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Microbiological and clinical evaluation of ultrasonic debridement with/without erythritol air polishing during supportive periodontal therapy in arches with full-arch fixed implant-supported prostheses: protocol for a randomised controlled trial

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ABSTRACT

Introduction Implant-supported prostheses are often successfully used in edentulous patients. However, the incidences of peri-implant mucositis and peri-implantitis increase over time. The accumulation of pathogenic bacteria adjacent to prostheses can induce peri-implant disease. Plaque removal is recommended to prevent and manage peri-implant diseases. The purpose of this study is to compare the plaque removal efficacy of ultrasonic debridement with/without erythritol air-polishing powder around implants and bridges in patients with full-arch fixed implant-supported prostheses as well as the effects of these two methods on the rates of peri-implant mucositis and peri-implantitis, and the submucosal microbiota composition over 5 years in patients undergoing supportive periodontal therapy.

Methods and analysis We plan to enrol 10 edentulous (maxilla and/or mandible) patients seeking full-arch fixed implant-supported prostheses. The study will use a split-mouth model in which contralateral quadrants are randomly assigned to two groups. Group 1: one contralateral quadrant of full-arch fixed implant-supported prostheses will undergo ultrasonic debridement combined with erythritol air-polishing powder. Group 2: a separate contralateral quadrant of full-arch fixed implant-supported prostheses will undergo ultrasonic debridement. The 5-year trial will involve a total of 10 re-examinations per participant. The mucosal conditions around the implants will be recorded at 6-month intervals after restoration. Peri-implant submucosal plaque will be collected at each re-examination, and the bacterial flora will be analysed by 16s ribosomal RNA gene sequencing. X-ray examinations will be conducted at 12-month intervals to evaluate the marginal bone level around implants.

Ethics and dissemination This prospective single-centre, randomised controlled trial (PKUSSIRB-202054045) has been approved by the Ethics Committee of Stomatology School and Hospital of Peking University. Data will be registered with the International Clinical Trials Registry Platform. Additionally, we will disseminate the results via publication in scientific journals.

Trial registration number ChiCTR-2000032431.

Strengths and limitations of this study

- This is a randomised, prospective, separately controlled trial.
- The follow-up duration is 5 years.
- We will evaluate the effects of erythritol air-polishing alone; we will not evaluate the effects of other air-polishing materials.
- The influences of local conditions will not be excluded, such as the local keratinised mucosa width and the dental arch contour.
- The study will include only generally healthy patients; it will exclude patients with systemic diseases.

INTRODUCTION

Implant-supported prostheses are often successfully used in edentulous patients.[1 2] However, the incidences of peri-implant mucositis and peri-implantitis increase over time.[3] In a long-term clinical study, 16%–29% of patients and 5%–6% of implants showed marginal bone loss indicative of peri-implantitis after 12–15 years of function.[4] The accumulation of pathogenic bacteria adjacent to prostheses can induce peri-implant disease.[5 6] Plaque removal is recommended to prevent and manage peri-implant diseases.[7] Professional intervention is needed for plaque control around implant prostheses, particularly in patients with full-arch fixed implant-supported prostheses.[8]

Professional plaque cleaning may be performed using manual curettes,[9] ultrasonic scalers,[10] air polishers[11] and lasers.[12]

Air polishing uses abrasive powder in a stream of air to polish a microrough surface. It is an efficient mechanical debridement method for peri-implantitis treatment.[13] Air polishing removes calculus and plaque,[14] reduces peri-implant mucosal inflammation[15 16] and has superior efficacy to manual curettes and ultrasonic scalers.[10 17] However, few studies have investigated the influence of regular air polishing on peri-implant inflammatory diseases, or the influence of peri-implant bacteria removal on full-arch fixed implant-supported prostheses.[18] The peri-implant microbiota are influenced by the flora of the remaining teeth in patients with partial edentulism[19]; our split-mouth randomised controlled trial will evaluate the effects of air polishing on the peri-implant microbiota.

This split-mouth randomised controlled trial is designed to compare the plaque removal efficacy of ultrasonic debridement with/without erythritol air-polishing powder around an implant and bridge in patients with full-arch fixed implant-supported prostheses as well as the effects of these two methods on the rates of peri-implant mucositis and peri-implantitis, and the submucosal microbiota composition over 5 years in patients undergoing supportive periodontal therapy.

METHODS AND ANALYSIS

Trial design

The proposed study is a 5-year randomised controlled trial. We plan to enrol 10 edentulous (maxilla and/or mandible) patients seeking full-arch fixed implant-supported prostheses. The study will use a split-mouth model in which contralateral quadrants are randomly assigned to two groups. Group 1: one contralateral quadrant of full-arch fixed implant-supported prostheses will undergo ultrasonic debridement (ultrasonic devices with polyetheretherketone-coated tips, EMS Master 750) combined with erythritol air-polishing powder (EMS AirFlow handy V.3.0, Perio). Group 2: a separate contralateral quadrant of full-arch fixed implant-supported prostheses will undergo ultrasonic debridement. The 5-year trial will involve a total of 10 re-examinations per participant. The mucosal conditions around the implants will be recorded at 6-month intervals after restoration. Peri-implant submucosal plaque will be collected at each re-examination, and the bacterial flora will be analysed by 16s ribosomal RNA (rRNA) gene sequencing. X-ray examinations will be conducted at 12-month intervals to evaluate the marginal bone level around implants (figures 1 and 2).

Study setting, ethical considerations and recruitment

This prospective randomised controlled trial (PKUSSIRB-202054045) has been approved by the Ethics Committee of Stomatology School and Hospital of Peking University, China. In addition, the study is registered in clinicaltrials.gov (ChiCTR2000032431). Participants will be recruited at Stomatology School and Hospital of Peking University. We will approach participants who meet inclusion criteria about their interest regarding this study. If interested, potential participants will be referred to our study team members who will provide a detailed description of the study procedures and invite the individual to participate. Written, informed consent will be

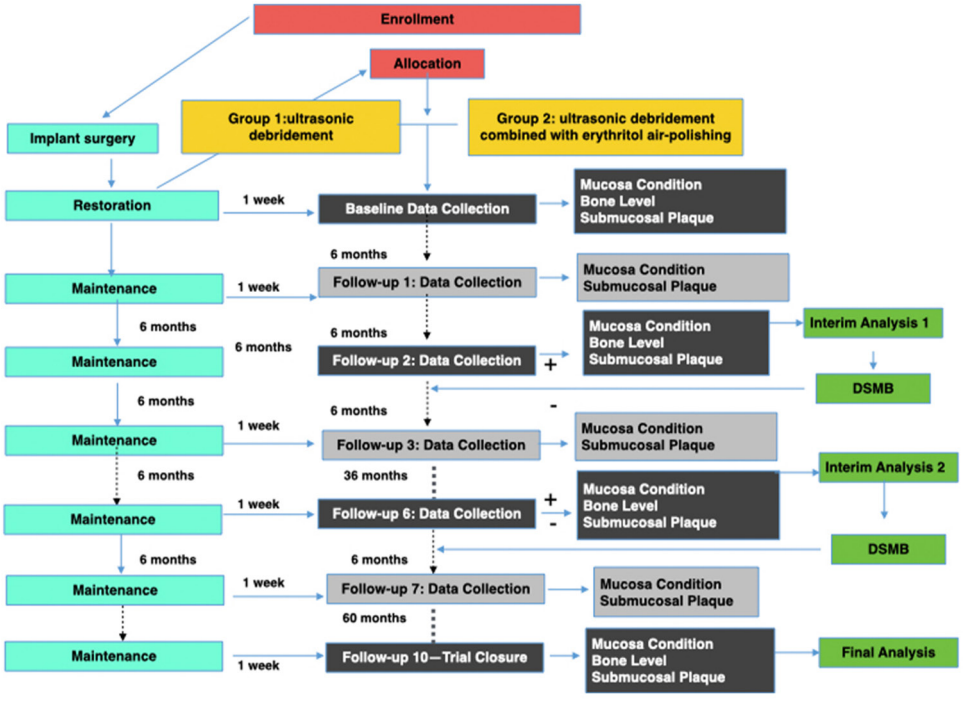

Figure 1 Consolidated Standards of Reporting Trials diagram.

	STUDY PERIOD												
	Enrolment			Allocation	Post-allocation								
TIMEPOINT	Prior to Allocation			Month0	Month6	Month12	Month18	Month24	Month30	Month36	Month 42	Month 48	Month 54	Month 60
ENROLMENT														
Implant surgery	X													
Eligibility screen	X													
Informed consent		X												
Restoration			X											
Allocation				X										
INTERVENTIONS														
Ultrasonic debridement combined with erythritol air-polishing powder				X										
Ultrasonic debridement				X										
ASSESSMENTS														
Implant survival rate						X				X				X
peri-implant plaque index				X	X	X	X	X	X	X	X	X	X	X
bleeding on probing				X	X	X	X	X	X	X	X	X	X	X
suppuration				X	X	X	X	X	X	X	X	X	X	X
probing depth				X	X	X	X	X	X	X	X	X	X	X
paralleling X-ray				X		X		X		X		X		X
Microbiotia sample collection				X	X	X	X	X	X	X	X	X	X	X

Figure 2 Participant timeline.

obtained prior to the collection of any study data. The clinical component of the study was initiated in May 2020 at the Stomatology School and Hospital of Peking University, China.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research. Patients meet the inclusion criteria of this study will be involved in the recruitment. The patient will assess the burden of the intervention by themselves. The outcome measures will not be informed by patients' priorities, experiences and preferences. Data will be registered with the International Clinical Trials Registry Platform and will be disseminated to study participants.

Eligibility

Inclusion criteria are as follows: edentulous jaw, American Society of Anesthesiologists physical status I–II (generally healthy), good oral hygiene and good compliance and never smoker status. Exclusion criteria are age <18 years; antibiotic use in the past 3 months: if a participant uses an antibiotic in the last 3 months before recruitment, we will exclude him/her from this trial; systemic disease, including uncontrolled diabetes mellitus, cardiovascular disease, immune-related diseases, blood disorders (eg, coagulation disorders) and severe osteoporosis; long-term use of steroids, antiepileptics or bisphosphonates; infection with HIV, hepatitis B or *Treponema pallidum*; bruxism, where sleep bruxism is rhythmic (phasic) or non-rhythmic (tonic) masticatory muscle activity during sleep, which is not a movement or sleep disorder in otherwise healthy individuals, while awake bruxism is repetitive or sustained tooth contact and/or bracing or thrusting of the mandible during wakefulness, which is not a movement disorder in otherwise healthy individuals[20 21]; uncontrolled infection in the area intended for implant placement or other areas; maxillofacial tumour; face–neck radiotherapy; mental illness and/or inability to provide informed consent.

Interventions

The treatment plan comprises placement of four to eight implants in the maxilla and/or mandible. Participants will receive the following oral hygiene instructions before entering the study: brush your teeth two times per day using a manual or electric toothbrush and fluoride toothpaste for at least 5 min, use a Waterpik at least once per day, floss under the bridge as much as possible and do not use mouthwash.

The study will use a split-mouth model in which contralateral quadrants are randomly assigned to two groups. Group 1, one contralateral quadrant of a full-arch fixed implant-supported prostheses will undergo ultrasonic debridement (ultrasonic devices with

polyetheretherketone-coated tips, EMS Master 750) combined with erythritol air-polishing powder (EMS Air-Flow handy V.3.0, Perio) at 6-month intervals. Group 2, a separate contralateral quadrant of a full-arch fixed implant-supported prostheses will undergo ultrasonic debridement at 6-month intervals. One week after each follow-up, clinical and X-ray assessments will be performed. Subsequently, the prosthesis will be removed for microbiota sampling as well as ultrasonic debridement in group 1 and ultrasonic debridement combined with air polishing in group 2. After ultrasonic debridement and air polishing, irrigation with 0.12% chlorhexidine (ie, the most effective antiplaque mouthwash)[22] will be performed for 1 min.

Outcome variables

The primary outcome variables will be the implant survival rate, peri-implant plaque index, peri-implant probing depth (PPD), peri-implant bleeding on probing (BOP), marginal bone loss and peri-implant submucosal bacteria. The secondary outcome variable will be peri-implant plaque staining.

Clinical assessment

Clinical examinations will be performed at baseline (immediately after prosthesis placement) and at 6-month intervals after final prosthesis placement. The following parameters will be evaluated during clinical examinations: peri-implant plaque index, BOP (0/1), suppuration (0/1) and PPD. The peri-implant plaque index, BOP, suppuration and PPD will be evaluated at six sites per implant: mesiobuccal, buccal, distobuccal, distolingual/palatal, lingual/palatal and mesiolingual/palatal.[23] PPD will be measured to the nearest millimetre using a graded probe (Hu-Friedy Manufacturing, Chicago, Illinois).

The peri-implant plaque index will be graded as follows: 0, no plaque in the gingival margin area; 1, thin plaque on the tooth surface of the gingival margin area not visible on scraping with the side of the probe tip; 2, medium amount of plaque on the adjacent surface; 3, large amount of soft dirt in the gingival sulcus or the gingival margin area and the adjacent surface.

Plaque staining will be performed as follows: a researcher will use tweezers to gently press a small cotton ball soaked with plaque stain (Sunstar, USA) on the bridge. Next, the patient will gargle two times. Digital images of the entire bridge area will be acquired after plaque staining using the standard imaging protocol.[24] Quantitative digital image analysis software (Image Pro Plus V.7.0) will be used to analyse the images. The Quigley-Hein plaque indices[25] of the bridge area will be evaluated by calculating the percent plaque-stained area.

To maximise reproducibility, the two examiners will be trained and calibrated prior to the trial.[26] The SE of continuous periodontal clinical parameters will be calculated. For the other clinical variables, >90% mean agreement between examiners will be considered satisfactory (Kappa test).

X-ray assessment

Marginal bone loss will be assessed as follows: periapical radiographs will be acquired immediately after final prosthesis placement, then annually thereafter. For standardisation, a paralleling technique will be used with an intramural digital system (Digora Toto, Soredex, Finland). Kodak Dental Imaging V.6.1 software (Carestream Health, Rochester, New York) will be used for radiographic analysis. The crestal bone level will be measured as the vertical distance from 2 mm below the implant–abutment interface to the most crestal part of the alveolar bone.[27 28] In each group, the mean mesial and distal peri-implant marginal bone losses will be measured to the nearest millimetre using Scion Image software (Scion, Fredrick, Maryland).

Peri-implantitis lesions will be defined as PPD ≥5 mm, with either suppuration or the presence of BOP plus radiographic evidence of bone loss (>2 mm); alternatively, they will be identified by consensus among the clinicians involved in the study.[29] Peri-implant mucositis lesions will be defined as the presence of suppuration or the presence of BOP without radiographic evidence of bone loss. Clinically healthy implant sites will be defined as a probing depth ≤4 mm, absence of BOP or suppuration and no radiographic evidence of bone loss. The rates of peri-implantitis and peri-implant mucositis will be calculated at 1, 3 and 5 years after the final restoration.

Laboratory assessment

Sample collection

Sulcus sampling will be performed immediately before prosthetic treatment and at 6-month intervals after final prosthesis placement. Antimicrobial mouthwash will not be used within 48 hours of sampling, and food will not be consumed within 1 hour of sampling. Briefly, prior to sampling, clinical sites will be isolated and dried; supramucosal plaque and calculus will be carefully removed. Submucosal plaque around a single implant will be sampled by insertion of four sterile paper points (Number 30) into the base of the sulcus or pocket for 20 s. The paper points will be placed in labelled Eppendorf tubes and frozen for transportation to the laboratory.

Processing of microbiological samples

Detection of periodontopathic bacteria by PCR will use specific primers designed from 16s rRNA sequences. Genomic DNA will be isolated from collected samples using a TIANamp Micro DNA Kit (TianGen Biotech, Beijing, China). Detection of *Porphyromonas gingivalis*, *Fusobacterium nucleatum* spp and *Prevotella intermedia* will be performed by PCR in a thermal cycler (Gene Amp PCR System 2700, Foster City, California) using primers reported elsewhere.[30] PCR products will be electrophoresed in 2% agarose gels, stained with Goldview DNA Stain (TaKaRa Biotechnology, Dalian, PR China) and examined under 300 nm ultraviolet light (Bio-Rad, USA).

Sample size

Sample size was calculated by NCSS-PASS software. At 3 months, the PPD reduction induced by glycine powder air polishing combined with Teflon curettes debridement was reportedly 1.3 mm (SD: 1.2 mm). The reductions in *Treponema denticola*, *P. gingivalis* and *Tannerella forsythia* numbers were reportedly 2×10^5, 5×10^5 and 2×10^5, respectively. The PPD reduction by ultrasonic debridement was 0.91 mm (SD: 0.98 mm).[9 14] The reduction in BOP% at 3 months after erythritol powder air polishing was 40.45%,[31] whereas it was 9% after ultrasonic debridement.[32] The criteria for significance were α=0.05 (type I error) and β=0.10 (type II error). The analysis was two tailed. Assuming a dropout rate of 30%, 18 implants per group and nine patients in total are needed.

Randomisation, allocation and blinding

The study will use a split-mouth model in which contralateral quadrants will be randomised by computer-generated permuted block randomisation with an allocation ratio of 1:1. Randomisation will be performed using sealed envelopes that will be opened after the final impression is recorded. Microbiota analysis will be performed in a blinded manner after assignment to interventions. Each sample will have a number associated with an allocation sequence, dental position and acquisition time. The PCR analyst will be blinded to sample identity.

Statistical methods

Statistical analysis will be conducted using Statistical Package for Social Sciences software (SPSS, V.19.0 for Macintosh, SPSS).

Clinical monitoring

Continuous variables will be described as means±SD or medians. Grade and quantitative data will be described as percentages. Age and other characteristics will be compared by independent t tests. Sex, implant survival rate, peri-implantitis rate and peri-implant mucositis will be compared by χ^2 tests. Clinical and X-ray indices will be compared by independent t tests. The mean percentages of sites with visible plaque, suppuration, PPD ≥5 mm and mean PPD will be computed for each participant and then averaged across participants in each group. Generalised estimating equations will be used to evaluate within-group and between-group differences. Actual p values will be reported; differences will be considered statistically significant when $p<0.05$.

Microbiological monitoring

The mean counts ($\times10^5$) of *P. gingivalis*, *F. nucleatum* spp and *P. intermedia* will be determined in each implant and each patient and then averaged across patients in the test and control groups. Between-group differences in microbiological parameters will be evaluated by the Wilcoxon signed rank test. Longitudinal differences in bacterial abundance will be analysed by the McNemar test. The level of statistical significance will be set at 5%.

Alpha and beta diversity analyses will be performed using Primer V.7 and QIIME V.2[33 34]; these will include alpha diversity, Shannon's diversity index of species number and distribution, Margalef's index of numbers and Pielou's index of evenness of distribution.[35] The significance of differences between control and test participants will be assessed by unpaired Student's t tests. Beta diversity analysis will include visualisation of data at multiple taxonomic levels; unweighted and weighted UniFrac distance metrics will be used to generate principal coordinates analysis plots.[36] Analyses of similarity will be performed to determine whether microbial communities are significantly different between groups. Between-group differences in taxonomic abundance will be evaluated by White's non-parametric test, typically with a false discovery rate cut-off of 0.005, using STAMP software.[37]

Interim analyses

Interim statistical analyses will be performed at 1 and 3 years after prosthesis placement. The analyst will be blinded to patient allocation and will submit the results to the Data and Safety Monitoring Board. The Data and Safety Monitoring Board will announce early termination of the study if the drop-out rate exceeds 20%.

Withdrawal

Patients will be informed at the beginning of study that they have the right to withdraw from the study at any time without providing a reason. Regardless of withdrawal, the required treatment will be provided to all patients. If a participant uses an antibiotic in the 3 months before a follow-up visit, we will collect submucosa samples, perform a clinical examination, record surface roughness and conduct an X-ray examination. We will discard the data from this follow-up. However, the participant will attend subsequent visits and undergo regular periodontal maintenance. If there is no antibiotic use within 3 months of the next follow-up, we will use the data from that follow-up.

DISCUSSION

Peri-implant diseases are common but lack a standard of care.[38 39] Treatment and prevention of peri-implant lesions typically involve mechanical debridement of biofilm and calculus. Mechanical cleaning of full-arch fixed implant-supported prostheses comprises the use of oral hygiene devices and professional oral hygiene interventions. Full-arch fixed implant-supported prostheses are difficult to clean because of their structural complexity, particularly around implant neck surfaces. Furthermore, bridge units exhibit a tight fit with respect to underlying mucosa and gingiva. Removal of plaque from the mucosal surface is indispensable for oral hygiene. Typical oral hygiene devices (eg, manual brushes, dental floss and interdental brushes) do not reach the mucosal surfaces of these bridge units.[40] Bridge-optimised dental

floss, powered brushes[41] and water flossers are recommended for this purpose. However, few patients with full-arch fixed implant-supported prostheses can maintain excellent oral hygiene in the absence of professional periodontal therapy.[41] The proposed technique may enable submucosal biofilm removal around implants and bridges in patients with full-arch fixed implant-supported prostheses.

The major professional mechanical debridement methods are manual debridement, ultrasonic scaling with non-metal tips and air polishing. The instruments involved should be effective but not damage the prosthesis surface or disrupt the implant–soft tissue interface.[42] Air polishing has been reported to significantly improve peri-implant mucosal health in peri-implant disease patients by reducing the plaque index and periodontal pathogen abundance.[9 17] This is the scientific basis of mechanical debridement and plaque control; it could prevent peri-implant inflammatory diseases. Furthermore, air-polishing powder has good biocompatibility[43] and causes few surface alterations.[44] However, air polishing has an unclear influence on the anti-inflammatory effects of ultrasonic scalers in patients with full-arch fixed implant-supported prostheses.

Glycine,[45] sodium carbonate[9] and erythritol[31] are the most frequently used air-polishing powders. Erythritol powder has a smaller particle size than glycine and sodium carbonate; it also exhibits low abrasiveness,[31] a better taste, greater post-treatment biofilm regrowth inhibition[46] and greater water solubility.[47] Additionally, erythritol powder inhibits periodontopathogenic bacteria such as *P. gingivalis*.[48] Therefore, air polishing using erythritol powder has potential for use in supramucosal and submucosal biofilm management around dental implants without eliciting marked surface changes.

Individual differences influence treatment effectiveness[49]; oral hygiene devices and plaque control affect the incidence and progression of peri-implant diseases.[37] This split-mouth randomised controlled study involving patients with full-arch fixed implant-supported prostheses will allow the comparison of plaque removal efficacy between ultrasonic debridement plus erythritol air-polishing powder versus ultrasonic debridement alone through the exclusion of other factors.

The limited evidence available precludes conclusions concerning the efficacy of air polishing for peri-implant diseases. Further studies of combined therapies for peri-implant diseases are needed.

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Contributors JY, PJ, JL and ZY proposed the concept. QL and ZL designed the trial. JY and PJ drafted the manuscript. LT, JH and QL revised the sections concerning randomisation and calculation of sample size. LT and ZL reviewed and finalised the manuscript. All authors read and approved the final version of the manuscript.

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Competing interests None declared.

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Patient consent for publication Consent obtained directly from patient(s)

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