Chlorhexidine as a Chemotherapeutic Agent In the Control of Periodontal Disease

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Introduction

At the present time, the safest and most predictable means of treating and/or preventing periodontal disease is mechanical therapy.[1,2] Bacterial deposits on and around teeth are removed by the dental profession and/or the dental patient through the use of various mechanical aids and techniques. Since periodontal disease represents a chronic inflammatory response to bacterial plaque,[3] it seems logical that a chemical agent that eliminates the plaque would result in an elimination or reduction of the inflammatory pathosis. It is the purpose of this paper to discuss the role of chlorhexidine as a posible chemotherapeutic agent to be used in the control of periodontal disease. This paper will discuss the chemical structure and pharmacology of chlorhexidine, modes of application, the effectiveness of the drug and its side effects.

Chemical Structure and Pharmacology

Chlorhexidine gluconate is a hexmythenebis (biguanide) that displays bactericidal activity on a wide range of bacteria upon contact. It is effective against gram-positive and gram-negative organisms and its effectiveness is not reduced by the presence of extraneous organic matter such as blood or pus. In vitro studies[5] have shown low concentrations of chlorhexidine absorb into the surface of cells causing a change in cellular permeability that results in leakage of vital cellular components. In higher concentrations, this chemical exerts its antimicrobial effect by precipiting cytoplasmic constituents.

Chlorhexidine is approved in the United States only for tropical use as a surgical scrub and cleanser of skin wounds, such as lacerations or burns and is marketed under the trade name of Hibiclens.[4] Chlorhexidine is not approved for general use as a prophylactic agent against periodontal disease in the United States at the present time.

The Effectiveness of Chlorhexidine Against Periodontal Disease

Loe and coworkers[6] demonstrated in a clinical study that topical application of a 0.20% chlorhexidine mouthrinse inhibits the formation of plaque and prevents gingivitis. In this study, 13 healthy male dental students were used who displayed excellent oral hygiene and an absence of gingival inflammation. The subjects were requested to withhold all oral hygiene procedures for a period of three weeks. At the end of this time, all of the students displayed plaque accumlations and gingivitis. Then, a scale and polish and regular oral hygiene regimen was reinstituted which resulted in disappearance of the plaque and reversal of the gingivitis. This exercise demonstrated (1) cessation of oral hygiene resulted in increased plaque accumulation; (2) accumulation of plaque resulted in the clinical appearance of gingivitis; (3) the gingivitis was reversed with resumption of good oral hygiene; and (4) the subjects in this study were susceptible to plaque accumulation and gingivitis.

In the next phrase of the study, the subjects were divided into three groups after the signs and symptoms of gingivitis had resolved. In the first group, four students omitted mechanical cleaning procedures and rinsed with 10 ml of 0.20% chlorhexidine for one minute five times a day for three weeks. The teeth stayed plaque free and gingivitis did not develop. This part of the experiment demonstrated that chlorhexidine was effective in preventing the formation of plaque on clean teeth.

In the second group, five students rinsed with 10 ml of 0.20% chlorhexidine for one minute twice a day. In this group, the teeth also remained plaque free and gingivitis failed to develop. In the third group, four students allowed plaque to accumulate on their teeth for 17 days and then rinsed with chlorhexidine six times in one hour and then twice daily for six days. By the end of the third day, the plaque had disappeared and their was no gingivitis present. This part of the experiment demonstrated that chlorhexidine not only

prevented formation of plaque on clean teeth but also removed accumulations of existing plaque.

In other well designed longitudinal studies, [7] [8] regular use of topical chlorhexidine resulted in reduced plaque and gingivitis formation.

Modes of Application

Chlorhexidine remains antibacterial in the mouth for several hours after topical application.[9] An explanation of this phenomenon may be related to the findings of an in vitro study[10] that demonstrated the binding of chlorhexidine to protein (albumin) in both serum and saliva. This binding occurs with proteins in solution as well as precipitated proteins. Although soluble proteins turn over rapidly with the saliva, the insoluble proteins are not removed as quickly and attached chlorhexidine exerts a longer effect as it is slowly released.

Some possible modes of topical application of chlorhexidine include mouthwashes, dentifrice and gel in cap splints. Mouthwash application is effective in the prevention and treatment of plaque accumulation and superficial gingivitis, as described in the above studies. However, chlorhexidine cannot cure or reverse established periodontitis with pocket formation and bone loss.[10]

Conventional treatment with debridement by instrumentation and pocket elimination surgery is still necessary to treat advanced periodontal disease.

Several studies[11],[12] have shown that a dentifrice serves as an adequate vehicle for application of chlorhexidine to obtain the desired result of controlling plaque and gingivitis.

In a study, involving a slightly handicaped population,[13] it was found that application of chlorhexidine gel (0.80%) in cap splints for four weeks without any other oral hygine measures resulted in a significant decrease in plaque indices when compared to the control patients. In the same study, a group of severely handicapped patients were submitted to the same treatment but the results were not as impressive. It is possible that the lack of cooperation of these severely handicapped individuals adversely affected the effectiveness of the chlorhexidine gel.

Side Effects of Chlorhexidine

The side effects of chlorhexidine seem to vary with its vehicle of application i.e., mouthwash, dentifrice or gel. In a study of side effect associated with chlorhexidine mouthwash,[14] tooth and filling discoloration, bad taste, interference with taste sensation, burning sensation, soreness and dryness in the mouth and desquamation of the oral mucosa occured. It was found that 15% of interpreximal tooth surfaces discolored, but only 7% of the buccal surfaces showed discoloration. This discoloration could be removed with routine brushing and a professional oral prophylaxis. Sixty-two percent of the fillings were permanently discolored. This discoloration phenomenon may be related to the ability of chlorhexidine to precipitate proteins in the oral cavity. The remaining subjective symptoms associated with mouthwash use were infrequently reported by the patient in the study. Discoloration is the only side effect that was observed with the use of chlorhexidine in the dentifrice or gel formulation.

A chemical similar to chlorhexidine (alexidine) has been evaluated in hopes of obtaining the same therapeutic effect but avoiding the undesired side effects of chlorhexidine. In a recent study[15] it was shown that alexidnine is a good antiplaque agent but it also causes the side effect of staining teeth.

Summary

Chlorhexidine is a possible chemotherapeutic agent to control plaque induced periodontal disease. The chemical structure, effectiveness, modes of application and side effects of chlorhexidine have been discussed.

Various studies have reported chlorhexidine to be an effective antiplaque agent, however there are undesirable side effects associated with its use. Chlorhexidine has no therapeutic value in the treatment of periodontal disease that has progressed to the point of osseous involvement. Chlorhexidine is effective only in the prevention and reversal of superficial gingivitis.

I feel the use of chlorhexidine in a patient with periodontitis could give a superficial appearance of health, while a deeper pathological process would continue unnoticed and untreated. Periodontal disease already has too few signs and symptoms to alert the dentist and/or patient to the amount of underlying destruction taking place. Furthermore, I feel that if chlorhexidine was approved for general use, it would be very easy for some enterprising individuals, or companies, to falsely present it to the general public as a cure-all for periodontal disease, which would be far from the truth. A patient could conceivably spend more time visiting a dentist for the removal of stains from his teeth and the replacement of stained fillings than a good oral

hygiene program would require, using presently accepted therapeutic measures.

At the present time. I do not feel chlorhexidine should be used to prevent periodontal disease for the reasons stated. Research should be continued with this agent because it may have application in a certain limited population, such as handicapped individuals who are totally dependent on others for their dental care or very young individuals whose periodontal disease is usually limited to gingivitis.

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Dr. Britt is a native of Shreveport, Louisiana who obtained his secondary education at Murphy High School in Mobile. He received a B.S. degree in chemistry from the University of South Alabama and a M.S. degree in human anatomy from the University of Alabama Medical Center in Birmingham before entering the University of Alabama School of Dentistry in 1974. After receiving his D.M.D. degree in June, 1978, he completed a two-year residency in periodontology at the University of Alabama School of Dentistry in July, 1980.

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