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Prophylactic Metformin After Antenatal Corticosteroids

Submission date
13/01/2017

Recruitment status
No longer recruiting

Registration date
04/05/2017

Overall study status
Completed

Last Edited
14/10/2022

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
Steroids are a type of medication used to treat a wide range of conditions. They contain a man-made version of hormones that are normally produced in the body. In women who are at risk of giving birth too early (prematurely), steroids are often given to help the reduce any negative effects on the baby once he or she is born. A common side effect of taking steriods is an increase in the mother's blood sugar levels, which can last for up to five days. High blood sugar (hyperglycaemia) for prolonged periods can be dangerous for both mother and baby, can cause problems for pregnancy and baby. However, it is not established whether a short period (up to 5 days) of higher blood sugar level in mothers who receive steroids will lead to long-term effects. Metformin is a medication used to control blood sugar levels in people with diabetes and is the first line treatment for diabetes in pregnancy in Malaysia. Metformin should also be effective in lowering high blood sugar due to administration of steroids. The aim of this study is to find out whether giving metformin at the same time as steroid treatment can help to control blood sugar levels and possibly leads to better outcomes for mother and baby after birth.

Who can participate?
Pregnant women between 24-38 weeks who are about to receive or within 6 hours of first dose of antenatal corticosteroids.

What does the study involve?
Pregnant women who are about to receive or within 6 hours of first dose of antenatal steroids spaced 12 hours apart are randomly allocated to one of two study groups, ensuring there are an equal number of diabetic and non-diabetic women in each group.

What are the possible benefits and risks of participating?
All participants benefit from in-depth blood sugar monitoring, which would quickly identify if a woman's blood sugar is too high and she needs treatment. Participants who receive the metformin may benefit from having fewer episodes of high blood sugar levels. There is a risk that participants who receive the metformin may experience side effects from the medication such as nausea, stomach upset, vomiting and diarrhea. There is a small risk that that metformin may cause low blood sugar.

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?
September 2016 to January 2018

Who is funding the study?
University Malaya Medical Centre (Malaysia)

Who is the main contact?
1. Dr Jesrine Hong (scientific)
2. Professor Peng Chiong Tan (scientific)
3. Professor Siti Zawiah binti Omar (scientific)

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
MREC ID NO: 20161019-4384

Study information

Scientific Title
Prophylactic Metformin After Antenatal Corticosteroids (PROMAC): A Double Blind Randomised Controlled Trial

Acronym
PROMAC

Study objectives
The aim of this study is to show that metformin given prophylactically after administration of antenatal corticosteroids will ameliorate the hyperglycemic effect.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Medical Research Ethics Committee, University Malaya Medical Centre, 30/11/2016, ref: 20161019-4384

Study design
Double blind single-centre prospective randomised controlled trial

Primary study design
Interventional

Secondary study design

Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Pregnancy

Interventions
Eligible patients receiving or about to receive intramuscular dexamethasone 12 mg for 2 doses 12 hours apart as per our institution's antenatal corticosteroid protocol to improve neonatal outcome will be approached to participate. Participants will be stratified to Gestational Diabetes Mellitus (GDM) and non-GDM pregnancies for separate randomisation using sequential assignment of sealed numbered envelopes which contained the study drug (a pack of six 500 mg metformin tablets or identical placebo).

Participants will be observed to take the first dose of their allocated study drug (500 mg metformin or identical placebo tablet) with the remaining five tablets to be taken twice daily with their breakfast and dinner over the following 3 days. If the second dose (at the next breakfast or dinner) is within 6 hours of the first dose, it should be omitted, with the second dose to be taken at the subsequent breakfast or dinner. If delivery occurs within the 3-day study period, the study drug will be stopped.

Point of care capillary blood glucose is to be tested at recruitment and repeated 6 times per day (before and 2 hours after each breakfast, lunch and dinner for up to three consecutive days (18 readings). If delivery occurs within the 3-day study period, the blood glucose monitoring will be stopped. Patients will be provided with blood glucose monitoring system (to be returned), test strips, lancets and taught to self-monitor their blood glucose level and record it in a record sheet. Participants will be told to continue their usual diet during the study.

The participants will be instructed that if blood glucose level is more than 11 mmol/L during monitoring, they are to contact investigator immediately through the hand phone number provided (if already discharged from hospital). Open label 500 mg metformin tablets will be provided to all participants in a separate sealed pack labeled as "Rescue Metformin, Use Only as Instructed". In the event that glucose level is > 11 mmol/L whether pre or post prandial at any meal, 500 mg of open label metformin will be administered. Study drug shall continue at breakfast and dinner as planned e.g. if the pre breakfast capillary glucose is > 11 mmol/L, the participant will take a 500 mg metformin (open label) plus the scheduled study tablet. A maximum of three open label 500 mg metformin may be taken per day. If control is insufficient, despite three open label metformin doses (plus study drug regimen), subcutaneous insulin will be used as per usual institutional practice for uncontrolled hyperglycaemia in pregnancy following rehospitalisation if the patient is already discharged.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure
Hyperglycemia episodes in the 24 hours following administration of antenatal corticosteroids. Hyperglycemia is defined as pre meal blood glucose level of more than 5.3 mmol/L and 2 hours post prandial/meal blood glucose of more than 6.7 mmol/L and these are measured by point of care capillary blood glucose monitoring system at 6 points (pre and post breakfast, lunch and dinner).

Secondary outcome measures
1. Neonatal outcome, as assessed by reviewing patient's and baby's notes after delivery:
1.1 Birth weight
1.2 Umbilical cord arterial blood pH at birth
1.3 Apgar score at 1st and 5th minute of life/ birth
1.4 Special care nursery/ neonatal intensive care unit admission during birth admission
2. Maternal outcome, as assessed by reviewing patient's notes after delivery:
2.1 Mode of delivery
2.2 Estimated blood loss during delivery
3. Need for additional or unplanned hypoglycaemic agent (metformin or other) use. This is indicated by capillary blood glucose level more than 11 mmol/L during the monitoring
4. Hyperglycaemia episodes (hyperglycaemia as defined in primary outcome measure) up to 48 hours after administration of antenatal corticosteroids (if still undelivered)
5. Hyperglycaemia episodes (hyperglycaemia as defined in primary outcome measure) up to 72 hours after administration of antenatal corticosteroids (if still undelivered)
6. Hypoglycaemia episodes (hypoglycaemia is defined as capillary blood glucose level equal or less than 3.9 mmol/L)
7. Diarrhoea is recorded using a yes/no question during study period up to Day 3 or delivery
8. Vomiting is recorded using a yes/no question during study period up to Day 3 or delivery

Overall study start date
01/09/2016

Completion date
31/01/2018

Eligibility

Key inclusion criteria
1. All antenatal cases between 24-38 weeks who are about to receive or within 6 hours of first dose of antenatal corticosteroids for improvement of neonatal outcome in anticipation of premature delivery
2. Age more than 18 years old
3. Singleton pregnancy

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
60

Total final enrolment
103

Key exclusion criteria
1. Patients on hypoglycaemic agent
2. Pre-existing Type 1 or Type 2 diabetes mellitus
3. Baseline capillary blood glucose more than 11mmol/L (at recruitment)
4. Patients in active labour or may deliver within the next 24 hours after administration of antenatal corticosteroids
5. Evidence of chorioamnionitis or other maternal or fetal infection
6. Twin/ multiple pregnancies
7. Patients on terbutaline or other beta-mimetic agents
8. Diet restrictions in anticipation of Caesarean birth

Date of first enrolment
25/05/2017

Date of final enrolment
14/11/2017

Locations

Countries of recruitment
Malaysia

Study participating centre
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Sponsor information

Organisation
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Sponsor type
University/education

ROR
https://ror.org/00vkrxq08

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
University Malaya Medical Centre

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal.

Intention to publish date
01/02/2020

Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version V1.0	21/10/2016	14/06/2017	No	Yes
Results article		15/02/2021	16/08/2022	Yes	No
Protocol file			14/10/2022	No	No