Developmental Effects of Antenatal Exposure to Antipsychotics

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Primary Objective:To investigate efficacy and adverse effects of AP treatment for pregnant women with SMI.Aim 1a: Efficacy of AP treatment for pregnant women with SMI. Hypothesis: Women taking either APs or non-AP mood stabilizers will be less...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Postpartum and puerperal disorders
Study type	Observational invasive

Summary

ID

NL-OMON56645

Source
ToetsingOnline

Brief title
MAIA

Condition

- Postpartum and puerperal disorders
- Psychiatric disorders NEC

Synonym
psychotic disorders, servere mental illness

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: National Institutes of Health

Intervention

Keyword: Antipsychotics, child development, Relaps, Severe Mental Illness

Outcome measures

Primary outcome

Main study parameter is relapse with mood or psychotic episode as determined by MINI psychiatric interview during the peripartum period.

Secondary outcome

Secondary parameters for adverse pregnancy outcomes are total weight gain in pregnancy and body size measurements at 20 weeks* gestation and delivery.

Medication concentrations in maternal blood at 6 months postpartum.

Neonatal adaptation in neonates will be assessed using Finnegan scale in hospital after delivery.

At six months of age sensory gating (P50) from EEG measurements will be measured. Infant development will be measured by Bayley Infant Development and Vineland Adaptive Behavior scales.

Investigate how biological and (epi-)genetic factors in parents and offspring influence development in offspring.

Study description

Background summary

Antipsychotic (AP) medications are widely prescribed for a range of mental illnesses including bipolar disorder and non-affective psychosis (1,2). These disorders usually onset in adolescence or early adulthood (3); thus, women of childbearing age are among those prescribed APs. The number of pregnancies exposed to APs has been increasing over time (4,5,6). In the USA, prevalence of AP use in pregnancy increased from 0.3-0.4% to 0.8-1.3% (4,5) over the first

decade of the twenty-first century. APs cross the placenta, and in some cases the fetus is exposed to a higher concentration than the mother*s serum level (7). APs block dopamine (DA) D2 receptors, which are functional in the developing fetus (8), including influencing the proliferation and differentiation of neural progenitor cells (9). Increased DA signaling in early development results in increased numbers of inhibitory cortical interneurons and decreased numbers of pyramidal cells, while decreased DA signaling has the reverse effect. Thus, tonic DA blockade in utero could alter the excitatory/inhibitory balance in mature prefrontal cortex, which could affect fear processing, social functioning, and spatial or working memory in the long term. At present very limited data exist on developmental outcomes associated with antenatal exposure to APs (10). This study aims to investigate efficacy and adverse effects of AP exposure in pregnant women with severe mental illness (SMI). Our overall goal is to precisely describe the risk/benefit ratio associated with AP treatment in pregnancy, in order to allow pregnant women with SMI to make informed decisions about their care.

Study objective

Primary Objective:
To investigate efficacy and adverse effects of AP treatment for pregnant women with SMI.

Aim 1a: Efficacy of AP treatment for pregnant women with SMI.
Hypothesis: Women taking either APs or non-AP mood stabilizers will be less likely to relapse with mood or psychotic episodes than those not medicated.

Aim 1b: Adverse pregnancy outcomes with AP treatment for pregnant women.
Hypothesis: Women taking Aps will be more likely to develop gestational diabetes than women taking non-APs or women taking no medication.

We will recruit women in pregnancy with SMI (bipolar or primary psychotic disorder, in three groups: women taking AP, women taking other psychotropic medication, and women taking no psychotropic medication. Women will be followed naturalistically and assessed for psychiatric relapse in pregnancy and the postpartum period, as well as complications of pregnancy, including gestational diabetes, pre-eclampsia, and hemorrhage.

Secondary Objectives:

Aim 2:To describe neonatal adaptation and physical growth in neonates of the mothers either exposed or unexposed to APs during pregnancy.

Aim 2a:Neonatal adaptation in neonates either exposed or unexposed to APs during pregnancy.
Hypothesis: Neonates of mothers who took APs during pregnancy will evince poorer neonatal adaptation than neonates of mothers who took either non-AP

psychotropic medication or no medication.

Aim 2b:Physical growth in neonates either exposed or unexposed to APs during pregnancy.
Hypothesis: Neonates of mothers who took APs during pregnancy will have larger body sizes than neonates of mothers who took either non-AP psychotropic medication or no medication.

We will examine obstetric and neonatal outcomes of infants of women with SMI, including neonatal adaptation syndrome (NAS), with control for maternal diagnosis and level of functioning.

Aim 3: To investigate sensory gating and development through 6 months in children of the mothers either exposed or unexposed to APs during pregnancy.

Aim 3a: To investigate sensory gating in children exposed to AP antenatally.
Hypothesis: All infants prenatally exposed to APs will have reduced inhibitory activity as demonstrated by reduced auditory sensory gating, measured by the P50 component in the EEG.

Aim 3b (Exploratory): Investigation of development through 6 months in children exposed to AP antenatally.
Hypothesis: We expect to find lower scores on the Socialization Domain of the Vineland and on the Social-Emotional scale of the Bayley. Further we hypothesize that we might find a sex specific effect for the associations between socioemotional outcomes associated with AP exposure.

Aim 3c (Exploratory): Investigate how biological and (epi-)genetic factors in parents and offspring influence development in offspring.

Aim 4 (Exploratory): To describe AP serum level changes during the peripartum period in mothers.
Hypothesis: We expect serum level fluctuations during pregnancy and postpartum period as a result of blood volume changes in mothers.

Study design

Design: Longitudinal naturalistic prospective cohort study
Duration: 5 years
Follow up: from first trimester of pregnancy until 6 months postpartum
Setting: Women treated in outpatient reproductive psychiatric and obstetric clinics of the Erasmus Medical Center in the Netherlands and at Mount Sinai NY, USA .

This study will be a longitudinal clinical cohort study to investigate efficacy and adverse effects of AP exposure in pregnant women with serious mental illness (SMI).

Our overall goal is to precisely describe the risk/benefit ratio associated with AP treatment in pregnancy, in order to allow pregnant women with SMI to make informed decisions about their care.

Study burden and risks

Study assessments are optimally aligned with routine clinical care. There are no risks associated with an one hour diagnostic interview. The risks of obtaining a venous blood sample can be considered negligible. Blood sampling is combined with clinical blood withdrawals as much as possible. To our knowledge there are no medical risks associated with an EEG. Collection times coincide as much as possible with regular care.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Babies and toddlers (28 days-23 months)
Newborns

Inclusion criteria

- Pregnant
- Severe mental illness
• Psychotic disorder (affective and non-affective)
• Bipolar disorder
• History of psychiatric hospitalization, regardless of diagnosis.
- Able to complete study interviews and measures in Dutch or English

Exclusion criteria

- Acute psychotic or bipolar episode
- Active substance use disorder in pregnancy
- Insufficiently high-functioning to provide full informed consent and/or participate in study procedures

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-03-2024
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO Date:	08-03-2024
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-10-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL84427.078.23