# AAO Foundation Award Final Report

Type of Award: Research Aid Award

Name of Principal Investigator: Tingxi Wu

Title of Project: Conducting a Pilot Clinical Study to Evaluate the Safety and Efficacy of a Newly Developed Chemical Formula for Managing Bracket-Induced Plaque Formation

Period of AAOF Support: 6/30/2016 – 12/30/2017

Amount of Funding: $5000


Summary/Abstract

Orthodontic brackets hamper effective oral hygiene with heavy accumulation of dental plaques in the area, leading to the negative consequences such as decalcification of enamel surface (white spot lesions), caries, as well as gingival inflammation. So far, no effective methods could control the dental plaque in orthodontic patients. Thus, I specifically focused my research effort on developing new ways to inhibit bracket-induced plaque formation. My previous research led to the discovery of several anti-plaque formation chemical compounds that were formulated into toothpaste with strong inhibitory effect against bracket-induced plaque *in vitro*. In this study, building on the strong preliminary data, a randomized, double-blinded, placebo-controlled, pilot clinical study was conducted to evaluate the *in vivo* safety and efficacy of this newly formulated toothpaste on managing bracket-induced plaque formation.

The proposed study was reviewed and approved by the IRB at University of California, Los Angeles. The objectives and protocols, as well as possible drawbacks and risks due to the study, were explained to each subject orally and in writing. They were also informed of the option to withdrawal from the study at any time without disrupting their current orthodontic treatment. All subjects were informed and signed their consent forms.

Participants were all screened for enrollment based on the inclusion and exclusion criteria listed in the proposal. After the enrollment period, 4 volunteers were randomly assigned to join safety study group. the rest of participants were randomized assigned to efficacy study groups to receive either toothpaste without new formula (placebo group) or toothpaste with new formula (treatment group). Once randomized, volunteers received a toothpaste and Oral-B toothbrush. The toothpastes were packaged the same manner in treatment group and control group without identified information. Participants applied toothpaste twice per day (morning and night) for 28 days. The investigator, study staff/clinicians and the sponsor's assigned team members (e.g., the Clinical Monitor and the Medical Monitor) were blinded as to whether subjects were receiving active or placebo until the study was formally unblinded for data analysis purposes.

For safety study group, 4 volunteers applied toothpaste with new formula twice per day for 28 days and were monitored at day 0, 7, 14, and 28. No adverse events were observed including the change of vital signs and targeted physical examination, and intraoral change of hard and soft tissues.

As there were no safety concerns identified, the efficacy study was initiated with 28 days of newly formulated toothpaste administration. Due to the late approval of IRB 3 month before my residency graduation, we were only able to recruit 29 patients to this study with limited time. 15 patients have been recruited as treatment group with the average age of 13.6y, while 14 patients have been recruited as control group with the average age of 13.4 y.

Plaque index and gingival scores in full dentition of the participants were recorded as baseline at day 0 (Visit 0) and then were provided toothpastes. To evaluate anti-plaque effect, study subjects were recalled to the clinic and examined for bracket-induced plaque index and gingival index at day 7, 14, 28 (Visit 2-4). Results of plaque index and gingival scores were expressed as median with the interquartile range (IQR) shown in Fig. 1 and Fig. 2. Variables were compared using non-parametrical tests, Wilcoxon rank-sum test was used for paired data analysis and Mann-Whitney test was used for non-paired data. The level of significance was established at the 0.05 level (two-sided). The analysis was performed using SPSS (SPSS Inc., USA).

Comparing with placebo group, treatment group demonstrated no statistically significance of the changes in plaque index and gingival scores of full dentitions through Wilcoxon paired test; and no detectable significant differences were found in the changes of plaque index and gingival scores after administering toothpaste in either treatment group or placebo group through Mann-Whitney test as shown in Fig. 1 and Fig. 2. However, when we further focused our analysis of the patients with heavy plaque (Plaque Index >=3), we found that the difference of the gingival score on days 14 and 28 when comparing day 0 in treatment group has significant decrease compare to the placebo group on the buccal surface of teeth with bands. The test group for day 14 had a 39.3% difference compared to the placebo, which had a p-value of .0362. For day 28, it was shown even a larger difference of 42.2% with a p-value of .0107. In addition, the gingival score of day 14 on the buccal side of teeth with brackets had a 18.8% reduction for the treatment group in comparison with the placebo. While this was a p-value of .1080 and not statistically significant, we do believe this could be clinically significant.

In summary, the study showed that the new formula is safe as no adverse event was observed during the entire study. On the efficacy part, while study did not observe the statistically significant deduction in plaque index and gingival scores of full dentitions for all subjects, when we focused on patients with heavy plaque (Plaque Index >=3), we did find some statistically and clinically significant reduction in gingival scores within the treatment group, suggesting this newly formulated toothpaste could potentially increase the gingival health in orthodontic patients with heavy plaques.

In discussion, we believe the treatment result would be much more significant when the sample size is increased, and the treatment time is extended beyond 28 days. Starting all patients from the same baseline with prophylaxis at first visit prior to administrating toothpaste may also improve the treatment result. These would be the next steps as I started my assistant professor position at University at Buffalo.

Special acknowledgement to people who were also contributed to this study: Dr. Kendrick Park, Joseph Mullen, Dr. Edward Viloria, Dr. Melissa Agnello, Kenneth Chang Chien, Dr. Nini Tran, Dr. Renate Lux, Dr. Kang Ting, and Dr. Wenyuan Shi.

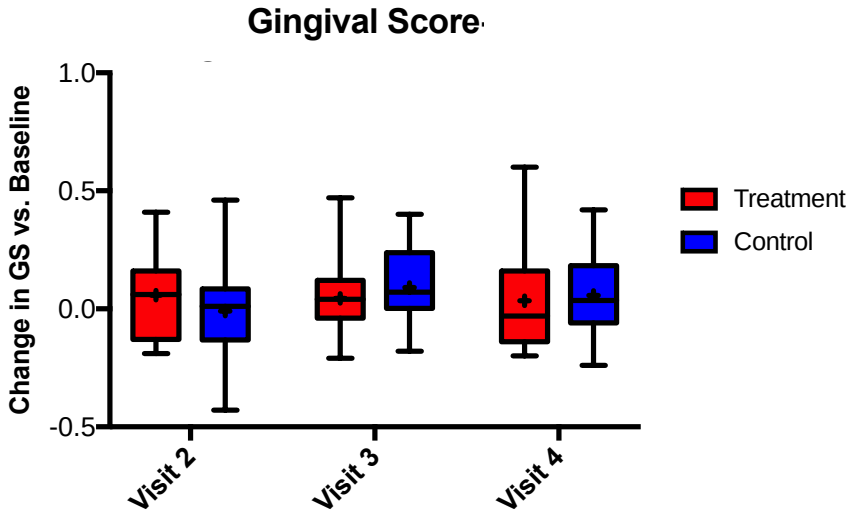


Fig 1. Change of Gingival Score (Visit 2-4, day 7-day 28) compare to baseline (Visit 0, day 0) in treatment group and placebo group. Plots are shown with median, IQR.

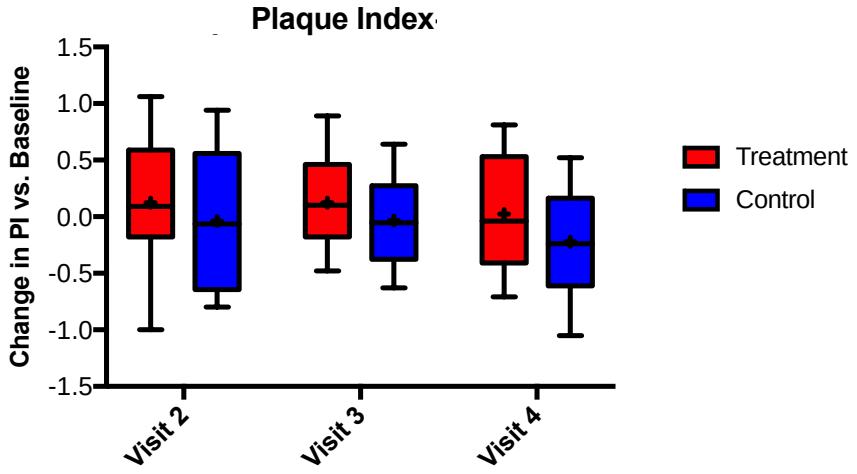


Fig 2. Change of the Plaque Index (Visit 2-4, day 7-day 28) compare to baseline (Visit 0, day 0) in treatment group and placebo group. Plots are shown with median, IQR.

Response to the following questions:

1. Were the original, specific aims of the proposal realized?
Yes, the original specific aims were achieved.

2. Were the results published?
The results have not been published yet. A final manuscript is under preparation and will be submitted to AJODO.

3. Have the results of this proposal been presented?
The results are being planned to present in 2019 AAO annual meeting. AAOF support will be acknowledged.

4. To what extent have you used, or how do you intend to use, AAOF funding to further your career?
The AAOF funding provided by RAA award has allowed me to develop my research program during my residency, which is the key reason for me to obtain tenure track assistant professor position at University of Buffalo. I have full intention to continue applying AAOF funding (such as Orthodontic Faculty Development Fellowship Award) to continue my career development as an academic clinician.