To test the use of a Microdialysate Automated Collection Device for cortisol sampling and to assure reproducibility in the LUMC of data reported by others

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- To assure reproducibility of results reported by other groups to see whether the current SOP should be adjusted for local use in order to let the device be of value to future research projects of our department. - To confirm the ability to measure...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON47911

Source
ToetsingOnline

Brief title
To test the use of a Microdialysate Automated Collection Device

Condition

- Other condition
- Adrenal gland disorders

Synonym
adrenal insufficiency, healthy people, physiological situation

Health condition

onderzoek heeft in eerste instantie betrekking op normale fysiologische situatie, in tweede instantie patienten met bijnierinsufficientie

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Cortisol, Microdialysis

Outcome measures

Primary outcome

- Peripheral tissue cortisol profiles/day rhythms

- Reproducibility results reported by other groups

Secondary outcome

not applicable

Study description

Background summary

Accurate determination of cortisol and its circadian rhythm is essential not only in the diagnostic evaluation of the HPA axis, but also in the evaluation of patients with adrenal insufficiency. Measuring circulating free cortisol has been recognized to be the most optimal diagnostic tool. However, the currently available biochemical screening tests all have their limitations. In addition, stress-free sampling is cumbersome, because for example a venepuncture causes a reactive stress response thereby affecting ACTH and (for later measurements) cortisol levels. To accurately measure the changes in hormone concentrations frequent measurements over extended periods are necessary. For this purpose, a computerized, automated sampling system, which allows repeated stress-free sample collection for the measurement of hormones in tissue using a small subcutaneous microdialysis probe was developed. In Leiden, we have been able to successfully test this sampling system in 2015 in 3 healthy subjects without any complications or problems during the procedure. However, the cortisol values measured in the dialysate in Leiden (at mid-day) were lower than the values measured by our colleagues in Bristol, despite the use of the same

materials and analysis in the same laboratory. These differences in measured values are not well understood. We believe it is important to prove the ability to measure subcutaneous cortisol profiles with this device before the start of a larger research protocol using this measurement technique, which is true for the comparability to other centres and for intra individual (pulsatile) profiles. There is a particular interest to know whether we can detect a circadian profile and whether physiological morning levels are indeed higher than the previously measured mid-day values. When physiological profiles turn out to be not measurable, it would be interesting to see whether supraphysiological cortisol levels (e.g. after hydrocortisone intake in adrenal insufficient patients) are to be detectable.

Study objective

- To assure reproducibility of results reported by other groups to see whether the current SOP should be adjusted for local use in order to let the device be of value to future research projects of our department.
- To confirm the ability to measure a pulsatile profile in participants (and patients with adrenal insufficiency with temporary supraphysiological levels intake of their usual medication if necessary).
- To finalize a new research proposal and protocol using the results of this pilot study.

Study design

Step 1:
We will connect the device to a maximum of ten healthy subjects and take microdialysis samples within 24 hours before disconnecting the device again. This will enable us to measure the physiological morning cortisol peak.

Step 2 (only performed when step 1 produces insufficient data):
We will connect the device to a maximum of ten patients with adrenal insufficiency on hydrocortisone replacement therapy and take microdialysis samples within 24 hours before disconnecting the device again. Because these subjects are on hydrocortisone therapy, supraphysiological cortisol levels after medication intake should be visible in their tissue cortisol profiles in case of reliable measurements with the Microdialysate Automated Collection Device. We will not discontinue or change prescribed medication.

Study burden and risks

The device is currently used for research purposes by different international groups. We work closely together with colleagues from Bristol, whom have developed this system and have a lot of experience using it. Complications during or after use of this device have never been reported. No problems have

occurred during our former measurements using this technique.

Placement of a subcutaneous catheter and the sequential draws of extracellular fluid is a safe procedure, with a low chance of malfunctioning of the catheter requiring placement of a new one. During positioning of the catheter, the skin will be locally anesthetized, so no pain will be experienced by the subject. Also after placement during sampling and while removing the catheter, the subject will not experience any pain. Theoretically, an infection of the insertion side could occur, despite sterile placement . This has not been reported in earlier studies with the device, nor has been the case in any of our former participants. In case this does happen, the probe will be removed and (local or oral) antibiotics will be prescribed if necessary. There is a minimal risk of development of subcutaneous oedema or hematoma on the insertion site.

The anesthetization can be somewhat sore/painful, however this is limited. Showering with the catheter in situ is not possible and sleeping while the pump makes a buzzing sound can be experienced as uncomfortable.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

First: Healthy adult males or females, aged between 20-60 years
Only if insufficient data, also adults with adrenal insufficiency, males or females, aged between 20-60 years

Exclusion criteria

Pregnancy, Allergy to local anaesthetic, hydrocortisone replacement therapy or any known abnormalities to the HPA axis (the latter only in case of healthy persons, first step of the protocol).

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-08-2018
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO Date:	26-10-2017
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	22-10-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

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
CCMO	NL61741.058.17