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Use of patient's own blood to help in the treatment of leprosy ulcers

Submission date
20/05/2020

Recruitment status
No longer recruiting

Registration date
16/06/2020

Overall study status
Completed

Last Edited
03/05/2024

Condition category
Skin and Connective Tissue Diseases

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Leprosy ulcers are not caused by the leprosy germ but by loss of sensation leading to repetitive injury. Treatment consists of keeping the ulcer clean and fresh and also applying wet bandages regularly (dressing changes). The purpose of this study is to test a new method that may help the ulcer to heal faster. The proposed treatment involves creating a membrane from the patient's blood and then placing this membrane over the ulcer during a dressing change. Patients will typically have dressing changes every 3 or 4 days. At present, this treatment appears to be very safe, although currently it is not known whether it is effective. This study only looks at ulcers on the feet or legs and not anywhere else.

Some people think ulcers heal faster using this membrane but others do not think so. It has not yet been properly tested. That is what this study aims to do, a ‘fair test’ to see if this membrane really does make healing faster.

Who can participate?
Adult patients with ulcers on their legs or feet

What does the study involve?
Participants are randomly allocated to one of two groups. One group will have blood taken from their vein in order to create a membrane. Participants in this group will have dressing changes every 3 or 4 days, during this a membrane will be placed over the ulcer. The second group will have dressing changes as normal without the membrane being created or placed.

What are the possible benefits and risks of participating?
The possible risk for participants is an infection of the wound and anaemia (lowered numbers of red blood cells or a lowered ability of red blood cells to carry oxygen). But there is minimal chance of infection as we use the patient's own blood during the procedure, and we use vitamins (Iron and Folic acid) from the day of enrolment to prevent anaemia.

The possible benefit for the participants is fast healing of the wounds without any surgical procedure like skin grafts.

Where is the study run from?
The study is being conducted at and organised by the Anandaban Hospital, The Leprosy Mission Nepal (Nepal) in collaboration with the University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
From July 2020 to December 2023

Who is funding the study?
The National Institute for Health Research (NIHR) Research and Innovation for Global Health Transformation (RIGHT) Programme (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
NIHR RIGHT Leprosy and BU Research Protocol WP3 Efficacy Trial, NHRC 303/2020 P

Study information

Scientific Title
Trial of Autologous Blood products to promote ulcer healing in LEprosy: TABLE

Acronym
TABLE

Study objectives
To evaluate the efficacy of L-PRF on healing rates for leprosy ulcers and on the duration of hospital stay in a randomised controlled trial.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 20/05/2020, Science, Technology, Engineering and Mathematics Ethical Review Committee, University of Birmingham (Room 137 C Block Dome, Aston Webb Building, University of Birmingham, Edgbaston B15 2TT UK; +44 (0)121 414 8825; s.l.cottam@bham.ac.uk), ref: ERN_19-1960

Study design
Randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Non-healing skin ulcers in patients with leprosy

Interventions
Participants will be individually randomized at a ratio of 1:1 to one of two groups:
1. Platelet enriched plasma
2. Control

The patient enriched plasma intervention uses the patient's own blood to prepare strips of leukocyte and platelet-rich material (L-PRF) to apply to wounds. The maximum volume of blood taken at one time is 80ml depending on the size of the ulcer. Blood will be taken twice per week at the time of dressing change in the intervention group. The control group will have only Normal saline dressing. All patients (including those in the control group) will be given iron and folic acid tablets. Patients in both groups have twice-weekly dressing changes during their hospital stay until ulcers are healed. The whole procedure is done in line with universal safety

precautions using sterile technique for procedure. Blood collection from patients, centrifuge procedure, and application of L-PRF is done in a minor operation room with sterile technique. All the patients will be followed up at 6 months from randomization.

Randomization:
The randomization procedure will follow a “digital sealed envelope” method since patients are enrolled sequentially, over time, into the trial. An allocation table will be generated at the University of Birmingham by the trial statistician to give a 1:1 ratio to treatment and control groups over the course of the trial. A random number generator will be used to generate a random sequence of the numbers 1 to N which will be used to ‘shuffle’ the list of treatment and control indicators. No blocking or other modifications to this table will be used. The generated table will be uploaded into the REDCap software to be used for patient enrolment and baseline. Trial staff in Nepal will not have access to the allocation table. When a patient’s details are irreversibly submitted, the trial arm and a unique study number will be assigned and revealed to the local clinician so that the randomized group that the patient is assigned to cannot be tampered with.

Assessment:
Photographic data are collected at each dressing change – twice per week. The research fellow will record data at each of these dressing changes by completing a form on the electronic tablet. The type of treatment administered (i.e. intervention or control) will be recorded so that adherence to allocated treatment can be observed. A short clinical form will also be completed at each dressing change to record the clinical appearance of the wound (e.g. any residual exudate) and the time taken to complete the dressing change (from patient entering to leaving the room).

Ulcer metrics will be based on photographs taken during dressing changes in a standardised manner, as recommended in the literature. The photographs will be obtained in Nepal by researchers employed on the grant using the camera in the data collection tablet. A clean ruler is placed in the photograph frame at the level of the ulcer. The trial number will be linked electronically to each frame. The photographs will be assessed completely independently of the local research site in Nepal by a research fellow at the University of Birmingham. This will ensure that the main outcomes are assessed blind to intervention status. In Nepal the photographs will be assessed (i.e. ulcer size measured) in two ways. First, a research fellow, not involved in the patient’s treatment, will measure the length and breadth from which area may be estimated. Second, we will use a validated software tool to measure ulcer surface area – the ARANZ tool (Silhouette Wound assessment tool). This dual assessment and dual site assessment will be of methodological interest. None of the pictures or videotapes will include patient identification information apart from the patient’s trial number. From the imagery we will determine the area of the wound (cm2) at each time point and from that determine the change in surface between two observation points. The outcome is a repeated measure within each trial participant.

The above photographic observations will be taken at dressing changes twice per week during inpatient stay from intervention and control patients. The proportion of ulcers healed at 70 days is a study end point. The majority of patients will be discharged at this point. They will either return to hospital for a follow-up appointment, or a home visit will be made by the local research fellow.

Quality of life measurements will be observed fortnightly by research fellow while the patient is in hospital and then at 70 days and 6 months from randomization. We will use the Health questionnaire -EQ5D3L for this Quality of life measurement.

Intervention Type
Biological/Vaccine

Phase
Phase III

Drug/device/biological/vaccine name(s)
Platelet enriched plasma

Primary outcome(s)
For all outcome measures, healing is defined as the complete re-epithelialization of the index ulcer
1. Rate of healing based on two observations per week (cm^2 per unit time) measured from an independent assessment and software assessment (the ARANZ tool) of photographs where a clean ruler is placed at the level or the ulcer taken during dressing changes twice weekly between baseline and 70 days
2. Proportion healed at 42 days measured by from an independent assessment and software assessment (the ARANZ tool) of photographs at 42 days
3. Time to healing (days) measured by from an independent assessment and software assessment (the ARANZ tool) of photographs from baseline to 70 days, or until the ulcer is healed

Key secondary outcome(s))
1. Proportion healed at 70 days measured by from an independent assessment and software assessment (the ARANZ tool) of photographs at 70 days
2. Generic quality of life measured using a Nepalese version of the EuroQoL five-dimensional instrument (EQ-5D 3L) fortnightly between baseline and discharge and at 70 days
3. Long-term end-points measured at 6 months from randomization
3.1. Recurrence of same/different ulcer measured using investigator notes and the Follow up Clinical Record Form at 6 months
3.2. Anatomical changes in the limb measured using investigator notes and the Follow up Clinical Record Form at 6 months
3.3. Generic quality of life measured using a Nepalese version of the EuroQoL five-dimensional instrument (EQ-5D 3L)
4. Days hospitalized, both duration of initial admission and total, measured from patient notes at discharge and at 6 months
5. Health economic outcomes:
5.1. Number of visits to any healthcare facility from discharge to the end of follow-up assessed from patient notes at 6 months
5.2. Time taken to change dressings assessed from investigator notes during twice weekly dressing changes between baseline and discharge

Completion date
31/12/2023

Eligibility

Key inclusion criteria
1. Chronic trophic ulcer on the feet or legs
2. Aged ≥18 years at the time of signing the informed consent

3. No blood-related abnormalities, haemoglobin (Hb) >9 g%, and Platelets >100 x10^3 /µl
4. No other health-related complications and any other severe chronic illness (such as HIV, chronic Hepatitis B, chronic Hepatitis C, or TB patients under active treatment)
5. Ulcer surface area should be between 2 cm^2 and 20 cm^2
6. Ulcer should be clean, dry and free from infection
7. Understands and voluntarily signs an informed consent document prior to any study-related assessments
8. Able to adhere to the study schedule and other protocol requirements

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
130

Key exclusion criteria
1. Any significant medical condition, laboratory abnormality, or psychiatric illness that would prevent the participants from participating in the study
2. High blood pressure (>150 mmHg systolic)
3. Pregnant or breastfeeding
4. Erythema Nodosum Leprosum (ENL) or a leprosy reaction under steroid treatment
5. Any wound that has a clinical diagnosis of microbial infections

Date of first enrolment
15/09/2020

Date of final enrolment
24/05/2022

Locations

Countries of recruitment
Nepal

Study participating centre
Anandaban Hospital
The Leprosy Mission Nepal

Satdobato Road
Lalitpur
Nepal
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Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
UK National Institute for Health Research (NIHR) Research and Innovation for Global Health Transformation (RIGHT) Programme

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Chief Investigator Professor Richard Lilford (r.j.lilford@bham.ac.uk). The data will be made available after the analysis and result dissemination is over. The data will be available for a period of 10 years after the study ends. Only anonymised data will be made available. Those accessing the data will abide by the same rules as are applicable throughout the project. Consents from participants have been already received to use the data for further research activities being held in future.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		02/05/2024	03/05/2024	Yes	No
Protocol article		15/07/2021	03/09/2021	Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes