Bioequivalence study of prednisolone and dexamethasone – The CORE study

No registrations found.

Ethical review	Not applicable
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24470

Source
NTR

Brief title
CORE study

Health condition

N.A.

Sponsors and support

Primary sponsor: N.A.
Source(s) of monetary or material Support: This study is investigator initiated and financed

Intervention

Outcome measures

Primary outcome

The main study endpoint is the difference in total cortisol excretion as measured in 24h-urine at between the lower doses of prednisolone and dexamethasone as well as between and the higher doses of prednisolone and dexamethasone doses.

Secondary outcome

- The effect of a dosage increase from low dose to high dose prednisolone and from low dose to high dose dexamethasone on total cortisol excretion in 24h-urine.
- Suppression of the HPA-axis measured by plasma cortisol, adrenocorticotropic hormone, and metabolites in the steroid profile in 24h-urine (e.g. free and total cortisol, tetrahydrocortisol, tetrahydrocortisone, and allo-tetrahydrocortisol).
- Suppression of the HPG-axis measured by testosterone, LH, FSH, SHBG, dihydrotestosterone, and steroid profile in 24h-urine (e.g. androsterone, etiocholanolone, and dehydroepiandrosterone).
- The pharmacokinetics and pharmacodynamics of prednisolone and dexamethasone.
- Suppression of the immune system measured by leucocyte count, granulocyte count (neutrophils, eosinophil's, and basophils), monocyte count, absolute B cell (CD19+) count, absolute T cell (CD3+, CD4+ and CD8+) count, absolute natural killer cell (CD16+ en CD56+) count, and RNA.
- Renin–angiotensin–aldosterone system measured by plasma renin, aldosterone, potassium, 24h-urine potassium, and trans-tubular potassium gradient.
- Muscle mass measured by 24h urinary creatinine excretion rate and creatine kinase.
- Metabolic parameters measured by fasting glucose, fasting insulin, HbA1c, cholesterol, triglycerides, glycerol, and non-esterified fatty acids.
- Bone parameters as measured by calcium and osteocalcin.
- Clinical parameters: body weight, height, waist circumference, hip circumference, and blood pressure

Study description

Background summary

Rationale: Corticosteroids are among the most important contributions to the medical field from the last century. Over the years, multiple new synthetic corticosteroids have been development and numerous studies have been performed, uncovering the important and beneficial anti-inflammatory and immunosuppressive characteristics of corticosteroids. Nowadays, corticosteroids are widely used in clinical practice, as their immunosuppressive characteristics are essential in treatment regimens for many chronic diseases, such as auto-immune diseases, lymphatic malignancies, and pulmonary diseases.
Unfortunately, to date, the efficacy data of corticosteroids are based on bioequivalency studies performed in the sixties and seventies of the last century, when randomized controlled trials (RCT) were rarely performed and not yet considered to be the golden standard. Prednisolone and dexamethasone are the two most widely used glucocorticoids. Their bioequivalence are estimated to be 1: 0.15, this is however, based on dated studies. Additionally, clinicians assume that all organ specific effects are similar between the different types of corticosteroids. However, according to recent insight, it could very well be that glucocorticoid sensitivity differs between variable tissues like the immune system, kidney,

and brain. This is of importance as many clinicians, prescribe glucocorticoids in a standardized manner assuming that one size fits all. Yet, as there is a lack of modern era studies with a good quality, this is assumption may not be a justified approach.
Objective: The purpose of this study is to compare two different glucocorticoids, prednisolone and dexamethasone at two different doses for their organ specific effects, utilizing modern day standards.
Study design: A randomized, double blind, cross-over clinical trial.
Study population: healthy human adult volunteers including 12 males and 12 females aged 18-75 years old.
Intervention: In random order, subjects will receive 7.5 mg prednisolone for one week, directly followed by 30 mg of prednisolone for one week. After a washout period of 4 weeks (or by exception 8 weeks), subjects will receive 1.125 mg dexamethasone for one week, directly followed by 4.5 mg dexamethasone for one week.
Main study parameters/endpoints: The main study endpoint is the difference in total cortisol excretion as measured in 24h-urine at between the lower doses of prednisolone and dexamethasone as well as between and the higher doses of prednisolone and dexamethasone doses.

Study objective

Due to the difference in mineralocorticoid characteristics between prednisolone and dexamethasone, it is hypothesized that dexamethasone will have a greater effect then prednisolone, especially when assessing neurocognitive function and blood pressure.

Study design

Duration of participation is 2 months.
Subjects will visit the UMC Groningen six times. Once for a screening visit, when included once for a baseline measurement, and four times for a study visit.

Intervention

In random order, subjects will receive 7.5 mg prednisolone for one week, directly followed by 30 mg of prednisolone for one week. After a washout period of 4 weeks (or by exception 8 weeks), subjects will receive 1.125 mg dexamethasone for one week, directly followed by 4.5 mg dexamethasone for one week.

Contacts

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Eligibility criteria

Inclusion criteria

1. Participants must be healthy with no relevant medical history (e.g. astma, solid organ transplantation, secondary adrenal insufficiency) and no use of medication.
2. Female participants aged <50 years must be using oral contraceptives and female participants age ≥50 years must be in the postmenopausal state
3. Command of the Dutch language
4. Providing written IC
5. BMI between 18.5 and 30 kg/m2
6. Participants must be between 18 and 75 years of age

Exclusion criteria

1. Potential participants who are unlikely to adhere to the study protocol (for instance subjects which have a history of substance abuse or non-compliance)
2. Potential participants with a medical history of:
a. Diseases affecting the HPA-axis: e.g. primary and secondary adrenal insufficiency, pituitary tumors, and nightshift workers
b. Diseases affecting the HPG-axis: e.g. Cushing disease.
c. Chronic inflammatory diseases: e.g. rheumatoid arthritis, polymyalgia rheumatic, and asthma
d. Psychiatric diseases
e. Diabetes
3. Shift workers.
4. Potential participants with a kidney function <60 ml/min/1.73m2, abnormalities in liver enzymes, and/or abnormalities in thyroid function
5. Potential participants who are dependent on corticosteroids, e.g. asthmatic patients, and transplant recipients

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-03-2021
Enrollment:	24
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Not applicable

Application type:	Not applicable

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL9138
Other	METc Groningen : 2020.398

Study results