

# Metronidazole in periodontal surgical therapy

<b>Submission date</b> 22/11/2020	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 04/12/2020	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 27/09/2022	<b>Condition category</b> Oral Health	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Periodontitis, 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.

Some studies have shown that the use of antibiotics can provide some benefits. However, there are no studies that have evaluated how well metronidazole works as an antibiotic in surgical periodontal therapy. Therefore, the objective of our study was to determine whether the use of an antibiotic (metronidazole), as an added treatment to periodontal surgery, provides additional clinical and microbiological benefits, in patients with generalized severe periodontitis.

### Who can participate?

Systemically healthy patients of both genders, aged 18 years or older, diagnosed with generalized severe periodontitis.

### What does the study involve?

Participants are randomly allocated to receive adjunctive metronidazole or placebo. Clinical variables were recorded at baseline, 6 weeks after subgingival instrumentation, and after 3, 6 and 12 months. Microbiological samples were taken at the initial and final visits and analyzed by multiplex quantitative polymerase chain reaction (qPCR).

### What are the possible benefits and risks of participating?

In this study, patients will benefit from non-surgical and surgical periodontal treatment of periodontitis. The treatment is expected to obtain improvements in periodontal clinical parameters such as a decrease in probing depth, gain in the level of clinical attachment, and resolution of inflammation. A greater decrease in bacterias would also be expected in the test group receiving the antibiotics. Although the adverse and unwanted effects associated with the use of systemic antibiotics must be taken into consideration.

### Where is the study run from?

Pontificia Universidad Católica Madre y Maestra (Dominican Republic)

### When is the study starting and how long is it expected to run for?

April 2014 to May 2019

Who is funding the study?  
Pontificia Universidad Católica Madre y Maestra (Dominican Republic)

Who is the main contact?  
Dr James R. Collins  
jamescollins@pucmm.edu.do

## Contact information

**Type(s)**  
Scientific

**Contact name**  
Prof James Collins

**Contact details**  
Av Abraham Lincoln esq. Simón Bolívar  
Santo Domingo  
Dominican Republic  
1101  
+1 (0)8094810572  
jamescollins@pucmm.edu.do

## Additional identifiers

**EudraCT/CTIS number**  
Nil known

**IRAS number**

**ClinicalTrials.gov number**  
Nil known

**Secondary identifying numbers**  
Nil known

## Study information

**Scientific Title**  
Adjunctive efficacy of systemic metronidazole in the surgical treatment of periodontitis: a randomized placebo-controlled clinical trial

**Study objectives**  
To determine whether the use of a systemic antimicrobial (metronidazole), as an adjunctive treatment to periodontal surgery (step 3), provides additional clinical and microbiological benefits, in patients with severe generalised chronic periodontitis (generalised stages III-IV, grades B-C periodontitis).

**Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Approved 12/03/2015, Ethical Committee of the Faculty of Health (COBE) of the Pontificia Universidad Católica Madre y Maestra (PUCMM) (Autopista Duarte Km 1 1/2, Santiago, República Dominicana; +1 (809) 580-1962, ext. 4416; brodriguez@pucmm.edu.do), ref: COBE-FACS-EXT-003-1-2014-2015

### **Study design**

Randomized parallel placebo-controlled double-blinded clinical trial

### **Primary study design**

Interventional

### **Secondary study design**

Randomised controlled trial

### **Study setting(s)**

Hospital

### **Study type(s)**

Treatment

### **Participant information sheet**

No participant information sheet available

### **Health condition(s) or problem(s) studied**

Severe generalised chronic periodontitis (generalised stages III-IV, grades B-C periodontitis)

### **Interventions**

Participants are randomly assigned to treatment groups in ascending order, at the time of surgery, according to a balanced distribution system (random block design, block size = 6).

1. Test group: blisters consisted of 500 mg metronidazole, to be taken three times per day for 7 days after the last surgery
2. Placebo group

In the initial evaluation, a clinical examination is carried out to establish the periodontal diagnosis. Clinical measurements include: PD and gingival recession/overgrowth (REC), measured to the nearest millimeter; CAL, calculated as the sum/rest of PD and REC; bleeding on probing (BOP), assessed dichotomously. Plaque index (PII) is also assessed. In each quadrant, the most accessible location with the deepest PD and BOP is selected. Subgingival plaque samples are obtained at the same sites throughout the study at the deepest site of each quadrant. All participants receive motivational sessions on oral hygiene instructions and scaling and root planning. Six weeks after the last session of SRP, the re-evaluation is performed and a new full periodontal examination is performed. Those presenting multiple locations with PD  $\geq 5$  mm with BOP  $\geq 1$  quadrant received periodontal surgery through open flap debridement. After the last surgical procedure is performed, the medication is provided to the participants, with the instructions to start with the drug regime, three times a day for 7 days. Clinical parameters are recorded 3 months after the last surgery session, and then after 6 and 12 months. Following the

active treatment, at 3, 6, 9 and 12 months all patients receive a full mouth professional mechanical plaque removal (PMPR), including SRP as needed and polishing of all dental surfaces present, in both groups.

### **Intervention Type**

Mixed

### **Primary outcome measure**

Probing Depth (PD), measured using a UNC-15 mm periodontal probe (Hu-Friedy, Leinmen, Germany) at baseline and 12-month visit

### **Secondary outcome measures**

At baseline, 3 months after the last surgery session, and then after 6 and 12 months:

1. Probing Depth distribution [overgrowth (measured to the nearest millimeter), Clinical Attachment Loss (calculated as the sum/rest of PD and REC) and open pockets measured using a UNC-15 mm periodontal probe (Hu-Friedy, Leinmen, Germany)
2. Plaque Index recorded using the O'Leary Index
3. Bleeding on Probing measured using a dichotomous analysis (presence or absence)
4. Microbiological variables (frequency of detection and counts of each targeted bacteria) samples analysed by multiplex quantitative polymerase chain reaction (qPCR), at baseline and after 12 months following surgical therapy

### **Overall study start date**

29/04/2014

### **Completion date**

15/05/2019

## **Eligibility**

### **Key inclusion criteria**

1. Severe generalized chronic periodontitis (Armitage, 1999), corresponding to generalized stage III-IV periodontitis, with grades B-C (Caton et al., 2018; Papapanou et al., 2018; Tonetti, Greenwell, & Kornman, 2018)
2. A least 10 teeth in function, excluding third molars
3. Sites with PD > 5 mm, in  $\geq 2$  teeth in  $\geq 1$  quadrant
4. Radiographic evidence of bone loss  $\geq 30\%$  in, at least, 30% of the dentition
5. Older than 18 years

### **Participant type(s)**

Patient

### **Age group**

Adult

### **Lower age limit**

18 Years

### **Sex**

Both

**Target number of participants**

Two groups with 25 patients each

**Total final enrolment**

40

**Key exclusion criteria**

1. Pregnant or breastfeeding women
2. Systemic diseases and/or chronic medications that may affect the periodontal status and /or requiring antibiotic prophylaxis
3. Having received systemic antimicrobial treatment in the previous 3 months
4. Have received periodontal treatment in the 6 months prior to the start of the study
5. Allergic to metronidazole, or to any of the components of their commercial formulations (Metrex 500 mg®, Laboratorio Union SRL, Santo Domingo, República Dominicana)
6. Refuse to sign the informed consent
7. Smokers  $\geq 10$  cigarettes/day

**Date of first enrolment**

10/02/2015

**Date of final enrolment**

15/02/2018

## Locations

**Countries of recruitment**

Dominican Republic

**Study participating centre**

**Pontificia Universidad Católica Madre y Maestra (PUCMM-CSD)**

Av Abraham Lincoln esq. Simón Bolívar

Santo Domingo

Dominican Republic

10109

## Sponsor information

**Organisation**

Pontificia Universidad Católica Madre y Maestra

**Sponsor details**

Av Abraham Lincoln esq. Simón Bolívar

Santo Domingo

Dominican Republic  
10109  
+1 (0)8095350111 Ext. 2094  
jeanmybautista@pucmm.edu.do

**Sponsor type**

University/education

**Website**

<https://www.pucmm.edu.do/>

## Funder(s)

**Funder type**

University/education

**Funder Name**

Pontificia Universidad Católica Madre y Maestra

## Results and Publications

**Publication and dissemination plan**

Study protocol can be available on request. Planned publication in a high-impact peer-reviewed journal.

**Intention to publish date**

10/03/2021

**Individual participant data (IPD) sharing plan**

Not provided at registration

**IPD sharing plan summary**

Available on request

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		05/02/2022	14/03/2022	Yes	No
<a href="#">Protocol file</a>	in Spanish		27/09/2022	No	No