

Linking Research to Clinical Practice

Non-Fluoride Caries-Preventive Agents

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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.

Rethman MP, Beltran-Aguilar ED, Billings RJ, et al. Nonfluoride caries-preventive agents: executive summary of evidence-based clinical recommendations. J Am Dent Assoc. 2011;142(9):1065-1071.

Background: In this article, the authors present evidence-based clinical recommendations regarding the use of nonfluoride caries preventive agents. The recommendations were developed by an expert panel convened by the American Dental Association (ADA) Council on Scientific Affairs. The panel addressed several questions regarding the efficacy of non-fluoride agents in reducing the incidence of caries and arresting or reversing the progression of caries.

Types of Studies Reviewed: A panel of experts convened by the ADA Council on Scientific Affairs, in collaboration with ADA Division of Science staff, conducted a MEDLINE search to identify all randomized and non-randomized clinical studies regarding the use of non-fluoride caries-preventive agents.

Results: The panel reviewed evidence from 50 randomized controlled trials and 15 non-randomized studies to assess the efficacy of various non-fluoride caries-preventive agents.

Clinical Implications: The panel concluded that certain non-fluoride agents may provide some benefit as adjunctive therapies in children and adults at higher risk of developing caries. These recommendations are presented as a resource for dentists to consider in the clinical decision-making process. As part of the evidence based approach to care, these clinical recommendations should be integrated with the practitioner's professional judgment and the patient's needs and preferences.

Commentary

An expert panel convened by the ADA conducted a systematic review to examine studies of non-fluoride agents in caries prevention and management. The research questions addressed whether non-fluoride agents could reduce incidence, arrest or reverse caries in the general population or in individuals at high caries risk. After identifying inclusion criteria for high quality studies, reviewing 2,697 articles from 1966 to 2010 and updating them through March 2011, the panel included 65 articles in its systematic review. Meta-analyses were performed when adequate numbers of similar studies were available to combine data and statistically control for effect size. In other words, studies with greater numbers of subjects and more statistical power were weighted more heavily than those with smaller samples.

The panel reviewed randomized clinical trials (RCTs, n=9) and non-randomized clinical studies (n=6) to evaluate the effectiveness of sucrose-free polyol (e.g., sugar alcohols such as xylitol and sorbitol) chewing gums in general populations. Meta-analysis found a statistically significant reduction in coronal caries in permanent teeth with use of xylitol gum (or combined polyol gum with xylitol and other sugar alcohols) compared with no gum or chewing gum with sorbitol. In children, a marginal reduction in caries incidence was found. Risk of choking in young children should be considered, and chewing gum should only be recommended for children over age 5 without neurological or swallowing problems. Xylitol-containing lozenges or hard candy were found to reduce incidence of coronal caries, although the evidence was not as strong as it was for gum. A dose of 5

to 8 grams/day divided into 2 or 3 doses (e.g., after meals) was suggested for maximum clinical benefits. Most chewing gums marketed in the U.S. with xylitol contain 0.50 to 0.72 grams per dose, meaning one would need to chew 7 to 12 pieces of gum daily, or 3 to 4 pieces 2 to 3 times a day. Chewing gum available in smaller pieces has an advantage over larger pieces because 3 pieces per dose are more practical to chew. Even with smaller units, that dosage is difficult to attain on a daily basis. Practitioners recommending xylitol gum or lozenges should be aware that large doses have been linked to adverse gastrointestinal effects.

When examining studies of antimicrobial agents in caries prevention, the panel concluded there is not sufficient evidence to support triclosan or iodine. Most of the studies reviewed by the panel were related to chlorhexidine (CHX) varnish or mouth rinses, however, neither of these products has been approved in the U.S. by the Food and Drug Administration for use in caries prevention. The products marketed in the U.S. include 1:1 chlorhexidine–thymol varnish and 0.12% chlorhexidine gluconate mouthrinse. Insufficient evidence is available to recommend use of CHX gels available outside of the U.S. for caries prevention in adults or children.

Evidence did not adequately support use of 10 to 40% CHX varnish for prevention of coronal caries in children or root caries in adults. However, when evaluating studies (n=6) of chlorhexidine–thymol varnish, the panel concluded a 1:1 mixture of chlorhexidine/thymol varnish applied every 3 months reduces the incidence of root caries in adults and elderly.

When evaluating 4 studies of 0.12% CHX mouth rinse in reducing caries in children and adults and 2 studies evaluating root caries in adults and older adults, the panel concluded that CHX rinse alone or in combination with fluoride does not reduce caries incidence in any of these groups. The panel concluded that CHX rinses should not be recommended as a non-fluoride therapy for reducing caries incidence, arresting or reversing caries. Since that time, however, a longitudinal RCT has been published to support combined daily 0.12% CHX rinse and fluoride therapy in adults with high caries risk. A discussion of this subsequent study follows.

The panel also evaluated studies (n=9) of calcium and/or phosphate agents with and without casein derivatives for caries prevention. It found that published clinical trials do not provide sufficient evidence that use of these agents lowers

incidence of either coronal or root caries.

The authors remind clinicians that caries risk assessment, patient motivation and readiness for change, oral health literacy, ability to accept and complete a recommended treatment plan and compliance all affect the outcome of a caries management care plan. Further, good evidence supports professional and home fluoride products including fluoridated toothpastes. Fluoride therapy and dental sealants remain the primary interventions for preventing caries, and clinicians should follow published evidence-based guidelines for these modalities.^{1,2}

Featherstone JD, White JM, Hoover CI, et al. A randomized clinical trial of anticaries therapies targeted according to risk assessment (caries management by risk assessment). *Caries Res.* 2012;46(2):118–129.

This randomized parallel group clinical trial assessed whether combined antibacterial and fluoride therapy benefits the balance between caries pathological and protective factors. Eligible, enrolled adults (n=231), with 1 to 7 baseline cavitated teeth, attending a dental school clinic were randomly assigned to a control or intervention group. Salivary mutans streptococci (MS), lactobacilli (LB), fluoride level and resulting caries risk status (low or high) assays were determined at baseline and every 6 months. After baseline, all cavitated teeth were restored. An examiner masked to group conducted caries exams at baseline and 2 years after completing restorations. The intervention group used fluoride dentifrice (1,100 ppm fluoride as NaF), 0.12% chlorhexidine gluconate rinse based upon bacterial challenge (MS and LB) and 0.05% NaF rinse based upon salivary fluoride. For the primary outcome, mean caries increment, no statistically significant difference was observed (24% difference between control and intervention groups, p=0.101). However, the supplemental adjusted zero-inflated Poisson caries increment (change in decayed, missing and filled surfaces, DMFS) model showed the intervention group had a statistically, significantly lower mean than the control group (24%, p=0.020). Overall, caries risk reduced significantly in intervention versus control over 2 years (baseline adjusted generalized linear mixed models odds ratio, (aOR=3.45; 95% CI: 1.67, 7.13). Change in MS bacterial challenge differed significantly between groups (aOR=6.70; 95% CI: 2.96, 15.13) but not for LB or fluoride. Targeted antibacterial and fluoride therapy based on salivary microbial and fluoride levels favorably altered the balance between pathological and protective caries risk factors.

Commentary

To date, very few randomized clinical trials have been conducted to evaluate use of a combination of fluoride therapy and 0.12% CHX gluconate rinse for caries prevention. Most of the published research related to CHX rinses has been related to the antimicrobial effect on gingivitis, and many studies have shown that CHX is an effective anti-gingivitis agent when used twice a day as directed. The objective of this study was to provide clinical evidence that a valid caries risk assessment combined with aggressive caries prevention methods and conservative dental restorations would result in a lower caries increment compared to not using this combined approach in adults. The hypothesis was that "caries management and conservative restorative treatment based on caries risk status (low or high) would significantly reduce 2-year caries increment compared to traditional, non-risk-based dental treatment."

Both groups (n=231) initially received a dental examination including radiographs and DMFS to confirm presence of 1 to 7 active caries lesions as well as a salivary assay analysis for salivary MS, LB and fluoride level to determine caries risk status (low/high). The examiner performing caries examinations before and after treatment was blinded to group assignment to reduce examiner-related bias. The control group received traditional treatment plans for restorative care and follow up. The intervention subjects were classified as high or low caries risk. Intervention group participants received information about their salivary analysis and their low or high caries risk status based on salivary analyses. Treatment plans included minimally invasive restorative care and sealants for all, as well as additional antibacterial/fluoride therapy for those in the high caries risk group. Subjects in both groups were instructed to reduce daily carbohydrate intake and brush daily with the 1,100 ppm sodium fluoride (NaF) dentifrice provided. Some subjects in both groups changed toothpastes over the 2 year study period, however, patient-selected dentifrices were similar. High caries risk subjects in the intervention group received an in-office 1.1% NaF treatment, instructions to use a 0.05% (225 ppm) NaF fluoride mouth rinse once daily, similar to most over-the-counter fluoride rinses sold in the U.S. and instructions to use a 0.12% CHX rinse. The protocol for the CHX rinse was once daily for 3 months through the restorative phase, followed by once daily for the first week of each month thereafter. This recommendation differs from the twice daily recommendation for gingivitis prevention and treatment. Compliance and self-recording of rinse use was encouraged and monitored. All subjects were recalled every

6 months for salivary assays and needed restorative care, and followed for 2 years. At the end of that period, final dental exams with radiographs and DMFS and salivary assays were performed. The authors defined the primary outcome measure as the caries increment (change in number of DMFS). Secondary measures included caries incidence (new), changes in decayed, missing and filled teeth, changes in number of decayed teeth (DT) or surfaces (DS), caries risk, salivary MS and LB levels and fluoride levels in saliva. Statistical analysis found no significant difference in baseline demographics or clinical characteristics of the groups, and demographics of those subjects who completed the study were comparable (control group=52, intervention subjects=60). Most attrition occurred early in the study because patients were unable to pay for and complete initial restorative treatment plans.

This study was designed to evaluate an aggressive caries management program with conservative restorative dental care based on caries risk assessment. This protocol has been suggested for some time, however, practitioners have been slow to adopt it. The complexity of this research protocol, especially for the intervention group, reflects the complexity of the suggested clinical approach to caries prevention, and that factor might be affecting adoption in practice. The authors of this manuscript stated that no practical caries risk assessment plan has been proven effective using a prescribed caries management plan. Nonetheless, a new approach to caries management in adults and children is needed. Although prevalence and incidence has been reduced since the 1960s, dental caries remains a major health problem. The status quo has not been shown to be an effective means of eradicating the disease. These authors have suggested, "With accurate risk assessment, noninvasive care modalities, including chlorhexidine antimicrobial and fluoride rinses, can be applied with confidence and invasive restorative procedures (if needed) can be more conservative, preserving tooth structure and better benefiting patient oral health."

Results showed lower caries increments (DMFS, DT, DS, DMFT) in the intervention group compared to the control group, although not statistically significant. No statistically significant differences between the groups were found in caries incidence over the 2 year study period. These results may have been impacted statistically by the fact that the distribution of scores was skewed by many 0 scores. A statistical model was used to adjust for this skewing by analyzing only the non-negative scores. This analysis indicated the

intervention group had a statistically significant 24% greater reduction in DMFS than the control group. A statistically significant reduction in caries risk and MS levels also favored the intervention group, however, no significant difference was found in salivary LB or fluoride levels. In short, the intervention resulted in a significantly lower percentage of subjects at high risk and high/medium bacterial challenge during the study period. Caries removal and dental restorations alone did not significantly change the MS bacterial challenge, caries increment or risk in either the control group or intervention subjects group. The use of an antimicrobial rinse, CHX, in conjunction with the dental treatment plan, did reduce the bacterial challenge by MS. The authors emphasized the need for combined fluoride therapy to remineralize tooth surfaces.

These authors based this study on the current approach to caries management by risk assessment which advocates improving the balance between protective factors (fluoride, calcium, phosphate, saliva and antibacterial agents) and pathological factors (cariogenic bacteria, dietary habits – especially frequent ingestion of fermentable carbohydrates and lack of saliva). Stepping up the caries risk assessment and management approach to include aggressive caries prevention methods in adults at high risk may be warranted based on the results of this randomized clinical trial.

The Bottom Line

Each of these studies addressed recommendations for use of CHX gluconate in an effective caries management program. The findings and conclusions do not agree because the first study was a systematic review and meta-analyses of studies conducted from 1966 to 2011. Results of the second study were published in 2012, so they were not a part of the findings of the systematic review. The new information must be confirmed through other studies but provides some evidence about how a CHX mouth rinse might be used to reduce caries risk in a comprehensive caries management program.

Both of these studies provide clarification regarding the value of nonfluoride agents in caries management. Based on the findings of one or both of these studies, the following conclusions can be drawn:

- For adults, xylitol chewing gum can be effective in reducing coronal caries with correct dosage. Adults can be advised to use xylitol

gum for 10 to 20 minutes after meals.

- The effect of xylitol chewing gum in children shows only a marginal reduction in caries. The risk of choking in young children should be considered, and chewing gum should only be recommended for children over age 5 without neurological or swallowing problems.
- There is not sufficient evidence to indicate that gum with other types of alcohol sugars (e.g., sorbitol) is effective in caries prevention and control.
- There is no evidence to show that CHX gel or 10 to 40% varnish prevents coronal or root caries in adults or children.
- There is evidence that CHX–thymol varnish applied every 3 months can prevent root caries in adults and older adults.
- There are conflicting views regarding use of a 0.12% CHX rinse for caries management. An ADA panel recommended in 2011 that clinicians avoid prescribing this rinse for caries prevention and control, however, a 2012 longitudinal RCT showed 0.12% CHX rinse plus fluoride therapy can be effective in reducing caries, decreasing MS levels and reducing caries risk in adults at high risk for caries. The latter finding was based on once daily CHX rinsing in combination with professional NaF application and daily use of fluoride toothpaste and an OTC fluoride rinse. Clinicians may recommend this protocol as a part of a comprehensive treatment plan including dietary advice to reduce carbohydrate intake, sealants and conservative restorative care but should avoid recommending CHX rinse alone for caries management.
- There is insufficient evidence from published clinical trials to support the use of calcium and/or phosphate agents with or without casein derivatives for prevention of coronal or root caries.

Summary

Evidence supports fluoride therapy and sealants for caries prevention and management. Evidence regarding non-fluoride agents indicates that xylitol chewing gum used after meals also can be effective in reducing coronal caries in adults and, to a lesser extent, children. Evidence does not support use of CHX gel or varnishes, however, CHX–thymol varnish can be applied 3 times a year to prevent root caries in adults and elders. There are conflicting views regarding use of 0.12% CHX rinse in combination with fluoride therapy for caries management. Recent findings indicate that use of a CHX rinse, in conjunction with caries risk assessment, fluoride therapy and a conserva-

tive dental treatment plan, reduced MS bacterial levels, caries increment (based on non-negative scores) and caries risk in adults with high caries risk. Insufficient evidence is available to recommend use of calcium and/or phosphate agents for caries management. Dental hygienists need to address caries risk based on a multi-pronged approach, especially in patients at high risk.

References

1. Professionally applied topical fluoride: evidence-based clinical recommendations. *J Am Dent Assoc* 2006;137(8):1151-1159.
2. Beauchamp J, Caufield PW, Crall JJ, Donly K, Feigal R, Gooch B, et al. Evidence-based clinical recommendations for the use of pit-and-fissure sealants: a report of the American Dental Association Council on Scientific Affairs. *J Am Dent Assoc* 2008;139(3):257-268.