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The contribution of inflamed gums to rheumatoid arthritis

Submission date
09/11/2019

Recruitment status
No longer recruiting

Registration date
14/11/2019

Overall study status
Completed

Last Edited
16/07/2024

Condition category
Musculoskeletal Diseases

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

Plain English summary of protocol

Background and study aims
Chronic Periodontitis (CP) is a destructive inflammatory disease affecting the supporting tissues of the teeth. Mounting evidence suggests a strong link between periodontitis and systemic diseases, such as rheumatoid arthritis (RA). Indeed, both diseases result in high concentrations of inflammatory markers such as C-reactive protein (CRP) in the circulation. Rheumatoid arthritis is a long-term condition that causes pain, swelling and stiffness in the joints. The condition usually affects the hands, feet and wrists.

This study aims at establishing the prevalence and impact of CP among patients with RA in different activity disease scores and studying the contribution of CP and its treatment towards RA progression and assessment

Who can participate?
Patients aged 18 – 70 years with chronic periodontitis and rheumatoid arthritis

What does the study involve?
Patients will be randomized, within each group, for subgroup 1: immediate treatment and subgroup 2: delayed treatment (to be started after 8 weeks).
Patients in subgroups 1 will start non-surgical periodontal treatment (NSPT) immediately and be submitted to rheumatologic re-assessment, periodontal revaluation and biological sample collection at 8 and 24 weeks.
Patients in subgroups 2 will start NSPT 8 weeks after first periodontal evaluation and be submitted to similar revaluations (at 8 and 24 weeks after treatment)

What are the possible benefits and risks of participating?
Risks: Physical discomfort or pain, brought about by the methods and procedures used for blood collection. The non-surgical periodontal treatment is accepted as gold standard in periodontitis treatment, and the risks are the ones associated with a deep cleaning (discomfort or teeth hypersensitivity)

Where is the study run from?
Centro Hospitalar e Universitário de Coimbra, Portugal

When is the study starting and how long is it expected to run for?
September 2018 to August 2020

Who is funding the study?
Coimbra Rheumatology Association (ARCo), Portugal

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
The contribution of periodontitis to the inflammatory burden in rheumatoid arthritis

Study objectives

1. The coexistence of Chronic Periodontitis (CP) may lead to overscoring of Rheumatoid Arthritis (RA) disease activity and consequently undue overtreatment
2. The coexistence of active CP may aggravate joint inflammation in patients with RA
3. Increased activity of RA due to CP is mediated by increased levels of ACPA
4. Effective treatment of CP in patients with RA will result in:
4.1. Improved RA disease score;
4.2. Improved actual joint inflammation;
4.3. Improved overall inflammatory burden and potentially, its systemic impact

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 07/09/2018, Ethical Committee of Centro Hospitalar e Universitário de Coimbra (Praceta Prof. Mota Pinto, 3000-075 Coimbra, Portugal; +351 239400408; secetica@chuc.min-saude.pt), ref: CHUC-130-17; 0194/CES

Study design
Phase 1. Cross-sectional study
Phase 2. Open prospective randomized controlled intervention study

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
Periodontitis
Rheumatoid Arthritis

Interventions
PHASE 1. A cross-sectional study of the prevalence of CP and its correlates in patients with RA

Tasks:
1. Assessment of prevalence of CP and its severity degrees in a population of RA patients
2. Establishment of a relationship between CP and its severity degrees with RA autoantibody profile
3. Validation of a self-reported periodontal screening questionnaire
4. Recruitment of patients for Phase 2

Methods:
Successive RA patients attending Rheumatology Department will be invited to participate. Clinical and routine lab results will be collected from the clinical files. Participants will be categorized according to Disease Activity (DAS28 CRP 3v), as follows:
Group A (Remission) – DAS 28-PCR 3v: < 2.4
Group B (Low Disease Activity)– DAS 28-PCR 3v: ≥ 2.4 ≤ 2.9
Group C (Moderate and High Disease Activity) – DAS 28-PCR 3v: > 2.9 ≤ 4.6 and DAS 28-PCR 3v: > 4.6

Participants will be asked to respond to a self-reported periodontal questionnaire.

Consenting patients will be invited for:
- Blood sample collection for deferred analysis (Biobank)
- Periodontal screening that will be performed by the screening PSR® method
- Full periodontal evaluation in patients with high probability of CP

Those RA patients with moderate and severe CP will proceed to Phase 2.

PHASE 2. Open prospective randomized controlled intervention study in patients with CP and RA
Tasks:
1. Rheumatologic, periodontal and biologic characterization of participants at baseline
2. Non-surgical periodontal treatment
3. Evaluation of the treatment effects upon clinical and biological parameters

Methods:
Consenting participants recruited in phase 1 will be submitted to periodontal biosamples collection and blood sampling for deferred analysis and biobanking.

Patients will then be randomized, within each group, for subgroup 1: immediate treatment and subgroup 2: delayed treatment (to be started after 8 weeks). The randomisation process is the sealed envelope system. Once a patient has consented to enter the trial an envelope is opened and the patient is then offered the allocated treatment regimen (immediate/deferred).

Patients in subgroups 1 will start non-surgical periodontal treatment (NSPT) immediately and be submitted to rheumatologic re-assessment, periodontal revaluation and biological sample collection at 8 and 24 weeks.
Patients in subgroups 2 will start NSPT 8 weeks after first periodontal evaluation and be submitted to similar revaluations (at 16 and 32 weeks).

Intervention Type
Procedure/Surgery

Primary outcome measure
CRP levels measured using blood sample analysis at baseline, 8weeks, 24 weeks

Secondary outcome measures
1. Periodontal and joint clinical parameters measured using medical evaluation at baseline, 8weeks, 24 weeks
2. Subgingival bacterial plaque: quantification of several known pathogens RT-PCR (P. gingivalis, T. forsythensis, T. denticola, P. intermedia, A.a. and F. Nucleatum) measured using laboratorial analysis (RT-PCR) of collected subgingival bacterial plaque at baseline, 8weeks, 24 weeks
3. Antibodies anti-citrullinated proteins measured using blood sample analysis at baseline,

8weeks, 24 weeks
4. Serum Cytokines (pro and anti-inflammatory) measured using blood sample analysis at baseline, 8weeks, 24 weeks

Overall study start date
01/09/2017

Completion date
01/07/2020

Eligibility

Key inclusion criteria
1. 18-70 years old
2. RA diagnosis according to ACR/EULAR 2010 criteria
3. Capable of understanding the study protocol and willing to provide informed consent for clinical evaluation.
4. DAS28 PCR ≤ 3,1 (with no change in medication, dose, or formulation in RA treatment during the 3 months preceding Phase 1 periodontal evaluation and 32 weeks after)
5. Presence of at least six natural teeth
6. Moderate to Severe CP diagnosis (Clinical Attachment Level > 3mm)
7. Available for all study visits over 32 weeks

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
70 Years

Sex
Both

Target number of participants
20

Total final enrolment
22

Key exclusion criteria
1. Pregnant or breastfeeding
2. Smoking habits (past or current)
4. Chronic respiratory disease that could lead to a present state of respiratory insufficiency
5. Presence of other conditions associated with increased CRP, namely:
5.1. Other inflammatory rheumatic diseases other than RA.

5.2. Other active inflammatory diseases (IBD, chronic infections, etc.)
5.3. Current/actual neoplastic diagnosis/treatment
6. History of infection/ antibiotic therapy within the preceding 4 weeks
7. History of periodontal therapy 6 months prior to the examination;
8. Planned hospitalization for pre-existing condition apart from RA within 32 weeks after Phase 1 periodontal evaluation
9. Hypersensitivity to chlorhexidine digluconate.
10. Contraindications to dental local anesthetic.
11. Current and past (last 6 months) participation in another intervention study

Date of first enrolment
01/09/2018

Date of final enrolment
31/12/2019

Locations

Countries of recruitment
Portugal

Study participating centre
Centro Hospitalar e Universitário de Coimbra
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Sponsor information

Organisation
Coimbra Rheumatology Association (ARCo)

Sponsor details
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Sponsor type
Research organisation

Funder(s)

Funder type
Research organisation

Funder Name
Coimbra Rheumatology Association (ARCo)

Results and Publications

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

Intention to publish date
01/06/2021

Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		13/07/2024	16/07/2024	Yes	No