Patient Information Sheet

Title: Acetazolamide as a chloride sparing Diuretic in patients Admitted with Heart Failure: a pilot and feasibility study – ADA-HF

(Randomised, open label, controlled trial of acetazolamide plus standard of care versus standard of care alone in patients admitted with heart failure. ADA-HF)

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Trial Centre: Castle Hill Hospital, Cottingham

Sponsor: Hull University Teaching Hospitals NHS Trust, R&D Department, Office 13, 2nd Floor Daisy Building, Castle Hill Hospital, Castle Rd, Cottingham, East Yorkshire HU16 5JQ

Invitation

You are being invited to take part in a trial. Before you decide whether or not to take part, 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. Talk to others about the trial if you wish.

Part 1: tells you the purpose of this trial and what will happen to you if you take part.

Part 2: gives you more detailed information about the conduct of the trial.

Note: Your GP will be informed of your involvement in the trial.

Part 1

Why have I been invited?

Your consultant believes you may be a suitable/ willing participant for a trial being carried out at Castle Hill Hospital. The trial is being carried out by the department of Cardiorespiratory Medicine, Castle Hill Hospital.

You are being asked to take part in this trial because you have a condition known as heart failure and have been admitted into hospital due to worsening of this condition. We are hoping to investigate how a drug called acetazolamide affects the amount of urine produced and the salt levels in the blood during treatment for heart failure.

What is the purpose of the study?

The heart is a muscular bag whose job it is to pump blood around the body. Heart failure is a condition where the heart does not have enough strength preventing blood being pumped around the body efficiently. The body detects this as a lack of blood reaching the vital organs. In response, the body retains more fluid to increase blood volume. However, the fluid retained does not remain within the bloodstream and pools in the tissues. This causes leg swelling as fluid pools in the skin and breathlessness as fluid pools in the lungs.

The treatment for excess fluid is to remove it from the body, the only non-invasive way to do this is by stimulating the kidneys to make more urine – a process called diuresis. Drugs that cause diuresis are called diuretics – you may have been taking a tablet diuretic before you came to hospital. However, in patients requiring hospital admission, tablet diuretics are often not strong enough to cause enough diuresis. So in order remove the excess fluid we give the diuretic medication through an intravenous drip.

However, the drip is sometimes not effective and other drugs are often added to encourage the body to make more urine. Lots of different strategies are available, but none are particularly effective. Also, the medications we currently give to cause diuresis can cause the body to lose excess salts in the urine such as chloride. People with heart failure who have low chloride have a worse prognosis than people with normal chloride levels in their blood. Whether or not we can prevent or correct low chloride levels in patients with heart failure is debated.

Acetazolamide is not a new medication – it is used as a treatment for glaucoma, an anti-epileptic drug in children, and as a treatment for mountain sickness. We believe that acetazolamide may have important but overlooked effects on the kidneys and may be able to increase diuresis without causing excessive loss of chloride.

We would therefore like to conduct a trial on the use of acetazolamide, taken orally in tablet form two times per day, on the amount of urine passed and blood levels of chloride while patients are receiving usual care for severe fluid retention in hospital. The aim is to see if acetazolamide increases the amount of urine produced while also reducing the amount of chloride lost in the urine.

To help you decide if you would like to take part, please read this information sheet. It gives you details of what will be involved if you decide to take part and also who to contact if you would like to discuss the trial or ask any questions.

Questions we want to answer

1. Does the acetazolamide increase the amount of fluid lost in patients receiving high dose intravenous diuretics?
2. Does acetazolamide reduce the amount of chloride lost in the urine during treatment with high dose intravenous diuretics?

Do I have to take part?

No, it is up to you to decide whether or not to take part the trial is entirely voluntary. If you do decide to participate you will be given this information sheet to keep and be asked to sign a Consent form. You are still free to withdraw at any time and do not have to give a reason. Your non-participation or dropping out of the trial will not affect your planned treatment and care in any way.

Before you can begin the trial

The recruiting doctor or nurse will tell you about any potential adverse events that could occur in this trial. You will be told exactly what the trial entails and what will be required of you. You are encouraged to ask questions to the research team until you are satisfied that you fully understand the nature of the trial and the requirements.

What happens in the study?

If you think you might be interested in taking part in the trial, you will have a discussion with one of the investigators to collect some medical details from you and make sure there is no reason not to include you in the trial. You will then be given time to consider your participation and, if you decide to participate, you will be asked to sign a consent form.

Once you are enrolled in the trial we carry out some preliminary assessments such as checking your blood pressure, heart rate and resting heart rhythm. Further investigations which include routine blood tests and an ultrasound scan of the heart will be performed at the bedside if not recently done.

You will then be “randomised” to either take acetazolamide tablets 250mg two times per day for 4 days in addition to standard treatment or to standard treatment alone. Acetazolamide can be taken alongside your usual treatment and should be taken at in the morning and again 6 hours

later – the nurses on the ward will provide you with the tablets at the appropriate times.

All patients admitted to hospital with severe fluid retention receive a continuous infusion of intravenous diuretic and have their urine output, fluid intake, body weight, kidney function, and blood salt levels measured on a daily basis – this is standard care. In addition to this we will require you to complete a brief diet diary and symptom questionnaire on a daily basis.

On days 1 and 4 we will perform an ultrasound scan of the large veins in the tummy at the bedside which will take around 2 minutes. On days 2 and 4 you will be asked to retain all urine passed in a collection bottle to measure the amount of salt lost in the urine on those days. After day 4 you will receive no more acetazolamide (if randomised to that group) but will be seen one more time by a member of the research team to debrief and answer any questions you may have. The treating team will continue to care for you until discharge.

After discharge we will contact you by telephone within 30 days to "check-in" and answer any questions you may have. We will have access to your electronic medical record for up to 6 months after the trial has finished.

During the trial we will require that you are on a low salt diet and are available for a member of the study team to visit you between 8 and 10 AM each day. All the data we collect will be confidential and processed in line with government guidelines for performing a clinical trial, and general data protection regulations (GDPR).

All samples taken (urine and blood) will be destroyed as per local protocols, no samples will be stored for future use.

Are there any risks to participating in the study?

Taking part in the trial will not alter any of the treatment or medication you would normally receive. It is unlikely to lead to any significant symptoms. The most common side effects of acetazolamide are nausea, diarrhoea, vomiting, and neurological symptoms such as headache, irritability, fatigue, loss of co-ordination or tingling in the limbs.. We will visit you on a daily basis as well as the treating team on ward rounds and will take blood tests every day as part of standard care to monitor any problems relating to being in the trial.

Are there any benefits to taking part?

You will be part of one of the first trials in the world to investigate how acetazolamide might benefit patients admitted to hospital with heart failure. If we find that acetazolamide does increase the amount of urine produced and reduces the amount of chloride loss it may become a very useful treatment for heart failure in the future. You will spend a lot of time with researchers during your admission and hopefully gain more understanding of your condition and your treatments.

Will taking part in this trial cost me anything and will I be paid?

No. You will not receive payment for taking part in the trial.

What happens when the trial stops?

When the trial is complete, you will continue to be treated on the ward by the treating team.

Part 2

What will happen if I don't want to carry on with the trial?

If you choose to take part, you may change your mind and choose to leave the study at any time for any reason. You will not need to explain your reasons for leaving the study. If you leave the study, the quality of your future care will not be affected in any way. We will be able to use any data collected from you up until the point of withdrawal of consent.

What happens if you become pregnant whilst on the trial?

If you or the partner, falls pregnant when participating in the trial, the trial participant should be withdrawn from the trial unless the Principal Investigator decides that the risk to the patient is not clinically significant.

What happens if new information becomes available?

Sometimes during a research trial, new information becomes available about the treatment that is being studied. If this happens, your trial doctor will discuss how this affects your care and participation. If you decide to withdraw, your doctor will make arrangements for your routine care to continue. If you decide to carry on in the trial you will be asked to sign an updated consent form.

Will my taking part in this trial be kept confidential?

Yes. All the information obtained about you in the course of the trial will be kept in a secure locked room. The trial doctors and nurses and a trial monitor

who works for the Hull University Teaching Hospitals NHS trust will have access to the data collected in this trial. The data may also be looked at by representatives of regulatory authorities and by authorised people from Castle Hill Hospital to check that the study is being carried out correctly. Everyone with access to the data has a duty of confidentiality and nothing that could reveal your identity will be disclosed outside the research site.

With your permission we will also write to your GP to inform them of the type of trial that you will be taking part in. We will not disclose any results to your GP, unless there is any medical information that they may need to know in order to provide medical care.

What will happen to the results of the research trial?

The results of this trial may be published or presented at medical meetings. You will not be identified in any report / publication or presentation. We would be happy to supply you with a copy of the results on request. If interested, you may also attend presentations of the results given at local or national events. We would be delighted to supply you with any details.

Who is organising and funding the trial?

The trial is funded by the British Heart Foundation's Research Development Fund. The trial is organised and run by the Hull University Teaching Hospitals Trust Research and Development department and the Department of Cardiorespiratory Medicine at Castle Hill Hospital.

Who has reviewed this trial?

The trial was designed by researchers from the local cardiology department and the Hull York Medical School. The British Society for Heart Failure has given their backing to the study. The INVOLVE-Hull public and patient feedback group have provided valuable insight and comments on the design of the trial. The ethical basis for performing the trial has been supported by the National Research Ethics Committee.

How we will use information about you?

We will need to use information from your medical records for this research project.
This information will include your [initials/ NHS number/ name/ contact details]. 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. We will keep all information about you safe and secure.
Once we have finished the trial, we will keep some of the data so we can check the results. We will write our reports in a way that your personal information and participation in the trial remains anonymous.

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

You can find out more about how we use your information

- At www.hra.nhs.uk/information-about-patients/
- our information available from https://www.hey.nhs.uk/privacy/data-protection/
- by asking one of the research team
- by sending an email to Information Governance at hyp-trheyig.nhs.net
- by ringing Carla Ramsay, Data Protection Officer on 01482 674920

What if something goes wrong?

If you have a concern about any aspect of the trial, you should ask to speak to the Principal Investigator on Tel: 01482 461806 or Email: joe.cuthbert@hyms.ac.uk who will do their best to answer your questions. If you remain unhappy and wish to complain, you can do so via the NHS Complaints Procedure. Details can be obtained from the Patients Advisory Liaison Service (PALS) using the details below:

Patient Experience, Alderson House, Hull Royal Infirmary, Anlaby road, Hull, HU3 2JZ.

Tel. 01482 623065 (CHH) or 675508 (HRI)
Or through the hospital switchboard 01482 875875
Email: hyp-tr.Pals.mailbox@nhs.net

Insurance and Indemnity

In the unlikely event that something does go wrong, and you are harmed during the research due to someone's negligence, you may have grounds for legal action for compensation against Hull University Teaching Hospitals NHS Trust. You may have to pay your legal costs. The normal National Health Service complaints mechanisms will be available to you.

What happens next?

Please discuss this information with your family, friends or GP if you wish. Any questions can be answered then or please do not hesitate to contact the research team on the number or email below.

Dr Joe Cuthbert
Tel: 01482 461806
Email: joe.cuthbert@hyms.ac.uk

Thank you very much for taking the time to read this information sheet and considering taking part in our research.

You will receive a copy of this information sheet and your signed consent form to keep if you decide that you wish to take part in the trial.