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PANTHEON-I: The peripheral effects of prednisolone on glucose metabolism, metabolic hormones, insulin sensitivity and insulin secretion in healthy young males and males with metabolic syndrome: a randomised, placebo controlled, double blind, dose-response, parallel group intervention study

Submission date
26/04/2007

Recruitment status
No longer recruiting

Registration date
03/07/2007

Overall study status
Completed

Last Edited
14/08/2013

Condition category
Nutritional, Metabolic, Endocrine

[X] 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
DCpred001

Study information

Scientific Title

Acronym
PANTHEON-I

Study objectives
Glucocorticoids (GCs), like prednisolone, are the most commonly prescribed anti-inflammatory and immunosuppressive drugs. Although GCs display excellent efficacy in a great number of (auto-immune) diseases, the side effect profile often limits their therapeutical benefit. Major side effects associated with GC treatment include changes in glucose, lipid and protein metabolism, leading to adult onset (a.o.) insulin resistance, glucose intolerance, muscle wasting and dyslipidemia. Currently a renewed interest exists in these poorly understood diabetogenic side effects, with the development of so called 'dissociated glucocorticoid receptor activators', which seem to be lacking these deleterious effects. With this trial, we expect to obtain results that will aid the development of such compounds by a pharmaceutical company that is involved in this study project. This novel class of drugs could become of great importance for the millions of people currently requiring glucocorticoid therapy.

Hypotheses:
What are the effects of a two-week treatment with 7.5 mg prednisolone daily or 30 mg prednisolone daily, versus placebo, on:
1. Various aspects of beta-cell function?
2. Whole-body insulin sensitivity?

This trial is linked to the PANTHEON II study, registered under ISRCTN83991850. Although these trials have the same interventions, the outcomes being looked at are different.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the Ethics Committee of the VU University Medical Centre on the 11th October 2007 (ref: 2007/179).

Study design
PANTHEON-I study is a randomised, placebo controlled, double blind, dose-response, parallel group intervention study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Metabolic syndrome

Interventions
The effects of a two-week treatment with either prednisolone 7.5 mg daily or prednisolone 30 mg daily versus placebo, will be evaluated.

Intervention Type
Drug

Phase
Not Specified

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

Primary outcome(s)
To assess the effects of a two-week treatment with 7.5 or 30 mg prednisolone daily, compared to placebo, in healthy males and males with the metabolic syndrome on:
1. Beta cell function (first phase insulin secretion, corrected for insulin sensitivity, during hyperglycaemic clamp procedure, measured at Day 14
2. Whole-body insulin sensitivity (insulin sensitivity index as measured during hyperinsulinaemic-euglycaemic clamp procedure), measured at Day 14

Key secondary outcome(s))
To assess the effects of a two-week treatment with 7.5 or 30 mg prednisolone daily, compared to placebo, in healthy males and males with the metabolic syndrome on:
1. Circulating biomarkers (plasma), measured at Day 13
2. Insulin-stimulated microvascular function, measured at Day 14
3. Blood pressure and haemodynamic parameters, measured at Day 13
4. Body fat distribution (Magnetic Resonance Imaging [MRI]), measured at Day 13
5. Molecular mechanisms underlying prednisolone effects, measured at Day 14

Completion date
01/09/2010

Eligibility

Key inclusion criteria
For all participants:
1. Written informed consent
2. Male caucasian
3. Smoking less than five cigarettes per day and capable of stopping during the trial period

For healthy participants:
1. Healthy as determined by history taking, physical examination, laboratory examinations and Electrocardiogram (ECG):
1.1. Aged 20 to 55 years
1.2. Body Mass Index (BMI) between 20 and 25 kg/m^2
1.3. Fasting glucose less than 5.6 mmol/L and glucose less than 7.8 mmol/L at two hours after intake of 75 g glucose (Oral Glucose Tolerance Test [OGTT])

For participants with metabolic syndrome:
1. Aged 20 to 55 years
2. Waist circumference more than 94 cm
3. Three of following criteria:
3.1. Triglycerides more than 1.7 mmol/L
3.2. High Density Lipoprotein (HDL) cholesterol less than 1.03 mmol/L
3.3. Blood pressure more than 130/85 mmHg
3.4. Fasting glucose level less than 6.1 mmol/L and glucose less than 11.0 mmol/L at two hours after intake of 75 g glucose (OGTT)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Male

Key exclusion criteria
For all participants:
1. Idiosyncrasy/sensitivity to Glucocorticoids (GC)
2. GC use during the last three months prior to first study dose
3. Participation in an investigational drug trial within 90 days prior to the first dose
4. Donation of blood (more than 100 mL) within 90 days prior to the first dose
5. History of or current abuse of drugs or alcohol
6. Serious mental impairment or language problems, i.e., preventing to understand the study protocol/aim

For healthy participants:
1. Presence of a medical disorder
2. Medication use, except for incidental analgesic agents
3. First degree relative with type two diabetes mellitus
4. Performing intensive physical activity more than twice a week

For participants with metabolic syndrome:
1. Serious pulmonary, cardiovascular, hepatic (Alanine Aminotransferase [ALT], Aspartate Aminotransferase [AST] more than 3 x Upper Limit of Normal [ULN]) or renal disease (serum creatinine more than 135 mmol/L)
2. History of cardiovascular disease, such as myocardial infarction, cerebrovascular accident
3. Major psychiatric disorder
4. Depression
5. All diseases that induce changes in the Hypothalamic-Pituitary-Adrenal (HPA) axis
6. Malignant disease
7. All other relevant medical disorders that potentially interfere with this trial*
8. All medication interfering with study drug or interfering with study endpoints/hypotheses*

* the study physician and internist will make an individual assessment per subject whether he is eligible for inclusion

Date of first enrolment
01/09/2007

Date of final enrolment
01/09/2010

Locations

Countries of recruitment
Netherlands

Study participating centre
De Boelelaan 1117
Amsterdam
Netherlands
1081 HV

Sponsor information

Organisation
Vrije University Medical Centre (VUMC) (The Netherlands)

ROR
https://ror.org/00q6h8f30

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Top Institute Pharma (TIP) (The Netherlands) - a collaborative structure consisting of industrial and academic research teams (www.tipharma.com)

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	islet-cell function results	01/04/2013		Yes	No
Results article	microvascular function results	01/11/2013		Yes	No