecular Teratology](#) - from John Wiley and Sons

Abstract:Background: Psychiatric conditions, such as schizophrenia, are common in women of child bearing age. Treatment with conventional antipsychotics has resulted in a reduction in fertility in this population due to hyperprolactenemia. With the emergence of second generation, or atypical antipsychotics, the rate of fertility in this group has increased dramatically. The second generation antipsychotics include: clozapine, olanzapine, risperidone, quetiapine, aripiprazole, and ziprasidone. In addition, these medications are used to treat other psychiatric disorders, such as bipolar. Consequently, a large group of pregnant women with psychiatric conditions may need to continue therapy in pregnancy, in order to maintain a stable mental state. Consequently, there is a need for investigation on the safety of atypical antipsychotics in pregnancy. Objective: To review available evidence on the safety of the use of the new generation antipsychotics in pregnancy. Method: Medline and Embase were searched for studies examining the fetal safety of the use of the new generation antipsychotics during pregnancy. Results: Data on the safety of the new generation antipsychotics in pregnancy is still limited. However, the available data is fairly reassuring and there are no reports of an increased risk in the rate of major malformations above the baseline risk with the use of atypical antipsychotics. An increased maternal weight gain and an increased risk for obesity and gestational diabetes has been observed, which may be a possible side effect of the antipsychotic. A lower birth weight was also reported. Conclusion: Further research is required with larger sample sizes to reach a definitive conclusion, however available data is reassuring. It is important to treat psychiatric conditions during pregnancy. Therefore, a benefit versus risk decision should be made when deciding to continue or initiate therapy with a new generation antipsychotic during pregnancy.

Database: EMBASE

Do psychiatric medications, especially antidepressants, adversely impact maternal metabolic outcomes?

Author(s): Lopez-Yarto, Maite; Ruiz-Mirazo, Eider; Holloway, Alison C; Taylor, Valerie H; McDonald, Sarah D

Source: Journal of affective disorders; Dec 2012; vol. 141 (no. 2-3); p. 120-129

Publication Date: Dec 2012

Publication Type(s): Research Support, Non-u.s. Gov't Meta-analysis Journal Article Review

Abstract:Psychiatric illnesses, particularly depression, are some of the most common complications of pregnancy. Accordingly, pharmacologic treatment of these illnesses is prevalent and increasing. Systematic reviews on psychiatric medication use during pregnancy have shown effects on obstetrical and neonatal outcomes and non-systematic reviews of maternal outcomes suggest higher weight gain and an increased risk of gestational diabetes. However, to date there has not been a systematic review of the effects of these medications on maternal metabolic outcomes. The objective of this study was to assess the relationship between psychiatric medication use during pregnancy and adverse maternal metabolic outcomes [gestational weight gain (GWG), gestational diabetes (GDM) and postpartum weight retention (PPWR)]. Systematic review and meta-analysis

were used. We searched Medline, EMBASE, PsychInfo and references. Two reviewers independently performed each step of the systematic review, following the MOOSE guidelines. Of 3080 non-duplicate titles and abstracts, 175 articles underwent full text review. Two moderate quality cohort studies were included. No differences were found for GWG, GDM and PPWR. There were only two studies which met our inclusion criteria, making it difficult to make any definitive conclusions regarding the effects of psychiatric medication on maternal metabolic outcomes. Despite the suggestions in non-systematic reviews that psychiatric medication use during pregnancy results in adverse maternal metabolic sequelae, in this systematic review, we found no evidence of an increased risk of GWG, GDM or PPWR in women with psychiatric illness who took psychiatric medications compared to non-medicated women with psychiatric illness. However, more, high quality studies are needed in this area to determine if there is an association between psychiatric medication use and maternal metabolic outcomes. Copyright © 2012 Elsevier B.V. All rights reserved.

Database: Medline

Risks of adverse pregnancy and birth outcomes in women treated or not treated with mood stabilisers for bipolar disorder: Population based cohort study

Author(s): Bodén, Robert; Lundgren, Maria; Brandt, Lena; Reutfors, Johan; Andersen, Morton; Kieler, Helle

Source: BMJ: British Medical Journal; Nov 2012; vol. 345

Publication Date: Nov 2012

Publication Type(s): Journal Peer Reviewed Journal Journal Article

Available in full text at [The BMJ](#) - from Highwire Press

Abstract:Objective: To investigate the risks of adverse pregnancy and birth outcomes for treated and untreated bipolar disorder during pregnancy. Design: Population based cohort study using data from national health registers. Setting: Sweden. Participants: 332 137 women with a last menstrual period anytime after 1 July 2005 and giving birth anytime before the end of 31 December 2009. Women with a record of at least two bipolar diagnoses were identified and grouped as treated (n = 320)—those who had filled a prescription for mood stabilisers (lithium, antipsychotics, or anticonvulsants) during pregnancy—or untreated (n = 554). Both groups were compared with all other women giving birth (n = 331 263). Main outcome measures: Preterm birth, mode of labour initiation, gestational diabetes, infants born small or large for gestational age, neonatal morbidity, and congenital malformations. Results: Of the untreated women, 30.9% (n = 171) were induced or had a planned caesarean delivery compared with 20.7% (n = 68 533) without bipolar disorder (odds ratio 1.57, 95% confidence interval 1.30 to 1.90). The corresponding values for the treated women were 37.5% (n = 120) (2.12, 1.68 to 2.67). The risks of preterm birth in both treated and untreated women were increased by 50%. Of the untreated women, 3.9% (n = 542) had a microcephalic infant compared with 2.3% (324 844) of the women without bipolar disorder (1.68, 1.07 to 2.62). The corresponding values for the treated women were 3.3% (n = 311) (1.26, 0.67 to 2.37). Similar trends were observed for risks of infants being small for gestational age infants for weight and length. Among infants of untreated women, 4.3% (n = 24) had neonatal hypoglycaemia compared with 2.5% (n = 8302) among infants of women without bipolar disorder (1.51, 1.04 to 2.43), and 3.4% (n = 11) of the treated women (1.18, 0.64 to 2.16). The analyses of variation in outcomes did not support any significant differences between treated and untreated women. Conclusions: Bipolar disorder in women during pregnancy, whether treated or not, was associated with increased risks of adverse pregnancy outcomes. (PsycINFO Database Record (c) 2016 APA, all rights reserved) (Source: journal abstract)

Database: PsycINFO

Antipsychotics during pregnancy-risk of fetal and maternal metabolic side effects

Author(s): Lundgren M.; Kieler H.; Brandt L.; Reutfors J.; Boden R.

Source: Hormone Research in Paediatrics; Sep 2012; vol. 78 ; p. 45

Publication Date: Sep 2012

Publication Type(s): Journal: Conference Abstract

Available in full text at [Hormone Research in Paediatrics](#) - from ProQuest

Abstract:Background: Despite the well-known risk of adverse metabolic effects caused by antipsychotics there is little knowledge concerning maternal and fetal effects related to such medication during pregnancy. Objective: To investigate effects of maternal use of antipsychotics during pregnancy on gestational diabetes and risk of fetal macrosomia. Methods: Data were obtained from Swedish national health registers. All women giving birth in Sweden between 2006 and 2009 were included. Exposure to medication was defined as pharmacy claims during pregnancy of any of the following two groups of antipsychotics: drugs with the most severe metabolic side effects, olanzapine or clozapine (n=169), and other antipsychotic drugs (n=338). The exposure groups were compared to the non-exposed population (n=357 696). Results: Exposure to olanzapine or clozapine was associated with increased risk of gestational diabetes (OR 2.39, 95% CI 1.12-5.13) as was exposure to other antipsychotics (OR 2.78, 95% CI 1.64-4.70), compared to women not exposed. Women exposed to antipsychotics had an increased risk of giving birth to infants small for gestational age (SGA) for weight; the OR for olanzapine or clozapine was 2.42 (95% CI 1.24-4.70) and for other antipsychotics 2.11 (95% CI 1.29-3.47). Further, fetuses exposed to other antipsychotics had a higher risk of being born SGA for length (OR 2.29, 95% CI 1.41-3.73) and microcephaly (OR 2.19, 95% CI 1.33-3.62). The risks for birth of SGA-infants decreased after adjustment for maternal factors. There was no increased risk of being born large for gestational age for weight and length for infants exposed to olanzapine or clozapine, but there was an increased risk of a macrocephaly (OR 2.59, 95% CI 1.38-4.88). Conclusions: Women using antipsychotics during pregnancy had a higher risk of gestational diabetes and of giving birth to an SGA infant. Exposure to the most metabolically adverse antipsychotic drugs was not associated with fetal macrosomia.

Database: EMBASE

Bipolar disorder, mood stabilizers and adverse pregnancy outcome-a population based cohort study

Author(s): Boden R.; Brandt L.; Reutfors J.; Andersen M.; Kieler H.; Lundgren M.

Source: Pharmacoepidemiology and Drug Safety; Aug 2012; vol. 21 ; p. 31

Publication Date: Aug 2012

Publication Type(s): Journal: Conference Abstract

Available in full text at [Pharmacoepidemiology and Drug Safety](#) - from John Wiley and Sons

Abstract:Background: Knowledge concerning treatment with mood stabilizers in pregnant women with bipolar disorder is limited. Objectives: To study risks of adverse outcomes for treated and untreated bipolar mothers and their infants. Methods: This is a population based cohort study. Data were retrieved from Swedish national health registers. All women with at least two recorded bipolar diagnoses giving birth in Sweden between 2005 and 2009 were identified. Drug use was determined through prescription fills. The women were grouped by use of mood stabilizing drugs during pregnancy (lithium, antipsychotics and anticonvulsants [n = 320]), or no use of these drugs (n = 554), and were compared to all other women who gave birth (n = 332,137). Outcome measures were congenital malformations, preterm birth, caesarian delivery, gestational diabetes, being born small for gestational age (SGA) or large for gestational age (LGA), and neonatal morbidity. Odds ratios

(ORs) were calculated in multivariate logistic regressions, adjusting for potential confounders: maternal age, country of origin, cohabitation, smoking, and height as well as the infants' birth order. Results: Bipolar mothers were more often smokers, overweight and abused alcohol and drugs. Moreover, they had increased risks of not having a spontaneous start of the delivery (ORs 1.64-2.24, 95% confidence intervals [CIs] 1.35-2.81), and a 50% increased risk of preterm birth. In contrast to the treated mothers the untreated had increased risks of giving birth to infants born symmetrically SGA for both weight and length (OR 2.24, 95% CI 1.20-4.19) and for microcephaly (OR 1.86, 95% CI 1.21- 2.86) and neonatal hypoglycemia (OR 1.63, 95% CI 1.07- 2.48). Conclusions: Women with bipolar disorders had increased risks of adverse birth outcomes. Refraining from medical treatment seems to be associated with growth restriction.

Database: EMBASE

Antipsychotics during pregnancy: Relation to fetal and maternal metabolic effects

Author(s): Boden R.; Brandt L.; Reutfors J.; Kieler H.; Lundgren M.

Source: Archives of General Psychiatry; Jul 2012; vol. 69 (no. 7); p. 715-721

Publication Date: Jul 2012

Publication Type(s): Journal: Article

Available in full text at [Archives of General Psychiatry](#) - from Silverchair Information Systems

Abstract:Context: Knowledge about the effects of exposure to the newer antipsychotics during pregnancy is limited. Objective: To investigate the effects of maternal use of antipsychotics during pregnancy on gestational diabetes and fetal growth. Design: Population-based cohort study comparing women exposed and not exposed to antipsychotics during pregnancy. Exposure was defined as prescriptions filled. Setting: Swedish national health registers. Participants: All women giving birth in Sweden from July 1, 2005, through December 31, 2009, grouped by filled prescriptions for (1) olanzapine and/or clozapine, the most obesogenic and diabetogenic antipsychotics (n=169), (2) other antipsychotics (n=338), or (3) no antipsychotics (n=357 696). Main Outcome Measures: Odds ratios (ORs) with 95% CIs for gestational diabetes and being small for gestational age (SGA) and large for gestational age for birth weight, birth length, and head circumference. Results: Exposure to other antipsychotics was associated with an increased risk of gestational diabetes (adjusted OR, 1.77 [95% CI, 1.04-3.03]). The risk increase with olanzapine and/or clozapine was of similar magnitude but not statistical significance (adjusted OR, 1.94 [95% CI, 0.97-3.91]). Infants exposed to either group of antipsychotics had increased risks of being SGA on birth weight, whereas only exposure to other antipsychotics yielded increased risks of being SGA for birth length and head circumference. None of the risks for SGA measurements remained significant after adjusting for maternal factors. There were no increased risks of being large for gestational age for birth weight or birth length after exposure to olanzapine and/or clozapine, but the risk increased for head circumference (OR, 3.02 [95% CI, 1.60-5.71]). Conclusions: Women who used antipsychotics during pregnancy had increased risks of gestational diabetes. The increased risks of giving birth to an SGA infant seemed to be an effect of confounders, such as smoking. Except for macrocephaly, olanzapine and/or clozapine exposure was not associated with anabolic fetal growth.

Database: EMBASE

Psychotropics in pregnancy: Safety and other considerations

Author(s): Oyebode F.; Rastogi A.; Berrisford G.; Coccia F.

Source: Pharmacology and Therapeutics; Jul 2012; vol. 135 (no. 1); p. 71-77

Publication Date: Jul 2012

Publication Type(s): Journal: Review

Abstract:Introduction: Perinatal psychiatric disorders are important because of their adverse effects on pregnancy outcomes. The aim of this review is investigate psychotropic drugs in the management of antenatal psychiatric disorders with emphasis on the risk of harmful effects. Method: A systematic review of published electronic literature between January 2000 and August 2011 was conducted using the following keywords: pregnancy, pregnancy complications, neonatal complications, congenital anomalies, infant/child development, antidepressants, antipsychotics, and lithium. The search was conducted for each class of psychotropic agents. Further hand searches were conducted. Anticonvulsants were excluded. Results: Antidepressants are associated with increased risk of spontaneous abortions, stillbirths, preterm deliveries, respiratory distress, endocrine and metabolic disturbance. There is evidence of discontinuation syndrome and of increased risk of cardiac defects. Antipsychotics are associated with increased gestational weight and diabetes and with increased risk of preterm birth. The effects of antipsychotics on birth weight are inconclusive. In addition, the findings in relation to malformations are inconclusive. Lithium is associated with increased birth complications such as polyhydramnios, pre-eclampsia, respiratory distress syndrome, hypotonia, and preterm birth. Lithium has previously been associated with markedly increased risk of Ebstein's anomaly. However, recent re-evaluation of the data casts doubt on the previous estimates. There is evidence that lithium is associated with cardiac septal defects. Conclusion: Psychotropic drugs remain an important treatment option during pregnancy to properly manage symptoms of psychiatric diseases. Clinicians need to remain aware of the potential risk of adverse effects associated with psychotropic drug treatment. © 2012 Elsevier Inc.

Database: EMBASE

Antipsychotic therapy during early and late pregnancy. a systematic review

Author(s): Gentile S.

Source: Schizophrenia Bulletin; 2010; vol. 36 (no. 3); p. 518-544

Publication Date: 2010

Publication Type(s): Journal: Review

Available in full text at [Schizophrenia Bulletin](#) - from National Library of Medicine

Abstract:Objective: Both first-(FGAs) and second-generation antipsychotics (SGAs) are routinely used in treating severe and persistent psychiatric disorders. However, until now no articles have analyzed systematically the safety of both classes of psychotropics during pregnancy. Data sources and search strategy: Medical literature information published in any language since 1950 was identified using MEDLINE/PubMed, TOXNET, EMBASE, and The Cochrane Library. Additional references were identified from the reference lists of published articles. Bibliographical information, including contributory unpublished data, was also requested from companies developing drugs. Search terms were pregnancy, psychotropic drugs, (a)typical-first-second-generation antipsychotics, and neuroleptics. A separate search was also conducted to complete the safety profile of each reviewed medication. Searches were last updated on July 2008. Data selection: All articles reporting primary data on the outcome of pregnancies exposed to antipsychotics were acquired, without methodological limitations. Conclusions: Reviewed information was too limited to draw definite conclusions on structural teratogenicity of FGAs and SGAs. Both classes of drugs seem to be associated with an increased risk of neonatal complications. However, most SGAs appear to increase

risk of gestational metabolic complications and babies large for gestational age and with mean birth weight significantly heavier as compared with those exposed to FGAs. These risks have been reported rarely with FGAs. Hence, the choice of the less harmful option in pregnancy should be limited to FGAs in drug-naïve patients. When pregnancy occurs during antipsychotic treatment, the choice to continue the previous therapy should be preferred. © The Author 2008.

Database: EMBASE

Maternal use of antipsychotics in early pregnancy and delivery outcome

Author(s): Reis, Margareta; Källén, Bengt

Source: Journal of Clinical Psychopharmacology; Jun 2008; vol. 28 (no. 3); p. 279-288

Publication Date: Jun 2008

Publication Type(s): Journal Peer Reviewed Journal Journal Article

Available in full text at [Journal of Clinical Psychopharmacology](#) - from Ovid

Abstract:The effect of various antipsychotics during pregnancy has repeatedly been studied, but for most atypical antipsychotics, only little information is available. We identified from the Swedish Medical Birth Register 2908 women who had reported the use of any antipsychotic or lithium in early pregnancy and studied malformation rates with data also from the Register of Congenital Malformations and the Hospital Discharge Register. Comparisons were made with all births (n = 958,729) after adjustment for some confounders. Risks were expressed as odds ratios (ORs). Most women had used dixyrazine or prochlorperazine mainly because of nausea and vomiting in early pregnancy. Seventy-nine women had used lithium, and these outcomes are reported separately. Hence, the main analysis was restricted to 570 women (576 infants) using other antipsychotics. There was a statistically significant increase in the risk for a congenital malformation--after exclusion of some common and minor conditions, the OR was 1.52 (95% confidence interval, 1.05-2.19). Exclusion of infants exposed to anticonvulsants reduced the OR only slightly. Most of the increased risk was caused by cardiovascular defects, mainly atrium or ventricular septum defect. No certain drug specificity was found. Except for an increased risk for congenital malformations, a nearly doubling of the risk for gestational diabetes and a 40% increased risk for cesarean delivery was noted. Because there seems to be little drug specificity, it is possible that underlying pathology or unidentified confounding explains the excess risk. (PsycINFO Database Record (c) 2016 APA, all rights reserved) (Source: journal abstract)

Database: PsycINFO

Second-generation (atypical) antipsychotics and metabolic effects: A comprehensive literature review

Author(s): Newcomer J.W.

Source: CNS Drugs; 2005; vol. 19 ; p. 1-93

Publication Date: 2005

Publication Type(s): Journal: Review

Abstract:Increasing numbers of reports concerning diabetes, ketoacidosis, hyperglycaemia and lipid dysregulation in patients treated with second-generation (or atypical) antipsychotics have raised concerns about a possible association between these metabolic effects and treatment with these medications. This comprehensive literature review considers the evidence for and against an association between glucose or lipid dysregulation and eight separate second-generation antipsychotics currently available in the US and/or Europe, specifically clozapine, olanzapine, risperidone, quetiapine, zotepine, amisulpride, ziprasidone and aripiprazole. This review also

includes an assessment of the potential contributory role of treatment-induced weight gain in conferring risk for hyperglycaemia and dyslipidaemia during treatment with different antipsychotic medications. Substantial evidence from a variety of human populations, including some recent confirmatory evidence in treated psychiatric patients, indicates that increased adiposity is associated with a variety of adverse physiological effects, including decreases in insulin sensitivity and changes in plasma glucose and lipid levels. Comparison of mean weight changes and relative percentages of patients experiencing specific levels of weight increase from controlled, randomised clinical trials indicates that weight gain liability varies significantly across the different second-generation antipsychotic agents. Clozapine and olanzapine treatment are associated with the greatest risk of clinically significant weight gain, with other agents producing relatively lower levels of risk. Risperidone, quetiapine, amisulpride and zotepine generally show low to moderate levels of mean weight gain and a modest risk of clinically significant increases in weight. Ziprasidone and aripiprazole treatment are generally associated with minimal mean weight gain and the lowest risk of more significant increases. Published studies including uncontrolled observations, large retrospective database analyses and controlled experimental studies, including randomised clinical trials, indicate that the different second-generation antipsychotics are associated with differing effects on glucose and lipid metabolism. These studies offer generally consistent evidence that clozapine and olanzapine treatment are associated with an increased risk of diabetes mellitus and dyslipidaemia. Inconsistent results, and a generally smaller effect in studies where an effect is reported, suggest limited if any increased risk for treatment-induced diabetes mellitus and dyslipidaemia during risperidone treatment, despite a comparable volume of published data. A similarly smaller and inconsistent signal suggests limited if any increased risk of diabetes or dyslipidaemia during quetiapine treatment, but this is based on less published data than is available for risperidone. The absence of retrospective database studies, and little or no relevant published data from clinical trials, makes it difficult to draw conclusions concerning risk for zotepine or amisulpride, although amisulpride appears to have less risk of treatment-emergent dyslipidaemia in comparison to olanzapine. With increasing data from clinical trials but little or no currently published data from large retrospective database analyses, there is no evidence at this time to suggest that ziprasidone and aripiprazole treatment are associated with an increase in risk for diabetes, dyslipidaemia or other adverse effects on glucose or lipid metabolism. In general, the rank order of risk observed for the second-generation antipsychotic medications suggests that the differing weight gain liability of atypical agents contributes to the differing relative risk of insulin resistance, dyslipidaemia and hyperglycaemia. This would be consistent with effects observed in nonpsychiatric samples, where risk for adverse metabolic changes tends to increase with increasing adiposity. From this perspective, a possible increase in risk would be predicted to occur in association with any treatment that produces increases in weight and adiposity. However, case reports tentatively suggest that substantial weight gain or obesity may not be a factor in up to one-quarter of cases of new-onset diabetes that occur during treatment. Pending further testing from preclinical and clinical studies, limited controlled studies support the hypothesis that clozapine and olanzapine may have a direct effect on glucose regulation independent of adiposity. The results of studies in this area are relevant to primary and secondary prevention efforts that aim to address the multiple factors that contribute to increased prevalence of type 2 diabetes mellitus and cardiovascular disease in populations that are often treated with second-generation antipsychotic medications. © Adis Data Information BV 2005. All rights reserved.

Database: EMBASE

DISCLAIMER: Results of database and or Internet searches are subject to the limitations of both the database(s) searched, and by your search request. It is the responsibility of the requestor to determine the accuracy, validity and interpretation of the results.

Strategy 107071

#	Database	Search term	Results
1	Medline	exp "ANTIPSYCHOTIC AGENTS"/	112100
2	Medline	(antipsychotic* OR "anti psychotic*").ti,ab	32241
3	Medline	(olanzapine).ti,ab	7107
4	Medline	(quetiapine).ti,ab	3792
5	Medline	(1 OR 2 OR 3 OR 4)	123755
6	Medline	(hyperglycemia OR hyperglycaemia).ti,ab	41640
7	Medline	exp HYPERGLYCEMIA/	30130
8	Medline	("blood glucose").ti,ab	54280
9	Medline	exp "BLOOD GLUCOSE"/	142213
10	Medline	(6 OR 7 OR 8 OR 9)	200791
11	Medline	(pregn*).ti,ab	388216
12	Medline	exp PREGNANCY/	799125
13	Medline	(11 OR 12)	878538
14	Medline	(5 AND 10 AND 13)	14
15	Medline	exp "DIABETES, GESTATIONAL"/	8921
16	Medline	(5 AND 15)	13
17	EMBASE	(antipsychotic* OR "anti psychotic*").ti,ab	49866
18	EMBASE	exp "NEUROLEPTIC AGENT"/	250392

19	EMBASE	(olanzapine).ti,ab	11019
20	EMBASE	(quetiapine).ti,ab	6674
21	EMBASE	exp "ATYPICAL ANTIPSYCHOTIC AGENT"/	88740
22	EMBASE	(17 OR 18 OR 19 OR 20 OR 21)	256626
23	EMBASE	(hyperglycemia OR hyperglycaemia).ti,ab	60515
24	EMBASE	exp HYPERGLYCEMIA/	83911
25	EMBASE	("blood glucose").ti,ab	82363
26	EMBASE	exp "BLOOD GLUCOSE"/	217094
27	EMBASE	exp "PREGNANCY DIABETES MELLITUS"/	27738
28	EMBASE	(gestational ADJ2 diabet*).ti,ab	16458
29	EMBASE	(23 OR 24 OR 25 OR 26)	294888
30	EMBASE	(27 OR 28)	28904
31	EMBASE	(pregn*).ti,ab	536701
32	EMBASE	exp PREGNANCY/	716655
33	EMBASE	(30 OR 31 OR 32)	863022
34	EMBASE	(22 AND 29 AND 33)	103
35	EMBASE	(22 AND 30)	129
36	EMBASE	(34 OR 35)	207
37	PsycINFO	(antipsychotic* OR "anti psychotic").ti,ab	24613
38	PsycINFO	(olanzapine).ti,ab	5567

39	PsycINFO	(quetiapine).ti,ab	3093
40	PsycINFO	exp "NEUROLEPTIC DRUGS"/	28004
41	PsycINFO	(37 OR 38 OR 39 OR 40)	37399
42	PsycINFO	(hyperglycemia OR hyperglycaemia).ti,ab	1297
43	PsycINFO	exp HYPERGLYCEMIA/	485
44	PsycINFO	exp "BLOOD SUGAR"/	996
45	PsycINFO	(42 OR 43 OR 44)	2266
46	PsycINFO	exp "GESTATIONAL DIABETES"/	127
47	PsycINFO	(gestational ADJ2 diabet*).ti,ab	396
48	PsycINFO	(pregn*).ti,ab	36980
49	PsycINFO	exp PREGNANCY/	21386
50	PsycINFO	(48 OR 49)	39790
51	PsycINFO	(46 OR 47)	399
52	PsycINFO	(41 OR 51)	37784
53	PsycINFO	(41 AND 45 AND 50)	1
54	PsycINFO	(41 AND 51)	14
55	Medline	(metabolic).ti,ab	393076
56	Medline	(5 AND 13 AND 55)	31
57	Medline	exp "METABOLIC DISEASES"/	883368
58	Medline	(5 AND 13 AND 57)	57