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Myo-inositol supplementation for the prevention of gestational diabetes

Submission date
12/02/2017

Recruitment status
No longer recruiting

Registration date
09/03/2017

Overall study status
Completed

Last Edited
15/08/2024

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
Gestational diabetes is high blood sugar (hyperglycemia) that develops during pregnancy and usually disappears after giving birth. It often occurs along with serious complications which increase the risk of illness and death, such as macrosomia, where the baby grows larger than usual. The combination of intensive monitoring of pregnancy and the use of newer forms of insulin makes it possible to control blood sugar levels. However, the incidence of macrosomia does not appear to be significantly reduced. The macrosomic newborns are at increased risk of obesity, high blood pressure and diabetes later in life. Myo-inositol is a dietary supplement which seems to improve the effects of endogenous insulin and could reduce the incidence of gestational diabetes or at least the incidence of gestational diabetes related morbidity.
The aim of this study is to investigate the effect of dietary myo-inositol supplements on the prevention of gestational diabetes.

Who can participate?
Women aged over 18 with single pregnancies and without pre-existing impaired glucose tolerance

What does the study involve?
Participants are randomly allocated to one of two groups. One group are given myo-inositol and folic acid supplements from the end of the first trimester of pregnancy until the time of gestational diabetes diagnosis (26-28 weeks of gestation), and the other group are given only folic acid supplements for the same period of time. Fasting blood sugar and glycated hemoglobin are measured at the time of study entry and at 19-20 weeks of gestation. At 26-28 weeks of gestation, an oral glucose tolerance test is performed on all participants for the diagnosis of gestational diabetes. The participants diagnosed with gestational diabetes and without gestational diabetes are recorded. At the same time (26-28 weeks of gestation), insulin levels are measured for the determination of insulin resistance.

What are the possible benefits and risks of participating?
Participants may benefit from better blood sugar control and lower risk of gestational diabetes as a result of taking part in the study. There are no notable risks involved for participants.

Where is the study run from?
The University of Athens, Alexandra Hospital (Greece)

When is the study starting and how long is it expected to run for?
December 2017 to August 2023

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Prof. George Daskalakis

Contact information

Type(s)
Public

Contact name
Mr Georgios Asimakopoulos

ORCID ID
http://orcid.org/0000-0001-6587-8226

Contact details
24, Agias Elenis Street
Athens
Greece
15772

Type(s)
Scientific

Contact name
Prof Georgios Daskalakis

Contact details
80, Vasilissis Sofias Avenue
Athens
Greece
11528

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

N/A

Study information

Scientific Title
The effect of dietary myo-inositol supplementation on the insulin resistance and the prevention of gestational diabetes

Study objectives
Current hypothesis as of 21/11/2017:
Myo-inositol supplementation improves insulin resistance and reduces the incidence of gestational diabetes.

Previous hypothesis:
Myo-inositol supplementation improves glycaemic control and perinatal outcome in patients with diet-treated gestational diabetes.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Scientific Board of Alexandra Hospital, 23/11/2016, ref: 717/09-11-2016
2. Scientific Board of Alexandra Hospital, 28/06/2017, ref: 520/22-06-2017

Study design
Single-centre open-label prospective randomised trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Gestational diabetes mellitus

Interventions
Current interventions as of 21/11/2017:
The participants will be randomized to two groups according to the ID number they get when they visit the hospital. According to this method, one group will consist of participants whose ID

numbers are even numbers and the other group will consist of participants whose ID numbers are odd numbers.

1. Treatment group: Myo-inositol and Folic acid from 11 – 13+6 weeks of gestation until the time of gestational diabetes diagnosis (26 – 28 weeks of gestation); myo-inositol, oral, 2g, two times per day; folic
acid, oral, 200 micrograms, two times per day
2. Control group: Folic acid from 11 – 13+6 weeks of gestation until the time of gestational diabetes diagnosis (26 – 28 weeks of gestation); folic acid, oral, 400 micrograms, one time per day

At the time of study entry (11-13+6 weeks of gestation), measurements of fasting blood glucose and glycated hemoglobin will be performed for all participants of both groups. At 19 – 20 weeks of gestation, the same measurements will be repeated for all participants. Finally, at 26 - 28 weeks of gestation, the 2 hour 75 gr Oral Glucose Tolerance Test (OGTT) will be offered for the diagnosis of gestational diabetes. Insulin resistance of all participants will also be evaluated via homeostasis model assessment of insulin resistance (HOMA-IR) and Matsuda Index. Also, the incidence rate of diet-treated gestational diabetes and diabetes requiring insulin therapy will be evaluated after the diagnosis of gestational diabetes at 26-28 weeks of gestation. All above parameters will be recorded in a database and analyzed with the appropriate statistical method.

Previous interventions:
The participants will be randomized to two groups according to the ID number they get when they visit the hospital. According to this method, one group will consist of participants whose ID numbers are even numbers and the other group will consist of participants whose ID numbers are odd numbers.

1. Treatment group: Myo-inositol and Folic acid after the diagnosis of diet-treated gestational diabetes (24 - 28 weeks of gestation); myo-inositol, oral, 2g, two times per day for 6 weeks; folic acid, oral, 200 micrograms, two times per day for 6 weeks
2. Control group: Folic acid after the diagnosis of diet-treated gestational diabetes (24 - 28 weeks of gestation); folic acid, oral, 400 micrograms, one time per day for 6 weeks

Both groups will also be treated with a diet of low glycemic index. After 6 weeks, measurements of blood glucose at 0-60 mins, glycated hemoglobin and fasting insulin will be performed and compared with the first measurements of 24 to 28 weeks of gestation. Insulin resistance will also be evaluated via homeostasis model assessment of insulin resistance (HOMA-IR) and compared with the first measurements of 24 to 28 weeks of gestation. Third trimester ultrasound measurements of fetal biometry will be recorded. Postnatally, perinatal outcome will be recorded, such in relation to the neonate as in relation to the mother. All above parameters will be recorded in a database and analyzed with the appropriate statistical method.

The total duration of follow-up extends from the end of the intervention till the end of the hospitalization of mother and neonate.

Intervention Type
Supplement

Primary outcome measure
Current primary outcome measures:
Gestational diabetes incidence rate, evaluated by the results of a 75 g oral glucose tolerance test at 26 - 28 weeks of gestation

Previous primary outcome measures:
Insulin resistance level, evaluated by homeostasis model assessment of insulin resistance (HOMA-IR) - measured at baseline (24-28 weeks of gestation) and after 6 weeks (after intervention)

Secondary outcome measures

Current secondary outcome measures as of 21/11/2017:
1. Fasting blood glucose levels, measured by blood test at 26-28 weeks of gestation (after intervention)
2. Glycated hemoglobin levels, measured by blood test at 26-28 weeks of gestation (after intervention)
3. Insulin resistance level, evaluated by homeostasis model assessment of insulin resistance (HOMA-IR) and Matsuda Index at 26-28 weeks of gestation (after intervention)
4. Incidence rate of diet-treated gestational diabetes and diabetes requiring insulin therapy, evaluated at 26-28 weeks of gestation (after intervention)

Previous secondary outcome measures:
1. Blood glucose at 0-60 mins, measured by blood test at baseline (24-28 weeks of gestation) and after 6 weeks (after intervention)
2. Glycated hemoglobin, measured by blood test at baseline (24-28 weeks of gestation) and after 6 weeks (after intervention)
3. Fasting insulin, measured by blood test at baseline (24-28 weeks of gestation) and after 6 weeks (after intervention)
4. Fetal biometry at third trimester, measured using ultrasound measurements (biparietal diameter [BPD], head circumference [HC], abdominal circumference [AC], femur length [FL]), measured at 32 - 34 weeks of gestation
5. Requiring insulin therapy, estimated during 6 weeks of intervention
6. Delivery data (gestational age at delivery, birth weight, mode of delivery, indication of labor induction or caesarean section, Apgar score measured using the Apgar Scoring System), estimated from the end of the 6 week intervention till delivery time
7. Adverse obstetric outcome, estimated from the end of the 6 week intervention till delivery time:
7.1. Macrosomia - birth weight greater than 4500g
7.2. Intrauterine growth restriction, estimated using the Fetal Growth Charts - fetal weight below the 10th percentile for the gestational age
7.3. Preeclampsia - systolic blood pressure (SBP) greater than or equal to 140 mm Hg or a diastolic blood pressure (DBP) greater than or equal to 90 mm Hg or higher, on two occasions at least 4 hours apart in a previously normotensive patient AND proteinuria of greater than or equal to 0.3 grams in a 24-hour urine specimen, a protein (mg/dL)/creatinine (mg/dL) ratio of 0.3 or higher, or a urine dipstick protein of 1+
7.4. Placental abruption, estimated by clinical symptoms and ultrasound imaging
7.5. Fetal death
7.6. Neonatal jaundice requiring phototherapy
7.7. Hospitalization in a neonatal care unit
7.8. The hospitalization period (days)
7.9. Acute respiratory distress syndrome (ARDS)
7.10. Necrotizing enterocolitis (NEC)
7.11. Intraventricular hemorrhage (IVH) Grade III and IV
7.12. Neonatal death
7.13. Postnatal maternal complications: fever (temperature under the arm (axillary) at or over 37.2 °C), wound suppuration, embolism

Overall study start date
01/12/2017

Completion date
01/08/2023

Eligibility

Key inclusion criteria
Current inclusion criteria as of 21/11/2017:
1. Female
2. Age over 18 years
3. Singleton pregnancies
4. Absence of pre-existing impaired glucose tolerance

Previous inclusion criteria:
1. Female
2. Age over 18 years
3. Singleton pregnancies
4. Diagnosis of diet-treated gestational diabetes (24 - 28 weeks of gestation)

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
160 (80 per group)

Key exclusion criteria
Current exclusion criteria as of 21/11/2017:
1. Age under 18 years
2. Multiple pregnancy
3. Pre-existing diabetes mellitus
4. Consumption of steroids
5. Hypertensive disorders
6. Hypothyroidism
7. Pre-existing renal or hepatic impairment
8. Beta thalassaemia carriers
9. Vaginal bleeding (e.g. placental abruption)
10. Special diets (e.g. lactose intolerance)
11. Inadequate monitoring during pregnancy

Previous exclusion criteria:
1. Age under 18 years
2. Multiple pregnancy
3. Diagnosed diabetes mellitus before 24 - 28 weeks of gestation
4. Requirement of insulin therapy during the period of myo-inositol supplementation
5. Chronic hypertension
6. Preeclampsia, eclampsia
7. Hypothyroidism
8. Pre-existing renal or hepatic impairment
9. Other chronic diseases (e.g. valvular heart disease)
10. Vaginal bleeding (e.g. placental abruption)
11. Special diets (e.g. lactose intolerance)
12. Inadequate monitoring during pregnancy

Date of first enrolment
01/01/2018

Date of final enrolment
01/01/2022

Locations

Countries of recruitment
Greece

Study participating centre
Alexandra Hospital
First Department of Obstetrics and Gynecology
80, Vasilissis Sofias Avenue
Athens
Greece
11528

Sponsor information

Organisation
Alexandra Hospital

Sponsor details
First Department of Obstetrics and Gynecology
80, Vasilissis Sofias Avenue
Athens
Greece
11528

Sponsor type

Hospital/treatment centre

ROR
https://ror.org/029hept94

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal. Study results will also be used in a PhD study.

Intention to publish date
01/12/2023

Individual participant data (IPD) sharing plan
The data of the participants are considered as medical records and include sensitive confidential information. Thus, it is not expected to be available to third party organisations and people. The data will be held electronically in computers of the First Department of Obstetrics and Gynecology, Alexandra Hospital.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	09/07/2020	13/07/2020	Yes	No
Results article		14/08/2024	15/08/2024	Yes	No