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Therapeutic irrigation procedures to treat apical periodontitis - TIPTAP

Submission date 09/09/2019	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 25/09/2019	**Overall study status** Completed	
Last Edited 11/04/2024	**Condition category** Oral Health	

Plain English summary of protocol

Background and study aims
Apical periodontitis is a dental infection which develops around the root of a tooth in the tooth socket and affects approximately 1 in 20 of the UK population. Current treatment aims to remove bacteria from within the root canal space during non-surgical root canal treatment (NSRCT). Despite improvements in techniques available to clear infection from root canals, over the last 20-30 years there has been little improvement in success rates, with one in five cases failing to demonstrate complete healing following NSRCT. This costs the health service and patients time and money in increased referrals to dental hospitals, long waiting lists and increased use of antibiotics.
Dentine is the softer layer of the tooth lying underneath the enamel, which is the hard outer layer. It contains substances that can inhibit bacterial growth. This study aims to investigate whether a dentist can stimulate the release of these substances from the dentine during NSRCT and whether this technique could improve healing of apical periodontitis.

Who can participate?
Medically fit adult patients aged over 18 years with apical periodontitis in single-rooted permanent teeth

What does the study involve?
The participants will be randomly allocated to one of two groups. Both groups will receive NSRCT as normal, but the irrigant solution used to rinse the tooth and root canal will be different for the two groups. Participants will return at 14 days after treatment for the root canal to be filled permanently.

What are the possible benefits and risks of participating?
Patients in both groups will benefit from receiving non-surgical root canal therapy. This will treat apical periodontitis and will aim to allow patients to keep the tooth. Although the substances released by dentine have been shown to have antibacterial and wound-healing actions in the laboratory, there is no guarantee they will provide any additional benefit to patients. However, the results obtained from these participants will contribute to a greater understanding of the treatment of apical disease.

Where is the study run from?
Birmingham Dental Hospital (UK)

When is the study starting and how long is it expected to run for?
January 2019 to October 2024

Who is funding the study?
The British Endodontic Society (UK)

Who is the main contact?
1. Dr Phillip Leo Thomson, p.l.tomson@bham.ac.uk
2. Mr Satnam Singh Virdee, s.s.virdee.1@bham.ac.uk

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
NCT03987659

Secondary identifying numbers
CPMS 41972

Study information

Scientific Title
A randomised controlled pilot study to determine the effect of irrigation techniques used to enhance the release of endogenous signalling molecules from dentine matrix to treat apical periodontitis.

Acronym
TIPTAP

Study objectives
The enhanced release of dentine extracellular matrix components (dEMCs) during irrigation will lead to:
1. Modified inflammatory mediator activity
2. An increased rate of clinical/radiographic periradicular healing

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/07/2019, West Midlands - Black Country Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS; +44 (0)207 1048106; nrescommittee.westmidlands-blackcountry@nhs.net), ref:19/WM/0149

Study design
Randomised; Interventional; Design type: Treatment, Other

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 below to request a patient information sheet

Health condition(s) or problem(s) studied
Apical periodontitis

Interventions
Study design:
A parallel group randomised clinical trial design has been selected to compare the outcomes for the aforementioned control and test groups. However, as there is no previous clinical data on the therapeutic effects of dEMCs, this study will be run as a pilot/feasibility study. A total sample size of up to 40 participants, with up to 20 per group, will be required to generate sufficient preliminary data. This number has been derived from similar studies which have previously analysed the impact of novel clinical interventions on inflammation and healing.

Participant recruitment:
Participants diagnosed with apical periodontitis will be initially identified and made aware of the study by a member of their direct care team on a routine consultation clinic held at the Birmingham Dental Hospital. Patients who express interest in the project will be given a patient information sheet (PIS) and referred (via letter or secure email) to a research screening clinic held at the Birmingham Dental Hospital. Here, a GCP trained clinical member of the research team will discuss the study with the potential participant, answer any questions and confirm that they are eligible against the predetermined inclusion/exclusion criteria. Those who are eligible for inclusion will then be consented by the GCP trained research member and subsequently booked onto 2 treatment sessions where they will be randomly allocated to receive either standard care (NSRCT with conventional irrigation techniques), or experimental care (NSRCT with irrigation protocol to optimise release of dEMCs). The 2 appointments will be 14 days apart and the patient will have to attend a 12-month review appointment for assessment and once completed they exit the study. These timelines comply with the routine care pathway of patients receiving treatment for apical periodontitis at the Birmingham Dental Hospital and are consistent with European Society of Endodontology (ESE)
quality guidelines (2006) so will place no extra burden on them or the patient or treatment site. Those who do not meet the eligibility criteria or are unwilling to take part will be discharged back to the referring clinician who will organise to have any outstanding treatment completed. For those wanting more time to think about participating, they will be contacted by a member of the research team 1 week following the discussion. At this point if the participant wants more time they will be discharged back to the referring clinician so they can pursue other treatment options and have the ability to directly contact the research team using details outlined on the PIS if and when they decide to participate. Withdrawing prior to enrolment or at any stage the trial will not result in any delay the patients' treatment along a conventional pathway.

Randomisation:
A third party provider 'Sealed Envelope', which provides its services free to PhD students, will be used to provide a web based randomisation service with a telephone as back up. Once eligibility criteria have been confirmed, consent is obtained and stratification variables determined

through clinical/radiographic examination, the randomisation can be performed. The allocation of participants into either control arm or intervention arm will be concealed to the operator until all outcome measures have been collected.
To ensure the test and control groups are matched and chance imbalances are avoided in important stratification variables, a computer-based 'minimisation' algorithm will be used. The variables chosen are:
- Age (18-30, 31-50, >51)
- Gender
- Ethnicity
- Size of apical lesion (1-5 mm, >6 mm)

Interventions:
All suitable participants that have volunteered to take part in this study will undergo 2 visits for NSRCT, each appointment being approximately 14 days apart. The treatment of patients in both groups follows conventional treatment protocols apart from the irrigant regime used to optimise release of dEMCs. Briefly on the first visit, the tooth will be anaesthetised with local anaesthetic and isolated with a rubber dam. Using cooled diamond burs, the root canal will then be accessed and shaped using rotary nickel-titanium files after the root length has been determined using an electronic apex locator in conjunction with a radiograph. In the control group, a conventional irrigant regime which does not release dentine matrix growth factors will be used whereas in the test group, a novel regime which has been optimised by our group to release dEMCs will be employed. The irrigants used in both groups are widely used solutions in endodontic therapy (Haapasalo et al., 2010) however, it is the timings at which these irrigants are used during root canal therapy which will allow the release of dentine matrix growth factors. Once these stages have been completed, a temporary filling will be placed onto the tooth and the patient recalled for the second visit approximately 14 days later. On the second visit, the temporary filling will be removed and the after the root canal filled followed by a permanent restoration to prevent bacterial ingress.

Intervention Type
Other

Primary outcome measure
Success rate measured using clinical/radiographic information (i.e. absence of pain and resolution of swelling, pain on percussion/palpation and reduction in size of periradicular lesion) collected immediately before treatment, after treatment and then again at a 12-month follow-up. - Treatment success will be determined based on criteria outlined by the European Society of Endodontology (ESE) Quality Guidelines for NSRCT. In these criteria, outcomes are defined as being 'favourable' (absence of pain, swelling and other symptoms, no sinus tract, no loss of function and radiological evidence of a complete healing), 'uncertain' (absence of pain, swelling and other symptoms, no sinus tract, no loss of function and radiographic evidence of some healing) and finally 'unfavourable' (tooth associated with clinical signs and symptoms of infection such as pain and swelling, sinus tract, loss of function and no radiographic evidence of healing.

Secondary outcome measures
Periradicular inflammatory mediator profile in periradicular tissue fluid retrieved through the root canal and collected on paper points quantified against the Olink Inflammation panel of 92 inflammation-related biomarkers using a Multiplex ELISA assay at baseline and 2 weeks post-intervention

Overall study start date
01/01/2019

Completion date
01/10/2024

Eligibility

Key inclusion criteria
1. Diagnosed with apical periodontitis
2. Permanent teeth
3. Medically fit
4. Adult patients (> = 18)
5. Voluntarily consent to partake in the study

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 40; UK Sample Size: 40

Total final enrolment
40

Key exclusion criteria
1. Teeth in sextants with active periodontal disease (i.e. pocketing of > 5 mm)
2. Tooth unable to retain a rubber dam
3. Teeth that have had previous endodontic treatment
4. Root apex in close proximity to the maxillary sinus
5. Antimicrobial therapy within 3 months prior to the screening clinic
6. Pregnant or breastfeeding women
7. Do not have capacity to consent
8. Systemic condition that would reduce immune function

Date of first enrolment
01/10/2019

Date of final enrolment
01/10/2023

Locations

Countries of recruitment
United Kingdom

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
University of Birmingham

Sponsor details
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Sponsor type
University/education

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Other

Funder Name
British Endodontic Society

Results and Publications

Publication and dissemination plan

Planned publication in a high-impact peer reviewed journal within one year of the end of the trial.

Intention to publish date
01/10/2025

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version V2.0	11/06/2019	25/09/2019	No	No
HRA research summary			26/07/2023	No	No