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Effect of FlowOx™ treatment on healing of lower limb ischaemic ulcers

Submission date
27/03/2017

Recruitment status
No longer recruiting

Registration date
02/05/2017

Overall study status
Completed

Last Edited
03/03/2020

Condition category
Circulatory System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Peripheral arterial disease (PAD) is a common condition in which the blood flow to the legs is restricted. This happens because of the buildup of a fatty substance (plaque) on the walls of arteries. Over time this can cause the main arteries in the legs to become narrowed (stenosed) or blocked (occluded). This can cause a severe cramping pain in the legs when exercising (claudication), as the restricted blood flow cannot deliver enough oxygen to the leg muscles. As the arteries become narrower, patients begin the feel pain even when at rest and are at severe risk of developing ulcers or gangrene (critical limb ischaemia), which in severe cases can lead to amputation. Many patients are treated with blood thinning medication or surgery to restore blood flow to the leg (revascularisation), however these treatments are not always successful. The development of home-use devices that apply compression to the foot or leg have been shown to improve blood flow, however there are safety risks associated with these devices as well as a lack of robust clinical evidence showing their effectiveness. Intermittent negative pressure (INP) is a new treatment system which works by applying oscillating (moving back and forth) pressure inside a boot which downs blood down the leg, improving circulation. The aim of this study is to look at the effectiveness of INP in the treatment long-term wounds caused by critical limb ischaemia.

Who can participate?
Adults with PAD who have been diagnosed with critical limb ischaemia and leg ulcers.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group are given a FlowOx™ device to take home and use for up to two hours every day for the duration of the study. Training to use the device will be provided on the first study appointment. The FlowOx treatment involves placing the leg in the FlowOx boot in a seated position and switching the device on at the main unit. Those in the second group will receive standard care, which involves assessment of the lower limb and ulcer and dressing the ulcer. At the start of the study and then after one, two and three months, participants in both groups are examined and complete a range of questionnaires to assess whether their condition has improved.

What are the possible benefits and risks of participating?
Participants are likely to benefit from a reduction in the size of the ulcer or healing it completely. There may also be a reduction in leg pain. However, this cannot be guaranteed. The information gained from this study may help to improve the treatment of ulcers of this kind better in the future. With regards to the FlowOx™ treatment there are some low risk potential side effects. There is a chance that any dressings worn during the treatment could be dislodged whilst putting the boot on and taking it off. If this should happen, participants will be encouraged to replace the dressings starting the treatment. Because of the suction pressure applied during the treatment, there is a possibility that the dressings may soak up wound fluid quicker than usual. If this happens the participant will need to dress the ulcer more frequently. There is a chance that the padding in the boot may cause skin irritation. The risk for this is low as medical grade materials are used for these parts. However, if any discomfort or irritation of the skin is experienced participants will be asked to stop using the device immediately and contact the vascular clinic, Research Assistant or the local Acute Response Services at the NHS site.

Where is the study run from?
1. Royal Oldham Hospital (UK)
2. Centre for Health Sciences Research, University of Salford (UK)

When is the study starting and how long is it expected to run for?
August 2016 to September 2019

Who is funding the study?
European Union (Belgium)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

Integrated Research Application System (IRAS)
214180

Protocol serial number
31847, IRAS 214180

Study information

Scientific Title
Pilot study to test the clinical efficacy of FlowOx™ home treatment compared to standard care in patients with critical limb ischemia and lower limb ulcers

Study objectives
The aim of this study is to test the effects of intermittent negative pressure (INP) therapy (trade name FlowOx™) on lower limb chronic ischaemic wounds compared to standard treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central – Oxford C Research Ethics Committee, 30/03/2017, ref: 17/SC/0089

Study design
Randomised; Interventional; Design type: Treatment, Process of Care, Device, Physical, Active Monitoring

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Specialty: Cardiovascular disease, Primary sub-specialty: Atherothrombosis; UKCRC code/ Disease: Cardiovascular/ Diseases of veins, lymphatic vessels and lymph nodes, not elsewhere classified

Interventions
Participants will be randomised with a 2:1 weighting between the two groups: FlowOx™ and standard clinical care, respectively. The random allocation sequence will be generated by the study statistician using block randomisation with randomly permuted block sizes. Allocations will be concealed in sequentially numbered, opaque, sealed envelopes kept at the University of

Salford. The allocations will be concealed from the RA enrolling the participants to the study. Once a patient is ready to be randomised, the RA recruiting the patient will ring the secure randomisation telephone number at the University of Salford for the treatment allocation.

Test intervention: FlowOx™ home treatment device. Daily use up to 2 hours per day for the duration of the study (3 months)

Control intervention: Standard clinical care of lower limb symptoms and wounds for the duration of the trial period (3 months)

Follow ups for all participants takes place 1, 2 and 3 months after baseline. The Test Intervention Group will receive a phone consultation 24 hours and 1 week after baseline to check for any usability or safety issues.

Intervention Type
Other

Primary outcome(s)
Ulcer size is measured using 3D camera images at baseline and 3 months.

Key secondary outcome(s))
1. Clinical improvement, defined as improvement in Rutherford and WIfI grading systems, is assessed by CRF at baseline, 1, 2 and 3 months
2. Bilateral Ankle Brachial Pressure Index (ABPI) is calculated by dividing the systolic blood pressure at the ankle (posterior tibial artery or dorsalis pedis artery) by the systolic blood pressure in the arm (brachial artery) at baseline, 1, 2 and 3 months
3. Bilateral Toe Brachial Pressure Index (TBPI) is measured by dividing the systolic blood pressure at the toe by the systolic blood pressure in the arm (brachial artery) at baseline, 1, 2 and 3 months
4. Rest pain is measured using centimeter Visual Analogue Scale (VAS) at baseline, 1, 2 and 3 months
5. Lower limb amputation incidence is measured by reviewing clinical records and CRF at baseline, 1, 2 and 3 months
6. Quality of life is measured using the VascuQol questionnaire at baseline, 1, 2 and 3 months
7. Generic health-related quality of life is measured using the EQ-5D-5L questionnaire at baseline, 1, 2 and 3 months
8. Quality of sleep is measured using the Pittsburgh Sleep Quality Index (PSQ) at baseline, 1, 2 and 3 months
9. Adherence to treatment program is assessed using FlowOx™ USB data and patient reports at baseline, 1, 2 and 3 months
10. Device usability data is measured using the QUEST questionnaire at baseline, 1, 2 and 3 months
11. Comfort is measured using the FlowOx™ comfort and usability questionnaire at baseline, 1, 2 and 3 months
12. Cost effectiveness (including capability outcome measures) are measured by ICECAP at baseline, 1, 2 and 3 months

Completion date
27/09/2019

Eligibility

Key inclusion criteria

Current participant inclusion criteria as of 07/08/2018:
1. Recent successful lower limb revascularization procedure
2. Male and female patients, aged 18 years and over with PAD, including patients with diabetes
3. Capacity to understand the nature of the study and provide informed consent
4. Diagnosis of critical lower limb ischaemia based on clinical signs and symptoms and confirmed by diagnostic imaging such as Duplex/computer tomographic angiography/magnetic resonance angiography/digital subtraction angiography
5. Critical lower limb ischaemia classified as based on recommendations of STAMP (43)
6. Critical limb ischaemia, Absent foot pulses AND monophasic or absent Doppler signals PLUS 2 of: Ischaemic Rest Pain, Ankle systolic
7. Grade 0 - 2 wound of the lower extremity (according to the WIfI, grading system (44)) present and non-healing for at least 6 weeks (45).
8. Treated foot/shoe size ≤ 46 (European size), which corresponds to approximate foot length ≤ 29.5 cm. This is required for the correct fitting of the FlowOx™ device.
9. Maximum circumference of calf should be 41cm for correct fitting of the FlowOx™ device
Participants who are not suitable for revascularisation but who meet all other inclusion /exclusion criteria will be invited to participate in a case study to evaluate the use of the device.

Previous participant inclusion criteria:
1. Male and female patients, aged 18 years and over with PAD including patients with diabetes
2. Capacity to understand the nature of the study and provide informed consent
3. Diagnosis of critical lower limb ischaemia based on clinical signs and symptoms and confirmed by diagnostic imaging such as Duplex/computer tomographic angiography/magnetic resonance angiography/digital subtraction angiography
4. Critical lower limb ischaemia classified as based on recommendations of STAMP
5. Critical limb ischaemia: absent foot pulses AND monophasic or absent Doppler signals PLUS 2 of: Ischaemic rest pain, ankle systolic <50mmHg, deteriorating wound
6. Grade 0 - 2 wound of the lower extremity (according to the WIfI, grading system) present and non-healing for at least 6 weeks.
7. Treated foot/shoe size ≤ 46 (European size), which corresponds to approximate foot length ≤ 29.5 cm. This is required for the correct fitting of the FlowOx™ device
8. Maximum circumference of calf should be 36cm for correct fitting of the FlowOx™ device
9. Patients not eligible for (or have declined) revascularization or other operative/interventional procedures OR have had operative/interventional procedures for the limb ischaemia which have failed

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

Total final enrolment
19

Key exclusion criteria
1. Pressure ulcers
2. Venous ulcers
3. Patients with the following: vasospastic and collagen vascular disease; vasculitis; acute limb ischaemia; atheroembolic disease, and arterial trauma.
4. Patients with active eczema, psoriasis or any inflammatory skin conditions
5. Patients with a history of recent above or below knee DVT
6. Patients with a with a history of multiple DVT in the past
7. Critical limb ischaemia that is limb threatening and requires immediate assessment and surgery by a vascular surgeon (the priority is to save the limb in this case).
8. Recent or anticipated (in the next 6 months) major surgery or lower extremity revascularisation
9. Current cardiac rehabilitation (these programmes involve exercise regimes which will alter ischemic limb signs and symptoms)
10. Currently participating in a study evaluating other treatments for lower limb ischaemia
11. Cellulitis
12. Unable, unwilling or does not have the capacity to give informed consent
13. Unable to don or doff the FlowOx system at home independently or with the help of a family member (aid).
14. Those with cancer, or those who are pregnant

Date of first enrolment
15/05/2017

Date of final enrolment
28/02/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Oldham Hospital
Rochdale Road
Manchester
United Kingdom
OL1 2JH

Study participating centre

University of Salford
Centre for Health Sciences Research
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Sponsor information

Organisation
University of Salford

ROR
https://ror.org/01tmqtf75

Funder(s)

Funder type
Government

Funder Name
European Union

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes