Henry Wellcome Laboratories for Integrative Neuroscience & Endocrinology
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Whitson Street
Bristol BS1 3NY, U.K.

Monitoring of congenital adrenal hyperplasia (CAH) by ULTRADIAN dynamic hormone measurements

Dynamic hormone diagnostics (ULTRADIAN)

Why have I been contacted?

You have been given this information sheet because you have a diagnosis of congenital adrenal hyperplasia (CAH). You may been told about this study by your hospital specialist, or you might you have responded to an advertisement or poster.

You are being invited to take part in a research study

Before you decide, it is important for you to understand why the research is being done and what it will involve.

Please take time to read the following information carefully and discuss it with friends, relatives or your GP if you wish.

Please ask us if there is anything that is not clear or if you would like more information.

Take time to decide whether or not you wish to take part and remember that your participation is voluntary. Participating will not affect the treatment of your condition.

What is the purpose of this research study?

CAH is a hereditary disorder of cortisol production and other hormones released from the adrenal gland. On one hand CAH leads to insufficient cortisol levels, which requires replacement, but on the other hand, overproduction of other hormones which need to be suppressed. Ideally, cortisol replacement treatment should copy the normal daily profile of cortisol as closely as possible. However, the cortisol dose also needs to be high enough to reduce levels of the overproduced hormones.

At the moment it is hard to monitor treatment accurately as we rely on isolated blood tests and other unreliable measures. This means medication may often be under or overdosed, leading to health problems and reduced quality of life. Frequent monitoring of hormones levels over a 24 hour period could give a much more accurate picture and enable individual dose adjustment but doing this using blood tests is not usually practical and is very invasive.

Our researchers have been developing a new method where samples are taken continuously from just below the skin rather than from samples of blood. This technique, called microdialysis, is much simpler and easier than multiple blood tests and should give a much more accurate reflection of hormone levels in CAH.

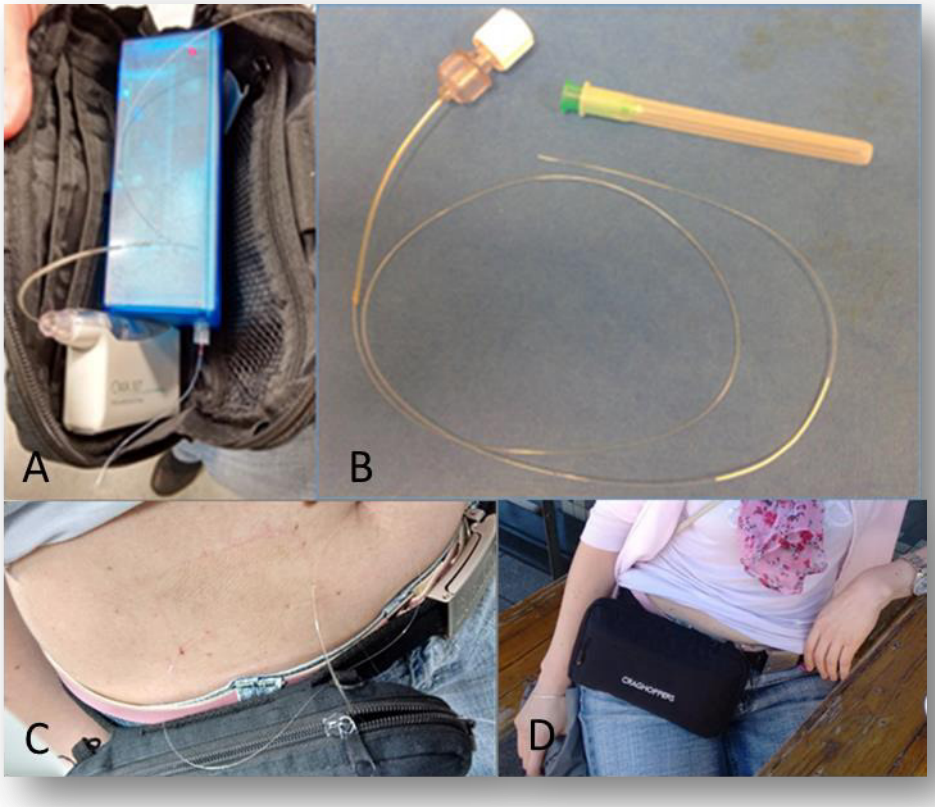
For this study we are looking for people who have an established diagnosis of congenital adrenal hyperplasia (CAH) and who take medication for their condition.

What is microdialysis?

The microdialysis probe is a very narrow tube (less than the width of a pin head) with tiny holes ("pores") through which certain molecules can pass. In this study the probe is placed just beneath the skin after making the area numb with local anaesthetic.

Once the probe is under the skin, it is connected to a small pump and a sample collector. These are both kept in a small bag, which is worn around the waist. Together, everything weighs less than a tin of baked beans. You can see a picture of the device on the next page.

The probe and pump are fully approved for use in humans (CE marked). The sample collector is a research device developed by our team. It does not have CE marking. However it has already been successfully used in several trials of healthy volunteers and patients with no problems reported. The device stores samples of fluid only – safety valves prevent any flow of liquid back toward the body.



The microdialysis system. The sample collector (oblong box) and pump (smaller box) and are carried in a small bag around the waist (A). The probe (B) is a very small plastic tube placed just below the skin, usually on the lower part of the abdomen (stomach) (C). A volunteer wearing the connected microdialysis system (D).

Do I have to take part?

Taking part is voluntary – it is up to you to decide whether or not to participate. If you do decide to take part we will ask you to sign a consent form and give you a copy of this information sheet and the consent form to keep. If you change your mind, you can

withdraw at any time. If you decide not to take part you do not have to give a reason, nobody will be upset.

What does the study involve and what will I be asked to do if I take part?

The study will require the insertion of a microdialysis probe as described above. Your participation in the study will not interfere with the planned treatment or management of your disease.

For the study you will be seen at the Joint Clinical Research Unit, UHBristol NHS Foundation Trust for brief periods.

Screening

If you are interested in taking part we will arrange a date for you to meet a study investigator and discuss all aspects of the study. We will discuss with you all aspects of the study and show you the microdialysis system. At that visit, if you would still like to be involved informed consent will be taken. It may then be necessary for a study investigator to review your medical notes in order to confirm your eligibility to take part.

Baseline study

We will ask you to abstain from alcohol from 2 days prior to and during the sampling period. We will also ask you to fill in an activity diary for the day prior to and during the sampling so that we can see what your usual routine is with regards to going to bed etc.

You will arrive at a mutually convenient time in the morning of the study visit - we ask that you do not have anything to eat or drink after midnight except for water. We will take a blood sample from you to look at your baseline hormone levels. We may also check other routine bloods (kidney, liver, thyroid, blood count) if these have not been done recently. Women of child bearing age may be asked to perform a pregnancy test if appropriate. Afterwards, you will be given breakfast (please let us know if you have any specific dietary requirements).

After breakfast we will measure height and weight to calculate your body mass index (BMI) as well as measure your waist/hip ratio and check your blood pressure. To help us understand your personal experience of CAH we will ask you to complete two brief quality of life and health care use questionnaires. We will talk to you about the best place on the stomach for the microdialysis probe. A local anaesthetic will be used to make the area numb. The probe will be inserted in the numbed area and connected to the collection system. It will automatically begin to collect samples without you having to do anything. This whole process will take about 1 hour.

Once the sampler has been started, it will need to remain on for the following 27 hours. We will contact or visit you about 12 hours after starting to check everything is working properly.

You will not be able to have a shower/bath whilst wearing the device and we also ask that you do not participate in any sport. Apart from that you will be free to carry on afterwards as you would on any other day.

At the end of the study

If there were any problems with the system during the study period, we may ask you if you are willing to wear the sampler for a maximum of a further 24 hours to achieve a complete collection (only if this is convenient for you).

Otherwise, at the end of the sampling period, you will return to the Research Unit and the device will be disconnected and removed from your skin. Finally, we will ask you to complete a questionnaire asking how you felt about using the microdialysis system.

Saliva samples

You will also be required to collect three saliva samples at home. Instructions for saliva sample collection will be provided separately.

Further sampling

We would like to keep in touch with you to find out if your treatment regimen changes at all over the lifetime of the study. If it does we would like to know so that we can repeat your microdialysis study on your new treatment regimen. Repeat sessions follow the same procedure described in the **Baseline study** section above. We would only repeat the sampling with your continued consent and on a maximum of 3 times in total.

Support

Throughout the study period, the researcher will be available for contact on a mobile telephone at all times.

What could prevent me from being in the study?

- If you are pregnant or planning pregnancy
- If you are known to be allergic to the local anaesthetic lignocaine
- If you are regularly taking certain types of corticosteroid other than your prescribed adrenal replacement
- If you take certain other interfering medication
- If you are on a special diet

What are the potential side effects and risks of taking part?

Microdialysis and blood tests

The microdialysis system is safe and we do not think there will be any significant side effects or risks to you as a participant. Minor bruising at the site of the microdialysis probe insertion or around the vein where you have your blood test might occur. Very occasionally people can faint while have a blood test – we will ask you if you have ever had any problems with fainting or blood tests before we start the study.

Like any other procedure there is a small risk of discomfort during insertion or at the site of the probe. There is theoretically a small risk of infection and localized allergic reaction at the site of the probe or blood sampling. This risk is considered to be extremely low as we use an aseptic (clean) method and the probe is made from low allergy material. If infection or allergy is suspected we will immediately remove the probe and stop the study.

If during the study your blood results reveal any unexpected abnormality we will arrange a meeting with you to explain these results. We will ask you if you wish for this information to be sent to your GP and if appropriate we will recommend an appointment with your GP.

If you have any questions regarding this you can either discuss with a researcher or take this information sheet to your GP to discuss matters of concern. If, at any time during the study, new information becomes available, the researchers will talk to you about this and discuss whether you want to continue in the study.

Will I receive any reimbursement for my time?

Yes. You can claim for expenses due to your participation in the study, such as for transport and accommodation, up to a maximum of £100 per session. Keep all receipts. Expense claims are subject to University of Bristol policy.

What will happen to my samples?

Some baseline blood tests will be analysed at the UH Bristol NHS laboratory. The rest of the microdialysis, blood and saliva samples will first be stored in a freezer within the University of Bristol and then sent away to the University of Bergen, Norway and a partner biotechnology company called OLINK, in Sweden. All samples will be totally anonymous and cannot be linked to you in any way. After initial analysis the samples taken for the research will be stored at a biobank at the University of Bergen for up to 5 years after the last person is recruited. Samples are kept in case analyses need to be repeated or if additional results are required to successfully complete the study. After this date your samples will be destroyed at the University of Bergen.

Results will be entered in to the protected project database with access limited to project investigators at the University of Bergen and Bristol.

If you decide to withdraw from the study, you can ask for your samples to be destroyed even if they have not already been analysed, or for any information obtained from analysing your samples to be destroyed.

What are my responsibilities?

We would like you to let us know of any changes in your health or any medication you may take. You will need to attend your appointments as per the agreed time.

How will I benefit from participating?

You will not benefit directly from results.

How will the results of this research be used?

The results of this study will be published in scientific journals and presented at medical meetings. A meeting of all research participants may be arranged to discuss our findings.

Who is organising and funding the research?

The Henry Wellcome Laboratories for Integrative Neuroscience (part of the University of Bristol) is carrying out the research in collaboration with the University of Bergen (Norway). The research is sponsored by the University of Bristol and is being funded by Horizon 2020, an EU Research and Innovation program.

It has full approval from the NHS Research Ethics Board and the Research and Innovation Department of UHBristol NHS Foundation Trust. Funding pays the salaries of some of the research staff and other direct costs of doing the research. Researchers are not receiving any payments other than their usual salaries.

Confidentiality

Once you have given consent your GP will be informed of your participation in the study. Any medical and research information from this study will remain confidential. Any information about you will be made anonymous so that you cannot be recognised from it. It will only be available to research staff, and to government bodies which regulate medical studies such as this one and make sure they are performed in a proper manner.

What do I do now?

Thank you for considering taking part in this study. If, after reading this information, you would like more information or decide that you would like to take part, please contact us.

Email us

ultradian-study@bristol.ac.uk

Call and speak to one of the study researchers

Dr. Georgie Russell	0117 331 3121
Dr. Thomas Upton	0117 331 3121
Prof. Stafford Lightman	0117 331 3167

If you would like more information

If you would like to discuss the science behind the study with an independent person, please phone Prof. Lightman's secretary on 0117 331 3167.

You can also visit the ULTRADIAN study website www.ultradian.net

If you have concerns

You should first speak with the researchers who will do their best to answer your questions. Otherwise you can contact Dr Tom Creed, head of the Joint Clinical Research Unit, UH Bristol (0117 342 4001).

If you wish to make a formal complaint, please write to:

Research Governance Team
Research and Enterprise Development
Senate House, University of Bristol
Tyndalls Ave
Bristol BS8 1TH

The University of Bristol, as the study Sponsor, operates a Clinical Trial protection scheme, which operates in respect of the University's legal liabilities for any injury arising specifically as a consequence of your participation in the study. Additionally, the standard provision of the NHS Indemnity Scheme will operate in respect of the provision of clinical treatment.