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Efficacy of non-thermal gas plasma on sub-clinical wound infection (biofilm) in patients with diabetic ulcers

Submission date 14/10/2016	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 20/10/2016	**Overall study status** Completed	
Last Edited 02/06/2023	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
People living with diabetes often have to live with long-term complications of the disease. One of the most common, disabling and costly complications are foot ulcers which do not heal. Infections of diabetic foot ulcers are a major cause of amputation and death. In many cases, the infection is resistant to antibiotic treatment, which can make them very difficult to treat. The infected wounds are also slow to heal due to a layer of bacteria on the surface of the wound called biofilms. Non-thermal gas plasma (NTGP) is known to be an effective and safe treatment for chronic (long term) infected wounds and does not lead to antibiotic resistance. This type of treatment consists of a five minute 'blast' of gas plasma held over the infected wound. The treatment head on the device contains a patented ionization chamber that bombards Argon gas (an unreactive gas) with electrons (negatively charged particles) emitted from multiple hot electric filaments. The resulting plasma ions mix with air creating reactive agents to generate a wide, constant treatment field that is capable of treating large tissue areas. The aim of this study is to find out if NTGP is an effective treatment for diabetic foot ulcers and establish a solution to a real life situation.

Who can participate?
Adults with diabetes, who have foot ulcers where healing is stalled for at least 4 weeks.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group receive standard wound care dressing twice per week. This involves having the wound cleaned with sterile water or normal saline (salt water) and then dressed with the usual dressing used at that site. Those in the second group also receive standard wound care dressing twice per week with the addition of NTGP. This involves five minutes of applying argon gas directly over the wound after it has been cleaned, before it is dressed. Participants in both groups have samples taken from the wound at the start of this study and then after 4 weeks in order to measure the amount of bacteria present on the surface of the wound. Photographs are also taken every week for four weeks in order to assess healing.

What are the possible benefits and risks of participating?
Participants who receive the NTGP treatment may benefit from improved quality of life as the technology should reduce stress, trauma and recovery time. There are no notable risks involved with participating.

Where is the study run from?
Leeds Teaching Hospital NHS Trust, UK
(updated 17/07/2019, previously: Salford Royal NHS Foundation Trust (UK))

When is study starting and how long is it expected to run for?
August 2016 to January 2018

Who is funding the study?
1. Innovate UK (UK)
2. Adtec Europe Limited (EU)

Who is the main contact?
Mrs Mary McGovern
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Contact information

Type(s)
Public

Contact name
Mrs Mary McGovern

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
59178-445167

Study information

Scientific Title
A randomised controlled trial to evaluate the efficacy of non-thermal gas plasma (NTGP) on sub-clinical wound infection (biofilm) in patients with diabetic foot ulcers compared to those treated with standard of care dressings

Acronym
Biofilm Project

Study objectives
The healing of chronic wounds that are stalled by sub clinical wound infection (biofilm) can be accelerated following intervention with non-thermal gas plasma.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East Midlands - Leicester South Research Ethics Committee, 20/01/2017, ref: 16/EM/0476
Health Research Authority, 25/01/2017, IRAS project ID: 198288

Study design
Single-centre prospective randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
Not available in web format. Please use contact details to request a participant information sheet. Telephone: 0113 392 3951, Email: leedsth-tr.VascularResearch@nhs.net

Health condition(s) or problem(s) studied
Chronic diabetic foot ulcers

Interventions
Participants are randomised to one of two groups using sealed, opaque sequentially numbered envelopes (SNOSE)

Intervention group: Participants receive local standard of care wound dressing (SOCD) plus 5 minutes treatment of NTGP twice weekly over a period of 30 days (4 weeks). SOCD involves cleansing the wound with sterile water or normal saline and then dressed with the local standard

of care dressing e.g. Aquacel Foam non-adhesive, Aquacel Foam adhesive, Biatain foam non adhesive, Biatain Foam adhesive. NTGP involves a two minute treatment of argon gas plasma directly over the wound.

Control group: Participants only receive local standard of care wound dressing (SOCD) twice weekly. This involves cleansing the wound with sterile water or normal saline and then dressed with the local standard of care dressing e.g. Aquacel Foam non-adhesive, Aquacel Foam adhesive, Biatain foam non adhesive, Biatain Foam adhesive.

Follow up for all study participants will occur after the 4 weeks, last samples and digital photographs will be taken at this time and participants will be informed when the results of the study will be completed and published.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
-

Primary outcome measure
Wound volume is measured using digital photographic imaging that will record, and measure the wound bed tissue type, wound dimensions and wound volume at baseline, 1, 2, 3 and 4 weeks.

Secondary outcome measures
1. The effect of gas plasma in regards to accelerated healing is measured using wound tissue biopsy's and wound slough samples taken from the 60 patients at baseline and week 4
2. Presence of biofilms is measured as the numbers of bacteria and comparison to bacteria quantified from the wound surface, using wound tissue biopsy's and wound slough samples, at baseline and week 4
3. Microbial populations are measured using digital photographic imaging, at baseline week 1, week 2, week 3, week 4 as well as wound tissue biopsy and wound slough samples at baseline and week 4

Overall study start date
01/08/2016

Completion date
31/05/2021

Eligibility

Key inclusion criteria
Inclusion criteria as of 04/04/2017:
1. Male or female,
2. Aged 18 years and over
3. Diabetics with HbA1c less than 10% (<86mm/mol) (Amended 12/09/2017 to Diabetics with HbA1c less than 12% (<108mm/mol)) that has been recorded within the previous 3 months

4. Foot ulcers with University of Texas grade/size A1or A2 or B1* sited below the ankle including plantar, dorsal and heel ulcers
*Texas grade B1 ulcers which have symptoms consistent with mild diabetic foot infection (IDSA 2012)14 including:
4.1. Pus or inflammation
4.2. Inflammation extends less than 2cm from the wound
4.3. Infection is limited to skin/soft tissue
4.4. Systemically well
5. Ulcers with dimension 1.0cm2 – 30cm2
6. Ulcer where there is less than 40% decrease in wound surface area in the previous 4 weeks
7. Ulcer has not been present for more than 2 years
8. If foot pulses not palpable the toe brachial pressure index (TBPI) should be greater than 0.5
9. If TBPI cannot be assessed then the ankle brachial pressure index (ABPI) should be 0.8 or above
10. If ABPI is 1.3 or above the Doppler sounds should be at least biphasic

Original inclusion criteria:
1. Aged 18 years and over
2. Diabetics with HbA1c less than 10% (<86mm/mol) that has been recorded within the previous 3 months.
3. Foot ulcers with University of Texas grade/size A1, A2, B1 sited below the ankle including plantar, dorsal and heel ulcers.
4. Diabetics whose wound/ulcer currently, or in the last 7 days, has symptoms consistent with mild diabetic foot infection (IDSA 2012)14 including:
4.1. Pus or inflammation
4.2. Inflammation extends less than 2cm from the wound
4.3. Infection is limited to skin/soft tissue
4.4. Systemically well
5. Ulcers with dimension 1.0cm2 – 30cm2
6. Ulcer where there is less than 40% decrease in wound surface area in the previous 4 weeks
7. Ulcer has not been present for more than 2 years
8. Adequate blood supply determined by palpable foot pulses or if not palpable a TBPI greater than 0.7
9. Loss of protective sensation to a 10g monofilament
10. Male or female

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
60 patients altogether. 30 patients in each arm will be randomised to receive local standard of care wound dressing (SOCD) or SOCD plus 5 minutes treatment of NTGP 5 twice weekly.

Total final enrolment
21

Key exclusion criteria
Exclusion criteria as of 04/04/2017:
1. HbA1c greater than 10% (>86mm/mol) Amended 12/09/2017: to HbA1c greater than 12% (>108mm/mol)
2. Those with malignancy or other immunosuppressive diseases
3. Those receiving radiotherapy or medications that actively delay healing (e.g. steroids, antimetabolites)
4. Those whose wound/ulcer currently has symptoms consistent with moderate diabetic foot infection (IDSA 201214) – including
4.1. Pus or inflamed wound in a patient who is systemically well and/or one of the following:
4.2. Inflammation extends greater than 2cm from wound
4.3. Lymphangitis
4.4. Localised necrosis/ gangrene
4.5. Involvement of muscle, tendon, joint or bone (active osteomyelitis)
5. Those whose wound/ulcer currently has symptoms consistent with severe diabetic foot infection (IDSA, 2012) as demonstrated by:
5.1. Extensive cellulitis,
5.3. Deep abscess with or without signs of systemic toxicity (fever, vomiting, hypotension, confusion, acidosis, renal failure, severe hyperglycaemia, leucocytosis)
6. Pregnant, or breast feeding
7. Women who are of child-bearing age not using reliable contraception
8. TBPI less than 0.5
9. ABPI less than 0.8
10. If ABPI above 1.3 and vessel sounds are monophasic
11. Those who have clinical evidence of gangrene at any location
12. Those who has a medical condition that in the opinion of the investigator would make the patient an inappropriate candidate for the study
13. Those who have necrotic toes on the study ulcer foot
14. Those who have undergone surgical procedure other than debridement on the study ulcer foot within 3 weeks prior to screening
15. Study ulcer over active Charcot's joint
16. Non study ulcer within 5.0 cm from the study ulcer at enrolment
17. Participation in other clinical study in the last 4 weeks

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5.1. Extensive cellulitis,
5.2. Deep abscess with or without signs of systemic toxicity (fever, vomiting, hypotension, confusion, acidosis, renal failure, severe hyperglycaemia, leukocytosis)
6. Pregnant, or breast feeding
7. Women who are of child-bearing age not using reliable contraception
8. TBPI less than 0.7
9. Those who have clinical evidence of gangrene at any location
10. Those who have a medical condition (e.g. diabetic nephropathy) that in the opinion of the investigator would make the patient an inappropriate candidate for the study
11. Those who have necrotic toes on the study ulcer foot
12. Those who have undergone surgical procedure other than debridement on the study ulcer foot within 3 weeks prior to screening
13. Study ulcer over active Charcot's joint
14. Non study ulcer within 5.0 cm from the study ulcer at enrolment
15. Participation in other clinical study in the last 4 weeks

Date of first enrolment
06/02/2017

Date of final enrolment
31/12/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
St James's Hospital
Leeds Teaching Hospital NHS Trust
Beckett Street
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LS9 7TF

Sponsor information

Organisation
Adtec Europe Limited

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Sponsor type
Industry

Website
http://www.adtecplasma.com/

ROR
https://ror.org/059gjhp96

Funder(s)

Funder type
Government

Funder Name
Innovate UK

Alternative Name(s)
innovateuk

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Adtec Europe Limited

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal and at wound care conferences.

Intention to publish date

31/12/2021

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?
Results article		08/12/2022	02/06/2023	Yes	No
HRA research summary			28/06/2023	No	No