

Study Title: Randomised controlled trial of topical chlorhexidine 0.2% versus topical natamycin 5% for fungal keratitis in East Africa

Participant Information Sheet and Consent Form - No 1: For baseline assessment and investigations

Introduction

You are being invited to take part in a medical 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 or listen to the following information carefully and to talk to others about the study, if you wish. Ask us if there is anything that is not clear or if you would like more information. Do not sign the consent form unless you are satisfied with the answers to your questions and decide that you want to be part of this study. Take time to decide whether or not you wish to take part.

Why have I been invited?

You have been invited to take part because you have a corneal infection. To guide the treatment of this it is helpful to do tests to find out the cause, to guide the choice of eye drop treatment. We are asking for your permission to carry out some tests that are listed below to find out what is causing the infection and to decide if you may be suitable for a trial comparing treatments for fungal eye infections.

What is this study about?

Infection of the clear part of the front of the eye (the cornea) is a corneal ulcer. It is an important cause of blindness. A scratch in the cornea allows infection to enter and an ulcer to begin. These infections can be very serious with some people losing the sight in the affected eye.

Different types of infectious organisms can cause corneal ulcers. These include bacteria and fungi which need to be treated with different types of eye drop medicines. To find out what type of infection is present it is necessary to collect a small sample from the ulcer and perform various laboratory tests. The test results guide the treatment. In Uganda and Tanzania about half of the infections are caused by fungus.

Fungal infections can be difficult to diagnose. No single test can reliably detect it. It may need several different tests to find it. Currently, in many countries where fungal ulcers are common laboratory services are limited or not available. Tests are expensive and may not detect all of the infections. There is a need to understand which of the current test options give the most useful information.

The first purpose of this study is to carefully evaluate your eye infection using several different diagnostic tests to try to find out what type of infection you have, and to learn which tests are most useful in this process.

There is a need for alternative, affordable and more easily available eye drop treatments for fungal infections. We are also conducting a clinical trial to compare two eye drop treatments for fungal infection, to try to find out which is better.

Therefore, the second purpose of this initial Assessment and Investigation study is to identify people who have a fungal corneal infection who may be eligible and willing to enrol in the clinical trial. If we find out that you do have a fungal corneal infection, we will then ask if you would be interested in hearing about the clinical trial. If you are interested, then at that stage we will explain about the treatment trial in detail, provide you with a second information sheet and go through a second consent process.

Do I have to take part?

No. Your involvement is entirely voluntary. If you agree to take part, we will then ask you to sign a consent form. If you decide to join and change your mind, you are free to withdraw at any time without giving a reason. This will not affect the standard of care you receive.

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What will happen to me if I take part?

If you agree to be part of this study, the following will happen:

- We will ask you a series of questions. This will include basic demographic information, the history of your current eye problem, and treatment you have had before arriving at the hospital.
- We will then carefully examine both eyes using a special microscope.
- Your eyes will be photographed with a camera. This is additional to standard care, and will help us to monitor the infection and the response to treatment.
- We will use a special microscope to look at the cornea to see if we can find a fungal infection. This involves putting anaesthetic drops on the eye. A soft plastic device then gently touches the eye so to see if you have a fungal infection. This is additional to standard care, and will help us to find out the type of infection you have more rapidly so that we can offer you the most appropriate treatment.
- We will collect samples from the corneal ulcer to test in the laboratory to try to identify what is causing the infection. Anaesthetic eye drops will be used numb the eye so you will not feel anything while we collect the sample by brushing the surface.
- We will check your blood sugar level for diabetes. This is done using a finger-prick blood sample. If this is raised, we will refer you to a separate group of doctors to help you with this.
- You will be offered a test for HIV infection. This will be done through the hospitals counselling and testing services. If you choose to accept this, then you will be separately counselled about the test and the implications of the results. This would involve the collection of a blood test sample from your arm. If the HIV test is positive, then you will be referred to the appropriate team for ongoing care. The result of this test will be shared with the us (cornea infection study team), with your consent, as it is potentially relevant to the treatment of your cornea infection.
- We will collect a sample of the cells from the inside of your cheek by gently rubbing a swab for a few seconds. This is additional to the standard of care. The purpose is to try to understand how the body fights the infection and why some people develop this eye problem and others do not.
- You will be asked to complete three short questionnaires to assess your quality of life and vision function. This is additional to standard care, and will help us to better understand the impact corneal ulcers can have on people's lives.

If we find evidence of fungus infecting your eye, then we will discuss the details of the trial with you further. At that point we will give you a second information sheet to read (or read to you), and if you meet all the eligibility criteria for the trial, to then go through a second consent process with you.

If you do not have a fungal infection, for example if the infection is caused by bacteria, then you will receive standard ongoing treatment for this by the same team at the hospital.

You may be withdrawn from the study without your consent if the researchers believe it is in your best interest or if you fail to follow study procedures.

What are the side effects or risks of taking part?

- The anaesthetic eye drops usually sting for a few seconds and then your eye should feel more comfortable. There is a very low risk of allergic reaction from the anaesthetic eye drops.
- The procedures including the history taking, examination, photography, in vivo confocal microscopy and sample collection are part of the standard of care for assessing a corneal infection. The risk associated with these are very low and no different from routine care. To minimise discomfort, topical anaesthetic will be given before examinations and sample collection.
- You will experience a little pain when a blood sample is collected. The people collecting the blood sample will ensure that this is done with as little discomfort as possible.
- The questions, tests and examinations will add about 15 minutes to your hospital visit above what we would usually expect in assessing a patient with this problem.

What are the benefits of taking part?

- The study will involve tests for the type of infection. This helps the doctor looking after you to choose the best type of treatment for your eyes
- The costs for the clinical assessment and the tests will be paid for by the study.
- By participating in this study, you will be helping to further research into this field so more informed decisions can be made when treating people with corneal infection.

What will happen to the clinical records, photographs and test results?

Your records will remain strictly confidential at all times. The information will be held in a secure office at your treating hospital. Only the people organizing or supervising the trial and regulatory authority auditors will have access to it. These include officials delegated by the Sponsor (London School of Hygiene and Tropical Medicine), the local National Ethics Committee, The local National Drug Regulatory Authority and trial Data Safety Monitoring Body (DSMB).

Your name will not be passed to anyone else outside the research team, unless we have your direct instruction to do so, for example to make a medical referral.

The photographs of the eye and the result of the laboratory test for infection will be shared with computer engineers to help develop a programme that can automatically analyse the image to see if this can provide some indication of the cause of the infection. Images of corneal infection may also be used for educational and teaching purposes, including in publications. All personal identifying information will be removed before sharing images.

What tests will we do on the sample?

The samples collected from the surface of your eye will be tested in several different ways to determine what is causing the infection. This work will be done in the hospital microbiology laboratory, where you are being treated. A portion of the infection sample will be transferred for additional special tests at KCMC Hospital Biotechnology (Tanzania), the London School of Hygiene and Tropical Medicine (UK) and Radboud University Nijmegen Medical Center (The Netherlands), as some of the tests will require additional special equipment that is not available at all sites.

- We will look for the type of infection using a microscope and by growing the organisms in the laboratory. We will test the organisms that grow to see which medicines work best to kill the infection, which is helpful in guiding the choice of treatment to be used.
- The swab samples from the ulcer will be used to test for infection using molecular diagnostic tests and to evaluate new tests that may be used to find the cause rapidly in the clinic.
- We will use study genetic material of the organism causing the infection to find out the exact type of infection and its ability to resist treatments. Samples from the ulcer may also be used to investigate your immune response to the infection, so that we can better understand what causes corneal scarring
- We will store a sample of the infection causing organism indefinitely for additional testing.
- The genetic material from the cells from your cheek will be sent to the UK or to KCMC Hospital in Tanzania. We would like to store it until a later time when a sufficiently large number of samples has been collected to conduct an analysis of this genetic material. The purpose would be to try to better understand how the human immune system fights the infection and why some people develop this eye problem and others do not. By doing these tests we hope that it will help us to develop approaches that will help to prevent or improve outcomes from this condition.
- As part of this consent we are asking that you give us permission to store this material to be able to test it at a later date as mentioned above. We do not know exactly for how long we shall store the genetic material before we have assembled a sufficiently large collection during the course of several planned studies to be able to proceed to the sample analysis, however, we anticipate a period of at least five years.

What will happen to the results of the research study?

The results of the study will be available after it finishes and will be included in peer reviewed medical and scientific journals and may be presented at medical meetings. Results will also be published on a publicly accessible trials database. The data will be anonymous and none of the patients involved in the trial will be identified in any report or publication. Should you wish to see the results, or the publication, please ask your study doctor.

Who is funding the research?

The research is being funded as part of a grant from the Wellcome Trust, UK.

Who is organising the research?

It is being organised through a research partnership between the London School of Hygiene and Tropical Medicine, Mbarara University of Science and Technology in Uganda and Kilimanjaro Christian Medical Centre in Tanzania.

What if relevant new information becomes available?

It is not anticipated that new information will become available during the course of this short study. The information from the microbiology tests will be available to the doctors to help select the most appropriate treatment for you.

What if something goes wrong?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the head of the hospital eye department or the named person on the following page. The London

School of Hygiene and Tropical Medicine holds insurance policies which apply to this study. If you experience harm or injury as a result of taking part in this study, you may be eligible to claim compensation.

Who has reviewed the study?

Prospective research such as this is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and approved by (1) the London School of Hygiene and Tropical Medicine Research Ethics Committee; (2) Mbarara University Ethics Committee, the Uganda National Council of Science and Technology; (3) Kilimanjaro Christian Medical Centre Ethics Committee, the Tanzanian National Institute for Medical Research.

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

Your participation in this study is entirely voluntary. You may refuse to participate or may withdraw from this study at any time without penalty or loss of any rights or benefits to which you are otherwise entitled. The study doctor may also stop your participation in the study at any time for safety reasons. If you decide to withdraw from the study you should contact a member of the study team immediately. You do not have to give a reason when stopping, however for safety reasons, it is suggested that you tell the study doctor if you decide to stop because of an unwanted side effect. If you withdraw from the study, we will only use data collected before this decision, unless you request this to also be withdrawn. If you withdraw from the study, researchers, authorized persons from the Sponsor and the regulatory authorities will still require access to your medical notes to verify the data collected up to the date of your withdrawal.

Contact Details

Uganda Study Site: Dr Simon Arunga, Department of Ophthalmology, Mbarara University of Science and Technology, Mbarara.

Tanzania Study Site: Dr William Makupa and Dr Eionoti Matayan, Eye Department, KCMC Hospital, Moshi, Tanzania

Study Coordinator: Dr Jeremy Hoffman: email: Jeremy.hoffman@lshtm.ac.uk

Chief Investigator: Prof. Matthew Burton: email: matthew.burton@lshtm.ac.uk

**You will be given a copy of the information sheet and a signed consent form to keep.
Thank you for considering taking the time to read this sheet.**

Randomised controlled trial of topical chlorhexidine 0.2% versus topical natamycin 5% for fungal keratitis

Consent Form No 1: Baseline assessment and investigations

Participant Name _____

Study ID Number: _____

**Please
initial box**

1. I confirm that I have read and understand the participant information sheet dated (version) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered fully.	
2. I understand that my participation is voluntary and I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	
3. I understand that sections of my medical notes and data collected during the study may be looked at by responsible individuals from the London School of Hygiene & Tropical Medicine, from national regulatory authorities or from this hospital, where it is relevant to my taking part in this research. I give permission for these individuals to access my records.	
4. I agree to take part in the above study.	
5. I agree to the collection, laboratory tests and storage for future analysis of the samples from the surface my eye infection to understand the disease as described above.	
6. I agree to the collection and storage for future analysis of the samples from the inside of my mouth to investigate how human genes affect this disease.	
7. I agree to having a blood sample collected to measure sugar levels	
8. I agree to being referred for a HIV pre-test counselling, testing and for the results to be shared with the research team.	
9. I agree for the photographs of the front of my eye to be used in the publication or report released on the study, and for teaching purposes, including on the internet.	
10. I understand that data about/from me/the participant may be shared via a public data repository or by sharing directly with other researchers, and that I will not be identifiable from this information.	

 Name of Participant (*printed*)

 Signature/Thumbprint

 Date

 Name of Person taking consent

 Signature

 Date

The participant is unable to sign. As a witness, I confirm that all the information about the study was given and the participant consented to taking part.

 Name of Impartial Witness
 (*if required*)

 Signature

 Date

1 copy for participant; 1 copy for Principal Investigator; 1 copy to be kept with hospital notes