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CURRENT OPINION

Fresh Mouth is a Gateway to a Healthy Body – An Overview of Current Use of Chlorhexidine

Ramandeep Kaur Sohi[1], Ramandeep Singh Gambhir[2], Amaninder Randhawa[3], Vikram Bansal[4], G.M Sogi[5], KL Veeresha[6]

ABSTRACT

For the past many years intensive research has been conducted on various chemical agents, as adjunct to mechanical plaque control measures, for the reduction of oral diseases. Various chemical formulations are available for control of plaque which is the causative factor in gingivitis. Extensive amount of literature is present, providing proof of efficacy of chlorhexidine in plaque control. After three decades of use by the dental profession, chlorhexidine is still recognized as the gold standard against which other antiplaque and antigingivitis agents are measured. It is both bacteriostatic and bacteriocidal in nature owing to different concentrations. Chlorhexidine is available in different forms like gels, sprays, mouth rinses etc. It appears to be mainly useful in situations where oral hygiene is difficult to maintain.

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[1]BDS, MDS, Senior Lecturer
Dept. of Preventive and Community Dentistry
M.M.College of Dental Sciences & Research,
Mullana, Ambala, Haryana, INDIA

[2]BDS, MDS, MPH, Senior Lecturer
Dept. of Preventive and Community Dentistry
Gian Sagar Dental College and Hospital,
Banur, Rajpura, Punjab, INDIA

[3]BDS, MDS, Senior Lecturer
Dept. of Preventive and Community Dentistry
Sri Guru Ram Dass Dental College,
Amritsar, Punjab, INDIA

[4]BDS, MDS, Senior Lecturer
Dept. of Preventive and Community Dentistry
M.M.College of Dental Sciences & Research,
Mullana, Ambala, Haryana, INDIA

[5]BDS, MDS, Professor,
Dept. of Preventive and Community Dentistry
M.M.College of Dental Sciences & Research,
Mullana, Ambala, Haryana, INDIA.

[6]BDS, MDS, Professor,
Dept. of Preventive and Community Dentistry
M.M.College of Dental Sciences & Research,
Mullana, Ambala, Haryana, INDIA.

Contact Author

Dr. Ramandeep Singh Gambhir
raman1g@yahoo.co.in

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INTRODUCTION

Health is a valuable asset for every individual. Oral health is an integral part of general health and has considerable effect on the quality of life and teeth are one of the essential elements of oral health.

Dental plaque, a bacterial biofilm, is one of the major etiologic agents involved in the initiation and progression of dental caries, gingivitis and periodontal disease. Removal of plaque and biofilm and the prevention of its accumulation on the teeth and adjacent gingival tissues is done by mechanical and chemical methods of plaque control for better health of the oral cavity. Mechanical plaque control is most commonly used for oral hygiene, which includes tooth brushing and interdental cleaning and professional prophylaxis. In recent years a concept of chemical plaque control has also been promoted along with the traditional concept of mechanical plaque control. Chemical plaque control agents have proven to be an ideal adjunct to mechanical plaque control procedures. Among the various chemical agents used as antiplaque agents, ***chlorhexidine*** is accepted as Gold Standard because of its property of substantivity in prevention of plaque formation (1).

Chlorhexidine was first marketed under the trade name "hibtane" in 1953 as an antiseptic cream. First sustained release dosage form of chlorhexidine diacetate for topical use was developed by Friedman and Golomb in 1982 (2). Chlorhexidine is poorly absorbed by the gastrointestinal tract and it therefore displays very low toxicity. Chlorhexidine is a dicationic bis-biguanide with broad antibacterial activity. It exhibits a wide spectrum of activity, encompassing gram-positive and gram-negative bacteria, yeasts, dermatophytes and some lipophilic viruses. Chlorhexidine has strong affinity for binding to skin and mucous membrane. Chlorhexidine shows different effects at different concentrations i.e. Bacteriostatic at low concentrations and Bactericidal at high concentrations (3).

SYNERGISTIC EFFECT OF CHLORHEXIDINE

CombinaLtions of Chlorhexidine with other agents such as fluoride or thymol in varnish resulted in additive or synergistic benefits, e.g. in preventing caries in high risk patients such as those receiving radiation therapy for head and neck cancer. In these patients, the radiation therapy affects the salivary glands, and the reduced salivary flow is conducive to rampant caries (4). Chlorhexidine and copper combination exerted a synergistic, growth-inhibitory effect on Actinomyces viscous, Actinomyces naeslundii, and Streptococcus mutans. Low concentrations of Chlorhexidine combined with copper (Cu^{2+}) could conceivably be used as a rinse for reducing cariogenic flora and /or treating gingivitis with potentially fewer adverse effects (5). The combination of calcium hydroxide ($Ca(OH)_2$) and chlorhexidine was used for faster eradication of P.micros and S.intermedius from infected root canals. Calcium hydroxide did not adversely effect the solubility and activity of chlorhexidine but rather exhibited an additive effect on some gram positive endodontic pathogens like P. micros and S.intermedius (6). The calcium hydroxide paste with 2% chlorhexidine was significantly more effective in killing Escheria faecalis in the dentinal tubules than calcium hydroxide with water (5). Chlorhexidine sodium gluconate mouth rinse was more effective in reducing plaque accumulation and gingivitis when compared to mouthrinse that contained only chlorhexidine (7).

PRODUCTS WITH CHLORHEXIDINE

Chlorhexidine has been formulated in a number of products:

Mouth rinses

Chlorhexidine mouthwash contains chlorhexidine gluconate solution in a suitable flavored and coloured vehicle. Varying concentrations of chlorhexidine are being used in various countries e.g- Aqueous alcohol solutions of 0.2% chlorhexidine have been made available twice daily use in Europe. Rinsing for 60 seconds with 10ml 0.2% chlorhexidine twice daily was considerable to be adequate for plaque inhibition. Chlorhexidine mouthwash with concentration 0.2% and 0.12% give equal efficacy when used at approximately at equal doses. Chlorhexidine (0.12%) mouth rinses are more efficient in reducing mutans streptococci count in salvia as compared to other mouth rinses like sodium fluoride and triclosan (8). Toothbrush rinsing with chlorhexidine mouth rinse (containing antimicrobial agent) after the normal oral hygiene is very convenient and cost effective to reduce toothbrush contamination. Chlorhexidine gluconate mouth rinse generally reduces more plaque than either Cetylpyridinium Chloride (CPC) or Essential Oils, a predictable outcome given its greater substantivity; the longer an antimicrobial agent stays in contact with plaque bacteria, the greater its effect. Both chlorhexidine gluconate and essential oils demonstrate greater reductions in supragingival plaque and gingivitis as compared with CPC (9).

Gels

1% Chlorhexidine gel product is available and can be delivered on a toothbrush or in trays. Uses of Chlorhexidine in trays is comfortable and effective, especially in handicapped children (10). More recently 0.2% and 0.12% chlorhexidine gels have also been available. Chlorhexidine appeared to be a promising agent to be used as final irrigant. 2% chlorhexidine gel formation was proposed as an alternative to 5.25 % sodium chloride solution for root canal disinfection. This lubricant is composed of a gel base (1% Natrosol), which is nonionic, highly efficient, inert, water- soluble agent that does not have antimicrobial ability comparable with that obtained with the other solutions (5.25% of NaOCl and 2% chlorhexidine liquid) tested. It appeared that chlorhexidine in a gel form required a much longer time to kill microorganisms than the corresponding concentration in liquid form. In addition 2% chlorhexidine gel has also been proposed as intracanal medication and sodium perborates vehicle for intracoronal bleaching (10). After biochemical preparation of root canal, residual pulp tissue, bacteria and dentin chips may persist in the irregularities of the root canal system, covering the canal walls or loged in the dentinal tubules even after careful instrumentation. The presence of smear layer and debris decreases the penetration ability of intracanal dressings and also prevents complete adaptation of obturation materials. The 2% chlorhexidine gel with the association of chelating agent 17 % EDTA (ethylenediaminetetraacetate) as an irrigating solution is effective in smear layer or debris removal. Thus use of chelating agent can contribute significantly for achievement of clean root canal walls with open tubules. 2% Chlorhexidine gel is an effective root canal disinfectant, and additional intracanal dressing did not significantly improve the disinfection. One-visit root canal treatment with 2% chlorhexidine gel can be performed without compromising its long term success. Gel can also be applied to teeth with finger and toothpicks (11).

Sprays

0.1% and 0.2% Chlorhexidine sprays are commercially available in some countries. Sprays appear to be particularly useful for the physically and mentally handicapped groups. Spraying with non-aerosol chlorhexidine spray, twice a day deliver approximately 1.4 to 2 ml of chlorhexidine, which is one seventh of the optimal mouth rinse dose of 0.2% Chlorhexidine. However, it has the same effect on plaque formation and gingival bleeding as the mouth rinse (11).

Toothpastes

Chlorhexidine is difficult to formulate into the toothpaste because of binding of Chlorhexidine to components in the toothpaste. This reduces the activity by decreasing the number of active cationic sites. However some formulations have been achieved which avoid this problem. More recently, some toothpaste have been specifically formulated to ensure a high availability of the contained antiseptic (12). Chlorhexidine interacts with calcium ions or anionic detergents such as sodium lauryl sulphate. Sodium synthetic detergent in dentifrices. Sodium lauryl sulfate and chlorhexidine digluconate are not compatible in vivo when applied subsequently and at concentration used for clinical purposes. Both compound will attach to oral tissues

and will bind to and denature proteins. There is reason to believe that a salt with low solubility and low antibacterial activity was formed in vivo, neutralizing Chlorhexidine, even when the agents were applied separately and with time intervals. Both acts as antagonists. It is therefore recommended that the interval between tooth brushing with toothpaste, containing sodium lauryl sulfate and rinsing with Chlorhexidine should be more than 30 min, probably close to 2 hours (2).

The frequent use of Chlorhexidine or metronidazole containing toothpaste alone or combined as an adjunction to existing oral hygiene procedures may reduce plaque levels and gingival bleeding tendency. The effect will be predominant in toothpaste when used as combined formulation of Chlorhexidine and metronidazole. This method could be an option of clinically effective treatment for dental professionals and their patients for long term management of adult periodontitis (13).

Chewing gums

Chewing gum as a delivery system for various topical dental prophylactic and therapeutic agents has been repeatedly studied, and a few dental chewing gum products are registered and marketed in various countries. Thus, there are gums containing fluoride, enzymes, mineral salts, metal salts, xylitol, carbamide and chlorhexidine diacetate. Chlorhexidine has also been incorporated into a sugar free chewing gum and in this form the chlorhexidine molecules remains unbound. The use of chlorhexidine gum could be a good method of using Chlorhexidine in longer terms (2).

Advantages of chewing gum as a chlorhexidine delivery system

Ease of intake (without water, anytime, anywhere), less pronounced bitter taste, less impairment of taste sensitivity, better oral distribution, less staining, less interference with surface active ingredients contained in toothpaste (11).

Indications for chlorhexidine containing chewing gum

Chlorhexidine containing chewing gum as a means to fight plaque and gingivitis is a valid choice for persons with high caries activity in general and especially for oligosialic (hypo salivary) and xerostomia patients. It is further indicated to fight bad breath and before and after undergoing periodontal therapy as an adjunct to other oral hygiene measures. Chlorhexidine chewing gum should not be chewed by all persons temporarily unable to perform for whatever reason. It is further indicated to help maintain the oral health in older dependent population and other at risk group unable to perform adequate oral hygiene (11).

Contraindications

Chlorhexidine containing chewing gum should not be used by persons who are known to be hypersensitive to chlorhexidine diacetate or other gum formula ingredients (11).

Dosage of chlorhexidine containing chewing gum

The daily recommended use of chlorhexidine chew gums is four to six pieces, ideally twice or three times daily two pieces at a time chewed for 20 min. One piece of Chlorhexidine chewing gum contains 5mg of chlorhexidine, thus the total daily dose is 20- 30 mg of chlorhexidine (11).

VARNISHES

Varnishes are the most effective form for professional application of chlorhexidine as they are easy to apply, do not require collaboration by patient and although they have unpleasant flavor, they do not cause discoloration. Currently, three chlorhexidine varnishes are manufactured-EC40, Chlorzoin and Cervitec (14).

The application of chlorhexidine varnishes seems to have beneficial effects in patients with chronic gingivitis, improving their plaque accumulation and bleeding levels and reducing their gingival index. It is possible to maintain this beneficial effect for prolonged periods of time, although this requires re-applications of varnish at intervals between for the best results over time (14). Chlorhexidine varnish can provide sustained release of Chlorhexidine and suppress S.mutans in dental plaque for 6 months after the application. It has similar effects when compared with topical fluoride applications in preventing dental caries in the permanent teeth of teenagers (15). The varnish may also be useful in the prevention of root-surface caries (16).

The standard varnishes (a natural resin soluble in ethanol and formerly used as a temporary filling material for carious teeth) containing high concentrations of Chlorhexidine can be used successfully for long term suppression of S. mutans in dental fissures. The sub gingival administration of a highly concentrated chlorhexidine varnish as an adjunct on the same day of full mouth root planing in non-smoking chronic periodontitis patients may benefit, at least in terms of pocket reduction at initially deep sites (e"7 mm) (17). In the long run, initially deep pockets seemed to benefit most from this chemo-mechanical treatment with an additive pocket reduction of nearly 1mm (18).

PERIOCHIP

Periochip, the controlled sub gingival delivery of chlorhexidine, was developed by Perio Products Ltd, Jerusalem, Israel and it is the only product available commercially. It is an orange brown, biodegradable, rectangular chip rounded at one end (19). This is a 5mm x 4mm x 0.3mm film containing 2.5mg of chlorhexidine gluconate which is incorporated in a biodegradable matrix of hydrolyzed gelatine cross linked with gluteraldehyde. The matrix also contains glycerin and purified water. It was first introduced in United States in 1998.

IMPORTANCE OF CHLORHEXIDINE CHIP IN PERIODONTAL THERAPY

If the progression of periodontitis can be arrested by chlorhexidine chip preventing complication, it can be accepted as a routine strategy. Disadvantage of flap surgery includes gingiva recession leading to tooth elongation and causing sensitivity and esthetic problems. If adjunctive use of sustained release chlorhexidine reduces

pocket depth, a second placement of the chip should be considered where pocket depth remains > 5mm. Chlorhexidine chip when used as an adjunct to scaling and root planning significantly reduces loss of alveolar bone and improve the clinical signs of periodontitis (19).

The most frequently observed adverse events in the two pivotal clinical trials were toothache, upper respiratory tract infection, and headache. The Perio Chip should not be used by persons who are known to be hypersensitive to chlorhexidine gluconate.

INDICATIONS OF CHLORHEXIDINE (20-22)

1. Sterilization
2. Used for disinfecting hands, skin, washing wound.
3. Oral rinses for sore gums, mouth ulcers, preventing plaque on teeth.
4. Effectively suppress the activity of Streptococcus mutans, thereby inhibiting acid production and preventing caries.
5. Chlorhexidine rinse has also found a place in fixed prosthodontics. For patients who are prone to candidal infection, 0.2% chlorhexidine can be used to disinfect dentures by soaking them overnight.
6. Reduce traumatic ulceration caused by orthodontic appliances.
7. Chlorhexidine 0.2 % can be used as endodontic irrigant and as intracanal, interappointment dressing. The pre surgical application of 0.5% of chlorhexidine significantly reduces microbial load, and lowers the risk of post operative infection.
8. For physically and mentally handicapped individuals.
9. Stomatitis and oral ulcers can be treated with chlorhexidine mouthwash. Twice daily chlorhexidine rinse markedly reduces oral infections in immuno-compromised patients including those with AIDS.
10. Reduce the severity of gingival overgrowth.
11. Reduce dry socket after extraction.
12. Reduce alveoilitis- Bio adhesive 0.2% chlorhexidine gel, applied only once after the extraction of impacted third molars in the alveolus seems to be an appropriate option for the reduction of alveolitis.
13. Intermittent treatment of ***dental unit waterlines*** with 0.12% chlorhexidine gluconate in a proprietary formulation, significantly reduced bacterial counts.
14. Chlorhexidine pretreatment rinse effective in reducing ***bacterial aerosols.***

ADVERSE EFFECTS OF CHLORHEXIDINE (19)

- Staining of teeth and mucous membrane (Brown staining).
- Bitter taste.
- Carcinogenicity- Parachloroaniline (PCA) an industrial chemical is found in chlorhexidine products as a trace contaminant. It forms a breakdown product subsequent to prolonged shelf life or exposure to high temperature. Keeping chlorhexidine solution in a dark refrigerated bottle can retard this. Risk assessment associated with chlorhexidine application must be based upon actual applied dosages. When the levels of PCA exceed 20 mg/litre of urine, workers in clinical plants should be referred for medical treatment.
- Enhances the formation of supragingival calculus formation.
- Mucosal desquamation.
- Parotid swelling.
- Neurosensory deafness- Can occur if chlorhexidine is introduced into the middle ear and the antiseptic should not be placed in the outer ear in case the ear drum is perforated.

§ Hypersensitivity reactions.

SUMMARY AND CONCLUSION

Traditionally, mechanical removal of plaque by tooth brushing and other methods was the most common approach to oral hygiene. Chemical plaque control agents have proved to be an ideal adjunct to mechanical plaque control measures. Amongst all antimicrobials, chlorhexidine digluconate has clearly received the greatest attention. For the past 35 years, it is being used to combat the two principle diseases (dental caries and periodontal disease) of oral cavity with varying degrees of success. Chlorhexidine is a strong cationic base. It is accepted as "***Gold Standard"*** as it shows both bacteriostatic and bactericidal effect, lasting more than 12 hours. This is due its property of "*Substantivity"*. Chlorhexidine helps in effective prevention of plaque accumulation on teeth, mucous membrane, restorations and appliances, hence in turn prevents dental caries, periodontal diseases, halitosis, secondary caries, dry socket and oral candidiasis. However, long term use of chlorhexidine is not advised because it causes brownish discoloration of the teeth. Chlorhexidine is mainly used these days in mouthrinses, gels, chewing gums, sprays, dentifrices, varnishes and periochips. Apart from this the chlorhexidine is used as an effective irrigant both in dental and medical surgeries. It is also used as an effective antiseptic in aerosol units. Chlorhexidine has proved to be an effective adjunctive chemotherapeutic agent in the prevention of oral diseases and in promotion and maintenance of health.

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