Original Article

A randomized controlled trial evaluating antioxidant–essential oil gel as a treatment for gingivitis in orthodontic patients

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ABSTRACT

Objective: To evaluate the treatment effect of an antioxidant–essential oil gel on orthodontic patients with generalized gingivitis. The gel contains the essential oils menthol and thymol and the antioxidants ferulic acid and phloretin.

Materials and Methods: Thirty patients from the university's orthodontic clinic were screened for gingivitis and randomly allocated into treatment and placebo-control groups. Each patient was evaluated at three orthodontic treatment visits (T1, T2, and T3). A periodontal examination, including probing depth (PD), bleeding on probing (BOP), gingival index (GI), and plaque index (PI) was performed at each visit. Between T1 and T2, patients were instructed to apply a topical gel (active or placebo) to their gingiva twice daily after brushing. From T2 to T3, patients were instructed to discontinue use of the gel.

Results: The treatment group showed statistically significant ($P < .05$) reductions of BOP (−13.6 percentage points) and GI (−0.14) between T1 and T2, and significant increases in BOP (13.3 percentage points) and GI (0.14) between T2 and T3. Except for an increase in the GI between T2 and T3, the control group showed no significant changes in BOP or GI over time. The only other significant changes that occurred pertained to the treatment group, which showed significant increases in PD (0.08 mm) and PI (0.18) between T2 and T3.

Conclusions: Application of a topical antioxidant-essential oil gel is an effective means of reducing inflammation in orthodontic patients with gingivitis. (*Angle Orthod.* 2016;86:407–412.)

KEY WORDS: RCT; Antioxidant; Essential oils; Gingivitis; Treatment

INTRODUCTION

Gingivitis is among the most common pathologies affecting the population, with a reported prevalence of over 50%.[1–3] While gingivitis is common in all age groups, prevalence increases with age. During puberty, the prevalence greatly increases, peaking between the ages of 9–14,[3,4] which is important for orthodontists, considering the high number of adolescents they treat. During the teen years, there is a tendency for the prevalence of gingivitis to decrease, followed by an increase throughout the adult years; by the sixth decade, prevalence approaches 100%.[3] Gingivitis is associated with poor oral hygiene, and increased mechanical plaque retention associated with fixed orthodontic appliances is one of the major reasons for higher rates of gingivitis among orthodontic patients.[5,6] More recently, oxidative stress and cytotoxic effects of materials in fixed appliances and bonding agents have been implicated as factors causing gingival inflammation.[7–10]

Several modalities are available for treating gingivitis, including proper oral hygiene instruction and various dentifrices, gels, and mouthwashes.[11–13] While essential oil mouth rinses provide effective therapy,[14] the current gold standard is use of chlorhexidine mouth rinse.[15] There is also a developing body of evidence to suggest that antioxidants are useful in the treatment of gingivitis.[16–18] The clinical trials evaluating the use of antioxidants for the treatment of gingivitis have found

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Accepted: June 2015. Submitted: April 2015.
Published Online: August 17, 2015

decreased severity of gingivitis, decreased bleeding on probing, and modest reduction in pocket depth.[19,20] However, none of the trials included orthodontic patients or used ferulic acid or phloretin in the treatment of gingivitis.

The aim of the present study was to evaluate the efficacy of a topical gel containing ferulic acid and phloretin, in addition to essential oils, in the treatment of gingivitis in orthodontic patients.

MATERIALS AND METHODS

The study pertains to 32 patients who were undergoing comprehensive treatment at Texas A&M University Baylor College of Dentistry. Power analyses showed that, assuming an effect size of 1, an alpha of 0.05, and a power of 80%, 14 subjects would be needed in each group. Eligible patients had to have their permanent teeth and have bonded brackets in both arches from first premolar to first premolar or from second premolar to second premolar if first premolars had been extracted. Patients also had to exhibit a minimum of 30% bleeding on probing at qualifying sites, including all bonded teeth mesial to the first molars and not adjacent to a banded tooth.

Exclusion criteria included syndromes or systemic diseases that could have contributed to inflammatory processes (such as lichen planus, systemic lupus erythematosus, and benign mucus membrane pemphigoid diseases), pregnancy, active caries, and periodontally compromised teeth. Informed consent to participate was obtained from each patient; the study was approved by the Institutional Review Board of the Texas A&M University Baylor College of Dentistry. Due to the discomfort associated with periodontal probing, one female from the treatment group and one male from the control group dropped out of the study.

The study was double-blinded and placebo controlled. Upon enrollment, patients were randomly assigned to either a placebo-controlled group or an active treatment group based on a predetermined randomly generated list. The treatment group included seven males (16.1 $\pm$ 1.1 years of age) and eight females (15.9 $\pm$ 2.2 years of age); the placebo group contained seven males (16.8 $\pm$ 2.1 of age) and eight females (15.1 $\pm$ 1.9 years of age). The placebo gel consisted of water, thickener, preservative, sorbitol, and a small amount of peppermint. The active treatment group received the same gel, along with the antioxidants phloretin and ferulic acid, in addition to essential oils (AO ProVantage Dental Gel, Periosciences, Dallas, Tex).

All the patients were shown how to apply a pea-sized amount of gel to their buccal and lingual/palatal gingiva twice a day immediately after brushing. They were then instructed to thoroughly expectorate after 30 seconds and to avoid rinsing, eating, or drinking for 30 minutes. Patients were further instructed to continue this regimen twice a day until their next regularly scheduled orthodontic treatment visit (most, approximately 4 to 6 weeks).

At the initial visit (T1), each patient received a periodontal examination, which included probing depth (PD), bleeding on probing (BOP), plaque index (PI), and gingival index (GI).[21] Each patient also received oral hygiene instructions; tooth brushing was demonstrated using the Bass technique,[22] which was modified to clean both gingival and occlusal to the brackets. Flossing was demonstrated using floss threaders (Gum Eez-Thru, Sunstar Americas Inc, Chicago, Ill).

At the patients' next regularly scheduled visit (T2), they received another periodontal examination, and were instructed to discontinue use of the gel, but to continue with a proper oral hygiene regimen until their next visit. At the follow-up visit (T3), each patient again received a periodontal examination (Figure 1).

The interval from T1 to T2 was 35.7 $\pm$ 10.8 days and 42.6 $\pm$ 23.5 days for the treatment and control groups, respectively. The entire study period, from T1 to T3, was 78.3 $\pm$ 29.5 days for the treatment group and 92.8 $\pm$ 33.9 days for the control group. Group differences in duration were due to variation in treatment intervals and missed appointments. There were no statistically significant group differences in duration between T1 and T2 ($P = .775$) or between T2 and T3 ($P = .239$). Based on the experimental gingivitis model, these intervals were judged to be sufficient for both the resolution and development of gingivitis.[21]

Evaluation

Each periodontal exam was performed by a single investigator using a UNC periodontal probe and No. 5 explorer (Hu-Friedy, Chicago, Ill). PD was recorded at six sites (distobuccal, facial, mesiobuccal, distolingual, lingual, mesiolingual) on each tooth. After a wait of 30 seconds, BOP was assessed visually at the same sites and recorded as present or absent. GI and PI were recorded using the GI and the Silness-Löe plaque index, respectively.[21] PI, GI, and PI were all expressed as averages for each tooth; BOP was expressed as a percentage of sites for each tooth.

Statistics

SPSS version 22 (SPSS Inc, Chicago, Ill) was used to analyze the data, using a $P < .05$ significance level. Mean and standard deviation were utilized as

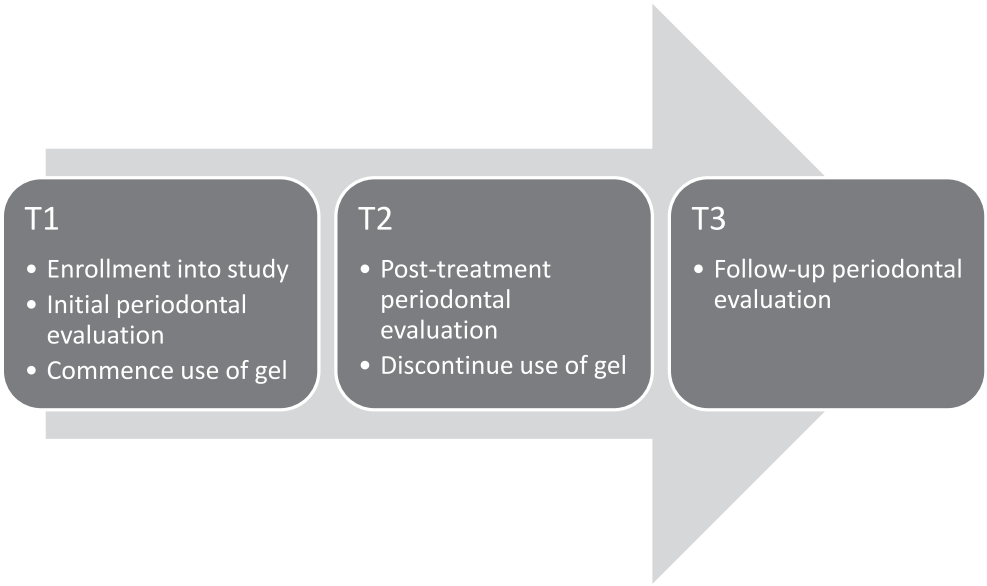

Figure 1. Patient flow through the study from T1 to T3.

descriptive statistics because the data were normally distributed. However, due to the small sample size, the Mann-Whitney *U* test was used to evaluate group differences, and the Wilcoxon signed ranks test was used to evaluate differences between time points.

RESULTS

Bleeding on Probing

At the initial T1 examination, BOP occurred at fewer sites in the treatment (62.9%) than in the control (72.1%) group, but the difference was not statistically significant after Bonferroni correction (Table 1). From T1 to T2, BOP decreased significantly in the treatment group and did not change significantly in the control group, resulting in a statistically significant group difference in the changes that occurred (Table 2) and a statistically significant group difference at T2. The treatment group also showed a statistically significant 13.3% increase in BOP between T2 and T3, while the 7.6% increase in the control group was not statistically significant. At T3, significantly fewer sites bled in the treatment than in the control group (61.2% vs 76.20%).

Probing Depth

At T1, the PDs of the treatment and control groups were not significantly different. There was a significant group difference in the changes between T1 and T2; PD decreased in the treatment group and increased in the control group. This produced a statistically significant difference at T2. From T2 to T3, the treatment group increased while the control group showed no statistically significant change, resulting in no statistically significant difference at T3.

Gingival Index

At T1, the GI was higher in the treatment than in the control group, but the difference was not statistically significant after Bonferroni correction. From T1 to T2, there was a statistically significant reduction in the GI of the treatment group and an insignificant reduction in the control group. At T2, the treatment group GI was significantly smaller than that of the control group. Between T2 and T3, the treatment and control groups showed similar increases. At T3, the GI of the

Table 1. Gingival Evaluation Scores at the Three Time Points and Probability (Prob) of Group Differences

% Sites with BOP[a]	T1	T2	T3
Treatment	62.9 ± 12.9	49.2 ± 15.7	61.2 ± 9.3
Control	72.1 ± 10.7	69.1 ± 16.7	76.2 ± 12.0
Prob group difference	0.042	0.002*	0.004*
Probing depth (mm)	T1	T2	T3
Treatment	2.58 ± 0.16	2.54 ± 0.09	2.61 ± 0.13
Control	2.60 ± 0.21	2.65 ± 0.11	2.66 ± 0.13
Prob group difference	0.748	0.008*	0.422
Gingival index	T1	T2	T3
Treatment	1.56 ± 0.14	1.42 ± 0.17	1.54 ± 0.14
Control	1.68 ± 0.12	1.61 ± 0.20	1.74 ± 0.14
Prob group difference	0.017	0.009*	0.001*
Plaque index	T1	T2	T3
Treatment	0.95 ± 0.28	0.87 ± 0.24	1.05 ± 0.32
Control	1.04 ± 0.36	1.17 ± 0.41	1.14 ± 0.32
Prob group difference	0.411	0.023	0.457

[a] Indicates bleeding on probing.
* Indicates statistically significant group differences after Bonferroni correction.

Table 2. Treatment and Posttreatment Changes in Gingival Condition and Probability of Change

	T1–T2	T2–T3	T1–T3
Percentage point change in sites with BOP[a]			
Treatment group	−13.6 ± 10.2[b]	+13.3 ± 14.4*	−1.2 ± 8.1
Control group	−3.0 ± 12.5	+7.6 ± 15.4	+4.1 ± 9.6
Prob group difference	0.025	0.523	0.045
Change in probing depth (mm)			
Treatment	−0.03 ± 0.15	+0.08 ± 0.12	+0.04 ± 0.14
Control	+0.05 ± 0.16	0.00 ± 0.10	+0.06 ± 0.15
Prob group difference	0.004*	0.051	0.442
Change in gingival index			
Treatment	−0.14 ± 0.11*	+0.13 ± 0.15*	−0.02 ± 0.13
Control	−0.07 ± 0.18	+0.13 ± 0.20	+0.06 ± 0.12
Prob group difference	0.174	0.681	0.014*
Change in plaque index			
Treatment	−0.08 ± 0.24	+0.18 ± 0.25	+0.07 ± 0.31
Control	+0.13 ± 0.43	−0.01 ± 0.34	+0.10 ± 0.49
Prob group difference	0.034	0.161	0.525

[a] Indicates bleeding on probing.

[b] Indicates statistically significant intragroup longitudinal changes after Bonferroni correction.

* Indicates statistically significant group differences after Bonferroni correction.

treatment group was significantly smaller than the GI of the control group.

Plaque Index

Initially, there was no group difference in the PI. From T1 to T2, the PI increased slightly in the control group and decreased slightly in the treatment group, but neither the changes that occurred nor the PI at T2 showed statistically significant group differences. From T2 to T3, the PI in the treatment and control groups increased and decreased, respectively, but neither group showed statistically significant changes. At T3, the PI showed no significant group difference.

DISCUSSION

Compared with the control group, the treatment group demonstrated decreased severity of gingivitis and inflammation. There was a 21.8% reduction in BOP and a 9.0% reduction in the GI. Reductions in gingivitis during treatment may have been due to decreases in inflammatory mediators and various interleukins brought about by the antioxidant component of the gel.[23,24] The essential oil component may also be a factor, since it has been shown to improve BOP and GI in in vivo studies.[11,15,25,26]

The treatment group also showed improvements in PD compared with the control group. The treatment group also showed a statistically significant increase in PD after cessation of the gel use, which further substantiates a treatment effect. As such, the antioxidant–essential oil gel had a positive but limited effect on pocket depth reductions. It must be remembered that both the treatment and control groups began the study with normal probing depths, leaving very little room for reduction of PD. Chapple et al.[19] showed minor gains in clinical attachment levels during the initial phases of treatment with a systemic antioxidant treatment. However, the sample pertained to adults with chronic periodontitis and at least two sites per quadrant having greater than 6 mm of attachment loss.

Plaque levels were also affected by treatment with the antioxidant–essential oil gel. The PI of the active treatment group decreased 8.4% from T1 to T2, while it increased 17% in the control group, resulting in a significant difference at T2. The lack of larger group differences in plaque reduction may have been due to the plaque retentive nature of orthodontic appliances.[6,27] While antioxidants have been shown to have an effect on plaque bacteria in vitro,[16,17] and essential oil mouth rinse has been shown to reduce plaque in vivo,[15,28] these effects may be limited during orthodontic treatment.[29] This is consistent with the findings of Tufekci et al.[25] and Chen et al.,[30] who showed small, and statistically insignificant, increases in PI over 6 months in orthodontic patients using essential oil mouth rinses.

Although the reduction in gingival inflammation with treatment was clinically significant, it is possible that this study underestimated the possible effect size of treatment with an antioxidant–essential oil gel. Other studies using the same GI criteria as this study[15,31,32] and evaluating essential-oil mouth rinses have shown larger reductions in the GI (≈20%) than has the present study (8.9%). However, none of these studies was conducted on patients with orthodontic appliances. The difference could have been due to compliance. In the present study, compliance was evaluated verbally only at T2, with all patients responding that they used the gel twice a day as instructed and seldom missed an application. However, estimates of compliance with home-care oral hygiene regimens have been reported to range between 68% and 82%.[33] It should also be noted that in self-reporting, compliance is often overestimated.[34,35] Use of a written reporting system or periodic reminders to the patients might have increased actual compliance[36] and provided a better estimate of the true effect size in the treatment group.

The oxidative stress,[9,37] cytotoxicity,[8,38] and increased plaque retention[6] associated with orthodontic appliances may also account for the smaller effect size

in the present study. Two recent studies involving essential oil rinse in orthodontic patients report conflicting results. Tufekci et al.[25] showed a small, but statistically insignificant, increase in their modified gingival index (MGI) and bleeding index (BI) over 6 months, while Chen et al.[30] showed a 7% reduction in their MGI and a 66% reduction in BI.

Efforts need to be made to determine the effect of the individual components of the gel (antioxidants and essential oils). It is also necessary to make direct comparisons with currently accepted treatment modalities for orthodontic patients, including essential oil mouth rinses[25,30] and chlorhexidine rinses, which have been shown to decrease both PI and GI.[15] Because of the gel's formulation, it is impossible to determine whether the treatment effect was due to the antioxidants, the essential oils, or from a possible synergistic effect.

CONCLUSIONS

- Topical antioxidant–essential oil gel is an effective means of reducing gingival inflammation in orthodontic patients. It reduced BOP 22%, the GI 13.6%, and the PI approximately 9%.
- Treatment with antioxidant–essential oil gel may reduce the risk of attachment loss and white spot lesions associated with the generalized gingival inflammation that characterizes high-risk orthodontic patients.

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