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CHLORHEXIDINE – A MIRACLE CHEMICAL

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ABSTRACT

Chlorhexidine is a broad-spectrum antiseptic. It is recognized as Gold standard against which other antiplaque and antigingivitis agents are being compared. We are using it on medical devices and for skin preparation prior to procedures. It is well tolerated by patients and is a true life-saver in terms of prevention of infection and “multi-drug resistant organisms”. Hence it can be called as a “Miracle Chemical”. This article clearly suggests the properties and limitations of this miracle molecule “Chlorhexidine” ensuring the maximum efficacy and the minimum side effects of the agent. Thus, this is one unique chemical which is considered as the past, present and future agent in the ever-growing field of clinical periodontics.

Keywords: Chlorhexidine, Antimicrobial, Antigingivitis, Antiplaque agent, Mouth wash, Antiseptic.

INTRODUCTION

Chlorhexidine is a cationic bisbiguanide that has been used as a broad-spectrum antiseptic in medicine since 1950's. Its ability to inhibit the formation and development of bacterial plaque was demonstrated in 1970's. It is the most effective antiplaque, antigingivitis agent.^[1]

Structure

It is symmetrical molecule consisting of two 4 chlorophenyl rings, two biguanide groups and a central hexamethylene bridge connecting chlorophenyl & biguanide group. (Fig.1)

After 20 years of use by the dental profession, chlorhexidine is recognized as the Gold standard against which other antiplaque and gingivitis agents are measured. Chlorhexidine's antiplaque effect is a result of the dicationic nature of the chlorhexidine molecule, which affords the agent the property of persistence of antimicrobial effect

at the tooth surface, through both bactericidal and bacteriostatic effects.

Mechanism of action

Chlorhexidine is a broad-spectrum biocide effective against Gram positive bacteria, Gram negative bacteria and fungi^[16]. Chlorhexidine inactivates microorganisms with a broader spectrum than other antimicrobials (e.g. antibiotics) and has a quicker kill rate than other antimicrobials (e.g. povidone-iodine). Based on its concentration, it has an immediate bactericidal action and a prolonged bacteriostatic action due to adsorption onto the pellicle-coated enamel surface^[10]. Chlorhexidine kills by disrupting the cell membrane.^[28] (Fig. 2)

Effect on bacteria

Chlorhexidine is a positively charged molecule that binds to the negatively charged sites on the cell wall; it destabilizes the cell wall and interferes with osmosis.^[22] The bacterial uptake of the chlorhexidine is very rapid, typically working

within 20 seconds. In low concentration, it affects the integrity of the cell wall. Once the cell wall is damaged, it crosses into the cell itself and attacks the cytoplasm membrane. Damage to the cytoplasm's delicate semi permeable membrane allows for leakage of components leading to cell death. In high concentration chlorhexidine solidifies the cytoplasm. (Fig. 3)

Effect on fungi

Fungi uptakes chlorhexidine in a short period of time and the mechanism of action is very similar to bacteria.

Effect on biofilm

Bio films are a complex aggregation of microorganisms growing on a solid substrate. They can occur on organic (e.g. dental plaque) or inorganic surfaces. This matrix protects the cells within it and increases their resistance to antimicrobials. Many antimicrobial agents have a difficult time eliminating organisms in a bio film. Chlorhexidine has shown some ability to help inhibit adherence of microorganisms to a surface thereby preventing growth and development of bio films.^[14]

Effects on other microbial organisms

This includes bacterial spores and protozoa. It has also shown activity against enveloped viruses *in vitro* (e.g., herpes simplex virus, HIV, cytomegalovirus, influenza. But has substantially less activity against nonenveloped viruses (e.g., rotavirus, adenovirus, and enteroviruses).^[11]

Effect on skin, mucous membrane

In topical applications, chlorhexidine is shown to have the unique ability to bind to the proteins present in human tissues with limited systemic absorption. Protein bound chlorhexidine releases slowly leading to prolonged activity. This phenomenon is known as substantivity^[18] and allows for a longer duration of antimicrobial action against a broad spectrum of bacteria and fungi. In fact, it's antimicrobial activity has been documented to last at least 48 hours on the skin.^{[7][18]} Unlike povidone-iodine, it is not affected by the presence of body fluids such as blood.

Effect on medical equipments

Chlorhexidine has also been applied to medical devices such as dental implants, vascular catheters, needleless connectors and antimicrobial dressings to kill organisms and protect against microbial colonization and subsequently bio film development.

Deactivation

Chlorhexidine is deactivated by anionic compounds, including the anionic surfactants commonly used as detergents in toothpastes and mouthwashes, anionic thickeners such as carbomer. For this reason, chlorhexidine mouth rinses should be used at least 30 minutes after other dental products^[4]. For best effectiveness, food, drink, smoking, and mouth rinses should be avoided for at least one hour after use. If it is not deactivated, chlorhexidine lasts longer in the mouth than other mouthwashes and this is partly why it is to be preferred over other treatments for gingivitis.

Safety

Chlorhexidine is harmful in high concentrations, but is used safely in low concentrations in many products, such as mouthwash and contact lens solution. However, numerous scientific papers have reported complications with low level exposure too. In UK, the Medicines and Health Care Products Regulatory Agency (MHRA) has issued a patient safety alert on the risk of anaphylactic reactions from the use of medical devices and medicinal products containing chlorhexidine. Adequate and well-controlled studies in pregnant women have not been done, so this drug should be used during pregnancy only if clearly needed. Caution should be exercised when chlorhexidine is administered to a nursing woman. Ingestion of 3-6ml of chlorhexidine by a small child (~10 kg body weight) might result in gastric distress, including nausea, or signs of alcohol intoxication. Medical attention should be sought if more than 12ml of chlorhexidine is ingested by a small child or if signs of alcohol intoxication develop.

Availability

Chlorhexidine is present in various forms such as oral rinses (0.2% and 0.12% concentration), skin cleansers, Gauze dressings, pre-operative skin preparation, surgical scrub, spray, rubbing agent, gel with and without combination of fluoride, soap, face wash, varnish, local drug delivery, chewing gums and in small quantities it is used as a preservative.(fig.4) As a mouth-rinse, chlorhexidine is sometimes marketed under the brand names Clohex, Foam Safe, Hexicleans, Peridex, and Perichlor. It is also available as a chlorhexidine-chip (PerioChip) in the UK, USA and in Germany. Quinoderm face wash is the brand name for its face wash. Its spray products are mainly marketed under the brand name Corsodyl. It is marketed as ethanol in Italy, Switzerland and other European countries, Chlorhexamed in Germany, Savacol in Australia and New Zealand, clohex in India, Peroxidina in Venezuela, chlorhex in UK. As a skin cleanser, it is marketed under brand names such as Hibiclens, Savinox plus or Dexidin. Surgical hand wash is marketed under the brand name Hexigard. It is also used in some acne skin washes. It is also used as part of a treatment for athlete's foot. In some countries, it is available by prescription only.

Various forms of chlorhexidine

Chlorhexidine mouth wash

Indications

- Antiplaque & antigingivitis agent.
- It is used to improve bad breath. Morning halitosis is reduced up to 90%.^[27]
- Improves gingival health for short periods in the absence of any mechanical oral hygiene procedure.^[15]
- It is used between dental visits as part of a professional program for the treatment of gingivitis^[6].
- It may also be of some prophylactic value against oral candidial infections.^[5]

- It decrease the speed and degree to which recurrence of drug-induced gingival enlargement occurs.^[24]
- During the first postoperative week after a periodontal surgery, patient advised to use twice daily to maintain good oral hygiene.^[19]
- It may help to reduce the mucositis.^[23]
- There are oral pathologic conditions like oral cysts, dental traumas etc. in which the maintenance of oral hygiene is required for healing and regeneration of the oral tissues^[29]^[30].

Side effects

The most common side effects are:

- An increase in staining of teeth and other oral surfaces including silicate and resin restorations due to continued use for long periods. ^[13] This brownish discoloration of teeth and tongue are due to the fact that the disintegration of bacterial membranes leads to the denaturation of bacterial proteins^[8]. Other discolorations might be caused by monosaccharide's such as glucose and fructose that are dissolved in saliva and that react with the amine functions of bacterial proteins(Maillard reaction)^[8].
- An increase in calculus formation,
- An alteration in taste perception^[12]
- Minor irritation and superficial desquamation of the oral mucosa.
- Parotid gland swelling and inflammation of the salivary glands (sialadenitis).
- Frequently reported oral mucosal symptoms are Stomatitis, Gingivitis, Glossitis, Ulcer, Dry mouth, Hypesthesia, Glossal edema, Paresthesia.

Study comparing efficacy of two different concentrations of chlorhexidine mouth-rinse on plaque re growth suggests both are almost equally effective for their plaque inhibiting capacity.^[9]

Study evaluating the role of chlorhexidine in caries prevention suggests that it has not been highly effective in preventing caries.^[3]

Topical chlorhexidine

Chlorhexidine is used as a topical antiseptic skin scrub in hospital and household settings. It is also used for general skin cleansing, surgical scrub, pre-operative skin preparation and as a rubbing agent prior to the use of hypodermic or intravenous needles in place of iodine. (Fig. 5)

It is contraindicated for use near the meninges, in body cavities, and near the eyes and ears because at 2% concentration, it can cause serious and permanent injury.

Chlorhexidine Spray

It acts as an antiseptic and disinfectant agent. It kills micro-organisms in the areas it is in contact with.

Indications

- Aid for preventing build-up of plaque on the teeth and maintaining oral hygiene.
- Prevention and treatment of gingivitis.
- Promoting gum healing after dental surgery.
- Management of aphthous ulcers.
- Management of candidiasis.
- Management of inflammation of the lining of the mouth due to denture irritation.

Side effects

- Temporary taste disturbance.
- Burning sensation on the tongue.
- Brown, non-permanent staining of the teeth avoided by brushing the teeth before using the spray.
- Peeling inside the mouth.
- Swelling of the salivary glands.
- Skin irritation.

Study comparing chlorhexidine spray and mouthwash in the control of dental plaque after periodontal surgery indicates that the efficacy of CHX spray in the post-surgical control of dental plaque is not different from that of CHX mouthwash, but, tooth staining on the contrary was significantly lower in the group using CHX spray^[12].

Chlorhexidine gel

It acts as an antiseptic and disinfectant agent. One inch of gel should be used to brush the teeth once or twice a day for about a minute. The brushing aids in both mechanical and chemical plaque control. Indications and side effects are similar to that of spray. It additionally helps in preventing tooth decay in people at high risk, for example people with a dry mouth due to poorly functioning salivary glands (xerostomia).

Chlor-fluro gel

It is used on trays or tooth brush or direct application. It is available in 30 and 250 ml with the composition of 0.2% of chlorhexidine gluconate and 0.003% of sodium fluoride. Chlorhexidine helps control plaque and eases localised gingival and oral infections whereas Fluoride ions present are taken up by tooth structure and help to increase resistance to dental caries^[20].

Indications

- Used for the control of minor infections and to ease associated discomfort.
- Used as an aid to oral hygiene after oral surgical procedures or jaw fixation.
- Used to control plaque growth on RPD or orthodontic appliances.

Contraindications

- Not recommended for people who cannot expectorate.

Directions to use

Place approximately 1cm on toothbrush, brush thoroughly spit out. No rinsing for approximately 15 minutes once a day.

When using a tray system place a small amount of gel in each tooth segment, gently seat tray into mouth. To achieve full benefit, keep tray seated in the mouth for 1 hour.

Chlorhexidine Soap

It is used to reduce the germs on your skin. It works for a longer time than other soaps and it works when other body fluids such as blood are

present. It is found to be more active against Hospital Acquired Infections.

Study evaluating effect of daily chlorhexidine bathing on hospital-acquired infection reveals daily bathing with chlorhexidine-impregnated washcloths significantly reduced the risks of acquisition of MDROs and development of hospital-acquired bloodstream infections^[21].

Side effects

Itchiness, redness, and irritation of the skin. But, these side effects often go away quickly.

Chlorhexidine face wash

It has an antibacterial action and prevents spots in the face. Composition includes Chlorhexidine gluconate 0.15% & cetrimide 1.5%. (Fig.6)

Chlorhexidine varnish

The protective varnish containing chlorhexidine & thymol protects exposed root surfaces and controls bacteria.

Indications

- Protection of exposed root surface
- Treatment of open dentin tubules
- Bacterial control in patients e.g. Ortho patients
- Inadequate oral hygiene
- Gingivitis

Study evaluating the use of chlorhexidine varnishes in preventing and treating periodontal disease indicates that the application of varnishes seems to have beneficial effects in patients with chronic gingivitis, improving their plaque accumulation and bleeding levels and reducing their gingival index. It also suggests that it is possible to maintain beneficial effect for prolonged periods of time, although this requires re-applications of the varnish. Additionally, sub gingival application of high-concentration varnishes following SRP gives greater reductions in pocket depth than those obtained solely by mechanical treatment of the pockets^[17].

Local drug delivery of Chlorhexidine

Periochip is a small chip (4.0*5.0*0.35mm) composed of biodegradable hydrolyzed gelatin matrix, cross linked with glutaraldehyde and also containing glycerine & water, into which 2.5mg of chlorhexidine gluconate (36%) has been incorporated. This delivery system releases chlorhexidine and maintains drug concentration in GCF for at least 7 days.^[26]

Availability

Periochip 2.5mg is supplied as a small, orange-brown rectangular chip. It is supplied in cartoons of 10 & 20 chips. Each chip is individually packed in a separate compartment of an aluminum blister pack.

Indications

- Adjunct to scaling & root planning for reduction of pocket depth.
- Used as a part of a periodontal maintenance program.

Dosage and administration

1 periochip is inserted into a periodontal pocket with probing pocket depth 5mm. Up to 8 periochips may be inserted in a single visit.

Chlorhexidine chewing gums

Chewing gum as a delivery system for various topical dental prophylactic and therapeutic agents has been repeatedly studied. 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 CHX diacetate. Chlorhexidine containing chewing gum consists of 5 mg of chlorhexidine diacetate.

Indications

- To fight against plaque and gingivitis.
- Valid choice for persons with high caries activity in general and especially for oligosialic (hyposalivary) and xerostomic patients.
- To fight against halitosis and before and after undergoing periodontal therapy as an adjunct to other oral hygiene measures.

- Used by all persons temporarily unable to perform mechanical oral hygiene for whatever reason.

The advantages of chewing gum over traditional methods of application of chlorhexidine are obvious

- Ease of intake (without water, any time, everywhere)
- Less pronounced bitter taste
- Less impairment of taste sensitivity
- Better oral distribution
- Longer oral presence
- Less staining
- Less interference with surface active ingredients contained in toothpastes.

A study done to compare dental plaque formation without mechanical oral hygiene when chewing five pieces per day of Chlorhexidine containing gum (5 mg CHX acetate per gum, total daily CHX = 25 mg), xylitol gum (0.8 g xylitol per gum) and sorbitol gum (1.0 g sorbitol per gum) resulted in significantly reduced plaque values using Chlorhexidine containing gums compared to the sorbitol- and xylitol-containing gums ^[25].

DISCUSSION

The perfection obtained in various tools being used, still even after doing strict practice of plaque control, mechanical methods have not got 100% success. Therefore, it is in practice today that tooth mechanical and chemical methods of plaque control can produce a double action and can be further effective than mechanical methods alone. A number of chemical agents which have antimicrobial actions have been used with variable success to inhibit supragingival plaque formation and the development of gingivitis.

Among all chemical agents, Chlorhexidine appears to meet all criteria of an ideal anti-plaque agent, which explains its superior efficacy. Chlorhexidine's exceptional anti-plaque activity can be attributed to its ability to adsorb onto dental surfaces and desorb there from gradually,

providing in effect, a timed release of the antimicrobial agent.

Apart from anti-plaque effect, chlorhexidine provides its maximum optimal clinical benefits when used in the hands of dental professionals.

CONCLUSION

Thus, by understanding the properties and limitations of the chlorhexidine molecule, the dental profession can ensure that the efficacy of the agent is maximized, & the side effects associated with the agent are minimized, allowing chlorhexidine to rightly remain the gold standard against which other antiplaque agents are measured.

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FIGURES

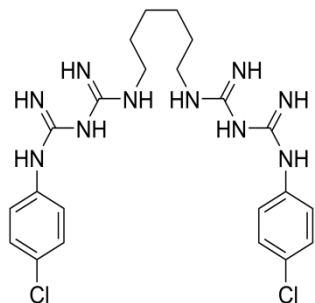


FIG.1: STRUCTURE OF CHLORHEXIDINE

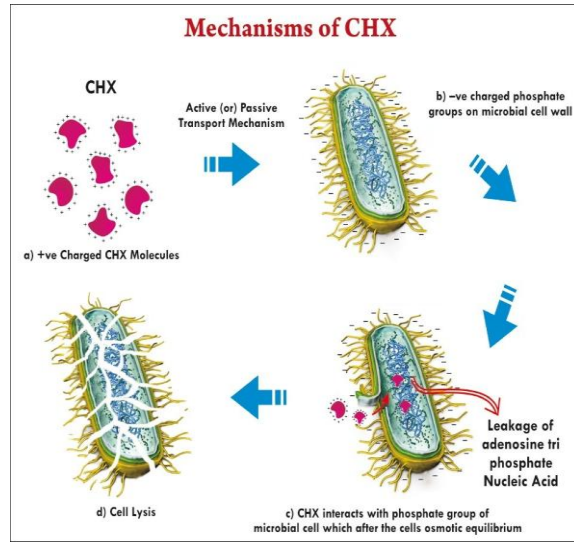


FIG. 2: MECHANISM OF ACTION

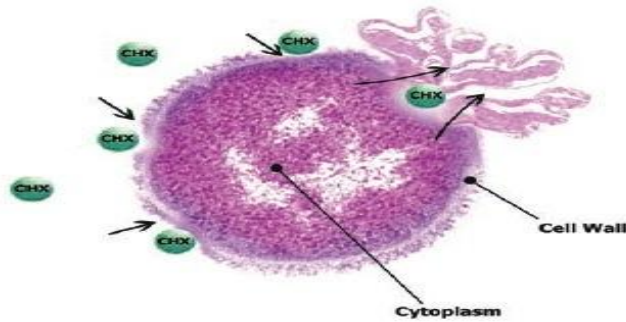


Figure 1. When the chlorhexidine molecules adhere to and damage the surface of bacteria, osmotic imbalance and the precipitation of cytoplasm ensue and result in cell death.

FIG. 3: EFFECT ON BACTERIA



FIG.4: CHLORHEXIDINE GAUZE DRESSING



FIG.5 : TOPICAL CHLORHEXIDINE PRODUCTS



FIG.6: CHLORHEXIDINE FACE WASH