Novel treatment of adrenal crisis: an early clinical trial with nebulized prednisolone

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Ethical review	Approved WMO
Status	Completed
Health condition type	Adrenal gland disorders
Study type	Interventional

Summary

ID

NL-OMON51709

Source
ToetsingOnline

Brief title
The treatment of adrenal crisis with inhaled prednisolone

Condition

- Adrenal gland disorders

Synonym
Adrenal insufficiency

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Adrenal crisis, Prednisolone, Treatment

Outcome measures

Primary outcome

Pharmacokinetic parameters: Tmax and AUC

Secondary outcome

Other pharmacokinetic parameters

Renal clearace of prednisolone

Study description

Background summary

Patients with adrenal insufficiency rely on glucocorticoid substitution therapy (hydrocortisone or cortisone acetate). In case of an acute stressful situation, e.g. illness, trauma or psychological stress, the standard substitution dose fall short and patients need to increase their glucocorticoid dose to prevent a cortisol deficiency which could ultimately lead to an adrenal crisis. The incidence of an adrenal crisis is about 5-10 per year 100 patient years and is characterized by hypotension, nausea, hyponatremia, hyperkalemia, hypoglycemia, and a circulatory shock with the risk of a fatal outcome. Acute administration of glucocorticoids in case of an adrenal crisis is of vital importance.
Currently, patients have to inject themselves with an intramuscular injection of 100 mg hydrocortisone. Hydrocortisone is an unstable product in solution, it is therefore given to the patient as a powder and the patient must prepare the medication (with the so-called *Act-O-Vial*), and then self-administer the hydrocortisone solution by an intramuscular injection. If the injection is insufficient, sometimes a second injection is necessary.
Patients with an adrenal crisis in an early stage can already experience confusion, drowsiness, dizziness and nausea. Furthermore, many patients fear needles, because the procedure of preparing the emergency medication is not routine for them. It is therefore logical that this method of drug administration is often not sufficiently used and easily leads to errors. The patients always have to carry the Solu-Cortef® Carry Act-O-vial, syringe and needle with them. This is often believed to be impractical and many patients do not carry their emergency medication with them. In addition, we recently published data about adrenal crisis in our own UMCG population, and concluded

that less than half of the patients who experienced an adrenal crisis used their emergency medication.
A small inhaler containing prednisolone could possibly replace the hydrocortisone injection. It is known that for several drugs that the time from administration to its effect is similar after inhalation and after injection. Examples are adrenaline, levodopa, morphine and insulin. Based upon of the physicochemical properties, prednisolone is expected to be as rapidly distributed in the bloodstream after inhalation compared to an intramuscular injection. In addition, previous application of inhaled prednisolone for patients with asthma and COPD has proven that the inhalation of prednisolone is safe. The patient*s resistance against inhalation is much smaller than against the injection.
The above advantages make the prednisolone inhaler a much safer and more patient-friendly product than the injection currently being used.

As the first step in the development of this prednisone inhaler we will investigate if therapeutic plasma concentrations of prednisolone can be reached by nebulizing prednisolone. In this study, we administer nebulized prednisolone in two different dosages to healthy volunteers.
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Study objective

The aim of this study is to establish pharmacokinetic data on inhaled nebulized prednisolone: Time from start nebulizing to serum peak prednisolone concentration (Tmax) and prednisolone area under. We derive this pharmacokinetic data from two different dosages of nebulized prednisolone: a lower and a higher dose

Study design

Single center, open label

Intervention

Every subject receives a lower dose of nebulized prednisolone. After a wash out of one week, every subject receives a higher dose of nebulized prednisolone.

Study burden and risks

The chance of serious or long term side-effects is very limited. There is a small risk of an AE during blood-sampling (formation of hematoma, infection and bruising). If the prednisolone inhaler is a reliable alternative for a hydrocortisone injection, the patients with adrenal insufficiency will greatly benefit.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

• Age: 18 - 75 years
• Woman who use reliable contraceptives or with a negative pregnancy test
• Equal sex distribution

Exclusion criteria

• Heart failure
• Known liver or kidney disease
• Dependency on glucocorticoids
• Adrenogenital syndrome
• Infectious disease
• Uncontrolled hypertension defined as a blood pressure > 180/110 mmHg

• Pregnancy or breastfeeding
• Use of medication that interferes with cytochrome P450 (e.g. carbamazepine)

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	06-10-2022
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	PREDNISOLONE NATRIUMSUCCINAAT
Generic name:	Di-Adreson-F aquosum
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	06-10-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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
EudraCT	EUCTR2022-002355-19-NL
CCMO	NL81816.056.22