Safety of the second generation antipsychotics during pregnancy (Second generation antipsychotics and pregnancy)

First published: 23/09/2013
Last updated: 23/04/2024

Study | Finalised

Administrative details

PURI
https://redirect.ema.europa.eu/resource/42972

EU PAS number
EUPAS4799

Study ID
42972

DARWIN EU® study
No

Study countries
Finland

Study description
Second generation antipsychotics have largely replaced first generation antipsychotics but little is known about their safety during pregnancy. This is a population based study based on national register data in Finland. Data from the National Birth Register, the Register of Congenital Malformations, and the Drug Prescription Register have been linked through years 1996-2012 in the Drugs and Pregnancy project, and data in this study are extracted from the Drugs and Pregnancy project database. The data include all births (live and still births), pregnancy terminations due to major congenital anomaly, and information on drug purchases during pregnancy and 3 months before pregnancy. There are appr. 55,000-

60,000 births per year in Finland, and we expect to have a baseline study population with appr. 1 mil. pregnancies. Appr. 0.2-0.6% of pregnant women during the study period used antipsychotics and we expect to include appr.2,000 pregnancies exposed to second generation antipsychotics. The primary aims of the study are i.) to assess the risk of major congenital anomalies after first trimester exposure to second generation antipsychotics and ii.) to investigate the prevalence of other perinatal outcomes, including large for gestational age, preterm birth, low birth weight, and perinatal mortality after continuous exposure. The exposed group is compared i) to women and their offspring exposed to first generation antipsychotics during the period of theree months prior to pregnancy until the end of pregnancy (to control for maternal illness), and ii) to unexposed women. Logistic regression is used to evaluate associations between exposure and outcome, and covariates to be considered include year of birth, mother's age, parity, tobacco use, prepregnancy diabetes, use of other psychiatric drugs and use of drugs classified as potentially harmful. The results will provide important information on the safety of second generation antipsychotics during pregnancy.

Study status
Finalised

Research institution and networks

Institutions

Finnish Institute for Health and Welfare (THL)

Finland
First published: 01/02/2024
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01/02/2024

Institution

Educational Institution

Laboratory/Research/Testing facility

Contact details

Study institution contact
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Primary lead investigator

Study timelines

Date when funding contract was signed
Planned:
01/01/2012
Actual:
01/01/2012

Study start date
Planned:
15/05/2014
Actual:
15/05/2014

Data analysis start date
Planned:
15/09/2014
Actual:
01/09/2016

Date of interim report, if expected
Planned:
31/10/2018

Date of final study report
Planned:
01/09/2019
Actual:
03/11/2019

Sources of funding

- Other

More details on funding

Finnish Medicines Agency

Study protocol

NEW_antipsychotics_HM.pdf(88.33 KB)

NEW_antipsychotics_HM__09052014.pdf(95.42 KB)

Regulatory

Was the study required by a regulatory body?
No

Is the study required by a Risk Management Plan (RMP)?
Not applicable

Methodological aspects

Study type

Study type list

Study topic:
Human medicinal product
Disease /health condition

Study type:
Non-interventional study

Scope of the study:
Assessment of risk minimisation measure implementation or effectiveness
Safety study (incl. comparative)

Data collection methods:
Secondary data collection

Main study objective:
To assess pregnancy-related risks associated with the use of second generation antipsychotics. These include major congenital anomalies and perinatal outcomes including preterm birth, birth weight, perinatal death etc.

Study Design

Non-interventional study design
Cohort

Population studied

Short description of the study population
Exposed cohort:
The definition of exposure includes pregnancies where the woman has purchased second generation antipsychotics (4th level ATC code N05AE, N05AH, N05AL, N05AX) at any time during pregnancy and/ or one month before pregnancy. Major congenital anomalies will be analyzed in the cohort with purchase(s) during one month prior to pregnancy or during the first trimester
The two unexposed reference groups consist of:
- 1. All pregnant women and their offspring not exposed to second generation antipsychotics during pregnancy and three months before pregnancy, but exposed to first generation antipsychotics (ATC codes N05AA, N05AB, N05AC, N05AD, N05AF) at any time during the period of three months before pregnancy until the end of pregnancy
- 2. Pregnant women and their offspring unexposed to second generation antipsychotics during the period of three months prior to pregnancy until the end of pregnancy

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Age groups
Preterm newborn infants (0 – 27 days)
Term newborn infants (0 – 27 days)
Adolescents (12 to < 18 years)
Adults (18 to < 46 years)

Special population of interest
Pregnant women

Estimated number of subjects
10000

Study design details

Outcomes
Major congenital anomalies, perinatal outcomes including preterm birth>37 weeks and very preterm birth (<32 weeks), low birth weight (<2500g) and very low birth weight (<1500g), perinatal death, mode of delivery, neonatal outcome (Apgar score, hypoxia, need for treatment in neonatal care unit, etc.

Data analysis plan
All data are anonymized and coded prior to statistical analysis. The prevalence of specific outcomes is compared between exposed and unexposed pregnant women and their offspring. Univariate analyses are used to study demographic differences between the study cohorts, and logistic regression to assess the association between new generation antipsychotic use during pregnancy and major congenital anomalies (MCA) and perinatal outcomes. With an estimated of 2,000 exposed births and fetuses from elective terminations of pregnancy due to fetal anomaly, the study has a 98.3% power to detect a 60% relative increase (1.8% absolute increase) in the prevalence of MCAs presuming a baseline prevalence of 3% in the control cohort (alpha = 0.05, two-sided), and for perinatal

complications that have a prevalence of 6% (as preterm birth) we have a 98.3% power to detect a 40% relative risk increase (2.4% absolute risk increase).

Documents

Study results
ABSTRACT_121019.pdf(2.99 KB)
SGA_malformations_Ellfolk et al..pdf(352.71 KB)

Study publications
Ellfolk M, Leinonen MK, Gissler M, Lahesmaa-Korpinen AM, Saastamoinen L, Nurmin…
Ellfolk M, Leinonen MK, Gissler M, Kiuru-Kuhlefelt S, Saastamoinen L, Malm H. S…

Data management

ENCePP Seal

This study has been awarded the ENCePP seal

Conflicts of interest of investigators
CI_M-LN.pdf(1.39 MB)

Composition of steering group and observers
Specification of steering group.pdf(17.06 KB)

Data sources

Data source(s), other
Drugs and Pregnancy Finland

Data sources (types)
Administrative data (e.g. claims)

Use of a Common Data Model (CDM)

CDM mapping
No

Data quality specifications

Check conformance
Unknown

Check completeness
Unknown

Check stability
Unknown

Check logical consistency
Unknown

Data characterisation

Data characterisation conducted
No