INFORMED CONSENT

for participation in the study

THE IMPACT OF LOCAL VS. SYSTEMIC ADJUVANT ANTIBIOTICS DURING NON-SURGICAL PERIODONTITIS THERAPY ON CLINICAL PARAMETERS, BACTERIAL COUNT AND CYTOKINE LEVELS – A RANDOMIZED CLINICAL TRIAL

NCT05608564

Date: 20.01.2022.

Study Purpose

The study aims to compare the clinical outcomes, total bacterial load, and relative expression levels of pro-inflammatory mediators after using local versus systemic adjuvant antibiotics during non-surgical periodontitis therapy. Specifically, it evaluates the effects of local antibiotic - piperacillin and tazobactam in gel form (Gelcide ®, Italmed MedTechDental, Florence, Italy), and systemic antibiotics - a combination of Amoxicillin (Amoxicillin ®, 500 mg) and Metronidazole (Orvagyl ®, 400 mg), on periodontal health over six months.

Procedures:

- Participants will undergo non-surgical periodontal therapy (NSPT) using a full-mouth disinfection protocol. NSPT is a deep cleaning treatment to remove bacteria and inflammation from the gums without surgery. The full-mouth disinfection protocol means that all teeth and periodontal and/or gum pockets are cleaned within 24 hours to prevent bacteria from spreading again. This includes scaling and root planing to remove plaque and tartar, along with antiseptic rinsing to disinfect the mouth. In some cases, additional treatments like antibiotics may be used to improve healing and prevent reinfection.
- Before treatment, gingival crevicular fluid (GCF) samples will be collected for laboratory analysis. To collect samples, the area will be gently dried using paper rolls and air. Then, three small absorbent paper strips will be placed in a deep periodontal pocket (over 5 mm) near a premolar or molar tooth for 30 seconds to absorb fluids. This process will be repeated in the same spot to ensure accurate results.
- Participants will be randomly assigned to one of two groups:
    - **Local antibiotic group (LA):** Local antibiotics will be applied subgingivally (between tooth and gums) 24h after NSPT.
    - **Systemic antibiotic group (SA):** Participants will take amoxicillin (500 mg, three times/day) and metronidazole (400 mg, three times/day) for seven days after NSPT.
- Follow-up appointments will be conducted six months after treatment for clinical assessments and additional GCF sampling.
- Laboratory analyses will include:
    - Quantification of total bacterial load through real-time polymerase chain reaction (qPCR) method;
    - Measurement of relative gene expression levels of IL-17 and TNF-α using qPCR method.

Risks:

- **General risks associated with periodontal treatment:** Mild discomfort, temporary gum irritation, and bleeding may occur after NSPT.
- **Risks related to antibiotic use:**
    - **Local antibiotics:** Potential for temporary sensitivity, mild irritation, or allergic reaction to piperacillin/tazobactam.
    - **Systemic antibiotics:** Possible side effects such as gastrointestinal discomfort (nausea, diarrhea), allergic reactions (in individuals with penicillin allergy), or development of antibiotic resistance.
- **Sampling risks:** Minor discomfort or irritation from the collection of GCF samples.

Potential Benefits:

- Participants may experience significant improvement in periodontal health, including reduced gum inflammation, bleeding, and bacterial load.
- The study may provide insights into optimizing antibiotic protocols for periodontitis treatment, potentially benefiting future patients.
- No significant differences in outcomes are expected between the two antibiotic groups, but the study may help determine if locally applied antibiotics are a viable alternative to systemic therapy.

The initiation of this study is approved by the Ethical Committee of the School of Dental Medicine, University of Belgrade (No 36/6) – approval is attached at the end of this document.

All information and dilemmas related to this examination were explained to me. I have read and understand this consent statement. All my questions were answered adequately. I voluntarily agree to participate in this clinical trial and to the release of my medical records as explained in this informed consent. I am not waiving my legal rights by signing this informed consent. I will receive a signed and dated copy of this informed consent.

Participant

Name and surname Signature Date

Attorney authorized by law (if required)

Name and surname Signature Date

A person who obtained consent (researcher)

Name and surname Signature Date

Witness* (if needed)

Name and surname Signature Date

*A witness is not required, unless the subject is unable to read (e.g. blindness or illiteracy), or if specified in the examination plan. If a witness is present, the witness must supervise the entire process of signing the informed consent.

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ISO 9001 BUREAU VERITAS Certification

ETHIC COMMITEE

N° 36/6

11-03-2020

On the ground of request of Assist. Prof. Iva Milinkovic, Ethic Committee of the School of Dental Medicine University of Belgrade, on the day of February 13th 2020, hereby signs the following

AGREEMENT

We hereby agree with the methodology of research suggested by Assist. Prof. Iva Milinkovic within the following study

Adjunctive effect of local and systemic antimicrobials in non surgical treatment of periodontitis grade II and III

Translation of the seal:
University of Belgrade
School oh dental medicine
1948, Belgrade

President of the Ethic Committee

Assoc. Prof. dr Natasa Nikolic Jakoba
(signature)

Belgrade, March 10th 2020.