Original Article

Local drug delivery systems for periodontal diseases - A review

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Abstract

Periodontitis is an immuno-inflammatory disease of the tissues surrounding the teeth. Elimination or adequate suppression of putative periodontopathic microorganisms in the subgingival microbiota is essential for periodontal healing. Antimicrobial treatments in periodontics range from mechanical debridement of tooth surfaces and home plaque removal to local and systemic delivery of chemical antimicrobial agents. Recent development of science and technology has revolutionized the basic outlook and approach to the problems of periodontal disease. 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. The local delivery of antimicrobial therapy to periodontal pockets has the benefit of administering more drugs at the target site while minimizing the exposure of complete body to the drug and the sustained release of antimicrobial in the periodontal pockets.

Keywords: Local drug delivery, periodontitis, periodontal pocket, antimicrobial therapy, tetracycline, chlorhexidine.

Introduction

Periodontitis is amongst the most widespread inflammatory diseases in the adult population initiated by the Gram negative anaerobic bacteria harbouring the subgingival biofilm region which poses a challenge to patients in performing oral hygiene procedures.[1] It is characterized by connective tissue breakdown and attachment loss, pathological apical migration of the junctional epithelium leading to formation of pocket, mobility of tooth, and complete loss of tooth.[2] Eliminating infections by conventional mechanical therapy aims at removal of subgingival plaque through scaling and root planning and inhibiting bacterial growth by means of periodontal therapy which halts the progression of periodontal and prevents the recurrence of disease.[3] Recurrence of disease is observed in patients due to poor oral hygiene and bacterial infection.[2]

Local and systemic antimicrobial drugs are used as an adjunct to mechanical periodontal therapy.[1] Despite various advantages, one of the most frequent drawback of the systemic drugs is poor patient compliance.[4] In contrast, the local drug delivery allows the therapeutic drug to be directly delivered at the diseased site (periodontal pocket) with minimal side effects.[3] The effectiveness of local delivery agents can be observed by visualising the decreased gingival inflammation and reduced pocket depth clinically and reduced pathogen microbiologicaly.[5]

Various Modes of Local drug delivery

Dr. Max Goodson et al in 1979 first gave the concept of controlled delivery for the treatment of periodontitis.[1] The choice of Local drug delivery agent depends on the bacterial aetiology of the periodontal infection. Many antibiotics are proven to be beneficial in periodontal diseases.[6] These antimicrobial agents are useful adjunctive treatment to scaling and root.[7] It can also be safely used in medically compromised patients for whom surgery is not an option or those who refuse surgical treatment.[6]

Classification of LDD agents based on:

Their action [8]: Controlled systems – Diffusion and chemically and Solvent activated systems.

Their Mode of application [1]: Personally applied and professionally applied. These can further be further divided into sustainable and non-sustainable.

Their Mode of release: Sustained release devices and Controlled release devices.

The Vehicle of delivery:[8] Films / slabs e.g., Chlorhexidine chips,[1] fibres e.g., Tetracycline and Injectable systems e.g. Minocycline.

Today, a host of local drug delivery system to treat periodontitis like injectable systems [3], vesicular system, microparticles, nanoparticles, gels, strips and fibres are currently present in market. Here is a quick glance at the currently available locally delivery agents used in the management of periodontitis.[1]

TETRACYCLINE:

Gels comprising of tetracycline seratiopeptidase were assessed by Maheshwari et al in 2005.[1] It is a bacteriostatic antibiotic that were first available local drug to treat periodontitis.[8]

Available forms:

Fibres: The biological inert and non-resorbable material originally marketed as ethylene and vinyl-acetate impregnated with 25%w/w tetracycline HCL powder, these are packed in form of thread of 0.5mm in diameter and 23cm in length.[8] **PERIODONTAL PLUS AB** is recently introduced bio resorbable tetracycline fibre which is developed with a base of collagen film.[4]

Gels: Tetracycline serratiopeptidase containing periodontal gel, Bio-erodible injectable poly for tetracycline-controlled delivery formulations loaded with tetracycline.[8]

DOXYCYCLINE

This being is a bacteriostatic agent has a biodegradable formulation of 10% doxycycline by weight and DL-Lactide is 33% by weight. It is bio absorbable polymer which is almost entirely expelled from the periodontal pocket in 28 days.[8]

MINOCYCLINE

It is a tetracycline with semi synthetic nature which is the most active anti biotic against microbes causing periodontitis. This has a potent anti-collagenase effect along with anti-microbial activity against a lot of organisms.[8]

Minocycline as a monotherapy could improve periodontal health when locally delivered. The effect of applying minocycline 2 percent gel after root planning has been evaluated and reported in many clinical trials.[5] It is available in different modes of application like ointment, film, microsphere.[8]

FDA approved 10% doxycycline is available in the market as **Atridox** dispensed as a gel, delivered using a syringe.[1]

CHLORHEXIDINE

It is used as an antifungal and antibacterial agent and has bacteriostatic at low and bactericidal at high concentrations. Chlorhexidine belongs to biguanide family. Although used as mouth rinse it has a short-lived effect on deep periodontal pocket. Different forms of delivery are: Gels, Varnishes, Mouth rinses, Chips.[8]

An agent comprising of 1.5% chlorhexidine of xanthan type is marketed with the name of **Chlo-Site**.[4]

Preliminary data indicated that administration of Chlorhexidine reduced subgingival bacteria and improved clinical health.[5]

METRONIDAZOLE

An oil-based metronidazole gel containing benzoate in a matrix of gylceryl mono oleate and sesame oil which is subgingivally injected with the help of syringe and cannula and is market with the brand name of **Elyzol.**[5]

The drug concentration is crevicular fluid follows an exponential pattern which is compatible with sustained drug delivery.[8] Metronidazole gel was effective at reducing subgingival anaerobes.[5]

NATURE IS THE BEST MEDICINE- HERBAL AGENTS USED AS LDD NEEM

The concentration of drug in the GCF mimics the exponential pattern in compatibility with sustained delivery. A significant reduction in bacterial and plaque levels is seen with the help of neem leaf. The bioactive materials found in neem increases the presence of gallotannins and effectively reduces the number of bacteria available for binding to the tooth surface.[9] Also inhibition of glucosyltransferase activity which reduces bacterial adhesion adhesion to saliva coated hydroxyl appetite shows anti plaque activity.[2]

SIMVASTATIN (SMV)

Simvastatin (SMV), lovastatin, and pravastatin which belong to statin group are inhibitors of 3- hydroxy-2-methyl-glutaryl coenzyme A (HMGCoA) reductase.[2] They are also used in lowering cholesterol hence providing an important and effective approach in treating hyperlipidemia and arteriosclerosis. By increasing the expression of BMP (bone morphogenetic protein) inflammation, and angiogenesis, they provide a new direction in the treatment of periodontitis.[9]

ALOE VERA

Aloe vera is a cactus plant that belongs to the Liliaceae family.[9] Aloe Vera has been used medicinally for a few thousand years. Its history of health benefits was first recorded in Egyptian medical writings in 1500BC.[10] pharmacological actions of Aloe vera include anti-inflammatory, antibacterial, antioxidant, antiviral and antifungal actions as well as producing hypoglycemic effects. It not only reduces bleeding and inflammation but also swelling of the gums. It also acts as a powerful antiseptic in treating periodontal pockets. It is a powerful healing promoter and can be used following extractions. [9]

TURMERIC

Turmeric (Curcuma longa L.),a common household name has immense medicinal properties used extensively in Ayurveda, Unani and Siddha medicine.[10] The active constituents of turmeric include the three curcuminoids: Curcumin (diferuloylmethane), demethoxycurcumin, and bisdemethoxycurcumin, as well as volatile oils (turmerone, atlantone, and zingiberone), sugars, proteins, and resins. Curcumin exhibits anti-- inflammatory, anti-oxidant, anticarcinogenic, antiviral, and antimicrobial activities.[9]

CONCLUSION

Systemic antimicrobial therapy has certain short comings which includes the absorption and distribution of the drug throughout the body and blood circulation, hypersensitivity, gastrointestinal intolerance and development of bacterial resistance.[6] Thus, leading to poor patient compliance due to its toxicity and acquired bacterial resistance.[7] These disadvantages can markedly reduced if antimicrobial agents could be delivered locally. However, some side effects like as gastrointestinal disturbances and development of antibiotic resistance cannot be totally ruled out.[6] The concentration of a drug in the local tissue can be markedly enhanced by incorporating the active agent into controlled release delivery systems delivered directly into the periodontal pocket.[6] The other advantages include no systemic overdose, simple formulation, availability and affordability.[3]Hence making these agents a material of choice in the non-surgical management of chronic periodontitis patients.

CONFLICT OF INTREST

None

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