Local Drug Delivery in Periodontics

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Abstract

Periodontitis is a multifactorial disease which results in inflammation of gingival and adjacent supporting periodontal tissue resulting in hard and soft tissue destruction and tooth loss. The effectiveness of mechanical therapy along with local delivery of antimicrobials has been investigated to overcome the limitation of conventional therapy. These control release antimicrobials are available in various forms like gels, films, fibres etc. The main aim of these local delivery devices is to establish a drug reservoir that maintains effective concentration of the drug at the site of action for longer period of time. The present review approaches the various drugs used for periodontal therapy.

Keywords: Periodontitis, antimicrobials, delivery devices.

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Introduction

Periodontal diseases are bacterial infections characterized by inflammation and destruction of the attachment apparatus, often leading to tooth loss. Periodontitis is defined as "An inflammatory disease of the supporting tissues of the teeth caused by specific microorganisms or groups of specific microorganisms, resulting in progressive destruction of the periodontal ligament and alveolar bone with pocket formation, recession, or both[1]".

Elevated proportions of some subgingival microbial species have been associated with destructive periodontal disease activity. So elimination or suppression of periodonto-pathogenic microorganisms in the subgingival microbiota is important for periodontal healing[2]. Periodontal therapy is helpful in altering the periodontal environment to the one, which is less conducive to retention of bacterial plaque in the vicinity of gingival tissue[3].

The aim of current periodontal therapy is to remove thebacterial flora from the tooth surface and to shift thepathogenic microbiota to one which is compatible with periodontalhealth. Therapeutic approaches include mechanical scalingand root planing sometime surgery. As a result oftreatment, there is a decrease in the gingival inflammation aswell as clinical probing depth. Unfortunately, in some instances, the complex anatomy of the root and the contours of the lesion prevent sufficient reduction of the bacterial load to make the tooth surface biologically acceptable[4].

The local delivery of antimicrobials to periodontal pockets has the benefit of administring more drugs to the target site while minimizing the exposure of total body to the drug and the sustained release of antimicrobial in the periodontal disease. Natural herbs are also known to affect the progression of periodontal disease[5].

Classification[2]

Classification of local delivery system

Based on type of therapy

A) Personally applied (patient home care)
   1.Non Sustained (Oral irrigation)
   2.Sustained (not developed till now)
B) Professionally applied (in dental office)
   1. Non Sustained (Supra and subgingival irrigation)
   2. Sustained (Controlled release device)

Based on degradability of the device

A) Biodegradable
B) Non- Biodegradable

Based on duration of action

A) **Sustained released devices** - These are the devices that last for less than 24 hours therefore require multiple applications. It follows the first order kinetics.
B) **Controlled delivery devices** -These are the devices which follows whose actions last longer than 24 hours and follow zero order kinetics, thereby decreasing the number applications.

Pharmacokinetic Parameters For Local Application

In order to achieve the pharmacological objectives of a locally delivered agent, Greenstein and Tonetti (2000)[6] have proposed following three pharmacokinetic parameters for the local drug delivery). z

1. Site of Action: The drug must reach the intended site of action. Local application of drug targets bacteria in the periodontal pocket, soft tissue wall of the pocket, exposed cementum or radicular dentin. Presence of subgingival calculus, anatomic anomalies, deep pockets and furcation lesions may result in physical difficulty in placing the drug at intended site, thereby impeding the drug efficacy at the site e.g. agents in mouth rinses and those used during supragingival irrigation do not predictably reach beyond 5mm into the periodontal pocket. However, irrigating solutions delivered intracrevicularly, via a cannula or other device can be projected into deep periodontal pockets[6].

2. Adequate Concentration: Biofilm experiments have shown that the minimum inhibitory concentrations of antimicrobial agents are around 50 time higher than for bacteria growing under planktonic conditions, as highly organized aggregates of adherent bacteria (biofilms) may impair diffusion or inactivate pharmacologic agents. Therefore, adequate drug concentration must be maintained at the local site to achieve the desired results[6].

3. Sufficient duration of Time : Once a drug reaches the site of action at an adequate concentration, it must remain at the site long enough for the pharmacological effect(s) to occur. The duration of action required is dependent upon the mechanism by which the antimicrobial agent inhibits or destroys target bacteria, e.g. chlorhexidine, a bactericidal agent, kills microorganisms by destroying the cell membrane and requires a shorter exposure time than a bacteriostatic agent.

Drug Delivery Devices

There are two possible approaches to improve the drug action:

(i) Sustained and controlled drug release to reduce or eliminate side effects by improving the therapeutic index;
(ii) Site-specific drug delivery to minimize systemic effects.

Non-biodegradablesystems must be removed after complete drug release, which may cause irritation and inflammation of the treated site. Conversely, a biodegradable sustain edrelease drug delivery system which can be placed into the periodontal pocket and maintain therapeutic concentrations for prolonged periods of time would be effective[4].

Drugs Used For Local Delivery

1) Tetracycline: Goodson et al in 1979 first proposed the concept of controlled drug delivery in the treatment of periodontitis. The first delivery devices involved hollow fibers of cellulose acetate filled with tetracycline.[7] Tetracyclines are a group of bacteriostatic antimicrobials. They have been frequently used in treating refractory periodontitis, including localized aggressive periodontitis.

Fibers: The ACTISITE tetracycline fibres have been approved for the treatment of adult periodontitis both by the United States Food and Drug Administration (FDA) and by the European Union's regulatory agencies. It maintains constant concentrations of active drug in the crevicular fluid in excess of 1000 µg/mL for a period of 10 days[8]. Following application of tetracycline fibres aexplicit reduction in the subgingival microbiota has been observed. Recently bioresorbable tetracycline fiber has been formed with base of collagen film, which is commercially available as Periodontal Plus Ab. It has the advantage of no second appointment for removal as it biodegrades within 7 days.

2) Subgingival Doxycycline: Doxycycline is a bacteriostatic agent which has the ability to downregulate MMP's a family of zinc dependent. The only FDA approved 10% doxycycline in a gel system ATRIDOX (42.5 mg doxycycline) is a subgingival controlled-release product composed of a 2 syringe mixing system. Doxycycline levels in GCF spiked to 1,500 - 2000 µg/mL in 2 hours following treatment with

ATRIDOX. In the first 18 hours, these levels remained above 1000 µg/mL after which time the levels began to decline gradually. Local concentration of doxycycline has been found to remain well above the minimum inhibitory concentration for periodontal pathogens (6.0 µg/mL) at the end of seventh day. Approximately 95% of the polymer is bio absorbed or expelled from the pocket naturally within 28 days[9].

3) Subgingival Minocycline: Local delivery of minocycline, a bacteriostatic antibiotic has been
tried clinically via in three different modes i.e. film, microspheres, and ointment.

4) Subgingival Chlorhexidine: The use of chlorhexidine as an antifungal and antibacterial agent is well known. Chlorhexidine is used as mouth rinses and is highly recommended in the hygiene phase of treatment as an adjunct to tooth brush. The major application is for the control of dental plaque and gingivitis. Its mechanism of action is to reduce pellicle formation, alteration of bacterial adherence to teeth and an alteration of bacterial cell walls causing lysis. Its antibacterial action is due to an increase of the cellular membrane permeability followed by the coagulation of intracellular cytoplasmic macromolecules. As the chlorhexidine is highly cationic, it exhibits high substantivity. The long term efficacy of chlorhexidine on the periodontal pocket flora is dependent on the duration of exposure. However, intracrevicular irrigation of the periodontal pocket with chlorhexidine has only a short lived effect on the pocket flora[10]. Chlorhexidine is available in the form of mouthrinses, Gels, varnishes, and chip to be used as a local drug delivery agent for the treatment of periodontal diseases.

5) Subgingival Metronidazole: Among the antibiotics that have been considered for periodontal treatment, Metronidazole has often been chosen because of its selective efficacy against obligate anaerobes. It acts by inhibiting DNA synthesis. It is known to convert into azally anaerobic rods and spirochetes in subgingival microflora[11]. After application of Elyzol 25% dental gel, Metronidazole concentrations of above 100 µ/ml were measurable in the periodontal pocket for at least 8 hours and concentrations above 1 µ/ml were found at 36 hours. A topical medication ELYZOL contains an oil-based metronidazole 25% dental gel (glyceryl mono-oleate and sesame oil). It is applied in viscous consistency to the pocket, where it is liquidized by the body heat and then hardens again, forming crystals in contact with water[12].

Conclusion

There are various drugs such as tetracycline, doxycycline, minocycline, chlorhexidine and metronidazole as well as herbal products like neem that are used and are under further trial for their administration as local drug into the periodontal pocket. Local Drug Delivery system with controlled release has the potential to be used as a therapeutic agent. There is ample evidence to show that locally delivered anti microbials can reduce clinical and microbial parameters.These devices are proving to be more convenient and more effective than the drugs used systemically.

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