ISRCTN00928792 https://doi.org/10.1186/ISRCTN00928792

The effect of Metformin in women with Type 2 diabetes during pregnancy

Submission date	Recruitment status
21/03/2011	No longer recruiting
Registration date	**Overall study status**
26/07/2011	Completed
Last Edited	**Condition category**
29/01/2021	Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title
Metformin in Women with Type 2 Diabetes in Pregnancy a randomized controlled trial

Acronym
MiTy

Study objectives
Among pregnant women with diagnosed type 2 diabetes mellitus, does the addition of metformin to a standard regimen of insulin increase or decrease the incidence of adverse perinatal outcomes as defined by a composite of: pregnancy loss, preterm birth, birth injury, respiratory distress, neonatal hypoglycemia, and neonatal intensive care unit (NICU) admission > 24 hours, compared with women treated with insulin plus placebo?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Mount Sinai Hospital Research Ethics Board approved on February 16, 2011; Ref :10-0129A

Study design
Randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Type 2 diabetes mellitus

Interventions
Addition of metformin to a standard regimen of insulin among pregnant women with diagnosed type 2 diabetes mellitus compared with women treated with insulin plus placebo

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Metformin, insulin

Primary outcome(s)
1. Pregnancy loss
2. Preterm birth
3. Birth injury
4. Moderate/severe respiratory distress (RDS)
5. Neonatal hypoglycemia
6. Neonatal intensive care unit (NICU) admission > 24 hours

Key secondary outcome(s))
1. Incidence of large for gestational age infants defined as greater than the 90th percentile for weight, based on the National Canadian fetal growth standards for singleton boys and girls
2. Pregnancy loss

3. Preterm birth (will record if spontaneous or indicated)
4. Birth injury
5. Respiratory distress
6. Neonatal hypoglycemia
7. NICU admission > 24 hours
8. Cord blood gases < 7.0
9. Elevated cord blood C-peptide
10. Fetal fat mass as measured by neonatal anthropometric measurements as measured by Catalano et al
11. Maternal glycemic control as measured by HbA1c and capillary glucose measurements. Gestational age at testing will be recorded. All downloaded glucose results will be transmitted on a regular basis to a central site for future analysis. Monthly correlations will be done with the laboratory during routine monthly blood draws.
12. Maternal hypoglycemia defined as mild (<3.6, symptomatic and asymptomatic or requiring treatment), or severe (loss of consciousness or confusion requiring assistance) will be documented at each visit
13. Maternal weight gain. The first and last weight will be obtained at the first and last visit in pregnancy, whether they be done by the endocrinologist, family physician or obstetrician. Consent from the mother will be obtained for this.
14. Maternal insulin doses (overall amount and number of patients that are taking high insulin doses defined as 2 units/kg or more per day)
15. Incidence of pre-eclampsia and/or gestational hypertension
16. Number of hospitalizations prior to admission for delivery and the duration of hospital stays for the mother prior to admission for delivery and associated with delivery
17. Rate of cesarean-section
18. Duration of hospital stay for infant associated with his/her birth until the first discharge home

Completion date
31/12/2019

Eligibility

Key inclusion criteria
1. Women between the ages of 18-45
2. Women diagnosed with type 2 diabetes prior to pregnancy or women with undiagnosed type 2 diabetes diagnosed prior to 20 weeks gestation [defined as women presenting with gestational diabetes before 20 weeks gestation with an elevated glycosylated hemoglobin (HbA1c) which is 8% or more above the upper normal range (i.e. HbA1c of 6.5% if upper normal is 6.0%, or HbA1c 7% if upper normal is 6.5%) or fasting glucose >= 7.0 mmol/L]
3. Pregnancy gestation between 12 weeks 0 days - 22 weeks 6 days
4. Live singleton fetus

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
45 years

Sex
Female

Total final enrolment
502

Key exclusion criteria
1. Women who are not on insulin
2. Women who are on oral hypoglycemic agents should be switched to insulin prior to randomization
3. Diabetes diagnosed after 20 weeks gestation
4. Type 1 diabetes
5. Known intolerance to metformin
6. Contraindications to metformin use which include:
6.1 Renal insufficiency (defined as serum creatinine of greater than 130 umol/L or creatinine clearance < 60 ml/min
6.2 Moderate to severe liver dysfunction (defined as liver enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT)) greater than three times the upper limit of normal)
6.3 Shock or sepsis
6.4 Previous hypersensitivity to metformin
7. Women with significant gastrointestinal problems such as severe vomiting requiring intravenous fluids or hospitalization, or active Crohn's or colitis
8. Previous participation in the trial
9. Patients who have a fetus with a known potentially lethal anomaly will be excluded. Information regarding congenital anomalies diagnosed after randomization will be recorded.
10. Known higher order pregnancies (twins, triplets, etc). These women will be excluded as they have a higher rate of adverse outcomes and we want to avoid any inequalities if they are unequally distributed between the groups
11. Presence of acute or chronic metabolic acidosis, including diabetic ketoacidosis
12. History of diabetic ketoacidosis or history of lactic acidosis
13. Presence of excessive alcohol intake, acute or chronic
14. Presence of congestive heart failure or history of congestive heart failure

Date of first enrolment
01/05/2011

Date of final enrolment
11/10/2018

Locations

Countries of recruitment
Canada

Study participating centre
C8-2075 Bayview Ave.
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Sponsor information

Organisation
The Centre for Mother, Infant, and Child Research (CMICR) (Canada)

ROR
https://ror.org/03wefcv03

Funder(s)

Funder type
Research organisation

Funder Name
Canadian Institutes of Health Research (CIHR) (Canada)

Alternative Name(s)
Instituts de Recherche en Santé du Canada, Canadian Institutes of Health Research (CIHR), CIHR_IRSC, Canadian Institutes of Health Research | Ottawa ON, CIHR - Welcome to the Canadian Institutes of Health Research, CIHR, IRSC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Canada

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/10/2020	29/01/2021	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes