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Haemoglobin application to wounds study: A research trial of Granulox haemoglobin spray in addition to standard treatment for healing of diabetic foot ulcers

Submission date
31/07/2017

Recruitment status
No longer recruiting

Registration date
03/08/2017

Overall study status
Completed

Last Edited
21/10/2022

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Diabetes can lead to various complications in affected people, including diabetic foot ulcer (DFU). This causes a broken area in the foot that is unable to heal due to uncontrolled blood sugar levels. If a DFU develops, it is important to treat it appropriately in order to increase the chance of the DFU healing and minimise the risk of infection. Putting on dressings could reduce the strain on the wound area and keeps it clean. To allow the best healing of the wound, it is essential to have sufficiently high oxygen levels. Hypoxia (oxygen deficiency), can lead to necrosis (a death of cells or tissues) and make the wound worse. Oxygen promotes the formation of new blood vessels and subsequently the growth of new skin. New treatment types have been introduced to increase oxygen levels in wounds, including hyperbaric oxygen (HBO) treatment. However, such treatments tend to be cumbersome, time-intensive and costly. In the UK, InFirst Ltd has brought to market a new medical device for oxygen treatment, which is designed to be more straightforward to apply than HBO. The product, Granulox, contains porcine haemoglobin (made from the part of blood that carries oxygen) contained in a spray canister. It is applied twice weekly to a DFU wound during redressing, and can be used in a clinic or patient's home setting. Initial case series and retrospective comparative studies have shown that Granulox reduces the time for a DFU to heal. The aim of this study seeks to assess if Granulox has a significant positive impact on the rate of wound healing in DFUs.

Who can participate?
Adults aged 18 and older who have a DFU.

What does the study involve?
There are two stages of the study: the screening phase and the intervention phase. In the screening stage participants provide information about their wound and other health-related questions. Participants also have an ankle-brachial pressure measurement and a blood sample taken to measure their HbA1c levels. They have the size of the DFU measured. Participants attend a second appointment where they have their DFU measured again. If the wound has

healed less than 30% in the last two weeks, then the participant is eligible for the next phase of the study. Participants are then randomly allocated to one of two groups. Those in the first group receive treatment as usual. Those in the second group receive the usual treatment as well as the Granulox treatment, which is sprayed on the DFU wound twice per week for 12 weeks. Participants attend appointments at week three, six, nine and 12 to have their DFU measurement. Participants also complete four pain and quality of life questionnaires. Participants receive telephone calls after the study to see if the DFU has healed.

What are the possible benefits and risks of participating?
Participants may benefit from improvements in DFU wound healing. There are no notable risks however there is a risk of allergic reactions to the Granulox spray, however only a small amount is sprayed on the wound. Granulox is a licensed medical device with a CE mark so there should be no risk of infection from the medical device itself.

Where is the study run from?
1. Flatt Walks Community Health Centre (UK)
2. Workington Community Hospital (UK)

When is the study starting and how long is it expected to run for?
July 2017 to November 2018

Who is funding the study?
Infirst Healthcare Limited (UK)

Who is the main contact?
Dr Leon Jonker
leon.jonker@nihr.ac.uk

Contact information

Type(s)
Public

Contact name
Dr Leon Jonker

ORCID ID
https://orcid.org/0000-0001-5867-4663

Contact details
Science & Innovation Manager
Cumbria Partnership NHS Foundation Trust
R&D Department
The Carleton Clinic
Carlisle
United Kingdom
CA1 3SX
+44 176824 5975
leon.jonker@nihr.ac.uk

Additional identifiers

Protocol serial number
35097

Study information

Scientific Title
Haemoglobin Application to Wounds Study, a single-centre, controlled, prospective, randomized trial of Granulox haemoglobin spray for adjuvant treatment of diabetic foot ulcers

Acronym
HAWS

Study objectives
The aim of this randomised, controlled, prospective clinical trial is to determine the efficacy of the Granulox haemoglobin spray device as an adjuvant therapy for DFU, with a primary outcome measure of DFU healing at 12 weeks of treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East Midlands - Leicester South Research Ethics Committee, 17/07/2017, 17/WM/0244

Study design
Randomised; Interventional; Design type: Treatment, Device

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Specialty: Diabetes, Primary sub-specialty: Both; UKCRC code/ Disease: Metabolic and Endocrine/ Diabetes mellitus

Interventions
Following written consent, participants are observed for two weeks to establish healing rate. At the end of two weeks, patients are only eligible for the intervention phase if their wound has healed <30% in the preceding two weeks. This point is deemed as the the baseline and participants are allocated at random to the control or Granulox intervention group, using a randomised sequence from the freeware randomisation programme. The randomisation is stratified for ulcer size, with an ulcer size of below and above 3cm2 as the cut-off. This size is has been determined as the average size of a presenting DFU previously.

Sequential envelopes with each next randomisation allocation are used to achieve concealment and these are kept in the research department. The researcher then informs the regular healthcare professional for the participant in question, and the participant themselves, which

treatment they've been allocated to. As the study involves administration of a spray it is not possible to achieve blinding for the participants nor the researchers – it is recognised that this increases the risk of bias.

Treatment as usual arm: Patients are in the study for a period of 18 weeks, once they've qualified after the 2 week screening phase (ie their wound has insufficiently healed). Thereafter, the patient is followed up as they would be in normal clinical practice. In practice this means that for almost all patients this involves dressing of the DFU, and advice on off-loading of the affected area. For the latter, specialist footwear may be prescribed, or a foot/leg brace. During and after the trial, clinical staff redress the DFU as per routine care, and during the trial they conduct the measurement of the DFU (grid measurement tool and PUSH score). The researcher is in attendance at the beginning of the observation two weeks, baseline, and weeks three, six, nine, and 12 of study participation to randomise the patient, and conduct/collect the study participant questionnaires. The researcher phones the participant at week 18 to check on wound status and any adverse event reporting.

Granulox arm: Participants undergo the same steps as the treatment as usual arm. The only additional intervention is that Granulox is sprayed on the wound twice weekly. Where possible, this is fitted in with standard clinic appointments that the patient may have, and when dressings are changed anyway so that the wound is accessible. The Granulox treatment is done twice week for 12 weeks maximum, for around 24 applications. If the wound heals before 12 weeks have passed, then Granulox treatment will cease.

Intervention Type
Other

Primary outcome(s)
Efficacy of the Granulox spray in terms of wound healing is assessed using the DFU size, measured with Convatec grid tool at -2 weeks (two weeks observation), baseline, week three, six nine and 12.

Key secondary outcome(s))
1. Size and characteristics of DFU is measured using the PUSH score at -2 weeks (two weeks observation), baseline, week three, six nine and 12
2. Grading of DFU is assessed using Texas Univ grading score at -2 weeks (two weeks observation), baseline, week three, six nine and 12
3. Wound closure status is assesed as either open or closed by clinician at baseline, week three, six, nine and 12
4. Patient mobility score is measured using the LifeSpace questionnaire at baseline, week six and 12
5. Pain related to DFU is measured using the Visual Analogue Pain score at -2 weeks (two weeks observation), baseline, week three, six nine and 12
6. General Quality of life score is measured using the EQ5D-5L and wound-related quality of life score as measured by Charing Cross Venous Ulcer Questionnaire at baseline, week six and 12
7. Wound status check [healed, not healed, recurrence] and any incidences of adverse events at week 18
8. Patient withdrawal rates due to change in management (e.g. need for surgery)

Completion date
31/01/2019

Eligibility

Key inclusion criteria
1. Clinical diagnosis of Diabetic Foot Ulcer (DFU), present on plantar or calcaneus area
2. DFU present for at least 2 weeks.
3. Adult patients aged > 18 years
4. Patients with recurrent wounds, including multiple wounds, are eligible. The largest of the wounds, in plantar or calcaneus area, will be selected for the trial.
5. Patients who have undergone an episode of infection prior to the enrolment but are not currently receiving antibiotic therapy or antimicrobial dressings for the DFU in question are eligible – i.e. where a previous infection has resolved.
6. Mental capacity to give consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
79

Key exclusion criteria
1. Under the age of 18 years
2. Unable to fully understand the consent process and provide informed consent due to either language barriers or mental capacity
3. Limited life expectancy, i.e. undergoing palliative care
4. Active infection in DFU
5. Systemic antibiotic treatment
6. Any personal objection to being administered a product containing porcine material.
7. Patients who are participating in another research study involving an investigational product.
8. The patient has concurrent (medical) conditions that in the opinion of the investigator may compromise patient safety or study objectives, including alcohol or drug dependency.
9. DFU in other area of the foot (e.g. in between toes, which would make exact ulcer size measurement impossible)
10. Patient pregnant or lactating
11. Ankle brachial index < 0.5, measured within 3 months of baseline visit

Date of first enrolment
07/08/2017

Date of final enrolment
30/09/2018

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Flatt Walks Community Health Centre
Podiatry Service
3 Castle Meadows
Cumbria
Whitehaven
United Kingdom
CA28 7QE

Study participating centre
Workington Community Hospital
Podiatry Service
Park Lane
Workington
United Kingdom
CA14 2RW

Sponsor information

Organisation
Cumbria Partnership NHS Foundation Trust

Funder(s)

Funder type
Industry

Funder Name
Infirst Healthcare Limited

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary

Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/09/2021	21/10/2022	Yes	No
Participant information sheet	Participant information sheet version 6	11/11/2025	11/11/2025	No	Yes
Protocol file		10/07/2018	14/10/2022	No	No