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Review Article

Local drug delivery in periodontal diseases- A review

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ABSTRACT:
Periodontitis is an immuno-inflammatory disease of the tissues surrounding the teeth. Various treatment modalities like mechanical debridement and use of antimicrobials have been followed in the treatment of such conditions. Introduction of local drug delivery system in the periodontal pocket is a promising therapeutic modality for achieving better clinical outcomes when used as an adjunct to conventional non surgical periodontal therapy. Intensive research efforts are now focussed on the development of new strategies for more effective treatment.
Key words:- Local drug, Periodontitis, Tetracycline.

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INTRODUCTION

Periodontal disease is a general term which encompasses several pathological conditions affecting the tooth supporting structures. Periodontal diseases include conditions such as chronic periodontitis, aggressive periodontitis, systemic disease-associated periodontitis and necrotizing periodontitis. These conditions are characterized by a destruction of the periodontal ligament, a resorption of the alveolar bone and the migration of the junctional epithelium along the tooth surface. It is a localized inflammatory response caused by bacterial infection of a periodontal pocket associated with subgingival plaque.[1]

The inflammation in the periodontal tissue is initiated by microbial plaque and bacterial infection. In the periodontal pocket the bacteria form a highly structured and complex biofilm. As this continues, the biofilm reach far subgingivally and it becomes difficult for the patient to reach it during oral hygiene practices. Traditional treatment options for such conditions include mechanical debridement aimed at removing the subgingival flora and providing a clean, smooth and compatible root surfaces. But, in several instances, the complex anatomy of the root and the location of the lesion may hamper the treatment and prevent sufficient reduction of the bacterial load.[2]

HISTORY

Ever since the introduction of systemic antibiotics, various drugs have been used in the treatment of periodontitis. 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 the treatment option. It was in the year 1979, Dr. Max Goodson et al first proposed the concept of controlled delivery in the treatment of periodontitis. Since then, a number of studies have been

carried out over the years with different antimicrobial agents and in different clinical situations.
Ideal requirements for local antimicrobial agents-[3]

- 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
Various classification systems were evolved.
I Based on the application (Rams and Slots)

1. Personally applied (in patient home self-care)

A. Nonsustained subgingival drug delivery[4]
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. Nonsustained 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)[5]

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. These two strategies have been explored by the association of drugs with different vehicles, either naturals or synthetics. However, most of these systems failed to realize their potential in clinical phase studies. In this respect, it is critical not to under-estimate problems such as weak therapeutic activity resulting from a limited accessibility to the tissue to be treated or toxicity and/or immunogenicity of the delivery system. Synthetic polymers have proved to be extremely interesting because they can be tailor-made to meet pharmacological or biological requirements.[6]

FIBERS:
Fibers are placed circumferentially around the tooth. There are Hollow fibers and Ethylene vinyl acetate fibers. Hollow fibers -Released tetracycline at a first order rate with 95% of the drug released in the first 2 hrs – GCF - remained in the therapeutic range for 24 h and some effects on spirochetes. Study should be viewed primarily as an evaluation of drug delivery. Ethylene vinyl acetate fibers Tetracycline incorporated into different polymers (1) Polyethylene, (2) Polypropylene, (3) Polycaprolactone, (4) Polyurethane, (5) Cellulose

STRIPS AND COMPACTS:
Larsen–studied in vitro release of doxycycline from different bioabsorbable materials and acrylic strips Acrylic strip and Colla Cote decreased to low levels of both concentration and residual antibacterial activity in a few days Compacts. Compacts based on PHBA containing tetracycline hydrochloride, 50% (w/w) of tetracycline, the mean drug concentration obtained was in the therapeutic range over the 10 days.

FILMS:
A far more widely used form of intra-pocket delivery device has been in the shape of film, prepared either by solvent casting or direct milling. Films are matrix delivery systems in which drugs are distributed throughout the polymer and release occurs by drug diffusion and/or matrix dissolution or erosion. This dosage form has several advantageous physical properties for intra-pocket use. The dimensions and shape of the films can be easily controlled according to the dimensions of the pocket to be treated.[7]

INJECTABLE SYSTEMS:
Attractive for the delivery of antibiotic agents into the periodontal pocket, easily and rapidly carried out, without pain, by using a syringe and Cost of the therapy is considerably reduced compared to devices that need time to be placed and secured.

GELS:
Gels are mucoadhesive, various drugs have been developed in gel forms, and they are **1.** Metronidazole-

containing gel; **2.** Tetracycline containing gel; **3.** Gel containing 1% clindamycin hydrochloride; **4.** Gel formulation based on 2.5% hydroxy propylmethyl cellulose containing 0.125% histatin etc.[8]

NANOPARTICLE SYSTEM:
Nanoparticles, owing to their small size, penetrate regions that may be inaccessible to other delivery systems, such as the periodontal pocket areas below the gum line. These systems reduce the frequency of administration and further provide a uniform distribution of the active agent over an extended period of time. Modern drug delivery systems are designed for targeted controlled slow drug release.

VESICULAR LIPOSOMAL SYSTEMS:
Vesicular liposomal systems are designed to mimic the bio-membranes in terms of structure and biobehavior, and hence are investigated intensively for targeting periodontal biofilms. The anti-oralis immunoliposomes showed the greatest affinity for S. oralis and affinity was unaffected by net charge on the lipid bilayer or by the number of antibodies conjugated to the liposomal surface.[9]

MICRO PARTICLE SYSTEM:
Based on biodegradable poly(a-hydroxyacids) a) poly(lactide) (PLA) or b)poly(lactide-co-glycolide). Tetracycline release rate is influenced by the – polymer choice (lactide/glycolide ratio) – polymer molecular weight and crystallinity) – pH of the medium, Tetracycline release rate is increased as the pH increases.

TETRACYCLINE:
TC containing fibers are the first available local drug. It had ethylene/vinyl acetate copolymer fiber with diameter of 0.5 mm, containing tetracycline12.7mg per 91 inches. The Actisite tetracycline fibres have been approved both by the United States Food and Drug Administration (FDA) and by the European Union's regulatory agencies. These are non-resorbable, safe, inert copolymer loaded with 25% w/w tetracycline HCI. It maintains constant concentrations more than 1000 µg/mL for a period of 10 days. Follow up showed reduction in the 2 subgingival microbiota. Bioresorbable tetracycline fibre has been developed with base of collagen film, which is commercially available as Periodontal Plus AB. It offers the advantage of no second appointment for removal as it 10 degrades within 7 days.[10]

METRONIDAZOLE:
Elyzol is a topical medication containing an oil-based metronidazole 25% dental gel, applied in viscous consistency to the pocket.

CHLORHEXIDINE:
Periochip is a small chip composed of biodegradable hydrolysed gelatin matrix, cross-linked with glutaraldehyde and also containing glycerine and water, into which 2.5 mg of chlorhexidine gluconate has been incorporated per chip. It is a FDA approved small, orange brown, chip measuring 4.0x 0.5x 0.35mm in a biodegradable matrix of hydrolysed gelatin.[11]

DOXYCYCLINE:
Atridox is a FDA approved 10% doxycycline in a gel system using a syringe. GCF levels reached its peak to 1,500-2,000 in 2 hours following treatment with Atridox. These levels remained above 1000 µg/mL through 182 hours, and then levels gradually declined. Walker et al in an attempt to determine the effectiveness of sustained-release, biodegradable gel containing 8.5% doxycycline on the anaerobic flora and on antibiotic susceptibility patterns associated with subgingival plaque and saliva reported that the treatment significantly reduced the anaerobic population in plaque but did not result in change in either number of resistant bacteria or the acquisition of antibiotic resistance.[12]

CONCLUSION
The local drug delivery into the periodontal pocket can improve the periodontal health. However these drugs fail to completely replace the conventional scaling and root planning. Thus the benefit of these drugs as a mono therapy is questionable.

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