Curing chronic wounds with fibrin.

Published: 03-04-2017
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To cure chronic wounds with fibrin treatment.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON50490

Source
ToetsingOnline

Brief title
Fibrin as a cure for chronic wounds.

Condition

- Other condition
- Diabetic complications
- Epidermal and dermal conditions

Synonym
Chronic wounds, ulcers

Health condition

Chronische wonden

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Fibrin, Ulcer, Wounds

Outcome measures

Primary outcome

To determine the effect of the treatment: the number of completely healed

wounds during the trial period of 12 weeks.

Secondary outcome

Measurement of the wound area and depth (fortnightly) by the researcher as long

as the wound is open (max 12 weeks).

Improved perfusion in the wounded area.

Score Quality of Life by questionnaires (EQ5D and Cardiff Wound Impact

Questionnaire); VAS pain score).

Study description

Background summary

Recently, we finished a study in which we have found that applying fibrin onto wounds in diabetic rats improves wound healing, as well as wound perfusion. It is highly expected that fibrin will also have a positive effect on the healing of chronic foot ulcers in diabetic patients. In this project we will apply a fibrin gel onto chronic wounds in diabetic patients to improve wound healing. The application of fibrin is highly feasible in a clinical setting and fibrin is tolerated by patients. This is known because in high concentrations, fibrin is already used in the clinic as tissue glue (Tisseel).

In the EU only, chronic wound care costs approximately 20 billion euros. These chronic wounds, caused by among others few and bad blood vessels, will lead to amputation of the lower extremities in 24% of all patients. After amputation the mortality is 50-60% within the first 2 years. This mortality is even higher than the mortality of many forms of cancer. Chronic wounds also cause additional problems, such as pain, social isolation and loss of income.

We will apply fibrin to chronic wounds to fasten wound healing. Fibrin is one of the major components in coagulation. After wound infliction it stops the bleeding and, importantly, attracts new blood vessels to the wound site, thus improving angiogenesis. We were able to show this in our own in vitro endothelial (blood vessel) cell ingrowth model. This is essential for proper wound healing.

Additional to our in vitro data we have recently finished our study in which we have shown the positive effect of fibrin on wound healing and vessel formation in normal and diabetic rats. The wounds will get a boost, so the healing process will not be hampered in the first phase of healing, as in diabetic wounds. This is exactly what happens in patients with chronic wounds. Their blood vessels in wounds and lower extremities cause low nutrients and oxygen supply, causing delayed wound healing, eventually leading to chronic wounds. When we analyze the graphical representation of the wound size at the patient's first return to the outpatient clinic, following fibrin application, we observe that the majority of patients present themselveswith a decreased wound size. However, this decline in wound size reverts at subsequent outpatient clinic visits which isn't unexpected since fibrin will be rapidly resolved by the body. Therefore, we request authorisation for more frequent fibrin applications, within the trial period, whenever the medical person in charge considers this beneficial for his/her patient.

For this study, we will work with doctors from different departments within the Erasmus MC (Surgery and Dermatology), the Alrijne (Rijnland) hospital, the Ikazia Hospital, the Franciscus Gasthuis Hospital, the Groene Hart hospital, the Reinier de Graaf hospital, the Maasstad Hospital, the IJsselland hospital, the HMC Westeinde hospital and the Frankelandgroep nursing homes. These doctors deal with chronic wounds and their consequences on a daily basis.

After showing positive results in this study, clinical implementation will be fast and efficient, as fibrin is known in the clinic.

Summarized: the positive results of our in vitro and in vivo studies show that it is time for a proof-of-principle study in chronic wounds of patients.

Study objective

To cure chronic wounds with fibrin treatment.

Study design

Fibrinogen: In this project we will use commercial fibrinogen (Tisseel) that is currently used in the clinic as Fibrin Sealant (91 mg/mL) on wound edges. The fibrinogen will be diluted to an optimal concentration (2 mg/ml). Thrombin (also from Tisseel) will be used to form a fibrin matrix.

Patients: 33 patients with poor-healing wounds will be included in this study. The most important inclusion criteria are:
- Non-healing, non-infected wound on either the foot or leg (Texas classification 1 or 2) that is non-respondent to treatment for at least 6 weeks.
- Older than 18 years old.
- BMI <40 kg/m2.
- HbA1c <10%.
- Willing to participate in our study.

This group will receive a fibrin treatment on top of standard wound care. The treatment will be executed by Dr M.J.E. van Rijn (diabetic foot clinic, Surgery Department) and Dr. C. van Montfrans (Dermatology Department) of the Erasmus MC; by Drs W. Brekelmans of the Alrijne hospital wound center; by Dr G. Cazander of the Ikazia hospital Wound Expert Center; dr. E.M.L. Corten of the Franciscus Gasthuis hospital Wound Expert Center; dr E.J. Waasdorp of the Groene Hart hospital Wound Expert Center; dr O. Schouten of the Reinier de Graaf Wound Expert Center; nurse specialist mrs E.C. Punt of the Maasstad hospital Wound Expert Center, dr. S.E. Buijk of the IJsselland hospital Wond Expert Center; dr. K.E.A. van der Bogt (HMC Westeinde hospital) and by drs H.I.M. Ploeg (Frankelandgroep). Wounds of patients in the fibrin group will be filled with fibrin (2 mg/ml). Patients will be invited for evaluation of the wound fortnightly until the wound is healed or over a period of 12 weeks.

Intervention

During the first trial visit, a fibrin matrix will be created in the wound of all trial patients. At subsequent outpatient clinic visits during the trial period, the patient may receive a fibrin matrix at all instances where the medical person in charge considers this beneficial for his/her patient.

Study burden and risks

Not applicable (see p27, paragraph 11.4 and p29, paragraph 13.2 of the research protocol).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Chronic, non-infected wound on either the foot or leg (Texas classification 1 or 2) that is non-respondent to treatment for at least 6 weeks.
- The size of the wounds must be between 1-20 cm2.
- Older than 18 years.

Exclusion criteria

- Patient suffers from osteomyelitis, cellulitis, gangrene or any other type of infection on the investigated leg.
- Patient is known with alcohol or drug abuse.
- It is impossible to correctly inform the patient (language barrier, mental problems).

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	27-12-2018
Enrollment:	33
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Tisseel fibrin sealant
Generic name:	fibrin sealant
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	03-04-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-12-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-11-2018
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-11-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-01-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-01-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-04-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-07-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-07-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-07-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	09-08-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-08-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-09-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-10-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-11-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-11-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-02-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-03-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

(Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2017-000863-34-NL
CCMO	NL58590.078.17