ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
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Quaternary Ammonium Methacryloxy Silicate-containing Acrylic Resin

This study is currently recruiting participants.
Verified by Frank Tay, BDSc (Hons), PhD, Kimmerling Holdings Group, LLC, August 2015

Sponsor:	Frank Tay, BDSc (Hons), PhD
Collaborators:	Wuhan University Washington University School of Medicine Fourth Military Medical University Tongji Hospital Georgia Regents University
Information provided by (Responsible Party):	Frank Tay, BDSc (Hons), PhD, Kimmerling Holdings Group, LLC
ClinicalTrials.gov Identifier:	

Purpose

One of the major challenges in orthodontic treatment is long-term stability. Because removable retainers are worn for at least one year, bacteria and fungi may accumulate on the retainers in the form of multi-species plaque biofilms. This may result in increased incidence of proximal dental caries or oral candida infection. Thus, incorporation of antimicrobial activity in orthodontic acrylic resin to achieve plaque biofilm reduction is highly desirable. An antimicrobial and antifungal quaternary ammonium methacryloxy silicate molecule (QAMS) has been synthesized by sol-gel reaction and incorporated into orthodontic acrylic resin. The QAMS-copolymerized acrylic resin demonstrated contact-killing properties against single-species biofilms in previous in vitro studies and has received US FDA 510(K) clearance for marketing. The objective of the present randomized clinical trial is to determine the in vivo antimicrobial efficacy of the QAMS-containing orthodontic acrylic by using removable retainers that are worn by recruited subjects to create 48-hour multi-species plaque biofilms. The null hypothesis tested is that there is no difference in the antimicrobial activities between QAMS-free and QAMS-containing orthodontic acrylic resin on oral biofilms grown in vivo in human subjects.

Condition
Oral Health

Study Type: Observational
Study Design: Case-Control, Prospective
Official Title: Antimicrobial Activity of a Quaternary Ammonium Methacryloxy Silicate-containing Acrylic Resin: a Randomized Clinical Trial

Further study details as provided by Frank Tay, BDSc (Hons), PhD, Kimmerling Holdings Group, LLC:

Biospecimen Retention: None Retained
Primary Outcome Measure:

- Biofilm killing efficacy [Time Frame: 48 hours] [Designated as safety issue: No]
  In vivo antimicrobial efficacy of QAMS-containing PMMA disks placed in orthodontic retainers that are worn by subjects to create multi-species biofilms

Secondary Outcome Measures:

- Harms [Time Frame: 48 hours] [Designated as safety issue: Yes]
  Adverse effects in the form of redness, inflammation, ulceration or swelling of oral mucosa

Estimated Enrollment: 32
Study Start Date: July 2015
Estimated Primary Completion Date: October 2015
Estimated Study Completion Date: January 2016

Groups/Cohorts	Interventions
Split-mouth control and experimental QAMS-free PMMA disks placed in one side of Hawley retainer; QAMS-containing PMMA disks placed in the other side.	

Detailed Description:

There is increasing demand for orthodontic care worldwide. In the United States, approximately one-fifth of the adolescents and teenagers, and up to 1% of young adults are receiving some form of the orthodontic treatment. One of the major challenges in orthodontic treatment is long-term stability; removable and fixed retainers are required to stabilise the aligned dentition and prevent post-treatment relapse. Most removable retainers are constructed of polymethyl methacrylates (PMMA), which are held by metal clasps around the posterior teeth. Because removable retainers are worn in a moist intraoral environment with fluctuating pH for at least one year, bacteria and fungi may accumulate on or within the retainers in the form of multi-species plaque biofilms that act as reservoirs of these microorganisms. This may result in increased incidence of proximal dental caries or oral candidiasis. Moreover, other opportunistic pathogens such as methicillin-resistant Staphylococcus aureus have been identified from orthodontic retainers, which may potentially lead to local or systemic infection, particularly in orthodontic patients with complicated medical disorders. For adult patients, oral microorganisms derived from removable acrylic appliances have been implicated in bacteria endocarditis, pneumonia, chronic obstructive pulmonary disease and gastrointestinal infection. Production of volatile odoriferous compounds by colonized microorganisms also contributes to halitosis, which affects a person’s communication and psychological well-being.

Microbial plaque biofilm accumulation on removable orthodontic appliances and retainers is usually controlled by mechanical and chemical means. Despite their effectiveness, these procedures demand stringent patient compliance, which may not be readily achievable in those with restricted dexterity. Hence, incorporation of antimicrobial activity in orthodontic acrylic resin to achieve plaque biofilm reduction is highly desirable. Conventional PMMA-based antimicrobial approaches are based on leaching of antimicrobial agents of small molecular mass (e.g. chlorhexidine) into the intraoral environment, application of an antimicrobial coating on the surface of the material or incorporation of antibacterial silver nanoparticles into the PMMA resin. Antimicrobial polymers are rapidly becoming a new class of biomaterials that can be functionalized and tethered to materials and kill microbes without releasing the biocides. For methacrylates, anionic and phosphated PMMA polymers have been created that can copolymerize with PMMA to create acrylic resins with permanent, non-leaching antimicrobial properties.

Cationic polymers containing quaternary ammonium and phosphonium groups possess contact-killing antimicrobial activities. An antimicrobial and antifungal cationic quaternary ammonium methacryloxy silicate molecule (QAMS) has been synthesized by sol-gel reaction between a tetraalkoxysilane and two trialkoxysilanes. Containing a methacryloxy functional group and a long C-18 carbon chain, the QAMS molecule is soluble in MMA monomer and has been incorporated into PMMA orthodontic acrylic resin. The QAMS-copolymerised acrylic resin demonstrated improved fracture toughness without adversely affecting flexural modulus and strength of the orthodontic acrylic. In previous in vitro studies, orthodontic acrylic resins containing 4-6% QAMS were found to possess in vitro immediate diffusional as well as contact-killing antimicrobial properties when tested with Streptococcus mutans, Actinomyces naeslundii and Candida albicans. To investigate the antimicrobial durability of the QAMS-containing acrylic resin, specimens were aged in water for 3 months prior to evaluation of their antimicrobial activities. Even after 3 months of water-ageing wherein any residual effects of diffusional kill would have been completely eliminated, the QAMS-containing orthodontic acrylic resin still possessed antimicrobial activities against single-species biofilms generated from the three microbes. Antimicrobial polymers designed

for biomedical applications should also be minimally cytotoxic to host tissues. In a previous study, the viability of an odontoblast-like cell line derived from mouse dental papilla was examined by exposing these cells to QAMS-containing orthodontic acrylic resin. Results of the cell viability assays indicated that the QAMS-containing orthodontic acrylic resin is relatively non-cytotoxic. The QAMS-containing orthodontic acrylic has received 510(K) clearance for marketing by the U.S. Food and Drug Administration (FDA). Nevertheless, clinical trials are lacking that demonstrate the in vivo antimicrobial potential of QAMS-containing orthodontic acrylic on multi-species biofilms.

Although various multi-species oral biofilm models have been developed and have contributed to the understanding of intraoral microbial adhesion and biofilm formation, these models have drawbacks in that they are unlikely to replicate the variability and in vivo dynamics of plaque biofilms. Apart from differences in structural characteristics between in vitro and in vivo biofilms, the presence of host defenses such as antimicrobial peptides derived from saliva, is seldom take into account in in vitro multi-species biofilm models. More than 600 microbial species have been identified in the human oral microflora, of which approximately 280 species have been isolated in culture. Thus, plaque biofilm profiles are unique among individuals, being modulated by different environmental factors as well as variable quorum sensing signals derived from adjacent microorganisms. These confounding factors may temper the efficacy of antimicrobial polymers in vivo. Accordingly, the objective of the present randomised clinical trial was to determine the in vivo antimicrobial efficacy of the FDA-approved QAMS-containing orthodontic acrylic by using custom-made removable Hawley retainers that were worn intraorally by recruited subjects to create 48-hour multi-species plaque biofilms. Because of the anticipated high variability in the microbial composition of individual plaque biofilms, a split-mouth design was utilised to reduce inter-subject variability, with procedures taken to minimize unwanted carry-across effects. The null hypothesis tested was that there is no difference in the antimicrobial activities between QAMS-free and QAMS-containing orthodontic acrylic resin on oral biofilms grown in vivo in human subjects.

Eligibility

Population in Wuhan China

Sampling Method: Non-Probability Sample
Ages Eligible for Study: 21 Years to 60 Years
Genders Eligible for Study: Both
Accepts Healthy Volunteers: Yes

Criteria

Inclusion Criteria:

- Healthy individual with no history or presence of a systemic disease
- Absence of active caries or periodontal disease with pocket depths deeper than 4 mm

Exclusion Criteria:

- Extensive gag reflex that precludes taking of an intraoral alginate impression
- Presence of cleft palate that precludes the wearing of a Hawley retainer
- Have been using an antimicrobial mouthwash prior to enrolment in the study
- Have been taking antibiotics against infectious diseases in the half year preceding the study

Contacts and Locations

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More Information

Statistical Brief #368. Agency for Healthcare Research and Quality, Rockville, MD.
http://meps.ahrq.gov/mepsweb/data_files/publications/st368/stat368.shtml

25. U. S. Food and Drug Administration. 510(k) premarket notification
http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K141439

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