

Anticalculus efficacy of an antiseptic mouthrinse containing zinc chloride

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The use of zinc chloride as an anticalculus ingredient in dental care products has not been confirmed to be effective when used at a concentration of 0.09 percent and delivered in an antiplaque/antigingivitis mouthrinse.

Therefore, we undertook a controlled clinical study to determine the efficacy of an essential oil antiseptic mouthrinse containing zinc chloride in inhibiting the development of supragingival dental calculus. The antiseptic mouthrinse we tested—Tartar Control Listerine (Warner-Lambert Co.)—contains the same active ingredients that impart antiplaque, antigingivitis and oral malodor properties to several similar products (Original Listerine, Cool Mint Listerine and FreshBurst Listerine, all manufactured by Warner-Lambert Co.).

METHODS

Design. A multicenter clinical trial was conducted under the direction of the principal investigator (M.J.C.) in two New Jersey sites, Northfield and Cedar Knolls. The study occurred in two phases. Phase 1 consisted of an eight-week pretrial period designed to identify a population with a suitable rate of calculus formation. Phase 2 consisted of a 16-week test period in which we used a randomized, double-blind, parallel group design.

After providing informed consent at the start of phase 1, healthy men and women aged 18 to 75 years, each with a minimum of 16 natural teeth (including the six

Background. The authors undertook a controlled clinical study to determine the efficacy of a tartar-control antiseptic mouthrinse in inhibiting the development of supragingival dental calculus.

Methods. After undergoing a dental prophylaxis, 334 subjects with a moderate rate of calculus formation were stratified and randomly assigned to one of three groups: positive control (using a tartar-control toothpaste and an antiseptic rinse), negative control (using a regular toothpaste and an antiseptic mouthrinse) or experimental (using a regular dentifrice and a tartar-control mouthrinse). Subjects brushed and rinsed twice daily, unsupervised, for four months. The researchers assessed subjects' calculus levels using the Volpe-Manhold Index, or VMI, after 16 weeks.

Results. Using analysis of covariance, the authors found that both the experimental group (which used a tartar-control rinse containing zinc chloride) and the positive control group (which used a tartar-control dentifrice containing pyrophosphate) demonstrated statistically significantly lower VMI scores ($P = .001$) than the negative control group (which used a regular dentifrice and an antiseptic rinse). Both anticalculus agents provided a clinically relevant 21 percent reduction in calculus formation.

Conclusion. An antiseptic mouthrinse containing 0.09 percent zinc chloride as the anticalculus agent provides a clinically relevant reduction in calculus formation in people with a moderate rate of such formation.

Clinical Implications. A tartar-control mouthrinse with zinc chloride as the tartar-control ingredient is clinically effective in reducing the formation of calculus.

mandibular anterior teeth), received an oral soft- and hard-tissue examination and a thorough dental prophylaxis to remove dental plaque, stain and calculus. Subjects began brushing twice daily for 60 seconds with a regular (non-tartar-control) dentifrice (Crest Cavity Protection, Procter &

Gamble). After eight weeks, subjects received an oral examination during which we scored their calculus levels using the Volpe-Manhold Index, or VMI.¹⁻³ Subjects with a VMI score ≥ 7.0 and ≤ 30 were qualified to participate in phase 2. Qualified subjects were stratified by calculus scores and randomly assigned to a group using one of three treatment regimens:

- a tartar-control dentifrice (Crest Tartar Protection, Procter & Gamble) with an antiseptic rinse (the positive control group);
- a regular dentifrice (Crest Cavity Protection) with an antiseptic rinse (the negative control group);
- a tartar-control mouthrinse (Tartar Control Listerine, Warner Lambert) with a regular dentifrice (Crest Cavity Protection) (the experimental group).

At the start of phase 2, qualified subjects received a baseline oral soft- and hard-tissue examination and a thorough dental prophylaxis to remove all calculus. Subjects began a 16-week program of brushing twice daily for 60 seconds with their assigned dentifrice, then rinsing for 30 seconds with 20 milliliters of their assigned mouthrinse. All clinical test products dispensed were coded and identical in appearance. Timers were provided to help the subjects comply with the brushing and rinsing time instructions. All clinical examinations were repeated after 16 weeks.

During phase 2, subjects returned to the test site every four weeks for an assessment of their compliance. At these visits, we measured the returned test materials, reviewed use diaries to estimate compliance and distributed a resupply of products and diaries to each subject.

At the final visit (at 16 weeks), all materials were returned and clinical examinations were repeated. Subjects were considered compliant if they had completed at least 80 percent of the twice-daily rinses (as ascertained by diary review) and if the weights and volumes of materials they returned reflected at least 80 percent use of the designated amounts of materials.

Examinations. All examinations (including inspections of oral soft tissues) were performed by the same qualified dental examiner (M.J.C.) at each scheduled visit. He examined buccal, labial and sublingual mucosae; tongue; hard and soft palate; uvula; and oropharynx for inflammation, infection and ulcerations or other lesions. He recorded any aberrations, assessed their severity

and made a judgment as to whether they were attributable to the test materials.

Subjects brushed and rinsed with water only on the mornings of the examination days so as to preclude any bias that could occur from residual product odor in the mouth. Before the calculus examinations, the dental assistant rinsed the lingual surfaces of subjects' mandibular anterior teeth with water and thoroughly dried them. The dental examiner scored calculus at the end of phases 1 and 2 using the VMI¹⁻³ and a calibrated periodontal probe in three planes on the lingual surfaces of the six mandibular anterior teeth.

The examiner performed replicate calculus examinations on 15 subjects at baseline and on another 15 subjects at the final examinations to estimate repeatability.

Statistical methodology. The planned sample size of 339 evaluable subjects (113 per treatment group) provides at least 80 percent power to detect a difference in total VMI calculus score of 13 percent from the negative control mean. The negative control mean and standard deviation used in this calculation were 9.51 and 3.30, respectively. The efficacy variable for this trial was total supragingival calculus score at 16 weeks, determined by means of the VMI. We derived the total from three individual scores on each of six anterior teeth.

We compared the three treatment groups with respect to age and baseline total VMI score by means of a two-way analysis of variance, or ANOVA, with three factors: treatment, study site and treatment-by-study-site interaction. We used the Cochran-Mantel-Haenszel test with sites as strata with respect to race, sex and smoking status.

We made between-treatment comparisons for total VMI calculus scores at 16 weeks by means of pairwise comparisons using a two-way analysis of covariance; the factors were treatment, study site and treatment-by-study-site interaction, and the covariate was baseline total VMI calculus score. To examine homogeneity of treatment effects across study sites, we tested treatment-by-study-site interaction at the .05 level.

Paired *t*-tests were used for within-treatment comparisons. Each statistical test was performed at the .05 level of statistical significance, two-sided.

- If the mean for the positive control group (which used the tartar-control dentifrice and the antiseptic rinse) was statistically significantly

TABLE 1

AGE, SEX, RACE AND SMOKING STATUS OF STUDY GROUPS.

DEMOGRAPHIC VARIABLE	TREATMENT GROUP			P VALUES AMONG TREATMENTS
	Positive Control Group*	Negative Control Group†	Experimental Group‡	
Number of Subjects	113	111	110	—
Mean Age (SD)§	45.2 (12.1)	46.3 (12.0)	45.3 (12.0)	.746
Sex (%)				.964
Female	74.3	73.0	72.7	—
Male	25.7	27.0	27.3	—
Race (%)				.568
White	88.5	90.1	93.6	—
Black	8.8	7.2	4.5	—
Hispanic	1.8	2.7	0.9	—
American Indian	0.0	0.0	0.9	—
Pacific Islander	0.9	0.0	0.0	—
Smoking Status (%)				.458
Yes	21.2	15.3	16.4	—
No	78.8	84.7	83.6	—

* The positive control group used a tartar-control dentifrice and an antiseptic mouthrinse.
† The negative control group used a regular dentifrice and an antiseptic mouthrinse.
‡ The experimental group used a regular dentifrice and a tartar-control mouthrinse.
§ SD: Standard deviation.

lower than the mean for the negative control group (which used a regular dentifrice and an antiseptic rinse), then we deemed the study valid.

■ If the mean for the experimental group (which used the regular dentifrice and the tartar-control rinse) was statistically significantly lower than the mean for the negative control group (which used the regular dentifrice and the antiseptic rinse, then we considered the tartar-control rinse efficacious.

To investigate examiner repeatability, we re-evaluated 15 subjects at baseline and another 15 subjects at the end of the study, or 16 weeks post-baseline. We assessed repeatability by means of the intraclass correlation coefficient, which is defined from an ANOVA with subject as a factor. To calculate the intraclass correlation coefficient, we divided the differences of the between-subject and within-subject mean squares by the sum of their mean squares.⁴

RESULTS

Population. Four hundred nine (409) subjects

were enrolled in phase 1 of the study. Forty-five subjects did not qualify for phase 2 because they had baseline total calculus scores of less than 7.0 or greater than 30.0. Ten subjects discontinued participation during phase 1. Of the 354 subjects who were randomized and who entered phase 2, 20 discontinued participation, leaving 334 subjects as the final study population.

Table 1 presents summary statistics and between-treatment comparisons for demographics. There were no statistically significant differences among treatment groups with respect to age, sex, race, smoking status or baseline total calculus ($P \geq .458$).

Calculus index. We found no statistically significant treatment-by-study-site-interaction ($P = .220$). Table 2 shows the statistical analysis for all subjects (combining the study sites). The adjusted mean VMI scores at 16 weeks were 11.36, 8.98 and 9.03 for the negative control group, experimental group and positive control group, respectively.

TABLE 2

SUBJECTS' MEAN TOTAL CALCULUS (VOLPE-MANHOLD INDEX) SCORE AFTER 16 WEEKS' USE OF TREATMENT PROTOCOL.			
VARIABLE	TREATMENT GROUP		
	Positive Control Group*	Negative Control Group†	Experimental Group‡
Number of Subjects	113	111	110
Baseline Mean Calculus Score (SD§)	11.45 (5.11)	11.51 (5.21)	11.53 (5.27)
16 Weeks Mean Calculus Score (SD§)	8.99 (6.26)	11.53 (6.38)	8.55 (5.37)
Within-Treatment <i>P</i> Value	< .001	.965	< .001
Adjusted Mean	9.03	11.36	8.98
SE**	0.47	0.49	0.49
Comparison vs. Negative Control Group			
<i>P</i> Value Between Treatments	.001	—	.001
Difference	-2.33	—	-2.37
SE**	0.68	—	0.69
Difference (%)	-20.5	—	-20.9
* The positive control group used a tartar-control toothpaste and an antiseptic rinse. † The negative control group used a regular dentifrice and an antiseptic rinse. ‡ The experimental group used a regular dentifrice and a tartar-control mouthrinse. § SD: Standard deviation. ** SE: Pooled standard error from analysis of covariance (root mean square for errors = 4.33).			

The mean for the positive control group was statistically significantly lower ($P = .001$) than the mean for the negative control group; thus, the study was valid. The mean for the experimental group also was statistically significantly lower ($P = .001$) than the mean for the negative control group. Reductions in VMI score vs. the negative control group were 20.9 percent for the experimental group and 20.5 percent for the positive control group ($P = .001$).

Examiner repeatability. The intraclass correlation coefficients for total calculus score were at least 0.992 over the course of the study.

Safety. We observed at least one oral soft-tissue adverse effect in the study, in a subject in the positive control group. The subject reported oral discomfort and had inflamed tongue papillae and areas of redness on the palate, all of which resolved within a week of discontinuing use of the test materials.

DISCUSSION

Numerous clinical trials have confirmed the antical-

culus efficacy of several agents when applied in dentifrice formulations. The most commonly used anticalculus agents are soluble pyrophosphates. Several human clinical trials conducted using a study design similar to that reported here have confirmed the anticalculus efficacy of soluble pyrophosphates.⁵⁻⁹ The tartar-control dentifrice used in this study contains tetrapotassium pyrophosphate; polyethylene glycol-6; disodium pyrophosphate; and tetrasodium pyrophosphate. Anticalculus efficacy also has been reported for dentifrices containing zinc salts such as zinc citrate^{6,10} and zinc chloride.¹¹ Recent research has indicated that dentifrices containing 0.3 percent triclosan and 2 percent polyvinylmethyl ether and maleic acid, copolymer (Gantrez) have anticalculus activity.^{7,12}

Research also has been conducted on mouthrinses designed to impart anticalculus efficacy. Three clinical trials ranging in duration from three to six months¹³⁻¹⁵ demonstrated that a mouthrinse containing 1 percent soluble pyrophosphate and 0.25 percent copolymer (Gantrez) significantly

reduced calculus formation when used for one minute twice daily after brushing.

The calculus reductions seen in the patient population in our study were consistent with those reported previously.⁶⁻¹⁵ Additionally, the results we observed in our study are consistent with those of previous trials involving pyrophosphate-containing dentifrices, and they demonstrate that the mouthrinse containing zinc chloride has significant anticalculus efficacy.

CONCLUSION

Our study involved the unsupervised use of an essential oil mouthrinse containing zinc chloride as an adjunct to usual oral hygiene, twice daily, for four months by subjects who had been shown to develop moderate amounts of calculus in a two-month period (total calculus score ≥ 7 and ≤ 30). The essential oil/zinc chloride mouthrinse statistically significantly reduced calculus formation by 20.9 percent ($P = .001$), and the tartar-control dentifrice used with a placebo rinse reduced calculus formation by 20.5 percent ($P = .001$). Both anticalculus agents resulted in clinically relevant reductions in calculus formation.

The tartar-control mouthrinse containing zinc chloride was shown to provide demonstrable anticalculus benefit and to be a viable vehicle for delivery of a calculus-control agent. ■

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