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INFORMED CONSENT DOCUMENT

Study Title: **Cluster randomised controlled trial of a complex intervention package to reduce blindness from severe microbial keratitis in Uganda.**

Principal Investigator(s): **Dr. Simon Arunga, Prof. Matthew Burton**

INTRODUCTION

What you should know about this study:

You are being asked to join this research study. This consent form explains the research study and your role in the study. Please read it carefully and take your time to decide. You are a volunteer. You can choose not to take part and if you join, you may quit at any time. There will be no penalty if you decide to quit the study.

Provide here a brief background to the study

Infection of the cornea 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. In tropical regions about half of all corneal ulcers are caused by fungi. Bacteria and fungi need to be treated with different types of eye drop medicines. Treatments for fungal eye infections are frequently not very effective,

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in addition access to these treatments in many countries is very limited and can be expensive.

Many people with corneal infection end up with poor vision or other eye problems because of delays in the infection being recognised and treatment being started. With this delay the condition becomes very severe, by which stage there is often nothing that can be done to save the vision or the eye itself.

This study is about testing out a new strategy in the primary health care setting to reduce the delay in diagnosis of cornea infection and the starting of an eye drop treatment, called chlorhexidine, that covers many different types of infections. They person with the infection would then be referred urgently to the regional eye hospital.

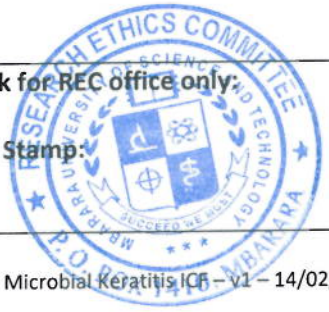
Chlorhexidine is an antiseptic. It is very effective at killing bacteria, fungi and other types of infectious organisms. It is used in medical care worldwide in several different ways. For example, it is used to clean skin before surgical operations, in antiseptic creams for skin cuts and as a mouth wash to prevent and treat mouth infections. It has been used in eye care for more than thirty years as an eye-drop preservative, for sterilizing contact lenses, for pre-operative topical antiseptic and for treating corneal infections.

If chlorohexidine eye drop were available at primary health care facilities, it would make this treatment much more easily accessible to many people with corneal infections and allow them to start appropriate treatment early in the course of the infection, as they proceed to an eye hospital to have a change of getting a good outcome.

Purpose of the research project:

This study will test if using this approach of an early intervention for people with corneal infection can reduce the risk of getting severe infections and blindness due to corneal infection.

Why you are being asked to participate:



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You have been invited to take part because you have a problem with the clear part of the front of your eye, which is called the cornea. This is either a scratch (corneal abrasion) or an infection of the cornea (microbial keratitis).

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

1) Baseline Assessment – In primary health centre:

- The health worker has already carefully examined your eyes thinks that you are eligible to join the study. We will ask you a few basic series of questions. This will include basic contact information, a short history of your current eye problem, and treatment you have had before arriving at the hospital.

- If have a corneal abrasion – a scratch without infection – the health worker will give you antibiotic eye ointment (called chloramphenicol) to tack three times each days for three days. You will be asked to come back after three days to re-check your affected eye.

- If you have a corneal infection you will be referred urgently to the Eye Unit in Mabrara. We strongly encourage you to attend this referral as quickly as you are able to, in order to be fully checked for the type of infection and to start treatment to match it.

- In half of the health centres the health workers are also going to give people with cornea infection a bottle of chlorhexidine eye drops to be taken one drop every hour. To be started straight away when you are in the health centre. To continue taking this until you are seen in the Eye Unit in Mabrara. In addition, we will send you reminder phone messages on the phone number that you have given us, to remind you to attend the eye clinic for additional treatment.

- In half of the health centres the health workers are also going to give people with cornea infection a bottle of chloramphenicol eye drops to be taken one drop every hour. To be started straight away when you are in the health centre. To continue taking this until you are seen in the Eye Unit in Mabrara.

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- As the risks to an unborn or breast-fed baby from eye drops use are unknown, pregnant and breastfeeding women will be excluded from participating in this study. They will be referred to the

2) Baseline Assessment – In Hospital Eye Clinic:

If you are referred to Mbarara eye clinic, your contact details will be communicated to our team at Mbarara who may contact you to provide additional guidance on your travel. On arrival at the clinic:

- 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.

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- 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 20 UL 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 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.

3) Treatment:

- Once the initial results of the tests for infection are available, the eye doctor will prescribe eye drop treatment that is appropriate to the infection type that is identified. If you were already started on chlorhexidine eye drops in the primary health centre you may be advised to continue taking these if there is evidence that they are working well.

- If your infection is severe, we may advise that you stay in hospital for daily review for the first few days. You will be treated with standard antibiotic or antifungal eye drops regularly for three weeks.

4) Follow-up Assessments:

- Initially, most people with corneal infections stay in hospital for several days so that the clinical team can monitor the response of the infection to the treatment.

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- We would like to review the response to treatment and document the clinical findings at the following times after you start treatment: two days, 1 week, 2 weeks, 3 weeks, 2 months and 3 months.

- On each occasion we will ask you a few questions about your eye and the treatment. We will measure your eyesight. We will examine the eye with a microscope and photograph it with a camera.

- At 1 week, 2 weeks and 3 weeks we will repeat the in vivo confocal microscopy test that was done at your first assessment. This is done to see how the infection is responding to treatment. This involves putting anaesthetic drops on the eye so that you do not feel any discomfort. A soft plastic device then gently touches the surface of the eye so that we can take special photographs of the front of your eye ("scan")

- At 1 week if you still have an open ulcer on the cornea we will repeat the sample collection to test for the ongoing presence of the infection. This involves first putting anaesthetic eye drops on the surface of the eye. Then gently scraping the surface of the corneal ulcer and testing for the presence of fungus and bacteria in the microbiology laboratory.

- Sometimes infections do not respond to the treatment. In such cases it may be necessary to alter the treatment or perform an operation. The eye doctors who will be looking after you will monitor your progress closely and advise you about further treatment might be needed.

- At three months, you will be contacted by a team from the main eye hospital in Mbarara and invited to have your vision checked to determine how well your eyes can see.

- 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.

Risks / discomforts:

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1. It is important to recognise that corneal infection is a serious, sight threatening condition. Many patients, whatever the treatment used, have reduced vision in the affected eye after it has resolved. In some people the affected eye will become blind. Sometimes the infection, despite lots of treatment, can progress to cause a hole to develop in the cornea (Perforation) and sometimes it is so severe it is necessary to perform an operation to remove the eye content.

2. Local Irritation: As with most eye drops, there is the risk of local irritation or stinging. This usually only lasts for a short time.

3. Allergic Response: Very rarely, eye drops can provoke a local allergic reaction on the surface of the eye or the eyelids.

4. Pregnancy and Breast Feeding: The risks to an unborn or breast-fed baby from these eye drops use are unknown. Therefore, pregnant and breastfeeding women are excluded from participating in this study.

5. Chlorhexidine 0.2% eye drops: Chlorhexidine eye drops are used on the surface of the eye as an antiseptic before procedures and also in the treatment of fungal and other eye infections. It has not been associated we any serious side effects. It may cause mild irritation and very rarely a local allergic response. This concentration of chlorhexidine is approved to be used in much larger volumes as a mouth wash. It is considered to be safe and is not associated with any systemic side effects.

6. Unknown Risks: The treatments in this study may have rare side effects that are currently not known. If during the course of the study new information becomes available, the researchers will share this with you.

Benefits:

- 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. These tests are not usually available for patients in Uganda.

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- By participating in this study, you will be helping to answer the question about whether or not this early intervention programme can reduce the risk of sight loss in the affected eye.

Incentives / rewards for participating:

There is absolutely no incentives/rewards e.g. monetary or any sort that will be given to you and others to participate in this study. The study is completely on a voluntary basis.

If you are referred to Mbarara hospital, the costs for your clinical assessment, tests, treatment and transport to the follow-up visit (after you initially come to Mbarara) will be paid for by the study at a public transport rate of 50,000 (fifty thousand only per visit).

Protecting data confidentiality:

The information collected about you will be kept confidentially in a controlled place. Your information will be identified by a participant number and not your name.

Protecting subject privacy during data collection:

The interview will be conducted in a quiet free room free from interference.

Right to refuse / withdraw:

The study is completely voluntary, and you are completely free to decline to participate or withdraw from the study at any time.

What happens if you leave the study?

There is no penalty for you if and when you decide to leave the study.

Who do I ask/call if I have questions or a problem?

Contact Principal investigator

Dr Simon Arunga

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What does your signature (or thumbprint/mark) on this consent form mean?

Your signature on this form means

- You have been informed about this study's purpose, procedures, possible benefits and risks
- You have been given the chance to ask questions before you sign
- You have voluntarily agreed to be in this study

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Print name of adult participant	Signature of adult participant/legally authorized representative	Date
_____	_____	_____
Print name of person obtaining consent	Signature	Date

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Thumbprint/mark signature of witness

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