Exploring the early healing potential of a novel thermosensitive hyaluronic acid gel with octenidine preservation system as an adjunct to non-surgical periodontal treatment: a split-mouth blinded pilot study with proteomic analysis

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This pilot study aims to assess the feasibility, safety and preliminary efficacy of a novel thermosensitive hyaluronic acid gel with an octenidine preservative system as an adjunct to standard non-surgical periodontal treatment. The use of a blinded...

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

Summary

ID

NL-OMON57208

Source
ToetsingOnline

Brief title
Pocket-X Gel : Early Healing Potential

Condition

- Other condition
- Bacterial infectious disorders
- Soft tissue therapeutic procedures

Synonym
periodontal disease, periodontitis

Health condition

periodontal disease

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit van Amsterdam
Source(s) of monetary or material Support: Ministerie van OC&W,Geistlich Pharma AG

Intervention

Keyword: Hyaluronic acid, Stage 3 periodontitis, Stage 4 periodontitis, Thermosensitive gel

Outcome measures

Primary outcome

The primary outcome of this study is a proteomic analysis of the patients'

gingival crevicular fluid so that we can understand in depth how (and if) the

gel promotes soft tissue healing after standard non-surgical periodontal

treatment.

Secondary outcome

The secondary outcomes of our study are the clinical periodontal markers, which

will be measured twice (baseline and control after 6 weeks): Probing Pocket

Depth (PPD), Bleeding On Probing (BOP), Clinical Attachment Loss (CAL).

Study description

Background summary

Oral diseases, surpassing all noncommunicable diseases in global prevalence, have become a major health concern, with caries and severe periodontitis at the forefront, affecting roughly 2 billion and 1 billion people worldwide, respectively. Periodontitis, a severe gum infection capable of destroying the

bone supporting teeth, signifies a threat to global health, linking to systemic diseases and underscoring the importance of oral hygiene and regular check-ups. This necessitates an integrated approach to oral health, highlighting the need for preventive measures, addressing oral health inequalities, and incorporating oral health into general healthcare systems for comprehensive management.

Currently available conventional treatment for periodontitis includes root surface debridement (RSD) or scaling and root planing (SRP), which remove subgingival plaque and tartar, thereby removing the causative factor for periodontal disease and inhibiting the natural healing process of the gums becomes possible. However, new bacteria can infiltrate the pockets after RSD or SRP and hinder the healing process.

To improve gingival healing and prevent recurrence of inflammation within the periodontal pockets, additional treatments have been developed, intended for use after RSD or SRP. These methods include antimicrobial laser therapy, host modulating agents that inhibit host collagen-degrading enzymes that cause tissue loss due to the inflammatory response, or the use of antibiotic or antibacterial agents that aid in the inhibition of bacterial recolonization in the periodontal pockets. The latter are available as rinses, toothpastes, or sustained-release products, which are inserted into the periodontal pockets and remain there for days or weeks. In addition, systemic antibiotics can be administered, with or without topical treatment. Another additional treatment option is the use of barrier agents that fill the periodontal pockets and prevent infiltration of bacteria from the oral cavity into the pockets.

Although the effectiveness of SRP has been proven to be statistically significant in numerous clinical studies, several complementary treatments have been shown to provide greater improvement in clinical parameters such as pocket depth, clinical attachment level and bleeding on probing.

The medical device under investigation, Pocket-X Gel, is a product of Israel-based Tree of Life Pharma Ltd. This device is designed to gel in place and serves as a physical barrier against the recolonization of bacteria in periodontal pockets after SRP. The gel is biodegradable and remains in the periodontal pocket for one to three weeks before breaking down or being expelled as part of the gums' natural healing process.

The study aims to assess the effectiveness of this patented Class IIa medical device in reducing bacterial load and promoting periodontal healing, which may provide a valuable alternative to traditional antibiotic treatments. This is of paramount importance in an era when the reduction of antibiotic use is extremely important. The study states two hypotheses: the null hypothesis (H0) claims that there will be no significant difference in clinical outcomes between the standard non-surgical treatment and the treatment with the integration of Pocket-X Gel, while the alternative hypothesis (H1) states a significant improvement in periodontal health is expected with the additional

use of this thermosensitive hyaluronic acid gel.

Study objective

This pilot study aims to assess the feasibility, safety and preliminary efficacy of a novel thermosensitive hyaluronic acid gel with an octenidine preservative system as an adjunct to standard non-surgical periodontal treatment. The use of a blinded design will strengthen the validity of the study. The primary outcome of this study is a proteomic analysis of the patients' gingival crevicular fluid so that we can understand in depth how (and if) the gel promotes soft tissue healing after standard non-surgical periodontal treatment.
Proteomic analysis provides a comprehensive view of the proteins in a biological sample, providing insights into cellular functions, disease markers and drug targets. It identifies differentially expressed proteins, post-translational modifications and interactions, and contributes to our understanding of complex biological processes. It is a very sensitive technique, therefore all collected samples will be sent to a specialized laboratory in Utrecht for analysis.
The secondary outcomes of our study are the clinical periodontal markers, which will be measured twice (baseline and control after 6 weeks): Probing Pocket Depth (PPD), Bleeding On Probing (BOP), Clinical Attachment Loss (CAL).

Study design

The pilot study allows us to use a smaller sample of participants (n=10) without a power calculation. We aim to recruit the patients within the timeline of the OHS Periodontology MSc. The patients will be recruited at the Periodontology Department of ACTA. Patients who come for an intake, diagnosed with Periodontintis stage III or IV, who meet the inclusion criteria will be asked to participate in this study. The study is prospective, randomized split-mouth and blinded (patients).

Intervention

User
- Recruitment of patients: patients who meet the inclusion criteria will be asked if they want to participate in this study (thinking period 2 weeks). They will be provided with the product's folder, extensive information about the research and the procedures, and an informed consent. The protocol is developed in order to provide as little inconvenience as possible to the patients in terms of time investment.
- Baseline: Full Periodontal status (POD, BOP, CAL) and Gingival Crevicular Fluid (GCF) sampling. The measurements and GCF collection will be performed by the head investigator (I.K. Vragkali). The treatment of the test and control sites as well as the application of the product will be performed by the head

investigator I.K. Vragkali, in order to provide standardization during the procedures.
- Patients will undergo the standard non- surgical periodontal treatment in 2 or 4 appointments (1 week apart) with adjunctive use of the product (Pocket-X gel) in a randomized split-mouth manner (1 quadrant with test product and 1 quadrant with placebo saline solution). Application of gel will be performed at the end of the 1st treatment appointment.
- At the second appointment (before the treatment), the second GCF sample will be taken.
- The patients will be required to come back for the 3rd GCF sampling after 3 weeks. This may be an additional appointment compared to the standard procedure, depending on if the patients would have their treatment in 2 or 4 appointments.
- During the 6 weeks check-up, the last (4th) GCF sample will be taken and new periodontal measurements will be performed (periodontal status).

The patients will undergo standard non-surgical periodontal treatment as it is offered to everyone who comes to our clinic. They will get a full mouth periodontal status, which is also a standartd procedure. The extra procedure that they will have to undergo is the Crevicular Gingival Fluid (CGF) sampling. GCF will be sampled using paper strips (Periopaper ® , Oraflow Inc., New York, USA) placed at the gingival margin of the test sites for 30 seconds. It is a painless procedure which will not burden the patient whatsover.

The gel comes in a pre-filled syringe with two application tips and is applied as a liquid by a dental professional. On contact with body temperature in the periodontal pocket, it turns into a gel, which effectively fills the pocket and blocks bacterial entry. The syringe is intended for single use on one patient, with the ability to treat multiple pockets on one individual. The ingredients are water, Poloxamer 407, hyaluronic acid, phenoxyethanol and octenidine dihydrochloride - all recognized as safe for oral use.

Study burden and risks

- There is minimal risk expected and/or associated with this research. In case of unknown allergies: Allergy to hyaluronic acid is reported to be rare and mostly associated with dermal fillers/injectables.
- There may be some post-treatment discomfort and sensitivity of the dentition, which would have happened anyway without the application of the product.
- There is possibly no additional effect in terms of early healing.

Benefits:
- The participants will receive the product for free.
- Potenitally improved healing of the periodontal tissues

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Adults above the age of 18 willing to sign the informed consent and comply with all the recall appointments
- No antibiotic therapy in the past 6 months
- No previous periodontal treatment, besides maintenance treatments at the oral hygienist/dentist
- Diagnosed with stage III or stage IV periodontitis (pockets > 5mm)
- Radiographic status of the entire mouth (multiple smaller radiographs; peri-apical and bitewings)

Exclusion criteria

- Pregnancy or nursing

- Known hypersensitivity to any of the device*s components as listed on the user leaflet
- Uncontrolled diabetes (HbA1c >= 7), rheumatoid arthritis, or other chronic disesses associated with immunosuppression
- History of radiotherapy or chemotherapy the last 12 months
- Mental disorders
- Patients undergoing orthodontic treatment
- Active carious and/or endodontic-periodontic lesions

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2024
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Generic name:	Pocket-X® Gel
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	24-10-2024

Application type:	First submission
Review commission:	METC Amsterdam UMC

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
CCMO	NL86516.018.24