

Review Article

Local drug delivery in periodontology

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Abstract

Periodontitis describes a group of related inflammatory disease resulting in destruction of the tissues that support the tooth. It results from extension of the inflammatory process initiated in the gingiva to the supporting periodontal tissues. Clinical features of periodontitis include bleeding, pus discharge, halitosis, tooth mobility, functional impairment and ultimately tooth loss. Scaling and root planning is the basic treatment modality for periodontal disease. Mechanical treatment is limited by physical impediments and biochemical considerations. Antimicrobial agents may be used as an adjunct to overcome limitations of mechanical therapy. Local delivery of antimicrobials has been investigated for the possibility of overcoming the limitations of conventional therapy. The use of sustained release formulations to deliver antibacterials to the site of infection (periodontal pocket) has recently gained interest. These products provide a long-term, effective treatment at the site of infection at much smaller doses. This review approaches the main local drug delivery systems for the administration of drugs to the periodontal pocket, their usefulness, as well as the advancement of these systems effectiveness in the periodontal therapy.

Keywords: Periodontal diseases, Periodontal pocket, Delivery systems, Periodontal pocket delivery

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Periodontal diseases are considered as infections of periodontium with a bacterial etiology, an immune response and subsequent tissue destruction [1]. Putative pathogens associated with periodontal disease are susceptible to a variety of antiseptics and antibiotics [2, 3]. Methods employed to convey antimicrobial agents into periodontal pockets include rinsing, irrigation, systemic administration and local application using sustained and controlled delivery devices.

Success of any drug delivery system designed to target periodontal infections depends upon its ability to deliver the antimicrobial agents to the base of the pocket at a bacteriostatic or bactericidal concentration [4]. It must also facilitate retention of the medicament long enough to ensure an efficacious results. Since local drug delivery can achieve the above requirements, it is important to critically assess the ability of these treatment methods to attain or maintain periodontal health. The use of locally delivered antimicrobials is a relatively new addition in the management of Periodontitis. The treatment method is primarily the result of more than 20 years of research pioneered by Goodson of Forsyth's Dental Research Center [5-7]. The commonly used drug delivery systems are:-

- a) Tetracycline fiber
- b) Metronidazole gel
- c) Chlorhexidine chip
- d) Minocycline gel
- e) Doxycycline polymer

Local Drug Delivery

Recently a new approach using local delivery systems containing antimicrobial has been introduced. This produces more constant and prolonged concentration profiles. Both topical delivery system and controlled release system have been termed

as local delivery. The term local delivery and site-specific delivery are sometimes used synonymously. The potential therapeutic advantage of local delivery approach has been claimed to be several fold. Local delivery devices are systems designed to deliver agents locally into periodontal pocket but without any mechanism to retain therapeutic levels for a prolonged period of time. The periodic use of local delivery systems in reducing probing depths, stabilizing attachment levels and minimizing bleeding would allow better control of the disease. Goodson et al in 1979 first proposed the concept of controlled delivery in the treatment of Periodontitis. The effectiveness of this form of therapy is that, it reaches the base of periodontal pocket and is maintained for an adequate time for the antimicrobial effect to occur. Periodontal pocket provides a natural reservoir bathed by gingival crevicular fluid that is easily accessible for the insertion of a delivery device. Controlled release delivery of antimicrobials directly into periodontal pocket has received great interest and appears to hold some promise in periodontal therapy. Some techniques for applying antimicrobial sub-gingivally, such as sub-gingival irrigation, involve local delivery but not controlled release. Controlled release local delivery systems, in which the antimicrobial is available at therapeutic levels for several days, have been evaluated in several forms and using different antimicrobials. Controlled delivery systems are designed to release drug slowly for more prolonged drug availability and sustained drug action. These delivery systems are also called sustained release, controlled release, prolonged release, timed release, slow release, sustained action, prolonged action or extended action.

There are distinct phases in a periodontal treatment plan where a dental practitioner can use this sustained release device

1. As an adjunct to Scaling and Root Planing
2. Periodontal maintenance therapy as recurrent Periodontitis usually involves only few teeth. These sites are ideal for the treatment with this device.

So patients with moderate Periodontitis should receive non-surgical therapy to halt periodontal disease and limit the extent of surgical intervention needed in the future. Intra pocket devices can be divided in two broad categories depending on degradability- non-degradable devices (first generation) and degradable devices (second generation). Non degradable devices have the advantage that the therapist controls the removal of the device and therefore has greater control over the time of exposure of the pocket environment to the drug. The degradable device have the advantage of requiring single visit by the patient to therapist for the insertion of the device. This minimizes the patient visits and ensures compliance. Patient revisit for the removal of the device can be avoided. Biodegradable devices that have been developed include fibers, films, slabs and injectable systems. First sustained release dosage form of chlorhexidine diacetate for topical use was developed by Friedman and Golomb in 1982.

Current status of intra-pocket delivery devices in periodontics

With the current availability of number of intra-pocket delivery systems containing antimicrobials for periodontal therapy, questions can be raised about the role of intra-pocket delivery devices in periodontics. Firstly, if intra-pocket delivery systems can deliver equivalent clinical results to scaling and root planning (SRP), should the use of these therapies be

considered in place of SRP. Better still, how will antimicrobials be incorporated into treatment strategies with or without mechanical intervention? Lastly, to be considered are the physical properties of delivery system, which may influence the acceptance by the patient and professional community. Most reports on the local delivery concepts have appeared in the periodontal literature but there are surprisingly few studies that demonstrate the clinical efficacy using intra-pocket delivery systems in Periodontitis patients. Despite the large number of studies, there are insufficient comparative data to support any one of the local delivery systems as superior to another because their treatment patterns differ widely. Great variability from site to site has been repeatedly noted by investigators showing that the same system could not work equally in all sites and in all patients. Many studies have failed to show real and clinically meaningful effects provided by the intra-pocket drug delivery systems when used as stand-alone monotherapies. Other studies have demonstrated that these systems have beneficial effects in terms of probing depth reduction; however, the statistical significance reached in these studies was not always clinically significant.

The strategic approaches with associated challenges and achievements towards the formation of periodontal drug delivery system [8-11]

Challenges Goals achieved

Strategy 1: Systemic delivery devices

- Low benefit to risk ratio, ingestion of large drug doses
- Inadequate drug concentration at periodontal site
- Rapid/non-sustained drug release

- Poor patient compliance: frequent administration
- No penetration of delivery system
- No adhesion/retention into periodontal pocket
- High incidence of bacterial resistance

Strategy 2: Local mouth rinses and dental irrigation

- Inadequate drug concentration at periodontal site Drug dose is reduced
- Rapid/non-sustained drug release Systemic toxicity is decreased
- Poor patient compliance: frequent administration
- No penetration of delivery system
- No adhesion/retention into periodontal pocket
- High incidence of bacterial resistance

Strategy 3: Non-biodegradable, intrapocket fibres, strips, films and microparticles

- Poor patient compliance: discomfort during the placement of device, at least two visits to therapist is required and development of foreign body response, if left in situ.
- Adequate drug concentration at periodontal site
- Poor penetration of system/drug Prolonged/sustain drug release
- Poor retention of system into periodontal pocket Less frequent administration
- Low incidence of bacterial resistance

Strategy 4: Biodegradable, intra-pocket fibers, strips, films and microparticles

- Poor patient compliance: discomfort during placement Visit to therapist is reduced

- Poor penetration of system/drug No foreign body response
- Poor retention of system into periodontal pocket
- Low incidence of bacterial resistance

Strategy 5: Biodegradable nanoparticles

- Poor retention of system into periodontal pocket Placement is easier
- Low incidence of bacterial resistance Good penetration due to nano-sized particles

Conclusion

As a monotherapy, local drug delivery systems incorporating a variety of drugs can improve periodontal health. Local drug delivery appears to be as effective as scaling and root planning with regards to reducing signs of periodontal inflammatory disease - redness, bleeding on probing, probing depth and loss of clinical attachment. Local delivery may be an adjunct to conventional therapy. The recent advances in periodontal drug delivery systems it can be said that the antibiotic-free, mucoadhesive, biodegradable nanoparticles technology has an immense opportunity for the designing of a novel, low-dose and effective treatment method by the use of the intra-pocket controlled device..These devices are proving to be more convenient, easy-to-use and more effective than the regular drugs and medicines which act systemically. These devices also do not probe the risk of overdose or systemic overload, simple for formulation, affordable and easily available.

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