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Understanding the link between gum disease and heart attacks

Submission date
07/03/2022

Recruitment status
No longer recruiting

Registration date
15/07/2022

Overall study status
Ongoing

Last Edited
14/03/2025

Condition category
Oral Health

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Heart attacks are the main cause of premature death in the UK. It is important to carry out research in this area in order to improve both the health and life expectancy for those at risk of heart disease. It is well known that inflammation within the blood vessels that supply the heart can lead to heart attacks. Inflammation occurs when specific cells within our blood, known as monocytes, respond to a signal and start to invade the cells lining the blood vessels. It is also known that individuals with gum disease (periodontitis) may be at greater risk of suffering a heart attack. However, this link is not fully understood and so further research is required. We have evidence from laboratory studies that gum disease may cause changes in monocytes that can lead to inflammation. This could help to explain why gum disease may promote the onset of heart attacks. We now need to confirm these findings. This study therefore aims to demonstrate that monocytes taken from patients with gum disease behave differently to those taken from healthy (good gum health) volunteers. A greater understanding of these processes may ultimately enable the design of improved therapeutic treatments for heart attacks.

Who can participate?
Clinicians or a member of the dental team at the University of Bristol Dental School will approach participants who are attending the hospital for either periodontal assessment or regular dental appointments (healthy volunteers)

What does the study involve?
1. A clinician will perform a basic periodontal examination to give your gum health a score. This score will allow the clinician to decide if you meet the criteria to be included in the study.
2. A blood sample will be taken by a dental practitioner in the dental chair of the clinic
3. A sample of saliva will be collected.
Some people who go on to have treatment for their gum disease at the Dental Hospital will be asked to provide additional blood and saliva samples during and after their treatment.
The whole process should take no more than 20minutes

What are the possible benefits and risks of participating?
The information gained from this study will help to further understand the link between gum disease and heart attacks and may enable improved treatment of people at risk of heart attack

When blood is taken there will be a sharp scratch from the needle but this should not last long. Slight discomfort and bruising may be experienced due to the withdrawal of blood, but this is no different to giving blood for a blood test.

Where is the study run from?
University of Bristol Dental School (UK)

When is the study starting and how long is it expected to run for?
January 2021 to December 2028

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Dr Daire Shanahan, ds17344@bristol.ac.uk

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
280626

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 50619, MR/V002007/1, IRAS 280626

Study information

Scientific Title
Determining the role of Wnt signalling & IGFBP6 in enhanced atherosclerosis risk in periodontal patients: biomarker & therapeutic potential evaluation

Study objectives
The aim of this study is to determine if the monocytes from people with periodontal disease behave differently from those taken from healthy individuals in a way that heightens the risk of atherosclerosis. We will test the hypothesis that reduced levels of IGFBP-6 and altered Wnt signalling contribute to altered monocyte/macrophage pro-atherosclerotic behaviour in patients with periodontitis. Consequently, modification of IGFBP-6 and/or Wnt signalling will retard atherosclerosis and IGFBP-6, and Wnt signalling proteins will act as suitable biomarkers of atherosclerosis disease progression

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 15/09/2021, London - Bromley REC (Temple Quay House, 2 The Square, Bristol Research Ethics Committee Centre, BS1 6PN, UK; +44 207 104 8105; bromley.rec@hra.nhs.uk), ref: 21/PR/1095

Study design
Observational clinical laboratory study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Understanding the link between gum disease and heart attacks

Interventions
Approximately 150 gum disease(periodontitis severe form of gum disease) subjects and 150 healthy volunteers (good gum health) will be approached once whilst attending a dental clinic

for the management of periodontitis or for a regular dental appointment at Bristol Dental Hospital. Participants will be approached only by members of their clinical care team and not by the researchers.

From these approaches we hope to obtain samples of blood from 125 participants with severe periodontitis and 125 healthy volunteers. This allows for approximately 1/6 of those approached to decline and still reach our targets. Sufficient participants with and without periodontal disease attend Bristol Dental Hospital for it to be possible to approach 250 to take part in this study, and without compromising any other ongoing studies. Saliva will be collected from 20 people with periodontitis and 20 healthy volunteers from the above sample.

Blood and saliva samples will also be collected from people with periodontal disease both pre and post treatment and from age and gender matched healthy volunteers at similar time points (n=12 per group).

Participants will be provided with a Participant Information Sheet.
The Patient Information Sheet explaining the study outlines:
1. What they can expect to happen for sample taking
2. What will happen to their samples – storage, testing
3. Who will have access to their samples
4. Who will have access to the results
5. When their samples will be destroyed
6. It also mentions that the clinician will score their gums for periodontal disease and that their scores will also be provided in anonymised form to the researchers

A sample of blood (2 tubes) will be taken from the participant by a trained clinician using standard venipuncture. A sample of saliva will be collected in a sterile tube (2mls). The clinician will also score the patient's gum health using the Basic Periodontal Exam (BPE). After donation, the participant will have no further participation in the study.

A member of the clinical team will allocate a code to the samples and periodontal scores for each participant and will keep a record of the link between the code and the patient. The researchers will not have access to this code.

Samples will be analysed using established laboratory techniques. It is anticipated that there will be differences in the behaviour of inflammatory cells (monocytes) isolated from the blood samples taken from people with good versus poor (periodontal) gum health. Furthermore, it is expected that successful periodontal treatment will result in a change in monocyte behaviour, allowing for the identification of potential biomarkers. This will be combined with the analysis of salivary biomarkers and allow for the development of a non-invasive diagnostic medium for disease detection.

Intervention Type
Other

Primary outcome measure
Behaviour of inflammatory blood cells (monocytes) will be measured using standard laboratory techniques including western blotting, specific enzyme-linked immunosorbent assays (ELISA), immunocytochemistry, fluorometry, and quantitative polymerase chain reaction at a single time point

Secondary outcome measures

1. Biomarkers to assess a person’s risk for developing heart disease from saliva and blood samples measured using standard laboratory techniques including ELISA and western blotting.
2. Biomarker change following treatment of their gum disease measured using ELISA and other standard laboratory techniques assessing bloods/saliva before periodontal treatment (baseline) and following treatment (typically 6 months later)

Overall study start date
04/01/2021

Completion date
31/12/2028

Eligibility

Key inclusion criteria
People with periodontitis:
1. All people over the age of 18 years
2. Capacity to consent
3. Attending a scheduled dental appointment at the University of Bristol Dental Hospital
4. People with unstable severe periodontitis or a high susceptibility to periodontitis (as defined by the British Society of Periodontology 2019 implementation of the 2017 World Workshop Classification of periodontal and peri-implant diseases and conditions: Stage III/IV and Grade C.)
5. At least 18 erupted teeth

Healthy volunteers:
6. All people over the age of 18 years
7. Capacity to consent
8. Attending a scheduled dental appointment
9. People with no evidence of periodontitis
10. At least 18 erupted teeth

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 274; UK Sample Size: 274

Key exclusion criteria
Exclusion criteria for people with periodontitis:
1. All people under the age of 18 years
2. Those who lack capacity to consent

3. History of cardiovascular disease such as hypertension, angina, previous myocardial infarction, heart failure, aortic disease, arrhythmia, heart valve disease.
4. History of autoimmune/autoinflammatory diseases such as Sjogren's syndrome, rheumatoid arthritis, inflammatory bowel disease, systemic lupus erythematosus, or systemic sclerosis
5. History of endocrine disease including diabetes mellitus types 1 and 2
6. Currently taking antibiotics or has had antibiotics in the preceding 6 months
7. People taking statins, non-steroidal anti-inflammatory medications, immunosuppressive medications or corticosteroids.
8. Smokers of tobacco (including Vaping/e-cigarettes)
9. History of salivary gland disease or oral mucosa disease

Exclusion criteria for healthy volunteers:
10. All people under the age of 18 years
11. Those who lack capacity to consent
12. History of cardiovascular disease such as hypertension, angina, previous myocardial infarction, heart failure, aortic disease, arrhythmia, heart valve disease
13. History of autoimmune/autoinflammatory diseases such as Sjogren's syndrome, rheumatoid arthritis, inflammatory bowel disease, systemic lupus erythematosus, or systemic sclerosis
14. History of endocrine disease including diabetes mellitus types 1 and 2
15. Currently taking antibiotics or has had antibiotics in the preceding 6 months
16. People taking statins, non-steroidal anti-inflammatory medications, immunosuppressive medications or corticosteroids.
17. Smokers of tobacco (including Vaping/e-cigarettes)
18. History of salivary gland disease or oral mucosa disease

Date of first enrolment
04/11/2021

Date of final enrolment
01/06/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University Hospitals Bristol and Weston NHS Foundation Trust
Trust Headquarters
Marlborough Street
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Sponsor information

Organisation
University of Bristol

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Sponsor type
University/education

Website
http://bristol.ac.uk/

ROR
https://ror.org/0524sp257

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

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

Intention to publish date
31/12/2029

Individual participant data (IPD) sharing plan
Anonymised study data will be stored on the University Research Data Storage Facility (RDSF) and analysed by the researchers. The RDSF is a secure facility that is backed up daily. Access is granted by the University Data Steward at the request of the project Chief Investigator, and will be restricted to members of the research team. After the study, with the consent of the participant, research data will be made available as “open data” on the data.bris Research Data Repository. This means the data will be publicly available and so able to be used by other researchers to support additional research in the future. All data relating to participants will be anonymised and so it will not be possible to identify participants from these data.

The University's Data Protection Officer (DPO) isHenry Stuart:
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University Secretary's Office
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Beacon House
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IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 2	07/09/2021	29/03/2022	No	Yes
Protocol file	version 2	17/08/2021	29/03/2022	No	No
HRA research summary			28/06/2023	No	No