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Reduction of residual and/or recurrent spaces or openings surrounding the teeth under the gum line using a sodium hypochlorite gel after completion of gum treatment

Submission date
14/10/2021

Recruitment status
No longer recruiting

Registration date
09/12/2021

Overall study status
Completed

Last Edited
14/07/2022

Condition category
Oral Health

[_] Prospectively registered
[_] Protocol
[X] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Periodontitis (per-e-o-don-TIE-tis), also called gum disease, is a serious gum infection that damages the soft tissue and, without treatment, can destroy the bone that supports your teeth. Periodontitis can cause teeth to loosen or lead to tooth loss.
Treatment may be performed by a periodontist, a dentist or a dental hygienist. The goal of periodontitis treatment is to thoroughly clean the pockets around teeth and prevent damage to surrounding bone.
If periodontitis isn't advanced, treatment may involve less invasive procedures:
Scaling removes tartar and bacteria from your tooth surfaces and beneath your gums. It may be performed using instruments, a laser or an ultrasonic device.
Root planing (air polishing) smooths the root surfaces, discouraging further buildup of tartar and bacteria, and removes bacterial byproducts that contribute to inflammation and delay healing or reattachment of the gum to the tooth surfaces.
Topical or oral antibiotics can help control bacterial infection. Topical antibiotics can include antibiotic mouth rinses or insertion of gels containing antibiotics in the space between your teeth and gums or into pockets after deep cleaning. However, oral antibiotics may be necessary to completely eliminate infection-causing bacteria.

Who can participate?
Men and women aged 20-80 years who have undergone systematic periodontal treatment for at least 6 months.

What does the study involve?
Participants will be randomly allocated to receive mechanical ultrasonic instrumentation and air polishing treatment accompanied by either PERISOLV® gel, Clorhexamed® 1% gel, or placebo (inactive) gel. Follow up will be at 3, 6, 9, and 12 months.

What are the possible benefits and risks of participating?
Participants will benefit of improved gum health and reduced inflammation; no risk is incurred by the use of any antimicrobial product.

Where is the study run from?
Department of Periodontology of the Victor Babes University Timisoara (Romania)

When is the study starting and how long is it expected to run for?
January 2018 to September 2019.

Who is funding the study?
The study is partially funded by Regedent AG, Zurich, Switzerland (supplied the investigated product).

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

Protocol serial number
01/2017

Study information

Scientific Title
Clinical and microbiological effects of a single application of a sodium hypochlorite gel in maintenance patients treated for periodontitis stages III-IV. A triple-blind randomized placebo-controlled clinical trial

Acronym
PerisolvSPT

Study objectives
A single adjunctive administration of Perisolv to mechanical ultrasonic instrumentation and air polishing provides better clinical and microbiological outcomes than the adjunctive administration of chlorhexidine gel or a placebo gel to mechanical ultrasonic instrumentation and air polishing (control groups) in patients with persistent pockets during supportive periodontal therapy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 21/01/2018, Commission of Research Ethics of the Victor Babes University of Medicine and Pharmacy Timisoara (Institutul de Medicina Legala, Str. Ciresului nr.1A, 300610 Timisoara, Romania; +40-256-466001; enache.alexandra@umft.ro), ref: no.1/21.01.2018

Primary study design
Interventional

Study design
Triple-blind randomized placebo-controlled clinical trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topical antimicrobial in supportive periodontal therapy

Interventions
Study design
This study is conducted as a triple-blind randomized placebo-controlled clinical trial of 12 months with a parallel design of three independent groups, with a 1:1:1 allocation ratio. The study is approved by the Committee of Research Ethics of the Victor Babes University of Medicine and Pharmacy Timisoara (approval no.1/21.01.2018). The study is conducted according to the principles outlined in the Declaration of Helsinki on human medical experimentation. All subjects are informed about the nature and purpose of the study, and each subject signed an Informed Consent document giving permission for the dental procedures and sampling of biological material. The study was carried out between January 2018 and September 2019.

Clinical examination
The team includes an examiner (experienced specialist of Periodontology), a randomizer, an operator (specialist of Periodontology) with at least 4 years of clinical experience. The intra-examiner calibration for reliability testing resulted in $\kappa = 0.92$ for repeated measurements of PD and AL in two quadrants of five patients, other than the patients recruited for the study.
The periodontal diagnosis is established according to the new classification scheme for periodontal and peri-implant diseases and conditions (2018).
The patient's medical history includes: systemic disease diagnosed from the beginning of the supportive periodontal treatment up to the present, the smoking status (former, active, non-smoker), and the compliance, to assess the availability of the patient to undergo the treatment procedures so as to avoid the reduction of the study population.

The clinical baseline evaluation (before therapy) and the 3, 6, 9 and 12 month re-evaluations are performed by the same investigator (SS) in all patients. Full-mouth plaque scores (FMPS) are recorded using six sites per tooth. Periodontal pocket depths (PPDs) are measured on six sites per tooth: mesiobuccal, midbuccal, distobuccal, disto-oral, midoral, and mesio-oral using PCP-UNC15 probes (Hu-Friedy, Chicago, IL, USA). Recession (REC) are recorded to the nearest millimeter at six sites per tooth. The clinical attachment level (CAL) is calculated using the PD and REC values. Measurements are rounded up to the next whole millimeter value. At the proximal surfaces, the evaluation is done in the proximity of the dental contact point, with moderate pressure. Bleeding on probing (BOP) is assessed dichotomously in 6 sites per tooth. Mobility is recorded in degrees, according to Miller classification system (1985).
The periodontal parameters are recorded in the periodontal chart (http://www.periodontalchart-online.com/uk/), saved in .pdf format, printed and included into each patient's observation file.
Microbiological examination

The microbiological samples are collected by the treating clinician (VR) from the teeth with the deepest PD recorded at the initial evaluation. These sites are used as reference sites for collecting the microbiological samples at 12-month re-evaluation time point. Subgingival plaque is collected for microbiological examination as follows: the site is isolated with cotton rolls; after removing the supragingival plaque and the debris with a sterile cotton gauze, the gingival surface is dried; the plaque samples is collected by inserting 2 sterile paper points ISO #30 in the reference site and allowing them 30 seconds in situ for saturation (Rusu et al., 2015).
Microbiological samples are collected at baseline (before applying each group's treatment procedure) and after 12 months. The samples are pooled and sent immediately to the laboratory for analysis.
In order to detect the 5 major keystone bacteria, Aggregatibacter actinomycetemcomitans (A. a.), Porphyromonas gingivalis (P.g.), Prevotella intermedia (P.i.), Tannerella forsythia (T.f.) and Treponema denticola (T.d.), a molecular genetic analysis is performed. The semi-quantitative analysis of bacteria is assessed using the commercial kit micro-IDent plus (Hain Lifescience GmbH, Nehren, Germany).
Randomization and therapy assignment

Randomization is achieved using a number generator (www.randomizer.org) by a randomizer who is independent from the operator or the evaluator.
Blinding is ensured by the randomizer, by using of a placebo gel similar in aspect and consistency to the test gel, and by the fact that neither the patients nor the operator and the examiner who evaluates the clinical parameters knew the group to which the patient was assigned.
The computerized randomization will assign the patients to one of the three groups, with an allocation ratio of 1:1:1. The randomizer performs the assignment to interventions, while a dental assistant performs the documentation. An allocation table will be created, containing all patients names, and will be used to assign each patient a treatment number as resulted from the randomization process. Each patient will be given a sealed opaque envelope containing the treatment number.

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patients names, and will be used to assign each patient a treatment number as resulted from the randomization process. Each patient will be given a sealed opaque envelope containing the treatment number.

Supportive periodontal treatment (SPT) procedures
Supra- and subgingival debridement using ultrasonic mechanical instrumentation (UMI) with the device EMS Piezon® Master (EMS, Nyon, Switzerland) and air polishing (AIRFLOW® CLASSIC powder, EMS, Nyon, Switzerland) at all sites will be performed. Teeth that showed after the periodontal re-evaluation PPD<4 mm or teeth with PPD=4mm without BOP will be instrumented supragingivally using ultrasonics, inserts A and B (EMS, Nyon, Switzerland) and air polishing (AIRFLOW® handpiece and AIRFLOW® CLASSIC powder, EMS Nyon, Switzerland). Teeth that presented after the periodontal reevaluation PPD> 4mm will be instrumented subgingivally using additionally the inserts PS, PL1 and PL2 for EMS (EMS, Nyon, Switzerland). The antimicrobial investigational product (Perisolv®, Regedent AG, Zürich, Switzerland) consists of two components contained in two separate interconnectable syringes: a transparent gel (the activating vehicle), containing amino acids (glutamic acid, leucine, lysine), carboxymethylcellulose, ultrapure water and a 0.95% sodium hypochlorite solution. The two components are mixed before use to generate chloramines (Megally 2019). The chlorhexidine product (Clorhexamed® 1% gel, GSK, Germany) and the placebo treatment consists of gels with similar aspect and consistency as the test product, packed in transparent syringes, identical with the syringe used to apply the test product.

In group A, the reference sites will be additionally treated as follows: Perisolv® is applied according to manufacturer's instructions by interconnecting the two syringes and mixing the liquids by alternately pushing the plungers, until the liquid becomes homogeneous (10-15 cycles) and will be pushed entirely in the transparent syringe. A blunt applicator will be applied to this syringe and will be inserted into the pocket mesially, lingually, distally and buccally to cover the full circumference of the teeth, and to reach the bottom of the pocket. After application, Perisolv® gel will be left in situ for 30 seconds, followed by UMI. After 15 minutes, Perisolv® will be applied again and teeth will be re-instrumented subgingivally using UMI. As a mean of destroying the biofilm, air polishing will be used on all teeth. In group B, the reference sites will be additionally treated as follows: Clorhexamed® 1% gel is applied inside the pockets mesially, lingually, distally and buccally, using a plastic nozzle, in order to cover the full circumference of the teeth and to reach the bottom of the pocket depth. After application, Clorhexamed® 1% gel is left in situ for 30 seconds and teeth are treated using UMI. After 15 minutes, the gel is re-applied and teeth are instrumented again, in the same manner. Air polishing is used identically to group A. At the end of the treatment appointment, Clorhexamed® is applied to all periodontal pockets, and the patient is advised not to rinse, drink fluids, or eat for half an hour. In group C, the reference sites are additionally treated with the placebo, applied in the same manner as Perisolv in group A.

Thus, the treatment according to the assignment of the patients in the three study groups is as follows:
Perisolv® (group A): UMI [EMS-Piezon® Master (EMS, Nyon, Switzerland), inserts A, B, PS, PL1, PL2]; air polishing (AIR FLOW® CLASSIC powder, EMS Nyon, Switzerland); PERISOLV® gel (REGEDENT AG, Zurich, Switzerland).
Clorhexamed® (group B): UMI [EMS-Piezon® Master (EMS, Nyon, Switzerland), inserts A, B, PS, PL1, PL2]; air polishing (AIR FLOW® CLASSIC powder, EMS, Nyon, Switzerland); Clorhexamed® 1% gel (GSK, Germany)
Placebo (group C): UMI [EMS-Piezon® Master (EMS, Nyon, Switzerland), inserts A, B, PS, PL1, PL2]; air polishing (AIR FLOW® CLASSIC powder, EMS, Nyon, Switzerland); placebo gel.
On the first periodontal reevaluation, patients will be asked by the investigator if any allergy or

adverse reaction occurred after the treatment procedure, or if they have used medication that might interfere with the inclusion criteria. If necessary, the individual oral hygiene will be reinforced.

Intervention Type
Procedure/Surgery

Primary outcome(s)
At baseline and 3-, 6-, 9- and 12-month re-evaluations the following are recorded using six sites per tooth by the same investigator:
1. Periodontal pocket depths (PPDs)
2. Full-mouth plaque scores (FMPS)
3. Full-mouth bleeding scores (FMBs)

Key secondary outcome(s)
Microbiological samples will be collected from teeth with the deepest PPD recorded at the initial evaluation and 12-months to detect the presence of bacteria: Aggregatibacter actinomycetemcomitans (A.a.), Porphyromonas gingivalis (P.g.), Prevotella intermedia (P.i.), Tannerella forsythia (T.f.) and Treponema denticola (T.d.) measured using a molecular genetic analysis.

Completion date
01/09/2019

Eligibility

Key inclusion criteria
1. Men and women aged 20-80 years
2. Treated periodontitis patients, that underwent supportive periodontal treatment for a minimum period of 6 months
3. At least 4 non-adjacent sites with PPDs ≥4 mm with BOP or PPDs >5 mm, but not deeper than 8 mm, with or without BOP, according to the criteria for the need of retreatment in SPT (rate of healing) (Tonetti, Lang & Cortellini 2012); the sites should not be associated with affected furcations, in third molars and in teeth severely malpositioned teeth. Ideally, the teeth should be in different quadrants
4. The teeth considered for assessment should be vital or should have an adequate root canal treatment
5. Compliant patients (mean BOP <25%, PCR <25%)
6. Patients who underwent systematic periodontal treatment in the same private practice where the study is conducted and have been documented regarding the periodontal evaluations, radiographs
7. Patients willing to provide written informed consent
8. Patients able to comply with 12-month study follow-up

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Adult

Sex
All

Total final enrolment
85

Key exclusion criteria
1. Known allergy or adverse reactions to hypochlorite
2. Clinically relevant psychological disorders
3. Alcohol abuse
4. Known HIV infection
5. Self-reported diabetes mellitus
6. Locally or systemic administration of antibiotics in the last 3 months
7. Pregnancy, breastfeeding

If progression of periodontal destruction was observed or if adverse reactions to the test product were reported, the subject was removed from the study. Progression of periodontal destruction was defined as attachment loss > 2mm or an increase of PPD >2 mm between subsequent evaluations.

Date of first enrolment
21/01/2018

Date of final enrolment
01/12/2018

Locations

Countries of recruitment
Romania

Study participating centre
Anton Sculean Center for Research of Periodontal and Periimplant Diseases, Department of Periodontology, Victor Babes University of Medicine and Pharmacy Timisoara
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Sponsor information

Organisation
Regedent (Switzerland)

ROR
https://ror.org/00nganv68

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 available from the corresponding author on reasonable request.
Dr. Viorelia Radulescu, viorelia.radulescu@umft.ro .
Type of data: periodontal charts, microbiological data,
Data will become available after publication of the study, and will be available for 5 years.
Data will be shared for similar studies, on request from the first author.
Written consent from participants was obtained.
Data from participants are anonymized. The key to the names of the participants is located in the repository.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		12/07/2022	14/07/2022	Yes	No
Statistical Analysis Plan			22/10/2021	No	No