REVIEW ARTICLE

ROLE OF CHLORHEXIDINE IN PERIODONTOLOGY – A WIDE RANGE NARRATIVE REVIEW SPECTRUM

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ABSTRACT

Chlorhexidine, the magical molecule proves to be the workhorse in treatment of wide range of gingival and periodontal diseases. It's imperative to take note of all the nitty-gritties of all details of this molecule. This article aims to provide all necessities and treatment criteria while using Chlorhexidine.

KEY WORDS

Bis-Biguanide, Substantivity, Pin Cushion Effect, Maillard Reaction

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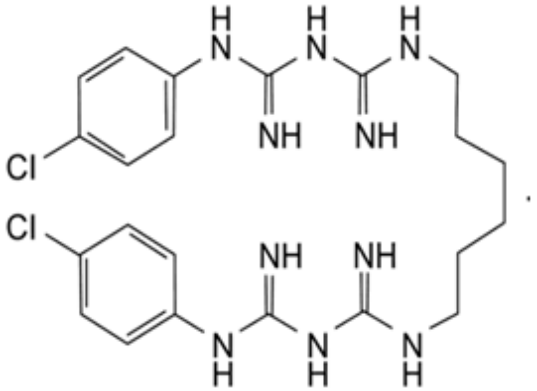
INTRODUCTION

Chlorhexidine gluconate, which is commonly known as chlorhexidine is a broad spectrum cationic bis-biguanide which is an effective against a wide array of microorganisms (including gram positive and gram negative microorganisms , fungi, yeasts and viruses). It exhibits both antiplaque and antibacterial properties. It is a second generation chemical plaque control agent. [1]

HISTORY

Chlorhexidine (CHX) was developed in the 1940s in UK and has been marketed as a general disinfectant. In the 1970s , its antiplaque activity was discovered and by the year 1976, it was available as a mouthwash. [2]

STRUCTURE [3]



Chemical Formula : $C_{22}H_{30}C_{l2}N_{10}$

Chlorhexidine is basic in nature and is mainly available in three forms. The three forms of chlorhexidine are as follows:

1. Chlorhexidine Digluconate (water soluble) – most commonly used form
2. Chlorhexidine Acetate (water soluble)
3. Chlorhexidine Hydrochloride (alcohol based)

PHARMACODYNAMICS [4,5]

- Available concentrations of chlorhexidine are 0.2% and 0.12%
- At low concentrations, chlorhexidine is bacteriostatic while at high concentrations it is bacteriocidal.
- Dosage of chlorhexidine : 18-20 mg
- Substantivity :12 hours

WHY 10 ml CHLORHEXIDINE MOUTHRINSE IS PRESCRIBED TO BE USED AT A TIME ? [4]

We know, that the available concentrations of chlorhexidine are 0.2% and 0.12%.

so, 0.2 gm of chlorhexidine is present in 100 mL of solution.

hence, 200 mg of chlorhexidine is present in 100 mL solution. therefore, as per the dosage of 18-20mg,

amount of chlorhexidine to be used is calculated as =

$$\frac{100}{200} \times 18 \text{ or } \frac{100}{200} \times 20 \cong 10\ mL$$

Hence, 10 ml of chlorhexidine mouthwash is prescribed to be used at a time to rinse the oral cavity.

PHARMACOKINETICS:

Oral Chlorhexidine rinses indicate that approximately 30% of the active ingredient is retained in the mouth following rinsing, which is subsequently released slowly in the oral cavity.

This ability to adsorb to dentin, is similar to tetracycline antibiotic agents and this ability is known as ***'Substantivity'*** or ***'Sustained Availability'***.[7]

MECHANISM OF ACTION

Chlorhexidine works by the following mechanism-

- There is a rapid attraction of a cationic CHX molecule to the surface of negatively charged bacterial cell containing phosphate groups and sulphate groups.
- The cationic properties of CHX result in its bonding with negatively charged sites within the biofilm including bacteria, extracellular polysaccharides and glycoproteins.
- This causes specific and strong adsorption to phosphate contacting components forming the surface of the bacterial cell.
- Penetration through the bacterial cell wall occurs as a result of passive diffusion, attracting it towards the cytoplasmic membrane of the cell, damaging it and compromising with its integrity.
- This allows the CHX molecule to infiltrate the inner cell membrane resulting into greater permeability.
- The result of this is an outflow of low molecular weight molecules an cytoplasmic components escaping from the microorganisms such as potassium ions leading to inhibition of activity of certain enzymes associated with the cytoplasmic membrane.[8]

PIN CUSHION EFFECT [4]

The di-cationic CHX molecule, attaches to the tooth surface by one cation, to the bacteria attempting to colonize the tooth surface with the other. This is called the Pin Cushion Effect. This prolongs the action of CHX upto 12 hours and hence is responsible for the property of Substantivity of Chlorhexidine.

ABSORPTION [6]

Topical application of chlorhexidine is unlikely to undergo any degree of systemic absorption. Orally administered chlorhexidine (as found in oral rinses) is very poorly absorbed from the gastrointestinal tract.

METABOLISM [6]

As chlorhexidine is very poorly absorbed from the gastrointestinal tract it is unlikely to undergo metabolic conversion to any significant extent.

ROUTE OF ELIMINATION [6]

Excretion occurs almost via faeces with less than 1% of an ingested dose being excreted in urine.

INSTRUCTIONS TO USE [1,4]

- 10 ml of 0.2% or, 15 ml of 0.12% chlorhexidine is used.
- We must not mix CHX with water.
- The solution is used to rinse the oral cavity for 30 seconds to 1 minute, for twice daily.
- It should not be used immediately after brushing. It must always be used 30 minutes to 1 hour later after brushing is done.

WHY CHX MUST NOT BE USED IMMEDIATELY AFTER BRUSHING : THE

EFFECT OF CHLORHEXIDINE ON TOOTHPASTE ? [1,4,9,10]

Chlorhexidine is cationic in nature and it forms salts of low solubility with anions such as phosphate, sulfate and carboxyl. Toothpastes contain anionic detergents, one of the most widely used being Sodium lauryl sulfate (SLS).

Chlorhexidine being a cationic compound binds non specifically with negatively charged phospholipid membrane of bacterial cell and provides antiplaque and antibacterial effect. However when anions like monofluoride phosphate and sodium lauryl sulfate present in toothpaste is introduced in the oral cavity along with CHX, they compete for the binding site of CHX and it leads to formation of insoluble salts of low solubility. Also, reaction between fluoride and chlorhexidine may result in decreased concentration of CHX. Hence, a 30 minute to 1 hour interval must be maintained between brushing and use of chlorhexidine mouthwash.

According to a study perfomed, which was affiliated by University Of Oslo, Norway which aimed to examine the possible interaction between chlorhexidine and the anionic components of toothpaste in vivo, the interference of sodium lauryl sulfate on the antiplaque potential of chlorhexidine was investigated.

The results of this study showed that even a 30 minute time interval between SLS and CHX rinsing gave a significantly reduced antiplaque effect of CHX. Whereas the neutralizing effect of SLS disappeared after 2 hours. It can be concluded that SLS is not compatible with CHX.

INDICATIONS [1]

Chlorhexidine is used in the following conditions:

- It is used as an adjunct to mechanical plaque control
- During post surgical period
- Patients wearing fixed orthodontic appliances/ intermaxillary fixation
- Patients with local oral infection such as denture induced stomatitis, aphthous ulcer .etc.
- Recommended level = 18-20mg per applications in mouthwash 10ml
- 0.12 – 0.2% Concentration range

Diseases	Concentration	Directions
Inflammatory(Mucositis Stomatitis Grades)	0.12%	10-15 ml rinse 30 sec 1 Week
Periodontal Diseases	0.12%	15ml rinse 30 sec thrice. SRP Re-evaluation
Prophylactic, Implant Periodontal Surgeries	0.2%	0.2% Clx 10ml 60 sec immediately before surgery and 0.12 % Clx 15 ml rinse 30 -60 sec twice a day following surgery for 2-3 weeks depending on procedures performed

ADVERSE EFFECTS OF CHLORHEXIDINE [1]

- Brownish staining of teeth on restorations. This staining however is reversible. This is called the Maillard reaction.
- Loss of taste sensation
- Rarely hypersensitivity to chlorhexidine has been reported.
- Stenosis of the parotid duct has also been reported.

RECENT STUDIES ON CHLORHEXIDINE [11]

An article was published by Bescos, Ashworth, Cutler, et.al titled 'Effects of Chlorhexidine mouthwash on the oral microbiome', on 24 March 2020.

This study showed that CHX mouthwash significantly changed the oral microbiome towards greater abundance of ***Firmicutes*** and ***Proteobacteria*** species, with lower abundance of ***Bacteroidetes, TM7, SR1 and Fusobacteria***, these changes were associated with an increase in oral acidic conditions, represented by lower acidic pH.

Saliva lactate and glucose concentrations were also elevated after using CHX. Additionally, CHX disrupted the ability of oral bacteria to reduce nitrate to nitrite. This study used genome sequencing with other general markers of oral health to analyse the impact of mouthwash containing CHX on oral and systemic health.

Results from this study hence showed that CHX lead to an increased abundance of some genera such as ***Neisseria, Streptococcus and Granulicatella*** and lowered the abundance of ***Actinomyces,*** but did not affect the abundance of ***Veillonella***. However, it remained difficult to determine that whether these changes in microbial environment suggest a shift towards a healthy oral environment or whether it increases the risk of oral diseases as it both increases and decreases certain bacterial load in the oral cavity.

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