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Local Drug Delivery: A Current Concept in Periodonlogy

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Introduction

Periodontal diseases are bacterial infections characterized by inflammation and destruction of the attachment apparatus, often leading to tooth loss. The most common forms of periodontal diseases, gingivitis and periodontitis are caused by bacteria adjacent to or associated with periodontal structures. These bacteria, along with calculus and other local factors, are the principal components that perpetuate the disease process [1]. The start and progression of the periodontal disease of the periodontium is given by the response of the immune system of the host to periodontal pathogens. These bacteria produce some enzymes (proteases, hyaluronidases and collagenases) which lead to a series of cellular events that induce the production of proinflammatory molecules: cytokines (interleukin-1b) and prostanoids (prostaglandins) causing tissue destruction. PGE2 is a proinflammatoryagent resulting from the cascade of the arachidonic acid. IL-1b and TNF are powerful stimulants of PGE2 through cyclooxygenase pathway COX2 in the human gingival fibroblast when attacked by lipopolysaccharides present in the periodontopathic bacteria [2].

Plaque constitutes of highly organized bacterial populations. Elevated proportions of some subgingival microbial species have been associated with destructive periodontal disease activity. Potential periodontal pathogens include Aggregtibacter actinomycetemcomitans, Porphyromonas gingivalis, Prevotella intermedia, Tannerella forsythus, Peptostreptococcous micros, Campylobacter rectus, Eiknella corrodens, Fusobacterium nucleatum, Eubacterium species,Treponema denticola, Selemonas species, Beta–hemolytic streptococci, a variety of enteric rods and pseudomonas, Enterococci, Staphylococci and possibly yeasts [3,4]. It is important to keep the pathogenic micro flora of the pocket suppressed in order to maintain health of the periodontal tissues [5,6]. Modalities of treatment may be non surgical approach or a surgical approach [5].

The most widely used approach has been scaling and root planning. Debridement of the root surface by scaling and root planing came into relatively common use in the first half of the past century and has become the central feature held in common by all currently used forms of periodontal therapy. Until the 1980s, the most commonly used treatment consisted of scaling and root planing, followed by respective surgery aimed at achieving zero pocket depth. During the 1980s, data were obtained demonstrating that the thoroughness of root debridement and subgingival infection control, not the presence or absence or periodontal pockets, is the major determinant of successful periodontal therapy; and nonsurgical became a commonly used treatment [7]. Scaling and root planning has been effective in immediately decreeing the microbial load but decolonization of the same can occur at early as 60 days after scaling and root planning. Hence chemical therapy has been advocated to inhibit pathogenic micro flora and encourage inhibition of non pathogenic micro flora [5,8-10].

In addition to mechanical treatment, the use of antimicrobial agents, both systemic and topical, has been increasing because of the realization that periodontal disease is not merely an overgrowth of bacteria, but also a shift in bacterial species [11]. Hence chemical therapy has been advocated to inhibit pathogenic micro flora and encourage inhibition of non pathogenic microflora. Common systemic antibiotics include Metronidazole [12] Tetracycline [13]. Amongst antibiotics, Tetracycline-hydrochloride became popular in 1970s due to its broad spectrum antimicrobial activity and low toxicity [14].

Systemic administration has been useful in treating periodontal pockets, but it involves a relatively high dose with repeated intake over a prolonged period of time to achieve the required inhibitory concentrations in the sulcular fluid. This increases the chances of development of resistance, of alteration of commensally flora and of increased potential for adverse effects like allergic/anaphylactic reaction, gastric disturbances, super infection, nausea, vomiting etc [15-19]. Local administrations, therefore, provide a useful answer to these problems; however, the important factor in the success of this treatment is the ability

to control and to prolong the release rate of the therapeutic agent from the device. Because the periodontal pocket is relatively inaccessible, various mechanisms for local delivery of chemotherapeutic agent have been devised which include subgingival irrigation, use of gels, hollow fibers, acrylic strips, dialysis tubings and collagen preparations [20].

Although research has shown that tetracycline concentration in the gingival crevice fluid varies substantially from patient to patient [11] an advantage of using antibiotics in the tetracycline family is that, in addition to their antimicrobial action, they also inhibit the activity and intracellular expression of metalloproteinases (MMPs) Zinc-dependent enzymes [21]. Tetracycline's cause chelation of zinc (as well as calcium), which inhibits the activity of the enzymes. This inhibitory action prevents the degradation of collagen in the periodontal ligaments and the resulting formation of gingival pockets and loss of tooth attachment.

Conclusion

With the realization that periodontitis is an infectious process, the use of antibiotics and other anti-infective agents came into common use as adjuncts to other standard therapies. Studies employing a variety of local delivery systems in corpora ting different drugs have addressed the utility of these devices as a mode of therapy. A substantial amount of information has become available and at present the following trends may be identified with regards to various local delivery systems.

A. As a immunotherapy local drug delivery systems incorporating a variety of drugs can improve periodontal health.

B. There is no single universal drug that would be effective in all situations. Therefore, at non-responsive sites, bacterial and antibiotic sensitivity testing may be necessary to determine putative pathogens and their susceptibility to specific antimicrobial agents.

C. Local drug delivery often appears to be as effective as scaling and root planing with regards to reducing signs of periodontal inflammatory disease, redness, bleeding upon probing, probing depth, and loss of clinical attachment.

D. Local drug delivery systems usually do not provide a benefit beyond what is achievable with conventional scaling and root planing in the treatment of adult periodontitis. Therefore, their routine utilization is unnecessary.

E. At present, there are insufficient data to indicate that one local drug delivery device is clearly superior to all the other systems. However, desired characteristics include ease of placement, controlled release of drugs and restorability.

F. In conjunction with conventional treatment, systemically administered drugs appear to be as effective as local drug delivery.

G. To date, results from studies assessing local drug delivery systems have not justified extending the time interval between supportive periodontal maintenance visits.

H. There are preliminary, but very limited data, regarding the ability of local delivery to help suppressing future disease progression.

I. There are insufficient data to indicate that the local drug delivery induces bacterial resistance to antimicrobial agents. Long term studies are needed to address this important issue.

J. There are limited term data (5 years) evaluating the efficacy of local drug delivery.

K. Additional studies are needed to evaluate if local delivery is effective against tissue invasive organisms.

L. There is a lack of data to support the impression that local drug delivery in conjunction with root planing reduces the need for periodontal surgery more than scaling and root planing alone.

Prudent administration of antimicrobial agents following judicious pharmacologic principles will preclude the abuse of chemotherapeutic agents and reduce the potential of developing or selecting drug resistant bacterial strains. Local drug delivery system with controlled release properties have the potential to be used as a therapeutic component in the management of periodontal diseases. However, additional randomized, controlled studies are needed to help delineate the types of lesions, periodontal diseases, or specific situations where local delivery systems would be most beneficial.

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