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Comparison of two adjunctive locally delivered antibiotic gel regimens for initial therapy in periodontitis patients

Submission date
16/10/2022

Recruitment status
No longer recruiting

Registration date
21/10/2022

Overall study status
Completed

Last Edited
20/04/2023

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 is the inflammation of the tissues around the teeth caused by dental plaque, without treatment, can destroy the bone that supports your teeth. Periodontitis can cause teeth to loosen or lead to tooth loss. The first step of treatment (removal of irritants) is called subgingival instrumentation (SI). Antibiotic gels may be additionally applied after the procedure because evidence indicates that local delivery of antimicrobials in periodontal pockets added to SI provides an additional benefit compared to SI alone as it aids in the control of the growth of pathogenic bacteria. Local drug delivery (LDD) systems provide a higher concentration of the antimicrobial with a sustained release over a longer duration of time.
Topical applied antibiotics gels can help control bacterial infection. Topical antibiotics gels can be applied in the space between your teeth and gums or into pockets after SI. However, oral antibiotics may be necessary to eliminate infection-causing bacteria.
The aim of this study is to evaluate the effect of a new piperacillin and tazobactam gel, in comparison with a standard commercially-available 14% doxycycline gel, in non-surgical therapy of stage III-IV periodontitis, after SI. Treatment may be performed by a periodontist or a dentist. Periodontitis treatment aims to thoroughly clean the pockets around teeth and prevent damage to the surrounding bone.

Who can participate?
Men and women aged 25 to 80 years who have suffered from long-term gum disease can take part.

What does the study involve?
Participants will be randomly allocated to receive SI accompanied by either Gelcide® gel, Ligosan® gel, or placebo (inactive) gel. Follow-up will be at 3 and 6 months.

What are the possible benefits and risks of participating?
Participants will benefit from improved gum health and reduced inflammation. No risks are expected to be 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?
September 2018 to August 2021

Who is funding the study?
Investigator initiated and funded (Romania)
MegaGen (supplied one of the investigated products) (Romania)

Who is the main contact?
Dr Ilyes Ioana, vejaioana@yahoo.com (Romania)

Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
2/2018

Study information

Scientific Title
A placebo-controlled trial to evaluate two locally delivered antibiotic-containing (piperacillin and tazobactam verus doxycycline) gels in stage III-IV periodontitis patients

Acronym
LDD-ATB-GELS

Study objectives
The adjunctive administration of a locally-delivered gel containing piperacillin and tazobactam in patients with stage III-IV periodontitis during subgingival instrumentation provides comparable, if not better clinical and microbiological results when compared with a doxycycline gel.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 03/09/2018, Research Ethics Committee of the Victor Babeş University of Medicine and Pharmacy Timişoara (Piata Eftimie Murgu 2A, 300041 Timisoara, Romania (EU); +40 (0)256 466001; esanda2000@yahoo.com), ref: 20/03.09.2018.

Study design
Prospective placebo-controlled double-blinded randomized clinical trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet.

Health condition(s) or problem(s) studied
Topical antibiotic gels applied adjunctively to subgingival instrumentation in stage III-IV periodontitis patients.

Interventions
The study includes a cohort of 100 patients equally divided into one of the three groups - A, B, and C. Subjects will be selected from patients of the Department of Periodontology of the Victor Babes University of Medicine and Pharmacy Timisoara, Romania. All subjects will be informed about the nature and purpose of the study, and sign an Informed Consent document permitting the dental procedures and sampling of biological material. The study will be carried out between November 2018 and February 2021.

Clinical and Paraclinical Examination
The following parameters will be measured in the initial evaluation and at 3 and 6 months: Overall Plaque Index (PlI) in 6 sites per tooth; Probing Pocket Depth (PPD) evaluation on the

vestibular and oral surfaces will be performed halfway between the line angles using the PCP – UNC 15 periodontal probe (Hu–Friedy, Chicago, IL., USA). On the interproximal faces, the evaluation will be performed near the contact point with moderate pressure; Overall Bleeding Index (BOP) evaluated in 6 sites per tooth at 30 seconds from the probing; Level of clinical attachment (CAL); Teeth mobility degrees; Involvement of furcation (FI) in multi-rooted teeth, all sites with furcation involvement were included into grade I, II or III; all clinical measurements will be performed by one clinician using a Nabers probe. Data will be recorded in the periodontal sheet of the University of Bern (http://www.periodontalchart-online.com/uk/index.asp), saved in PDF format, printed, and will be included in the observation file of each patient. Patients fulfilling the inclusion criteria received an informed agreement that he/she had 7 days to analyze and had to sign it, to be included in the study. During the study period, the attending examiner will be monitored the patients for disease progression. The patients will be excluded from the study in case of progressive attachment loss of 2 mm or more between two subsequent evaluation time points. If that occurred, the patients will receive treatment as necessary.

Microbiological examination
Microbiological samples will be obtained from sites with a depth of a minimum of 5 mm at the initial examination, with 4 sites being selected, 1 in each dial. These sites will be used as reference sites for samples collected at 0 and 6 months. The subgingival plaque will be sampled for microbiological evaluation as follows: the site will be isolated with rolled wool, the overgrowth plaque will be removed with a sterile compress and the gingival surface will be dried, and plaque samples will be obtained by inserting 2 sterile ISO #30 paper cones into the site, which will be left in place for 30 seconds for saturation. Plaque samples will be obtained at baseline (prior to treatment of the patient) and 6 months after the initial evaluation. The paper points will be pooled immediately into sterile sealed Eppendorf tubes and sent for polymerase chain reaction (PCR). The PCR testing will be conducted at the laboratories of the Department of Biochemistry of the “Victor Babeş” University of Medicine and Pharmacy.

Detection of the major periodontopathogens Aggregatibacter actinomycetemcomitans (A.a.), Porphyromonas gingivalis (P.g.), Prevotella intermedia (P.i.), Tannerella forsythia (T.f.), and Treponema denticola (T.d.) will be carried out by molecular genetic analysis of the samples taken. The presence of these bacteria will be assessed using a commercial kit (micro–IDent A Test). The same sites will be used to collect the microbiological samples during the 6-month re-evaluation time point. Periodontal treatment will be performed, including oral hygiene instruction, and supragingival ultrasonic instrumentation, by the person designated as the operator. Subgingival plaque samples will be collected from 4 tooth sites at baseline and 6 months (after supragingival ultrasonic instrumentation, at 7 days). Supra- and subgingival instrumentation by ultrasound and manual instrumentation will be performed at all sites: ultrasound instruments in 10 minutes, followed by manual SI with Gracey curettes; #5/6; 7/8; 11 /12; 13/14; instrumentation will be followed by subgingival gel application, depending on the patient’s group. Due to the physical properties of the products, only the patients and the evaluator will be blinded.

For patients assigned to Group A (test), GELCIDE® (piperacillin and tazobactam) will be applied according to the manufacturer's recommendations. The patients assigned to Group B (positive control) will receive LIGOSAN® (doxycycline). For the patients assigned to Group C (negative control), a placebo gel will be applied to the periodontal pocket in the most apical portion.

Patients from all groups will be instructed to gently brush and refrain from flossing for the first 36 h following treatment in the treated area. After 36 h, oral hygiene procedures will be resumed gentle brushing of the application area will be done twice a day, and the removal of interdental plaque, once a day.

Intervention Type
Drug

Drug/device/biological/vaccine name(s)
GELCIDE® (piperacillin + tazobactam gel), LIGOSAN® (doxycycline gel)

Primary outcome measure
Periodontal pocket depth measured using a periodontal probe at baseline (initial evaluation) and 3 and 6 months after surgery

Secondary outcome measures
Secondary outcome variables were evaluated at 3 and 6 months:
1. Full mouth bleeding score (FMBS) recorded using 6 sites per tooth, mesiobuccal, midbuccal, distobuccal, disto-oral, midoral, and mesio-oral] using PCP-UNC15 probes (Hu-Friedy, Chicago, IL, USA)
2. Mean full mouth plaque score (FMPS) evaluated in 6 sites per tooth at 30 seconds from the survey
3. Overall bleeding index (BOP) evaluated in 6 sites per tooth at 30 seconds from the survey
4. Pocket closure defined as the transition of sites with PPD>5 mm or 4 mm with BOP to non-bleeding sites with PPD ≤ 4 mm
5. Recession (REC) are recorded to the nearest millimeter at 6 sites per tooth.
6. Clinical attachment level (CAL) is calculated using the PD and REC values
7. Numbers of the following five keystone bacterial pathogens [using a molecular genetic analysis, micro–IDent A Test]: (baseline and 6 months):
7.1. Aggregatibacter actinomycetemcomitans
7.2. Porphyromonas gingivalis
7.3. Prevotella intermedia
7.4. Tannerella forsythia
7.5. Treponema denticola

Overall study start date
01/09/2018

Completion date
01/08/2021

Eligibility

Key inclusion criteria
1. All subjects were diagnosed with periodontitis stage III and IV
2. All participants fulfilled the following inclusion criteria:
2.1. Aged between 25 and 80 years old
2.2. At least 8 sites with PD ≥ 5 mm and showing bleeding on probing
2.3. Clinical attachment loss ≥3 mm
2.4. Patients who have not undergone periodontal therapy in the last 12 months

Participant type(s)
Patient

Age group

Adult

Sex
Both

Target number of participants
100

Total final enrolment
100

Key exclusion criteria
Patients with the following conditions were excluded:
1. Clinically relevant psychiatric disorders
2. Alcohol consumption
3. Autoimmune disorders
4. HIV infection
5. Untreated diabetes mellitus
6. Pregnancy or breastfeeding
7. Patients who have received periodontal therapy in the last 12 months
8. Patients who reported local and/or systemic antibiotic therapy within the 3 months before the baseline examination of the study
9. Candidiasis
10. Allergies to piperacillin, tazobactam, doxycycline, or to any tetracycline or penicillin or to any excipient of the products used
11. Systemic medication that can influence the clinical features of periodontitis
12. Patients who have rinsed or irrigated with antiseptics less than a month before the initial examination
12. Conditions that require antibiotic protection

Date of first enrolment
01/10/2018

Date of final enrolment
01/02/2021

Locations

Countries of recruitment
Romania

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

Organisation
MegaGen Dental Implant Romania

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Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Funder Name
MegaGen Dental Implant Romania

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact and peer-reviewed journal

Intention to publish date
01/12/2022

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 Ilyes Ioana (vejaioana@yahoo.com).
Type of data: periodontal charts, microbiological data.
Data will become available after the publication of the study results 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?
Participant information sheet			21/10/2022	No	Yes
Statistical Analysis Plan			21/10/2022	No	No
Results article		07/02/2023	20/04/2023	Yes	No