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Cold atmospheric plasma (CAP) for reduction of bacteria in chronic skin wounds – plasma care study

Submission date
27/09/2018

Recruitment status
No longer recruiting

Registration date
15/10/2018

Overall study status
Stopped

Last Edited
20/07/2020

Condition category
Infections and Infestations

[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
Cold atmospheric plasma (CAP, an ionized gas) offers a new method to effectively inactivate bacteria (independent from their antibiotic resistance level) without harming body cells or tissue. This makes cold atmospheric plasmas extremely suitable for different applications in medicine, especially in the field of chronic wounds. Chronic wounds are commonly colonized with microorganisms, and the wound healing process is delayed if more than four different bacterial species are found on a wound. Therefore, general wound management includes strategies for minimizing infection risks as well as prevention of the spread of pathogens throughout the bloodstream to avoid lethal sepsis. One of these strategies is antibiotic treatment. Chronic wound patients are a high-risk group for infection with antibiotic-resistant organisms and new methods, like CAP, for the inactivation of resistant pathogens in wounds are urgently needed. Up to now, there have been only a few clinical trials on patients with wounds using cold atmospheric plasma. More clinical data are urgently needed. Therefore, the aim of this study is to demonstrate that the reduction of bacterial load in chronic skin wounds is larger when using treatment with CAP in addition to standard wound care compared to standard wound care alone.

Who can participate?
Patients aged 18 and over with chronic (existing for over 8 weeks) treatable skin wounds that are colonised with bacteria

What does the study involve?
The study involves a CAP device (plasma care) and a placebo device (identical device but without cold atmospheric plasma/without impact). The placebo is necessary to have a reference in comparison to CAP treatment, meaning a comparison between the effect of standard treatment alone vs the effect of standard treatment and additional cold atmospheric plasma. Each patient is treated with both CAP and placebo on two different wounds. The patient does not know which wound is treated with CAP. Patients are also randomly allocated to 1, 2 or 3 minutes of treatment. Every participating patient also receives the previously used standard treatment and a thorough monitoring of all medical procedures. All patients are followed up to measure the

amount of bacteria in the treated wounds until six consecutive treatment sessions have been performed, which is usually reached two to three weeks after the first treatment session.

What are the possible benefits and risks of participating?
All patients have the benefit of careful standardised monitoring of their treatment and follow-up procedures by their study physicians as in routine clinical care but undergo in addition quality management by the CRO, the sponsor, and the Steering Committee (SC) of the trial. Patients with wounds in the CAP group might benefit from the add-on CAP treatment compared to those with wounds in the routine clinical care group. This is the assumption underlying this study. All medical products (devices and drugs) used in this trial are marketed products used in line with market authorisation and represent standard of care. This also applies to all medical procedures within the trial. Adverse events are expected to occur in similar ways and at a comparable rate as the known adverse events of the approved treatments applied in the trial. Thus, this trial is considered to be low risk with respect to adverse events in the control group. Within previous trials it has been shown that CAP treatment in comparable patients did not lead to any notable side effects, therefore there is no risk related to study treatment. The individual risk of patients concerning the placebo-control wound is equal to the risk in routine clinical care. The placebo device will be used in the same way as the marketed CAP device but with disabled function. The CAP procedure with disabled function does not add risk compared to standard care. Therefore, no additional risk is expected for wounds in the control group. The individual risk of study patients concerning the CAP-treated wound is expected to not be higher compared to the risk of the placebo-treated wound. In previous trials it has been shown that CAP treatment in comparable patients did not lead to any notable side effects.

Where is the study run from?
1. Dermatologische Klinik und Poliklinik - Universitätsklinikum Regensburg (Germany)
2. Klinik für Dermatologie und Allergologie - Klinikum Vest, Recklinghausen (Germany)
3. Dermatologie - Klinikum Lippe, Detmold (Germany)
(updated 20/07/2020, previously:
1. Klinik für Dermatologie und Allergologie - Universitätsklinikum Augsburg
2. Dermatologie - Klinikum Lippe Detmold
updated 11/07/2019, previously:
1. Dermatologische Klinik und Poliklinik - Universitätsklinikum Regensburg (Germany)
2. Klinik für Dermatologie und Allergologie - Klinikum Vest (Germany)
3. Klinik für Dermatologie, Allergologie & Umweltmedizin II - Klinik Thalkirchner Straße (Germany))

When is the study starting and how long is it expected to run for?
July 2018 to September 2020
(updated 11/07/2019, previously: February 2020)

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
PD Dr. Julia Zimmermann
(updated 11/07/2019, previously: Dr Sylvia Binder)

Contact information

Type(s)

Scientific

Contact name
Dr Julia Zimmermann

Contact details
Lichtenbergstr. 8
Garching
Germany
85748

Additional identifiers

Protocol serial number
1

Study information

Scientific Title
Cold atmospheric plasma (CAP) for reduction of bacteria in chronic skin wounds

Acronym
CAP

Study objectives
The trial will demonstrate that the reduction of bacterial load in chronic skin wounds is larger when using treatment with cold atmospheric plasma (CAP) in addition to standard wound care compared to standard wound care alone.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Current ethics approval as of 20/07/2020:
Approved 12/12/2018, Ethikkommission an der Universität Regensburg (93040 Regensburg, Germany)

Previous ethics approval:
Approved 12/12/2018, Ethikkommission an der Universität Regensburg (), ref:

Study design
Prospective multi-arm multi-stage (MAMS) randomised placebo-controlled single-blinded multi-centre superiority trial with medical devices with adaptive design

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic infected wounds

Interventions
Each study patient will serve as his/her own control by performing cold atmospheric plasma (CAP) treatment and placebo treatment on two different comparable wound locations within the same treatment session. Allocation of CAP and placebo treatment to wound locations is determined by randomisation.

A multi-arm multi-stage design has been chosen in order to maximize the methodologic power of the trial. Insufficient data are available before the start of the trial to define one major assumption with acceptable error margin: the optimal duration of CAP treatment per session in relation to maximal reduction of bacterial load.

Thus, patients will be equally randomised to three different groups with 1, 2 or 3 minutes duration of study treatment. In each patient in addition to standard wound care, CAP treatment (index device) and no CAP treatment (placebo device) will be randomly allocated to two comparable, numbered wound locations. Patients will be blinded for the type of treatment they receive on the two different wound locations within the same treatment session but treating physicians will know.

All randomised patients will usually be followed for the primary endpoint until six consecutive treatment sessions have been performed which is usually reached two to three weeks after the baseline treatment session. Secondary endpoints will be followed for a maximum of 12 weeks.

At least two planned unblinded interim analyses will be performed within the trial:

After about 10 patients have been enrolled and treated in each treatment duration group with study treatment according to protocol for at least 3 treatment sessions (within about one week of study treatment) enrolment of new patients will temporarily be ceased. The results for the primary endpoint after the first 3 treatment sessions of each patient will be assessed to determine which of the 3 treatment duration groups (1, 2 or 3 minutes) reveals the optimal duration of CAP treatment per session in relation to maximal reduction of bacterial load. Based on this analysis the SC will decide which stratum will be continued for further patient recruitment whilst the other two strata will be closed. However, all patients enrolled so far will be treated and followed according to protocol.

After study data for baseline and maximal follow-up of the primary endpoint of about 75% of study patients to be enrolled are available, the results for the primary endpoint will be assessed. The number of study patients needed might be adapted as a consequence of this analysis.

Intervention Type
Device

Primary outcome(s)
Current primary outcome measure:
Reduction of bacterial load in treated wounds: The difference between count of colony forming units (CFUs) in nitrocellulose contact smear filter culture immediately before and after study treatment, expressed as percentage of CFUs immediately before each study treatment.

Previous primary outcome measure:
1. Reduction of bacterial load in treated wounds: The difference between count of colony forming units (CFUs) per cm2 in nitrocellulose filter culture immediately before and after study treatment, expressed as percentage of CFUs per cm2 immediately before each study treatment session.
2. Time to optimal reduction of bacterial load: The timepoint after which the following reduction of bacterial load is smaller than 10% of the CFUs per cm² immediately before each study treatment session.

Key secondary outcome(s))
Followed for a maximum of 12 weeks:
1. Intensity of pain assessed with standardized visual analogue scale at each treatment session
2. Assessment of safety by means of reported SAEs and AEs of special interest

Completion date
04/05/2020

Reason abandoned (if study stopped)
Participant recruitment issues and complete recruitment stop during the coronavirus (SARS-CoV-2) pandemic in 2020

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 20/07/2020:
1. Age ≥ 18 years
2. Chronic (existing >8 weeks) treatable skin wound(s) of one or more of the following origins: arterial, venous, infectious, diabetic, neuropathic, traumatic
3. Chronic skin wound(s) colonised with bacteria, as confirmed by CFU count in nitrocellulose filter culture
4. Signed informed consent
5. Two comparable treatment sites, resulting of chronic, colonized skin wounds:
5.1 Two wounds each of a size of at least approx. 1.5 cm x 1.5 cm, or
5.2 One separable wound of a size of at least approx. 1.5 cm width and at least approx. 6 cm length

Previous participant inclusion criteria as 0f 11/07/2019:
1. Age ≥ 18 years
2. Chronic (existing >8 weeks) treatable skin wound(s) of one or more of the following origins: arterial, venous, infectious, diabetic, neuropathic, traumatic
3. Chronic skin wound(s) colonised with bacteria, as confirmed by CFU count in nitrocellulose filter culture
4. Signed informed consent
5. Two comparable treatment sites, resulting of chronic, colonized skin wounds:
5.1 Two wounds each of a size of at least approx. 2 cm x 2 cm, or
5.2 One separable wound of a size of at least approx. 2 cm width and at least approx. 8 cm length

Previous participant inclusion criteria:
1. Age ≥ 18 years
2. Chronic (existing >8 weeks) treatable skin wound(s) of one or more of the following origins:

arterial, venous, infectious, diabetic, neuropathic, traumatic
3. Chronic skin wound(s) colonised with bacteria, as confirmed by CFU count in nitrocellulose filter culture
4. Signed informed consent
5. 2 comparable treatment sites, each of a size of at least approx. 2 cm x 2 cm (2 wounds OR one large separable wound)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
11

Key exclusion criteria
1. Wounds with tumor origin
2. Wounds of vasculitic genesis
3. Pyoderma gangrenosum
4. Drug abuse or clinically manifest alcohol abuse
5. Participation in another clinical trial, either within the past 2 months or still ongoing
6. Previous participation in plasma care study

Date of first enrolment
01/07/2019

Date of final enrolment
04/05/2020

Locations

Countries of recruitment
Germany

Study participating centre
Klinik und Poliklinik für Dermatologie - Universitätsklinikum Regensburg
Franz-Josef-Strauss-Allee 11

Regensburg
Germany
93053

Study participating centre
Dermatologie - Klinikum Lippe, Detmold
Röntgenstr. 18
Detmold
Germany
32756

Study participating centre
Klinik für Dermatologie und Allergologie - Klinikum Vest
Dorstener Str. 151
Recklinghausen
Germany
45657

Sponsor information

Organisation
Terraplasma medical GmbH

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to the data protection act. All data obtained in the context of the clinical trial are subject to data protection. This applies to patients' data as well as to investigators' personal data which may be included in any database of the sponsor or the CRO. The

investigating physicians shall take care that patient documents (e.g. copies of reports on special findings) transmitted to the CRO or the sponsor contain no names, but only the year of birth and a relevant patient number. The storage of data for statistical analysis shall likewise be performed only under the patient’s random/study number.

IPD sharing plan summary

Not expected to be made available