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Metformin in mild gestational diabetes mellitus: a double-blind placebo-controlled randomised trial

Submission date
30/10/2017

Recruitment status
No longer recruiting

Registration date
07/11/2017

Overall study status
Completed

Last Edited
27/10/2022

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Gestational diabetes mellitus (GDM) is glucose intolerance (high blood sugar) first recognized in pregnancy. It occurs as the body is not able to produce enough insulin to control the blood sugar levels needed during pregnancy. The risk of adverse pregnancy outcomes increases in with increases h the mother's blood sugar level. This correlation is present even at maternal blood sugar levels within the normal range. GDM is usually managed by lifestyle control (mainly diet and exercise) and regular monitoring of blood sugar levels. Metformin is often the first line medical treatment if lifestyle change is insufficient. It is not known if preemptive use of metformin in combination with the standard lifestyle advisory compared to lifestyle advisory alone is better at lowering blood glucose in mild GDM cases. It could be possible that a combination will lower average blood glucose level and hence reduce the glycated haemoglobin (HbA1c) reading when assessed at 36 weeks of gestation in a placebo controlled trial. HbA1c reflects the average blood glucose in the preceding 2-3 months. The aim of this study is to examine if preemptive use of metformin by reducing maternal blood glucose level may reduce adverse maternal and baby outcome.

Who can participate?
Adults aged 18 to 45 years old who are diagnosed with gestational diabetes.

What does the study involve?
Participants provide blood sample for glycosylated haemoglobin (HbA1c) (a protein in the red blood cells that carries oxygen throughout the blood) when they join the study. They are then randomly allocated to one of two groups. Those in the first group take a 500 mg metformin pill. Those in the second group take an identical looking placebo or "dummy" pill) twice daily by mouth after breakfast and dinner. Participants are provided with a blood glucose monitor and test strips to monitor their BSP four times per day (before breakfast, two hours after lunch and dinner, before bed) at least weekly until delivery. If the BSP suggests that medical treatment is needed, open label metformin (up to 500 mg thrice daily) can be added. Insulin injection is added if control remains inadequate. Standard gestational diabetes care will be provided to all participants. Participant receive allocated study drug from recruitment, up until delivery.

What are the possible benefits and risks of participating?
Participants may benefit from better blood sugar control with metformin reducing adverse pregnancy outcomes like preterm birth, need for labour induction, big baby and maternal or baby injury. Common side effects of metformin are maternal gastrointestinal disturbances (diarrhoea, nausea and vomiting).

Where is the study run from?
University Malaya Medical Centre (Malaysia)

When is the study starting and how long is it expected to run for?
June 2017 to January 2019

Who is funding the study?
Obstetric and Gynaecology Department, University Malaya Medical Centre (Malaysia)

Who is the main contact?
1. Miss Min Ping Tew (Scientific)
2. Professor Peng Chiong Tan (Scientific)
3. Dr Rahmah Saaid (Scientific)

Contact information

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Additional identifiers

Protocol serial number
2017813-5489

Study information

Scientific Title
Metformin in Mild Gestational Diabetes Mellitus : a double-blind placebo-controlled randomised trial

Acronym
MIMGDM

Study objectives
Metformin compared to placebo in mild gestational diabetes reduces HbA1c by 0.2% by 36 weeks gestation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
University Malaya Medical Centre, 11/10/2017, ref: 2017813-5489

Study design
Randomised double-blind placebo-controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Mild gestational diabetes mellitus

Interventions
Participants who are diagnosed as gestational diabetes and fulfilled the inclusion and exclusion criteria will be recruited. Blood samples for HbA1c are obtained and analysed by centre's laboratory.

Participants are then randomised to either the metformin at a dose of 500 mg (1 tablet) twice daily or identical looking placebo tablet twice daily taken by mouth after breakfast and dinner. Trial interventions continue to delivery.

Randomisation sequence is generated using a random number generator by a co-investigator who is not involved in recruitment, numbered and with strict sequential allocation by recruitment order. Participants and investigators are blinded.

Both arms receive the same advice on diet and lifestyle modification. Participants are followed up in antenatal clinic at least biweekly and monitored with weekly 4 points blood sugar profile consisting of fasting pre breakfast and 2-hour post meals. Open label metformin to a maximum dose of 1500 mg daily in divided doses can be added if needed based on above target BSP readings with treatment threshold according to local practice. The open label metformin are from a different manufacturer and visually distinct from trial metformin/placebo tablets.

Standard institutional care for gestational diabetes applies to both arms. Blood is drawn at 36 weeks or as soon as possible thereafter to determine HbA1c level. Outcomes will be collected from participants' hospital and laboratory records.

Intervention Type
Drug

Phase
Not Specified

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

Primary outcome(s)
HbA1c is measured using blood samples at baseline and 36 weeks

Key secondary outcome(s))
1. Tolerability is measured using a symptom questionnaire at four weeks after recruitment and at 36 weeks gestation
2. Open label metformin use in pregnancy is measured by checking participants' hospital records after delivery
3. Insulin use in pregnancy is measured by checking participants' hospital records after delivery
4. Pregnancy induced hypertension is defined as blood pressure more than 140/90mmHg on 2 occasions with 4 hours apart after 20 weeks of gestation and established by checking participants' hospital records after delivery
5. Gestational age at delivery (preterm labour < 37 weeks)
6. Intervention to delivery interval is measured by checking participants' hospital records after delivery
7. Induction of labour is measured by checking participants' hospital records after delivery
8. Epidural analgesia in labour is measured by checking participants' hospital records after delivery

9. Mode of delivery
9.1. Indication for Caesarean delivery
10. Blood loss at delivery is measured as:
10.1. Postpartum haemorrhage ≥ 500 ml
10.2. Major postpartum haemorrhage ≥ 1000 ml
11. Third or fourth degree perineal tear as reported at birth
12. Reported shoulder dystocia
13. Birth weight is measured by checking participants' hospital records after delivery
14. Placenta weight is measured by checking participants' hospital records after delivery
15. Umbilical cord arterial pH at birth
16. Neonatal birth injury
17. Neonatal jaundice
18. Neonatal admission and indication

Completion date
31/01/2019

Eligibility

Key inclusion criteria
Current inclusion criteria as of 11/12/2017:
1. Aged 18 to 45 years
2. Singleton pregnancy
3. Gestational age at recruitment 16-30 weeks
4. Confirmed GDM: Fasting plasma glucose ≥ 5.1 mmol/L and/or the 2-hour ≥ 7.8 mmol/L by 75g OGTT
5. Normal 4-point blood sugar profile (BSP) in the preceding 2 weeks: fasting/pre-prandial ≤ 5.3, post prandial 1 hour of ≤ 7.8 or post prandial 2 hours of ≤ 6.7 mmol/L
6. Not on any hypoglycaemic drug treatment

Previous inclusion criteria:
1. Aged 18 to 45 years
2. Singleton pregnancy
3. Gestational age at recruitment 16-30 weeks
4. Confirmed GDM: Fasting plasma glucose ≥ 5.1 mmol/L and/or the 2-hour ≥ 7.8 mmol/L by 75g OGTT ≥ 16 weeks of pregnancy
5. Normal 4-point blood sugar profile (BSP) in the preceding 2 weeks: fasting/pre-prandial ≤ 5.3, post prandial 1 hour of ≤ 7.8 or post prandial 2 hours of ≤ 6.7 mmol/L
6. Not on any hypoglycaemic drug treatment

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Total final enrolment
106

Key exclusion criteria
1. Any contraindication to metformin
2. History of prepregnant hyperglycaemia
2.1. Type 2 diabetes,
2.2. Impaired glucose tolerance
2.3. Fasting glycaemia
3. Diagnostic 75g OGTT: fasting plasma glucose ≥ 7 or 2-hour glucose ≥ 11.1 mmol/L

Date of first enrolment
13/11/2017

Date of final enrolment
30/07/2018

Locations

Countries of recruitment
Malaysia

Study participating centre
University Malaya Medical Centre
Lembah Pantai
Kuala Lumpur
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59100

Sponsor information

Organisation
University Malaya Medical Centre

ROR
https://ror.org/00vkrxq08

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Obstetric and Gynaecology Department, University Malaya Medical Centre

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr. Tew Min Ping at loistew2@gmail.com.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/03/2022	27/10/2022	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes