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Metformin improves arterial stiffness in polycystic ovary syndrome (PCOS)

Submission date	Recruitment status
08/04/2009	No longer recruiting
Registration date	**Overall study status**
25/06/2009	Completed
Last Edited	**Condition category**
05/08/2019	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
Study Protocol Version 5

Study information

Scientific Title
Metformin improves arterial stiffness and endothelial function in young women with polycystic ovary syndrome: a randomised crossover trial

Study objectives
To determine whether metformin therapy improves endothelial function and arterial compliance in young women with polycystic ovary syndrome (PCOS).

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Wales Research Ethics Committee approved in May 2006 (ref: 06/WSE04/33)

Study design
Randomised double-blind placebo-controlled crossover trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Polycystic ovary syndrome

Interventions
The two treatment arms are metformin and placebo. During the study phase, patients received consecutive daily doses of metformin for 12 weeks (84 days) followed by placebo or placebo followed by metformin, separated by an 8-week wash-out period. Metformin has a short circulatory half-life and 8-week washout intervals have been employed on this basis in previous studies. Metformin is used widely in treating anovulation associated with PCOS in doses of up to 2 g daily. The majority of patients tolerate treatment well though gastrointestinal side-effects are common initially and the doses of metformin were built up gradually in an attempt to minimise these (500 mg once daily for the first week, 500 mg twice daily for the second week then 500 mg three times daily thereafter).

The total duration of treatment was 32 weeks and the total duration of follow-up was also 32 weeks for both arms of this trial.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
Changes in measures of arterial stiffness (pulse wave velocity and augmentation index as measured by pulse wave analysis post-salbutamol versus post-GTN) from baseline, recorded at enrolment and then repeated at 12 weeks, 20 weeks and 32 weeks.

Key secondary outcome(s))
1. Changes in testosterone, plasminogen activator inhibitor-1 (PAI-1), endothelin-1 (ET-1) and high sensitivity C-reactive protein (hsCRP)
2. Measures of insulin resistance
3. Lipid profile

Recorded at enrolment and then repeated at 12 weeks, 20 weeks and 32 weeks.

Completion date
01/05/2008

Eligibility

Key inclusion criteria
1. From the Endocrinology clinics at the University Hospital of Wales
2. Diagnosed with PCOS, based on androgen excess (clinical symptoms of hyperandrogenism and /or elevated testosterone) with ovulatory dysfunction (fewer than six menstrual cycles per year), supported by ovarian ultrasound where available
3. Congenital adrenal hyperplasia, Cushings syndrome, androgen-secreting neoplasms, hyperprolactinaemia and thyroid disease excluded by biochemical testing
4. Aged between 18 and 35 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
1. Pregnant
2. Breastfeeding
3. History of current or previous use (within 6 months) of oral contraceptives, anti-diabetics or anti-androgens
4. Contraindications to metformin therapy including renal or hepatic impairment, ketoacidosis, or conditions where tissue hypoxia is likely (e.g. sepsis, respiratory failure, recent myocardial infarction)
5. History of hypertension or diabetes
6. Able to use barrier methods of contraception if sexually active. In addition, pregnancy tests were performed at each study visit and patients were withdrawn from the study in the event of confirmed pregnancy.

Date of first enrolment
01/01/2007

Date of final enrolment
30/04/2008

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Department of Endocrinology
Cardiff
United Kingdom
CF144XW

Sponsor information

Organisation
Cardiff University (UK)

ROR
https://ror.org/03kk7td41

Funder(s)

Funder type
University/education

Funder Name
Royal College of Physicians (UK) - Lewis Thomas Gibbon Jenkins Fellowship

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/02/2010		Yes	No