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Cetylpyridinium Chloride Mouth rinse on Gingivitis and Plaque

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The purpose of *Linking Research to Clinical Practice* is to present evidence-based information to clinical dental hygienists so that they can make informed decisions regarding patient treatment and recommendations. Each issue will feature a different topic area of importance to clinical dental hygienists with A BOTTOM LINE to translate the research findings into clinical application.

A 6-month clinical trial to study the effects of a cetylpyridinium chloride mouth rinse on gingivitis and plaque. Am J Dent 2005;18 (special issue):9A-14A.

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Abstract

Purpose. To evaluate the effects of a novel mouth rinse containing 0.07% high bioavailable cetylpyridinium chloride (Crest Pro-Health Rinse) on the development of gingivitis and plaque versus a placebo control over a period of 6 months.

Methods. This was a randomized, 6-month, placebo-controlled, parallel groups, double-blind, single center clinical trial. One hundred thirty-nine generally healthy adults with mild-to-moderate gingivitis were enrolled in the study. Subjects were given Modified Gingival Index (MGI), Gingival Bleeding Index (GBI) and Modified Quigley-Hein Plaque Index (MQH) examinations followed by a dental prophylaxis. Subjects were then randomly assigned to either the cetylpyridinium chloride (CPC) rinse or placebo rinse and instructed to begin rinsing twice a day with 20 ml of their assigned mouth rinse

for 30 seconds after brushing their teeth. Subjects were assessed for MGI, GBI and MQH scores after 3 and 6 months of product use. Oral hard and soft tissue examinations were also performed at all visits.

Results. One hundred twenty-four subjects were evaluable at Month 3 and 119 at Month 6. After 6 months, subjects rinsing with the CPC rinse showed 15.4% less gingival inflammation, 33.3% less gingival bleeding, and 15.8% less plaque relative to the placebo group. All reductions were highly statistically significantly different ($P < 0.01$). Results were similar at 3 months. Both treatments were well-tolerated.

Clinical Significance. This study demonstrates that the Crest Pro-Health's 0.07% CPC mouthrinse provided significant antiplaque and antigingivitis benefits when used twice daily for 6 months as an adjunct to tooth brushing.

Commentary

Chemical plaque control as an adjunct to normal oral hygiene has been the subject of numerous research studies over the past 2 decades. Chlorhexidine gluconate oral rinse (CHG) is considered the gold standard for reducing plaque and gingival inflammation; however, it has well-documented side effects such as dental staining, increase in calculus formation and transient altered taste acuity. These side effects generally preclude long-term use. In addition, CHG rinses are generally formulated with an alcohol-based vehicle of 11.9%. Essential oil mouth rinses (EO) also have been shown to possess anti-plaque and antigingivitis effects, but without the unfavourable side effects common to CHG. EO rinses have the highest alcohol content of any oral rinses at 27.9%. Because of the alcohol content, both CHG and EO are contraindicated for individuals with xerostomia or past history of alcohol dependency. Recently, a cetylpyridinium chloride oral rinse (CPC) was formulated as an alcohol-free alternative to other anti-plaque and anti-gingivitis oral rinses. This study experimentally compared the antiplaque and antigingivitis effectiveness of CPC, 0.07% in a bioavailable matrix (Crest® PRO-HEALTH™ Rinse) to an alcohol-free placebo-control oral rinse over 6 months. This was a well-designed trial incorporating many study features recommended by the American Dental Association Council on Scientific Affairs. One-hundred and thirty-nine study subjects were randomly assigned to either the CPC or placebo-control oral rinse groups, and were instructed to brush normally and rinse twice daily with their assigned rinse. The study was conducted as a double-blind trial with neither study subjects nor examiners aware of which subjects received which oral rinse. In order to qualify for participation, subjects had to have mild gingival inflammation and a plaque score of at least 1.5 on the Modified Quigley-Hein Plaque Index (MQH). Comparison of subject characteristics at baseline showed that the experimental and placebo groups were equivalent with respect to age, gender, ethnicity, smoking status, and levels of oral health parameters. Subjects were recalled for assessment of plaque and gingivitis at 3 and 6-month intervals. A total of 124 subjects were available for the month 3 and 6 visits. At both 3 and 6-month time points, the CPC group demonstrated statistically significantly lower plaque (MQH) and gingival measures (MGI and Gingival Bleeding Index-GBI) compared to placebo. The difference between active and placebo group scores at 6 months were: 15.4% for gingivitis scores; 33.3% for bleeding scores; and 15.8% for plaque scores. The ADA Guidelines for Acceptance of Chemotherapeutic Products for Control of Gingivitis have set the minimal standard required for gingivitis reduction between the active therapy and the control at 15%. Given this standard, the CPC mouth rinse demonstrated acceptable gingivitis reduction. While it is not possible to compare the effectiveness of CPC to the gold-standard CHG in this study, previous research has demonstrated reductions in gingivitis ranging from 18-80%, depending on the sample selected for the study. In the current study, baseline bleeding scores were modest (12.2% and 11.4%, for placebo and experimental, respectively) suggesting that subjects did possess a mild level of gingival inflammation. Previous research has shown that the greater the level of gingivitis, the greater reductions can be expected with chemotherapy agents. Whether CPC would demonstrate greater effectiveness in individuals with moderate or severe gingivitis remains to be seen. The current study suggests that for subjects with mild gingival inflammation, CPC can be more effective than placebo at reducing plaque, gingival bleeding and gingival index scores. Future studies are needed to determine the relative effectiveness of CPC on subjects with higher levels of gingival inflammation, as well as to substantiate the therapeutic effect of CPC oral rinses. These preliminary results are promising, especially for individuals for whom alcohol rinses are contraindicated.

Comparison of the effects of cetylpyridinium chloride with an essential oil mouth rinse on dental plaque and gingivitis - a 6-month randomized controlled clinical trial. *J Clin Periodontol.* 2007 Aug; 34(8):658-67

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Abstract

Objective. To compare the effects of an experimental mouth rinse containing 0.07% cetylpyridinium chloride (CPC) (Crest Pro-Health) with those provided by a commercially available mouth rinse containing essential oils (EOs) (Listerine) on dental plaque accumulation and prevention of gingivitis in an unsupervised 6-month randomized clinical trial.

Material and Methods. This double-blind, 6-month, parallel group, positively controlled study involved 151 subjects balanced and randomly assigned to either positive control (EO) or experimental (CPC) mouth rinse treatment groups. At baseline, subjects received a dental prophylaxis procedure and began unsupervised rinsing twice a day with 20 ml of their assigned mouthwash for 30 s after brushing their teeth for 1 min. Subjects were assessed for gingivitis and gingival bleeding by the Gingival index (GI) of L oe & Silness (1963) and plaque by the Silness & L oe (1964) Plaque index at baseline and after 3 and 6 months of rinsing. At 3 and 6 months, oral soft tissue health was assessed. Microbiological samples were also taken for community profiling by the DNA checkerboard method.

Results. Results show that after 3 and 6 months of rinsing, there were no significant differences ($p=0.05$) between the experimental (CPC) and the positive control mouth rinse treatment groups for overall gingivitis status, gingival bleeding, and plaque accumulation. At 6 months, the covariant (baseline) adjusted mean GI and bleeding sites percentages for the CPC and the EO rinses were 0.52 and 0.53 and 8.7 and 9.3, respectively. Both mouth rinses were well-tolerated by the subjects. Microbiological community profiles were similar for the two treatment groups. Statistically, a significant greater reduction in bleeding sites was observed for the CPC rinse versus the EO rinse.

Conclusion. The essential findings of this study indicated that there was no statistically significant difference in the anti-plaque and anti-gingivitis benefits between the experimental CPC mouth rinse and the positive control EO mouth rinse over a 6-month period.

Commentary

This study examined the effect of unsupervised use of a CPC rinse (Crest® PRO-HEALTH™ Rinse) compared to an ADA approved EO mouth rinse (LISTERINE®) following a professionally delivered supragingival polishing. Since all subjects received a dental prophylaxis prior to initiating oral rinse use at home, the primary intent was to determine if the CPC and EO products differentially reduced gingivitis, plaque reaccumulation and shift in microbial composition. The study design did not include a placebo comparison group, thus the only comparisons possible were between the two active mouth rinses. The study population started with 151 subjects and, of those, 127 completed the 6-month study. The authors appropriately evaluated the characteristics of those individuals who dropped out of the study to those who completed the study and determined that the drop out of 24 subjects did not create a bias in results. Multiple statistical analyses were conducted to compare between groups at each time interval and compare within group over time. An intent-to-treat, analysis of covariance (ANCOVA) statistical procedure was used to compare GI scores for both 'site level' and 'subject averaged' data for the 3 month comparisons and 6 month comparisons while controlling for any potential baseline differences. Results showed no statistically significant differences between the CPC and EO groups at 3 months and 6 months for GI scores; however, both groups improved comparably from baseline. Similarly, for % sites with bleeding, there was a statistically significant difference favoring the CPC rinse. Baseline levels of gingival inflammation were relatively low for both groups, with average bleeding on probing of 14.6 and 13.3%, for CPC and EO, respectively. After 6 months of oral rinse use, the adjusted average bleeding on probing was 6.0 and 7.4 for CPC and EO. This difference was statistically significant; however, the authors were quick to point out that the difference was small, and not clinically meaningful. Plaque reaccumulation scores followed a similar trajectory as GI scores, decreasing from baseline in both groups, but with no differences between oral rinse groups at the 3 month and 6 month time intervals. Additionally, neither oral rinse was

effective at significantly reducing subgingival periodontal pathogens at either 3 or 6 months, despite the fact that all subjects received supragingival polishing at baseline. Assessment of 40 periodontal organisms was achieved at baseline, 3 month and 6 months using checkerboard DNA-DNA hybridization. Of interest, 50% of sites in both oral rinse groups harboured *P. gingivalis* at baseline, but did not show a statistically significant change over the study period. This is not terribly surprising as previous studies have shown that oral rinses have limited capacity for reaching subgingivally, and are not present for sufficient periods of time to achieve effectiveness against pathogens.

Overall, the results suggest that the anti-plaque and anti-gingivitis effectiveness of the CPC is comparable to that achieved by EO rinses in a population of individuals with mild gingivitis. The results of this study, as with the previous study, can be inferred to individuals with mild gingivitis and who are relatively young (mean age of 39.5 years) and healthy. As 76% of subjects were non-smokers, it is unknown whether similar results would be obtained in a population of individuals who smoke. The primary intent of this study was to assess the relative effectiveness of a CPC oral rinse compared to an EO rinse; however, the absence of a placebo control group makes it difficult to determine how much of the reduction in PI and GI is attributable to the active ingredients rather than increased attention to oral health. In the past, there have been numerous studies demonstrating the effectiveness of EO rinses to reduce plaque and gingivitis better than controls. These studies met the requirements of the ADA Guidelines for Acceptance of Chemotherapeutic Products for Control of Gingivitis and subsequently lead to the ADA seal for EO rinses as anti-plaque and anti-gingivitis products. As the observed reductions for the EO rinse group from baseline are within the range previously reported, the equivalence of clinical data between the EO and CPC groups suggests potential utility for the CPC product. More long-term trials comparing CPC to positive controls (EO and CHG) and negative controls (placebo) in samples with various levels of gingival disease are needed to provide the firm evidence needed to establish CPC as a therapeutic product.

The Bottom Line

The market is inundated with new oral rinses claiming to prevent or reduce plaque and gingivitis and improve dental aesthetics. Clients expect dental hygienists to provide direction in product selection and hygienists need to be aware of the state of evidence related to chemotherapeutic control of plaque and gingivitis. These two studies present preliminary evidence regarding the effectiveness of CPC for the reduction of plaque and gingivitis. CPC is thought to exert antimicrobial activity by disrupting the cell membrane of microbial organisms that then results in an alteration of cellular metabolism, cell growth and ultimately, cell death. The need for alcohol-free oral rinses that can effectively reduce dental plaque and gingival inflammation, especially in developing countries where polypharmacy-induced xerostomia is increasing, makes the results of these studies promising. Collectively, evidence from these two trials gives preliminary support for recommending these rinses, especially to individuals with mild gingivitis. However, dental hygienists are cautioned about extending this evidence to populations with more severe diseases. Making good evidence-based clinical decisions relies on clinicians' critical evaluation of the applicability of research findings (from a well-defined study population) to patients with various levels of gingival and periodontal disease. It is also prudent for dental hygienists to make recommendations considering the body of evidence available on any given topic. These two studies present preliminary findings on the effectiveness of CPC oral rinses for mild gingivitis. Clearly as more evidence is generated, clinicians will need to reconsider whether these recommendations remain timely.

Given the findings from these two studies, the following conclusions and recommendations can be made to dental hygiene clinicians:

- The CPC oral rinse (Crest® Pro Health Rinse) demonstrated 15.4% reductions in gingivitis and 15.8% for plaque scores at 6 months compared to a placebo control in populations with mild gingivitis;
- The CPC oral rinse also demonstrated comparable results in reducing plaque and gingivitis when compared to EO in subjects with mild gingivitis;
- In order for CPC to receive the ADA seal of acceptance for gingivitis, two long term studies showing gingivitis reductions of at least 15% are necessary providing that the study design meets ADA guidelines including the incorporation of negative controls. One of these studies meets those requirements;

- When interpreting study results, in addition to demonstrating statistically significant differences between groups (control and treatment), it is important to consider whether change from baseline in the outcome measure (i.e. plaque score, gingivitis score) is demonstrated between groups over time and is clinically meaningful.

Summary

Preliminary evidence has demonstrated a reduction in gingivitis scores of at least 15% between placebo controls and CPC oral rinse (Crest® Pro Health Rinse). While this is indeed promising, additional studies are needed to determine whether CPC would achieve similar levels of disease and plaque reduction, especially for individuals with more severe gingivitis and/or periodontitis. For those patients for whom alcohol-containing mouth rinses are contraindicated, CPC oral rinse may be a viable adjunct to the traditional home care regimen. Finally, dental hygienists should monitor the literature in this area closely as new research will likely be published on CPC effectiveness and increase the evidence base for making good clinical recommendations.