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Literature Review

The Role of Chlorhexidine in Caries Prevention

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Clinical Relevance

Chlorhexidine rinses should not be recommended for use in caries prevention due to the current lack of evidence for their effectiveness.

SUMMARY

The use of chlorhexidine for caries prevention has been a controversial topic among dental educators and clinicians. In several reviews, it has been concluded that the most persistent reduction of mutans streptococci have been achieved by chlorhexidine varnishes, followed by gels and, lastly, mouth rinses. Also, the evidence for using different chlorhexidine modes or a combination of chlorhexidine-fluoride therapy for caries prevention has been "suggestive but incomplete." Variable study designs and lack of data in high-risk children and adults support the need to continue conducting randomized, well-controlled clinical trials and to search for a practical, effective mode of antimicrobial treatment that augments the known effect of fluoride treatments.

Currently, the only chlorhexidine-containing products marketed in the United States (US) are mouthrinses containing 0.12 percent chlorhexidine. Based on the available reviews, chlorhexidine rinses have not been highly effective in preventing caries, or at least the clinical data are not convincing. Due to the current lack of long-term clinical evidence for caries prevention and reported side effects, chlorhexidine rinses should not be recommended for caries prevention. Due to the inconclusive literature and sparse clinical data on gels and varnishes, their use for caries prevention should also be studied further to develop evidence-based recommendations for their clinical role in caries prevention.

Since dental caries is a disease with a multifactoral etiology, it is currently more appropriate to use other established, evidence-based prevention methods, such as fluoride applications, diet modifications and good oral hygiene practices. Recent findings also indicate that the effect of an antimicrobial agent for reducing the levels of mutans streptococci or plaque reduction may not always correlate with eventual caries reduction. The clinically important outcome is proven reductions in caries.

Many advances in the treatment and prevention of dental caries have been introduced over the past century. The use of chlorhexidine in caries prevention has been referred to as a nonsurgical management of dental caries and has represented the modern medical model of caries treatment. However, there is a lack of consensus on evidence-based treatment protocols and controversy regarding the role of chlorhexidine in caries prevention among dental educators and

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clinicians. There is a need to standardize guidelines to optimize evidence-based non-surgical disease management to provide appropriate care.

This paper reviewed the literature on the effectiveness of different modes of chlorhexidine delivery for caries prevention and provides guidelines for chlorhexidine use in caries management. A literature search was conducted using the PubMed and Evidence-Based Medicine Reviews databases and the keywords "chlorhexidine" and "caries," limiting the search to "humans, "reviews" and "English."

Based on the published reviews, it was concluded that chlorhexidine rinses, gels and varnishes or combinations of these items with fluoride have variable effects. Additionally, the sparse clinical data that was reported weakens the conclusions. Due to the current lack of evidence on long-term clinical outcomes and reported side effects, chlorhexidine rinse, which is currently the only treatment mode available in the US, should not be recommended for caries prevention. Clinical evidence on gels and varnishes is also inconclusive. For the treatment of dental caries, there are alternative evidence-based prevention methods available, such as fluoride applications, diet modifications and good oral hygiene practices.

INTRODUCTION

Clinical decision-making and the balance between preventive, non-surgical and surgical intervention have become an important part of daily dental practice. There is a definite increase in interest among dental educators, scientists and practitioners in the United States (US) for non-surgical approaches to the management of dental caries. While non-surgical caries treatment modalities are taught in some dental schools in the US, treatment protocols can vary greatly.[1] Some dental schools and private practitioners have implemented specific non-surgical medical models for caries management and published their protocols.[2-4] The use of chlorhexidine for caries prevention has remained a controversial topic. Evidence-based consensus and standardized protocols are needed to evaluate the role of chlorhexidine in caries prevention to provide appropriate care and preserve and maintain healthy tooth structure.

It is known that dental caries is caused by the interplay of caries risk factors leading to demineralization. The disease can be considered an endogenous multibacterial infection. However, the presence of bacteria alone is not sufficient to cause enamel and dentin demineralization. In the presence of a diet high in sugar, it has been shown that subjects with high levels of *S mutans* develop more caries than those with low levels of *S mutans*.[5-6] Chlorhexidine, an antimicrobial agent that can suppress the growth of mutans streptococci, has been considered as having the potential to prevent dental caries.[5-6] A variety of delivery systems exist, but the only product currently marketed in the US is a mouthrinse containing 0.12 percent chlorhexidine gluconate. Due to the lack of other delivery systems with higher concentrations of chlorhexidine, this mode is still widely recommended for caries prevention in several caries management programs in the US.[2-4] This paper reviewed the literature on the effectiveness of different modes of chlorhexidine delivery for caries prevention and provided evidence-based guidelines.

METHODS AND MATERIALS

A search of the literature was carried out using the electronic databases available at the University of Florida College of Dentistry, such as PubMed (MEDLINE source from the year 1980) and Evidence-Based Medicine Reviews (Cochrane databases of systematic reviews from the year 1991). The search was intended to select systematic reviews and randomized controlled human trials with the following inclusion criteria: humans, English language and reviews. Also, recently published peer-reviewed articles on caries management by risk assessment protocols were reviewed. A PubMed search using the keywords "chlorhexidine" and "caries" resulted in 55 articles. After a review of these articles, three articles were identified that focused specifically on chlorhexidine and caries prevention. Also, a second search, using the additional keyword "rinse," revealed seven articles, with three papers that focused on chlorhexidine. A third search using the keywords "chlorhexidine," "mutans" and "caries," which was limited to reviews, resulted in 16 articles. In addition to earlier searches, four of the 16 articles focusing on chlorhexidine were found and included.

EFFECT OF DIFFERENT MODES IN CARIES PREVENTION

Mouthrinses

Early studies on the effect of chlorhexidine rinses, gels and varnishes on caries progression were reviewed by Luoma.[7] These studies reported a low-to-moderate reduction in *S mutans* counts in plaque and saliva but none-to-moderate caries-inhibiting effects when compared to a placebo treatment. However, the subjects had low or moderate caries activity.[8-9] After these early studies, conducted more than 20-25 years ago, there are very few published articles that describe evaluations of the effect of chlorhexidine rinse on caries. One clinical study by Spets-Happonen and others,[10] where the use of periodic chlorhexidine mouthwashes was followed over a period of two years and nine months, revealed no significant reduction in caries.

In 1989, a 0.12% solution of chlorhexidine gluconate was marketed in the US, and it is currently the only chlorhexidine treatment mode available. There are very few clinical studies on this chlorhexidine mode that assess the progression of caries. A clinical study by Wyatt and MacEntee[11] evaluated the effectiveness of either a 0.25% neutral sodium fluoride (NaF) solution or a 0.12 % chlorhexidine solution as a daily mouthrinse for controlling caries in a two-year randomized clinical trial among the elderly in long-term care facilities in Canada. The prevalence of caries increased in the chlorhexidine and placebo groups, whereas there was a 24% decrease in the NaF group. The investigators concluded that the daily rinse with 0.25% NaF solution was significantly better than with 0.12% chlorhexidine rinse. A double-blind clinical trial by Wyatt and others[12] also tested the impact of regular rinsing with a 0.12% chlorhexidine solution on caries in low-income elders in Seattle, WA, USA and Vancouver, Canada. The subjects alternated between daily rinsing for one month, followed by weekly rinsing for five months. Regular rinsing with chlorhexidine did not have a substantial effect on the preservation of sound tooth structure in older adults. In a randomized clinical trial by Powell and others,[13] a weekly rinse with 0.12% chlorhexidine over three years did not reduce caries development significantly in a low-income older subjects population. This study was the only clinical study using 0.12% chlorhexidine rinse that was included in the review by Twetman.[14] His review concluded that chlorhexidine has substantial antimicrobial properties against caries-causing bacteria, but its use as an anticaries agent remains controversial.

To be maximally effective, an antimicrobial agent must be used for a sufficient but definite period of time.[6] The lesser effect on mutans streptococci and surfaces at risk probably reflect a re-growth of mutans streptococci, because the reservoirs in the dentition are not sufficiently affected due to the low bio-availability of chlorhexidine from the mouthrinse solution.[6] Staining of the teeth, silicate fillings and the tongue, as well as disturbances of taste, raise concerns for maintaining prolonged daily use of 0.12% chlorhexidine acetate solution for caries prevention.[7]

Gels

Clinical studies of chlorhexidine gels have been mainly conducted on children, and the data are promising, but sparse. Emilson found that studies with chlorhexidine gel treatment in high caries-risk children showed significant reductions in dental decay.[6] This finding was based on the original study by Zickert and others,[15] which reported a great reduction in caries increment in children with high levels of *S mutans* in saliva and when treated with 1% chlorhexidine gel trays for five minutes daily for 14 days. After three years, the children in the control group had developed 9.6 new caries lesions, while the treated children only developed 4.2 new caries lesions (a 56% difference). Emilson's conclusions were also based on the original study by Linquist and others,[16] in which a 52% caries reduction was found in the 1% chlorhexidine gel group after two years, compared to the control group. In the chlorhexidine group, children with high levels of mutans streptococci in saliva were treated with 1% chlorhexidine gel every third month.

Longitudinal studies, in which the effect of chlorhexidine gel on approximal caries was evaluated, showed significant caries reduction ranging from 26% to 68%.[6] For example, in a study by Gisselsson and others,[17] a 1% chlorhexidine gel was applied four times a year to approximal spaces, followed by dental flossing. After three years, the caries increment reduced significantly (52%) compared to a control group.

A recent study by Petti and Hausen[18] assessed the effect of chlorhexidine gel among three-year old children whose regular fluoride exposure came from toothpaste. The subjects underwent chlorhexidine gel application for three days at three-month intervals for 15 months. The chlorhexidine gel applications showed a moderate reduction in mutans streptococci levels but no effect on caries prevention.[18] Twetman's conclusion that there is limited evidence on the effectiveness of chlorhexidine gels and rinses in preventing caries seems to still be current.[14]

Varnishes

Chlorhexidine-containing varnishes were developed to increase the substantivity, length of the time of suppression[19-20] and effectiveness of the delivery of chlorhexidine to sites colonized by *S mutans*.[21] Varnish has been shown to reduce the numbers of *S mutans* in several studies.[20,22] Suppression of *S mutans* for periods of up to five months has been achieved by the application of a varnish containing a high concentration of chlorhexidine (40%).[20-24] Twetman stated in his review that clinical data on caries prevention effects remain sparse and that the recent literature was inconclusive for the use of chlorhexidine varnishes for caries prevention in risk groups.[14] Studies of the effect of chlorhexidine varnishes on caries in young permanent teeth showed no statistically significant effect.[25-27] For example, Forgie and others[25] assessed the efficacy of chlorzoin, a chlorhexidine varnish containing 10% chlorhexidine acetate and 20% Sumatra benzoin, in reducing caries increment in 1,240 high-risk adolescents aged 11-13 in a three-year clinical trial. In the first year, the varnish was applied weekly for the first month. Patients received a minimum of four and a maximum of six varnish applications in the first year and a minimum of one and a maximum of three applications in each subsequent year. After three years, the

results indicated that the use of chlorzoin had an initial effect on *S mutans* levels, but no long-term reduction in caries increment was documented.

Four studies that were included in Twetman's review did not show any statistically significant effect of chlorhexidine on caries progression in approximal sites.[14] One study by Twetman and Petersson[28] evaluated the effect of chlorhexidine varnish treatments on both caries incidence and lesion progression in school children with a high risk for caries. One-hundred and ten children ages 8 to 10 years old with moderate to high counts of salivary *S mutans* were treated three times within two weeks with interdental spot applications of 1% Cervitec varnish. After two years, it was found that a reduction in caries incidence and lesion progression was clearly dependent on this antimicrobial treatment. A significantly higher progression score was found among children who exhibited less marked suppression of interdental *S mutans* levels when compared to those with high suppression and to the children in the reference group. It was suggested that the suppression of *S mutans* in interdental plaque might be important in preventing and arresting approximal caries development. Four studies on fissure caries showed favorable effects from chlorhexidine varnish; however, Twetman questioned the accuracy and reliability of the diagnosis on fissure caries.[14]

In other studies included in Twetman's review, no protective effect on initial white spot demineralization adjacent to orthodontic brackets was noted in children with orthodontic appliances; this occurred despite significant reductions in cariogenic microflora.[29-30] Rozier[31] summarized the evidence for the effectiveness of methods available for caries prevention. The studies in his review provided mixed evidence of the caries-preventive effects of chlorhexidine used as a varnish, and they were judged to provide insufficient evidence of effectiveness.

Combinations of Fluoride and Chlorhexidine

In the search for better clinical effects, combinations of chlorhexidine and fluoride have been tested. Some clinical trials and *in vitro* tests have shown that the combination of chlorhexidine and fluoride was effective against *S mutans* and that the effect was synergistic.[32-33] Chlorhexidine-fluoride gel has been shown to reduce numbers of *S mutans*.[34] It has also been shown that this suppression effect lasts for a longer period of time than after chlorhexidine treatment alone.[35] However, clinical data on the effects of caries prevention continues to remain sparse.

In a study by Luoma and others,[33] the combination of chlorhexidine and fluoride was tested when children rinsed every day for two years with either a 0.04% NaF solution or a solution containing both 0.04% NaF and 0.05% chlorhexidine, resulting in a caries reduction of 16% and 42%, respectively. Spet-Happonen and others[10] evaluated the effect of rinsing with a solution containing 0.05% chlorhexidine gluconate and 0.04% NaF on 11 year-old schoolchildren (n=243). Participating children had high DMFS scores and rinsed twice a day every third week. However, after two years and nine months, there were no differences in caries increment between the rinsing group and the basic control group.

In a study by Katz,[36] a regime of four topical applications of 1.0% NaF-1.0% chlorhexidine digluconate plus daily rinses with a combination of 0.05% NaF-0.2% chlorhexidine solution completely prevented radiation caries. Use of the chlorhexidine-fluoride rinses alone also stopped radiation caries but did not support remineralization.

Petersson and others[37] treated a test group of 12 year-old children (n=115) semi-annually with a mixture of varnish containing 0.1% F (Fluor Protector) and 1.0% chlorhexidine (Cervitec). A reference group (n=104) received fluoride varnish semi-annually. Approximal caries was recorded from bitewing radiographs at baseline and after three years. In this study, the differences in caries increments were not significant, and the combination of fluoride and chlorhexidine had no additional preventive effect. However, approximal caries incidence overall was low during the study period, which could weaken the statistical power of the study.

In a study by Ogaard and others,[38] the effect of chlorhexidine varnish in combination with a fluoride varnish was compared to a fluoride varnish alone in reducing white spot lesions in orthodontic patients. Patients received one application of 1% chlorhexidine varnish every week for three weeks and fluoride varnish at the next visit, six weeks later. The patients were seen every six weeks and each varnish was applied every 12 weeks. During the first 48 weeks of treatment, the combination with a chlorhexidine varnish (Cervitec, 1%) significantly reduced the number of *S mutans* in plaque. However, this effect did not result in significantly less development of white spot lesions compared with the group receiving only fluoride varnish.

RE-COLONIZATION AND SIDE EFFECTS

The main clinical problem with the use of chlorhexidine is the difficulty in suppressing or eliminating *S mutans* for an extended period of time. In many clinical studies, the organisms re-colonized the dentition.[6] However, the re-colonization time varied among subjects.

In cases where *S mutans* had been decreased to low or undetectable levels by the chlorhexidine gel, they generally reached the pre-treatment levels after two to six months.[6,34,39] The most likely explanation for the reappearance of *S mutans* is their regrowth.[40] This suggests that there must be reservoirs or retention sites in the dentition that are hardly affected or not affected at

all by this chlorhexidine treatment and from which the *S mutans* re-colonize the dentition after treatment. Patients with more retentive sites, such as faulty restorations, occlusal fissures, enamel cracks, incipient lesions or patients with orthodontic appliances, were more rapidly re-colonized with *S mutans*.[6]

Chlorhexidine has been shown to have some side effects, the most common of which is a yellow-brown staining of the teeth with a mouthrinse.[41-42] Staining tends to occur in the cervical third of the crown and in the interproximal areas and is most pronounced along any exposed cemento-enamel junction or root surface, in pits and fissures, on existing composite restorations and occasionally on the tongue.[43] Staining of the teeth occurs in one-third to one-half of patients and is usually evident within several days after the initiation of daily rinses. The stain is removable, with the exception of porous restorations or in open margins, and a professional dental prophylaxis is usually required after the use of chlorhexidine mouthrinse.

Another side effect is an altered taste sensation.[41-42] These alterations are uncommon and self-limiting, but they tend to persist for several hours.[43] Others have reported side effects, including burning sensations of the oral soft tissues, soreness and dryness of the oral tissues, and desquamative lesions and ulcerations of the gingival mucosa.[42] In addition, a strong, unpleasant taste of the rinse itself is a regular complaint among users of chlorhexidine rinses. Varnishes were developed to minimize these known side effects. Since varnishes are not available in the US, these unpleasant side effects from the use of rinse mode are still a problem among patients.

CONCLUSIONS

The use of chlorhexidine for caries prevention has been a controversial topic among dental educators and clinicians. In several reviews, it has been concluded that the most persistent reduction of mutans streptococci have been achieved by chlorhexidine varnishes, followed by gels and, lastly, mouth rinses. Also, the evidence for using different chlorhexidine modes or a combination of chlorhexidine-fluoride therapy for caries prevention has been "suggestive but incomplete." Variable study designs and lack of data in high-risk children and adults support the need to continue to conduct randomized, well-controlled clinical trials and to search for a practical, effective mode of antimicrobial treatment that augments the known effect of fluoride treatments.

Currently, the only chlorhexidine containing products marketed in the US are mouthrinses containing 0.12 percent chlorhexidine. Based on the available reviews, chlorhexidine rinses are not highly effective in preventing caries or at least the clinical data are not convincing. Due to the current lack of long-term clinical evidence for caries prevention and reported side effects, chlorhexidine rinses should not be recommended for caries prevention. Due to the inconclusive literature and sparse clinical data on gels and varnishes, their use for caries prevention should also be studied further to develop evidence-based recommendations for their clinical role in caries prevention.

Since dental caries is a disease with a multifactorial etiology, it is currently more appropriate to use other established, evidence-based prevention methods, such as fluoride applications, diet modifications and good oral hygiene practices. Recent findings also indicate that the effect of an antimicrobial agent for reducing the levels of mutans streptococci or plaque reduction may not always correlate with eventual caries reduction. The clinically important outcome is proven reductions in caries.

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