REVIEW ARTICLE

CHLORHEXIDINE FOR LOCAL DRUG DELIVERY IN PERIODONTITIS – A REVIEW

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ABSTRACT

Periodontitis is caused by host bacterial interactions, which leads to inflammation, pocket formation, destruction of attachment apparatus of teeth, eventually leading to tooth loss. Scaling and root planing (SRP) is considered as gold standard to attain and maintain periodontal health by elimination of bacterial plaque. Perioceutics, which includes the delivery of therapeutic agents via systemic and local means as an adjunct to mechanical therapy has revolutionized the arena of periodontal therapy. Irrigating systems, fibers, gels, strips, films, microparticles, nanoparticles and low dose antimicrobial agents are some of the local drug delivery (LDD) systems available in the field, which deliver antimicrobial agents to sub-gingival diseased sites with minimal side-effects. Over the year's chlorhexidine (CHX) has been used in the dental practice as an excellent antiplaque agent. Chlorhexidine not only exhibits special property of substantivity, it also possesses a broad antimicrobial spectrum which makes its use in wide variety of oral disorders. The aim of present review is to discuss the role of Chlorhexidine as local drug delivery in periodontitis.

Key words: Periodontitis, Scaling and root planning, Local drug delivery, Chlorhexidine

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INTRODUCTION

Periodontitis is caused by host bacterial interactions, which leads to inflammation, pocket formation, destruction of attachment apparatus of teeth, eventually leading to tooth loss. Scaling and root planing (SRP) is considered as a gold standard to attain and maintain periodontal health by elimination of bacterial plaque. As the probing depth increases, the effectiveness of SRP decreases because of limited access to deep pockets, which leads to incomplete removal of periodontopathogens.[1]

Antibacterial agents have been used along with mechanical debridement locally or systemically in the management of periodontal infections. For the effective treatment, the antibiotic must reach the depth of the pocket and produce gingival fluid concentration higher than the minimum inhibitory concentration (MIC) of the suspected pathogens.[2]

The disadvantages of systemic antibiotics like bacterial resistance, superimposed infections, uncertain patient compliance, nausea, vomiting and gastrointestinal disturbances led to the introduction of local drug delivery as a treatment option in the management of periodontitis by Dr. Max Goodson in the year 1979.[2]

Intrapocket administration, i.e., application of an antimicrobial agent at the site of infection, achieves greater concentration of the drug (sometimes 100 folds more than MIC), lessens the chance of developing drug resistance, enhances patient compliance, reduces the risk of extraoral super infections, and avoids gastrointestinal adverse reactions due to minimal systemic uptake.[3]

LOCAL DRUG DELIVERY (LDD)

An ideal LDD must be easy to administer, release the drug in a controlled fashion, sustain the drug concentration for prolonged period, should be biodegradable, biocompatible and not cause any irritation to the tissues. The placement of LDD is supported by presence of periodontal pocket, which acts as a natural reservoir in which gingival crevicular fluid (GCF) provides hydrated environment that increases distribution of the drug throughout the pocket.

Ideal requirements for local antimicrobial agents (Goodson 1985) :

- Must deliver the drug to the base of pocket
- Must have microbiologically effective concentrations in the pocket.
- Should sustain the concentration of the drug in the pocket for sufficient period of time & at a concentration to be clinically effective.
- Less undesirable side effects

Classification of Local Drug Delivery system[2] :

I. Based on the application [Rams and Slots] 1996:

1. Personally applied (self-care)

A. Non sustained subgingival drug delivery

- Home oral irrigation
- Home oral irrigation jet tips
- Traditional jet tips
- Oral irrigation (water pick)
- Soft cone rubber tips (pick pocket)

B. Sustained subgingival drug delivery

2. Professionally applied (in dental office)

A. Non sustained subgingival drug delivery

- Professional pocket irrigation

B. Sustained subgingival drug delivery

- Controlled release devices
- Hollow fibres
- Dialysis tubing
- Strips
- Films

II. Based on the duration of medicament release (Greenstein and Tonetti) 2000 :

A. Sustained release devices - Designed to provide drug delivery for less than 24 hours

B. Controlled release devices - Designed to provide drug release that at least exceeds 1 day or for at least 3 days following application (Kornman1993)

III. Depending on degradability:

1. Nondegradable devices (first generation)

2. Degradable devices (second generation)

Various drug delivery systems for treating periodontitis are fibres, films, injectable systems, gels, strips, compacts, vesicular system, microparticles and nanoparticles.

Various agents available in the market are :

AGENT	PRODUCT AVAILABLE	DOSAGE FORM
Tetracycline	Actisite (25% tetracycline Hcl) Periodontal plus AB (2mg of tetracycline in 25mg of collagen)	Non resorbable fiber Resorbable fiber
Doxycycline	Atridox (10% Doxycycline)	Biodegradable mix in syringe
Minocycline	Dentomycin gel (2% minocycline) Arestin (2% minocycline) Periocline (2.1% minocycline)	Biodegradable gel Biodegradable mix in syringe Ointment
Metronidazole	Elyzol (25% metronidazole)	Biodegradable gel
Chlorhexidine	Periochip (2.5 mg CHX) Periocol CG (2.5mg CHX) Chlosite (1.5% CHX) Cervitec (1% CHX and 1% Thymol)	Biodegradable chip Biodegradable chip Biodegradable gel Biodegradable varnish

CHLORHEXIDINE

Chlorhexidine (CHX) is a bisbiguanide antiseptic and a symmetrical molecule consisting of four chlorophenyl rings and two biguanide groups connected by a central hexamethylene bridge. It is a strong base and is di-cationic at pH levels >3.5, with two positive charges on either side of the hexamethylene bridge[5]. As an antimicrobrial agent, it is effective in vitro against both Gram-positive and Gram-negative bacteria including aerobes and anaerobes and also yeasts and fungi. It is poorly absorbed through gastrointestinal tract, metabolized in liver and kidney and excreted through faeces. It is free from systemic toxicity, microbial resistance & superinfection[5]. It is retained in the oral cavity and is progressively desorbed in bacteriostatic concentrations 8 hours after rinsing. It acts by altering integrity of cell membrane of bacteria and the mechanism of action includes plaque inhibitory effect, bacteriostatic and bactericidal effect, substantivity and pincushion effect.

When a low dose is used, the cellular transport of the bacterial cell is damaged with the creation of pores in the cellular membrane (Bacteriostatic). In higher concentration, the solution penetrates the bacterial cell and leads to microorganism destruction (Bactericidal)[5]. The ability of drugs to adsorb onto and bind to soft and hard tissues is known as Substantivity and was first described in the 1970s. It is influenced by the concentration of medication, its pH, temperature, and length of time of contact of solution with the oral structures. This property was associated with its ability to maintain effective concentrations for prolonged periods of time which made it suitable for the inhibition of plaque formation[5].One charged end of CHX molecule binds to the tooth surface and the other end interacts with bacterial membrane, as the microorganism approaches the tooth surface. This is known as the Pin cushion effect. This explains the lack of effectiveness of other antimicrobials in terms of them lacking a large, rigid molecule with two charged interactive ends[5].

The reported side effects of CXH are alteration in taste, increase in calculus formation, staining of teeth and mucous membranes and rarely, oral mucosa desquamation and parotid swelling. However, the most important side effects are the brown staining of the teeth, restorative materials and dorsum of the tongue as well as supragingival calculus formation. Non-enzymatic browning (Maillard reactions)

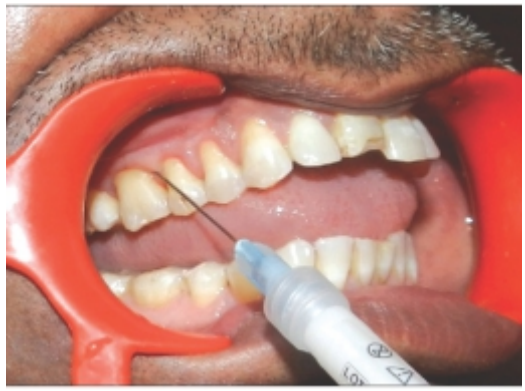
and formation of pigmented metal sulfides are considered the possible mechanisms of tooth discolorations[5].

The vehicles most often used to administer chlorhexidine are mouthrinses (at concentrations of 0.12% and 0.2%), aerosols (0.12% and 0.2%), gels (0.12% and 1%), CHX chip and varnishes[6].

CHLORHEXIDINE AS LOCAL DRUG DELIVERY

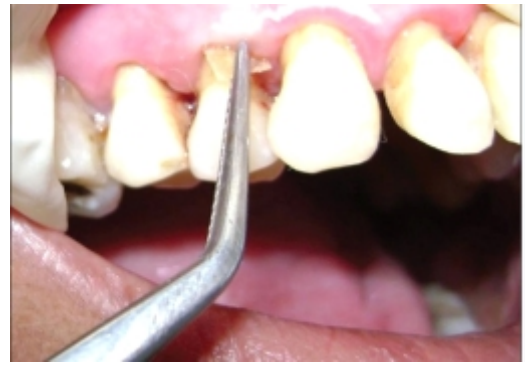
CHLORHEXIDINE GEL

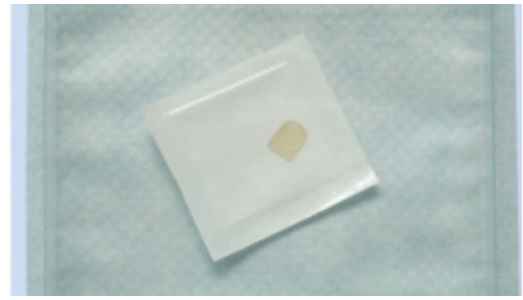
Chlosite TM gel is a xanthan based 1.5% CHX gel containing 0.5% fast releasing chlorhexidine gluconate and 1% slow releasing chlorhexidine dihydrochloride. Xanthan is an optimum substrate for formation of a stable gel that is easily extruded from 0.5ml syringe needle and is delivered into periodontal pocket[7]. It degrades spontaneously in the application site in 15-30 days and is well tolerated.



CHLORHEXIDINE CHIP

Periochip is a small chip composed of biodegradable hydrolysed gelatin matrix, cross-linked with glutaraldehyde and also containing glycerine and water, into which 2.5mg of chlorhexidine gluconate has been incorporated per chip. It is a FDA approved small, orange, brown chip measuring 4.0x0.5x0.35mm in a biodegradable matrix of hydrolysed gelatin[2]. Subgingival placement of a biodegradable chip, biodegrades and releases CHX within the pocket over 7 10 days maintaining an average concentration in the GCF greater than 12 mg/ml for 8 days[1].



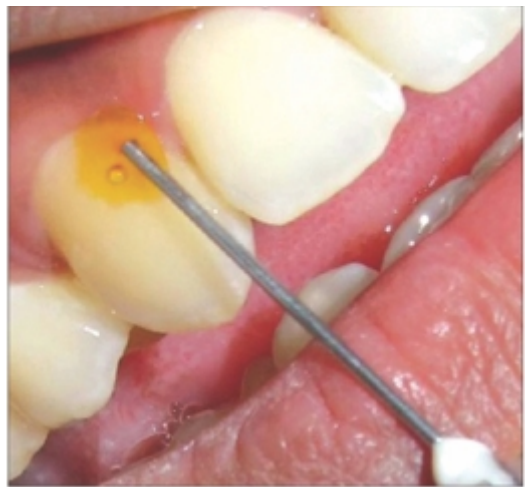


CHLORHEXIDINE VARNISH

Varnishes have been developed over the past decade. They are one of the most effective form for professional application of chlorhexidine, as they are easy to apply, do not require collaboration by the patient and although they have an unpleasant flavour, they do not cause discoloration[6]. They are a novel class of vehicles emerging for antimicrobial delivery in the management of oral infections. An ample dosage is administered and retained at the site of action, minimizing the associated adverse effects. The most salient advantage offered by this mode is prolonged direct contact of the drug with the affected tissue. It further allows multiple site intervention, thus enhancing its cost-effectiveness. Hence, they seem quite promising as vehicles for local drug delivery in periodontal milieu[3].

Varnishes containing chlorhexidine are available in the concentrations of 1% (Cervitec), 10% (chlorzoin), 40% (EC 40), and 20% (Bio C).

Varnish	Composition
EC40 ®	40% Chlorhexidine Sandarac Ethanol
Chlorzoin ®	10% Chlorhexidine Ethanol Polyurethane Methylene chloride Sumatra benzoin
Cervitec ®	1% Chlorhexidine 1% Thymol Ethanol/ethyl acetate Polyvinyl butyral



CONCLUSION

The application of chlorhexidine as an agent for LDD seems to have beneficial effects in patients with chronic gingivitis and periodontitis, improving their plaque accumulation and bleeding levels and reducing their gingival index and periodontal pocket. It is not only an excellent antiplaque agent but it also possesses very good antimicrobial properties. It's broad antimicrobial spectrum can be considered as boon for maintaining overall oral health. A wealth of research supports its use in various forms and in wide variety of oral disorders.

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