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Sildenafil citrate effect on in vivo human trophoblast research

Submission date	Recruitment status	[X] Prospectively registered
02/07/2017	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
13/07/2017	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
12/07/2017	Pregnancy and Childbirth	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
The placenta is an organ attached to the lining of the womb during pregnancy. It keeps the unborn baby's (fetus) blood supply separate from the mother’s blood supply, and provides a link between the two. Problems can occur during the development of the placenta that can cause the blood flow to the fetus to be too low (placental insufficiency). Sildenafil citrate is a drug which could be used to improve the development of the placenta. Early results show an improvement in blood flow and fetus weight but a failure to delay premature birth. The aim of this study is to assess sildenafil citrate's effect early in pregnancy in order to find the best time to give the drug to prevent placental insufficiency.

Who can participate?
Healthy pregnant women between 20-40 years old during the first trimester of pregnancy who are coming to hospital for a legal medical abortion

What does the study involve?
The participants undergo an ultrasound exam to assess the blood flow in the placenta, and are then randomly allocated to take either sildenafil citrate or a placebo (dummy drug). The participants stay in the waiting room for one hour before a second ultrasound scan is performed. Blood pressure and heart rate are measured every 15 minutes and any side effects are recorded. Participants are also contacted by telephone to record any side effects 12 hours later and 7 days after legal abortion has been carried out. Placental tissue samples are also taken.

What are the possible benefits and risks of participating?
Participants are informed that there are unlikely to be any direct benefits from participating, but the information obtained from this study may help to improve treatment for future patients. The studies of sildenafil in animals, non-pregnant adults, pregnant women and unborn babies have not shown harmful effects. It is not possible to say that sildenafil is 100% safe, but based on what is known it is unlikely that the use of sildenafil in pregnancy harms the patient or the baby. Sildenafil has been used in pregnant women and premature babies previously and no side effects have been reported in babies. However, people taking sildenafil can have some short-lasting side effects like headache, flushing, blurred vision and indigestion.

Where is the study run from?
Consorcio Hospital General Universitario (Spain)

When is the study starting and how long is it expected to run for?
September 2017 to June 2018

Who is funding the study?
La Fundación Investigación Hospital General Universitario de Valencia (Spain)

Who is the main contact?
Prof. Maria Begoña Pellicer

Contact information

Type(s)
Scientific

Contact name
Prof Maria Begoña Pellicer

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46014

Additional identifiers

EudraCT/CTIS number
2017-001878-42

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
11

Study information

Scientific Title
Sildenafil citrate placental effect evaluated by ultrasound: a randomised controlled trial

Acronym
SC pregnancy

Study objectives
Single dose of sildenafil citrate in pregnant women during 1st trimester improves vascular flow in placental territory.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee of Consorcio Hospital General Universitari de Valencia (Spain) - approval pending

Study design
Randomized double-blind placebo-controlled longitudinal study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

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

Health condition(s) or problem(s) studied
Placental vascular flow

Interventions
Once the patients have been properly advised about the study and the consent form has been signed as a part of their agreement, patients are sent to the hospital to undergo an initial ultrasound exam by the obstetrics doctor in charge or the fellow in training. Transvaginal ultrasound scan will be performed using a Voluson E6 (GE Medical Systems, Zipf, Austria) and a four-dimensional 6–9 MHz transvaginal probe. It is optional to the patient to see the fetus during the scan if they want to. Randomization will be performed using sealed envelopes by a clinician who does not belong to the research group. Patients are randomly assigned to two groups:
Group A (n=30) receive 5mg folate acid as a placebo
Group B (n=30) receive 50 mg sildenafil citrate

Patients will stay in the waiting room for one hour before a second ultrasound scan is performed. The trialsts calculate the three 3D power Doppler ultrasound vascular indices, the vascularization index (VI), flow index (FI) and vascularization flow index (VFI), the calculation is based on and related to the total and relative amounts of power Doppler information within the volume of interest. VI denotes the ratio of color-coded voxels to all voxels within the volume and is expressed as a percentage, FI represents the mean power Doppler signal intensity from all

color-coded voxels and VFI is the simple mathematical relationship derived from multiplying VI by FI and dividing the result by 100. Both FI and VFI are unit less and are expressed as a numerical value ranging from 0 to 100. The indices are thought to reflect the number of vessels within the volume of interest (VI), the intensity of flow at the time of the 3D sweep (FI), and both blood flow and vascularization.

Blood pressure and maternal heart rate is measured every 15 minutes and side effects are recorded. Patients are also contacted by telephone to record side effects 12 hours later and 7 days after legal abortion has been carried out. After abortion has been practised in the referred centre placental tissue samples (n= 10) from each studied group containing trophoblast tissue will be obtained and processed in order to examine angiogenic factors and histologic structure.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Sildenafil citrate

Primary outcome measure
Placental vascular flow, measured by standard vascular indexes acquired with three dimensional angiopower doppler output when the patient is admitted and one hour later (following drug or placebo administration)

Secondary outcome measures
1. Uterine artery hemodynamic flow effect, measured using an automated semiquantitative analysis of Doppler spectra before and 1 hour after Sildenafil oral administration
2. Maternal blood pressure, measured using an automated oscillometric blood pressure measurement device before and during one hour (every 15 minutes) after Sildenafil oral administration
3. Maternal heart frequency, calculated automatically using waveform spectra before and 1 hour after Sildenafil oral administration

Overall study start date
01/09/2017

Completion date
30/06/2018

Eligibility

Key inclusion criteria
1. Healthy women between 20-40 years old
2. Confirmed pregnant viability without any obstetric complication
3. First trimester gestational age
4. Coming to hospital for legal medical abortion

Participant type(s)

Healthy volunteer

Age group
Adult

Sex
Female

Target number of participants
Control group (n=30), treated group (n=30)

Key exclusion criteria
1. Obstetric risk factors: recurrent miscarriage, previous preeclamsia and hematology disease
2. Current use of vasoactive drugs (mainly related to hypertension treatment)
3. Toxic substances abuse
4. Threatened abortion symptoms
5. Sildenafil citrate contraindications, as are described in the prescribing information formulary (excluding pregnancy)

Date of first enrolment
01/09/2017

Date of final enrolment
01/09/2018

Locations

Countries of recruitment
Spain

Study participating centre
Consorcio Hospital General Universitario de Valencia
Avenida Tres Cruces, 2
Valencia
Spain
46014

Sponsor information

Organisation
Servicio Ginecologia y Obstetricia Hospital General de Valencia

Sponsor details
Avenida Tres Cruces, 2
Valencia

Spain
46014

Sponsor type
Hospital/treatment centre

Website
http://chguv.san.gva.es

ROR
https://ror.org/03sz8rb35

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Fundation Investigation Hospital General Universitari Valencia CIF G-96.792.221

Results and Publications

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

Intention to publish date
30/06/2019

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 Ander Morales Vicente.

IPD sharing plan summary
Available on request