Sodium intake effect on Aldosterone Level in real Time (SALT) study

PARTICIPATION INFORMATION SHEET

Chief Investigator: Dr Emma Hart, University of Bristol Medical School, Biomedical Sciences Building, University of Bristol, Bristol, BS8 1TD.

Co-investigator: Dr Tim Swinn, School of Physiology, Pharmacology and Neuroscience, Biomedical Sciences Building, University of Bristol, Bristol, BS8 1TD. Email: salt-study@bristol.ac.uk

Please contact Tim Swinn if you have any questions about this study.

Why am I being invited to participate in this study?

You are being invited to take part in a research study at the University of Bristol, which is looking at whether salt intake affects the concentration of the hormone aldosterone throughout the day. We are looking to recruit healthy volunteers who are willing to follow a high and low salt diet (each for a week) before having their aldosterone levels measured by wearing a novel device (U-Rhythm) for a day.

This information sheet will explain why the study is done and what happens during the visits. If you are interested in taking part in this study, please read this information sheet fully to understand what the study involves. Feel free to discuss this information with your family and friends or contact us if you have any queries.

Why is this study being done?

High blood pressure (hypertension) is a common medical condition and one that puts individuals at higher risk of heart attacks and stroke. The hormone aldosterone is raised in around 30% of patients with hypertension however diagnosing this is difficult as the protocols are complex and invasive. In a recent study, we developed a new technique for monitoring aldosterone continuously using a device called U-Rhythm (Upton et al. 2003). The pilot study showed that even healthy volunteers can display a variety of patterns of aldosterone concentration throughout the day, and we suspect that this may be explained (at least in part) by salt intake.

We aim to test this idea as, if correct, this may lead to quicker and easier methods to diagnose raised aldosterone and therefore allow targeted treatment to be started earlier in patients with hypertension and raised aldosterone.

What will taking part involve?

Full participation in the study involves a total of 6 visits to the NIHR clinical research facility (St. Michael's Hill, Bristol, BS2 8DX) plus adhering to a low and high salt diet (designed by NHS dietitians), each for a week. At the end of each dietary regime, participants will be asked to have the U-rhythm device fitted for 24 hours, collect a 24-hour urine sample and undergo blood tests.

You will be randomly assigned (using the research randomiser: randomizer.org) to have the low or high salt diet first.

Full details of the visits and protocol can be found below.

Study protocol

Screening questionnaire (telephone discussion: 30 minutes)

We will conduct the screening questionnaire over telephone. This will ask about your medical history to check whether you are safe and suitable to participate in the study. If you are eligible for the study, we will arrange a date and time for the first in-person visit.

Start of study (day 0). *Visit 1: 60 minutes*

1) **Consent**

We will go over what the study involves and answer any questions that you have about the study. If you agree, we will complete a written consent form.

2) **Additional medical information, examination and investigations**

- Height and weight measurements
- Blood pressure and heart rate measurements
- Electrocardiogram (ECG heart tracing)
- Urine dip test including pregnancy test
- Blood tests (to check kidney and thyroid function)

3) **Dietary preparation**

We will talk through the dietary regimes and you will be randomly assigned to receive either the high or low salt diet first (using the research randomiser tool: randomizer.org). We will give documentation on what the diet entails and will either give you the meals for the week at this time, or schedule a delivery for later.

4) **VO2 peak test**

On visit 1 of diet 1 we will ask you to undertake an exercise test known as a VO2 peak test. This involves around 20 minutes on an exercise bike whilst measuring your breathing. It will be a maximum effort. The reason we want to do this is so that we can appropriately gauge the subsequent exercise intensity level for visits 3 and 6 (which will be at 50-60% of maximum).

5) **Devices given and calibrated**

During the subsequent week, we will ask you to wear a wrist-based activity monitor (motion-watch or similar) and a wrist-based blood pressure monitor (Aktiia device). We will loan these for a week and calibrate them on the initial visit.
We will also provide a urine container that will be needed later in the week and will schedule subsequent visits

Day 1-6

We will ask you to adhere to the dietary protocol during these days however there will be no restriction on daily activities. You will be able to contact the researching team if there are any issues.

Day 7

Please start the 24-urine collection with the 2nd urine of the day. Please bring this with you.

Study visit 2: 60 minutes

1) **Review**

We will discuss how the week has been and answer any questions you may have about the next steps.

2) **U-rhythm device**

The U-rhythm device uses a technique called microdialysis, this does not cause discomfort whilst wearing the device however fitting of the minute probe involves a sharp scratch equivalent to undertaking a blood test. We will check the monitor has collected its first sample correctly (around 20 minutes after starting).

3) **Equipment and diary provision**

We will provide you with equipment to track your sleep for the next night (AcuPebble device or similar). We will also provide you with a document to record specific activities (e.g. sleep and wake times, meal times, any exercise undertaken).

Day 8

The 24-hour urine sample can stop after the first urine of the day.

Study visit 3: 4-5 hours

This is the longest visit as it is the one where we collect measurements. If there has been any issue with the U-Rhythm device then we may ask you to continue the diet for another day and conduct visit 3 on day 9 instead.

1) **Urine sample and devices returned**
2) **Weight and blood pressure measurement**
3) **Blood tests**

This is so that we can compare the U-rhythm readings with blood samples and check kidney function, as well as other hormones (including renin). We will ask you to undergo blood sampling twice, one after lying for 30 minutes then a second on standing.

4) **Exercise bike**

We will ask you to go on our exercise bike for 30 minutes whilst wearing U-rhythm so that we can assess the response of hormones to exercise. This will be at an intensity around 50-60% of the exercise test conducted during visit 1. We will ask you to remain seated for 2 hours after the exercise so that we can record enough data.

5) **U-rhythm disconnected and dietary protocol ends**
6) **End-of protocol questionnaire**

After completing visit 3, we will give you the £150 voucher as compensation for your time and arrange visits for the trial on the other diet regime (i.e. book in for the high salt diet if you started with the low salt diet, and vice versa).

The protocol above will then repeat with the second diet, meaning that there will be 6 visits in total to complete the study.

Must I take part?

No, It is completely your decision if you would like to take part. Signing a consent form only happens when you are completely happy that all your questions have been answered and feel confident to participate. You are free to withdraw from the study at any point without having to give a reason.

What are the possible side effects?

Due to the short duration of each diet, we do not anticipate any health impact from the high or low salt regimen. We have involved NHS dietitians to balance other nutritional components of each regime.

What are the possible benefits of taking part of this study?

Participants will be compensated up to £300 for their time (£150 for each arm of the trial completed). This will be in the form of a voucher for a retailer of their choice. Food will be provided for each dietary regime (all meals for a week).
You will get a blood pressure screen, blood tests and ECG. Taking part in this study will also help us understand more about the science underpinning the role of hormones in hypertension which may lead to tailored treatments or diagnostic methods in future.

Who can take part in this study?

- Healthy volunteers aged 18-40 who have a regular sleep pattern (usual bedtime 21:00-23:00 and usual wake time 06:00-08:00).

Who can't take part in this study

- Anyone with a history of hypertension, raised aldosterone (hyperaldosteronism), obstructive sleep apnoea, heart disease.
- Anyone on medication that could affect our results. This includes most blood pressure/kidney medicine and common inhalers.
- Anyone with a 1st degree family member who was diagnosed with hypertension below the age of 60 or has a diagnosis of primary hyperaldosteronism.
- Inability to understand spoken or written instructions given in English
- Body mass index ≥30 kg/m^2
- Pregnancy
- Alcohol consumption (>28 units/week), daily use of nicotine (including smoking and vaping) and daily use of recreational drugs
- Needle phobia
- Allergy to any ingredient within meal plans, or dietary requirements that cannot be catered for within the meal plans
- Anyone who has worked shifts finishing after midnight in the past 4 weeks
- Anyone with irregular sleep times (i.e. bedtime/wake time varies by more than +- 1 hour across a normal week)

How will we use information about you?

We will need to use information from you for this research project.
This information will include:

- Your name
- Contact details
- GP details
- Medical history

People will use this information to do the research or to check your records to make sure that the research is being done properly.
People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.
University of Bristol (UoB) is the sponsor of this research.
UoB is responsible for looking after your information. We will not share your information related to this research project with other organisations.
We will keep all information about you safe and secure by:

- Keeping written records in a locked filing cabinet on-site at UoB
- Storing electronic data in an encrypted database
- Your data will not be shared outside the UK.

How will we use information about you after the study ends?

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study. We will keep your study data for a maximum of 15 of years. The study data will then be fully anonymised and securely archived or destroyed.

What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have
You have the right to ask us to access, remove, change or delete data we hold about you for the purposes of the study. You can also object to our processing of your data. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this
If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

Where can you find out more about how your information is used?

You can find out more about how we use your information:
www.hra.nhs.uk/patientdataandresearch
Or you can find out more about how we use your information by contacting a member of the study team (Principal investigator: Dr. Tim Swinn, salt-study@bristol.ac.uk).

Will there be any risk to me?

All procedures will be conducted by a suitably qualified research investigator (specialised clinical research nurse or General Medical Council (GMC) registered physician) and the study

will present minimal risk to participants. The microdialysis procedure has previously been conducted in hundreds of participants with no significant adverse events and all components of the device are CE marked. The insertion may cause minor bruising but infection risk is minimal.
Blood samples will be collected by a suitably trained researcher. Aside from minor bruising or discomfort the risk of this procedure is extremely small and the total volume to be drawn will be small.
As each diet is only for a short time period, no adverse effect on long-term health is expected. Similarly, the exercise elements of the study will be conducted by a suitably trained researcher in a controlled environment so no risk to participant is expected.

What happens if something goes wrong?

In the unlikely event that you are harmed in this study, there are no specific compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. This study will be sponsored by the University of Bristol. The University has Public Liability insurance to cover the liability of the University to research participants. If you have any general complaints or concerns regarding the study please contact Dr. Tim Swinn or the University Research Ethics Committee (research-governance@bristol.ac.uk).
If you have queries during your time on the study, we will provide a phone number that you can call at any time to contact Dr Swinn.

What will happen if you discover any health-related findings on testing?

These research tests are not a medical screening test. If you volunteer to take part in the study, we will ask you for your permission to inform your GP. This is optional and you are welcome to decline this. This will not affect your participation in the study. Sometimes the researchers may be concerned that a possible abnormality is found on the ECG, blood pressure or blood tests. In this case, we will contact your GP and inform them of these results, if you have given permission for this. We will also inform you of any abnormal results. If the abnormal results make it unsafe for you to participate, you will not be able to take part in the rest of the study.

What happens to my samples?

Whole blood is not stored but serum/plasma is stored. Serum and urine samples will be stored anonymously in a locked freezer at a University of Bristol or an NHS University Hospitals Bristol and Weston site, with an ID number on the sample. After testing, samples will be disposed with in accordance with the Human Tissue Authorities Code of Practice however some serum samples will remain stored for future analysis of biomarkers of high blood pressure. Interstitial fluid and urine samples will be sent to the University of Bergen

for analysis and will be disposed of in line with local protocols after analysis. You have the right to ask for your samples to be withdrawn at any stage.

What happens if I don't want to carry on with the study?

You are free to withdraw your consent at any time, without giving a reason, even after signing the consent form. If you decide to withdraw from the study, your normal care, and relationship with the University of Bristol and University Hospitals Bristol and Weston will not be affected in any way. If you withdraw partway through the study, we will keep the data we have already collected about you. If you withdraw partway through the study, you will have the option to withdraw your samples from further use. You can withdraw by contacting the researching team at any stage (salt-study@bristol.ac.uk).

What happens at the end of the study and to the results of the study?

The full results of the study will not be known until the last participant has been tested, which could take up to a year. The results will be reported in professional publications and scientific meetings, but you will not be identified by name. Participants will be offered a plain-language summary of the results.

Who has reviewed the study?

The study has been approved be the University of Bristol Faculty of Human Sciences Research Ethics Committee (FREC) and has been submitted to the Healthcare Research Authority (HRA) for review.

Insurance

Insurance / indemnity will be provided by the Sponsor.

What time will I have to take to do this study

We will arrange your visits at a time that is convenient to you. The study visits will take place from Monday to Friday and between 09:00 and 17:00.

What do I do now?

If you're interested in taking part in this study or have any questions, please contact Dr. Tim Swinn (contact details can be found at start and end of this sheet).

Thank you for taking the time to read this information sheet and for considering whether you would like to take part in this study.

Contact Information

If you are interested in taking part in the study, or have any questions, please contact:
Tim Swinn: salt-study@bristol.ac.uk