Local Drug Delivery Systems as an Adjunct to Cure Periodontitis- The Novel Dental Applicant

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ABSTRACT

Periodontitis is a complex disease that involves the loss of attachment around teeth resulting from action of microorganisms and the response of the host to these organisms. The basic treatment of chronic periodontitis is a mechanical debridement of periodontal pockets by Scaling and root planing (SRP) in combination with efficient plaque control. The effectiveness of mechanical debridement of plaque and repeated topical and systemic administration of antibacterial agents are limited due to the lack of accessibility to periodontopathic organisms in the periodontal pocket. The introduction of a slow release and subgingival delivery of tetracycline has changed the rationale from a mechanical treatment towards a combined therapy for full mouth/sites disinfection. Various antibiotics, antiseptics and resorbable carriers are now proposed as Local drug delivery systems with similar targets to arrest disease progression. The dosage forms include fibers, film, injectable systems, liposomal system, micro or nanoparticle based systems, some of which are degradable while others are not and need to be removed at the termination of the treatment. These products provide a long-term, effective treatment at the site of infection at much smaller doses. This article reviews the current status of controlled local delivery their usefulness, as well as the advancement of these systems in the treatment of periodontitis.

Key wors: Chlorhexidine, Doxycycline, Local drug delivery systems, Minocycline, Metronidazole, Tetracyclines.

INTRODUCTION

The inflammatory periodontal diseases are caused by bacteria associated with dental plaque. The nature of the periodontal disease depend on the interaction among the bacterial agent, the environment, and the response of the host's defense mechanisms to the bacterial assault mainly composed of gram negative anaerobic bacteria.[1] The most common form of periodontitis is chronic periodontitis and it can be localized or generalized (more than 30% of the teeth) depending on the amount of clinical attachment loss.[2] The aim of current periodontal therapy is to remove the bacterial deposits from the tooth surface and to shift the pathogenic microbiota to one compatible with periodontal health. Therapeutic approaches include mechanical scaling and root planing (SRP) and in some cases surgery.

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After development of specific plaque hypothesis1 suggesting that specific bacteria caused specific forms of periodontal diseases newer treatment strategies, aiming primarily at suppression or elimination of specific periodontal diseases have been established. Putative pathogens associated with periodontal diseases are susceptible to a variety of antiseptics and antibiotics.[3,4] Antimicrobial agents may gain access into the periodontal pocket through systemic and local route of delivery. Systemic antimicrobial agents enter periodontal pockets following their intestinal absorption and passage from the blood stream into oral tissues, gingival crevicular fluid and saliva.[5]

Systemic administration has been useful in treating periodontal pockets, but repeated, long-term use of systemic antibiotics is fraught with potential danger including resistant strains and superimposed infections. Local administration, therefore provide a useful answer to these problems. The principle requirement for effectiveness of this form of therapy is that the agent reaches the base of the pocket and is maintained there by some means like

reservoir for an adequate time for the antimicrobial effect to occur.[6] Numerous local drug transport products have undergone preliminary assessments but only a few methods have been evaluated in several studies.[1,4]

LOCAL DRUG DELIVERY SYSTEMS

Goodson et al in 1979 first proposed the concept of controlled delivery in the treatment of periodontitis. It has been observed that the local route of drug delivery can attain 100-fold higher concentrations of an antimicrobial agent at subgingival sites compared with a systemic drug regimen. This reduces the total patient dose by over 400 fold thereby reducing the potential problems with the use of systemic antibiotic drug regimens and development of drug-resistant microbial populations at non oral body sites. These can be safely used in medically compromised patients for whom surgery is not an option and contraindicated in patients with known hypersensitivity to the antimicrobial used, asthmatics and infective conditions such as AIDS, Tuberculosis.[7]

Local delivery devices can be of 2 types according to the duration of medicament release-(a) Sustained release Formulations: It follows First order kinetics i.e. the rate of elimination is directly proportional to drug concentration, providing drug delivery for less than 24 hours.[8] (b) Controlled Release Formulation: It follows Zero order (linear) kinetics i.e. the rate of elimination remains constant irrespective of drug concentration, clearance decreases with increase in concentration; or a constant amount of the drug is eliminated in unit time.

Intra pocket devices can be divided in two broad categories depending on degradability. Nondegradable devices (first generation) and Degradable devices (second generation) Non degradable devices have the advantage that the therapist controls the removal and therefore has greater control over the time of exposure of the pocket environment to the drug. The degradable device has the advantage of requiring the patient pay only a single visit to therapist for the insertion of the device. Professionally applied sustained subgingival drug delivery systems may be attained with drugs possessing a high intrinsic substantivity for tooth root surfaces.[9] Various local drug delivery systems used in treatment of chronic periodontitis include-Fibers, Film, Injectable systems, Gels, Strips and compacts, Vesicular systems, Microparticle system, Nanoparticle system etc (Table 1).

Table 1: Summary of various Local Drug Delivery systems used

SYSTEM	POLYMER MATRIX	DRUG INCORPORATION
FIBRES	Cellulose acetate	Tetracycline HCl Chlorhexidine
	Ethylene vinyl acetate	Tetracycline HCl (ACTISITE Fibre)
	Poly (e-caprolactone) (PCL)	Tetracycline HCl
	Ethyl cellulose	Metronidazole, Minocycline Tetracycline HCl
FILMS	Cross-linked atelocollagen	Tetracycline
	Gelatin (BycoW protein)	Chlorhexidine diacetate
	Cross-linked gelatin + glycerine	Chlorhexidine digluconate (PERIOCHIP)
	PLGA-poly (dl-lactic-coglycolic acid)	Tetracycline
	HEC + polycarbophil	Metronidazole
	HEC (hydroxyethylcellulose) + polyvinylpyrrolidone	Tetracycline
	HEC + polycarbophil	Metronidazole
GELS	Glycerol monooleate + sesame oil	-
	Metronidazole (ELYZOL Dental gel)	-
	HEC + aminoalkyl-methacrylate + triacetine + glycerine	Minocycline
	Poly (DL-lactide) + N-methyl-2 pyrrolidone	Doxycycline (ATRIDOX gel)
	Aerosil + 0.5% wt/wt serratiopeptidase	Tetracycline (PLURONIC gel)
	Xanthan gel	Chlorhexidine (CHLOSITE gel)
VESICLES	Phosphatidylinositol	Triclosan
MICROPARTICLES	PLGA	Tetracycline Minocycline
	Hydroxypropyl Cellulose + Methacrylic Acid Copolymer S (MACS)	Ofloxacin
	Collagen + Gelatin	Fibroblast Growth Factor
NANOPARTICLES	PLGA	Harungana madagascariensis leaf extract
	Cellulose acetate phthalate	Triclosan

FIBRES

Monolithic Tetracycline containing fibers, using different acrylics like Polyethylene, Polypropylene, Polycaprolactone, Polyurethane cellulose propionate and Ethylene Vinyl Acetate (EVA) were first developed and tested by Goodson.[10]

ACTISITE tetracycline fibres have been approved for the treatment of adult periodontitis by the United States Food and Drug Administration (FDA). These are non-resorbable biologically inert, safe, plastic copolymer (ethylene and vinyl-acetate) loaded with 25% w/w tetracycline HCL powder packaged as a thread of 0.5 mm in diameter and 23 cm in length. It maintains constant concentrations of active drug in the crevicular fluid in excess of 1000 μg/ml for a period of 10 days.[11] Actisite, as an adjunct to SRP, showed significantly greater reductions in probing depths, bleeding on probing and significant reduction in A. a and P. gingivalis levels .than SRP alone.[12,13] Bio-resorbable form of fibre commercially available as PERIODONTAL PLUS AB offers the advantage of no second appointment for removal as it biodegrades within 7 days.

A new generation of semi-synthetic tetracycline compounds called glycylcyclines has recently been developed[14] which are effective not only against tetracycline-sensitive bacteria, but also against tetracycline-resistant gram-positive and negative microorganisms.

FILMS

Films are matrix delivery systems in which drug is distributed throughout the polymer and release occurs by drug diffusion and/or matrix dissolution.[15] These films were made by casting ethanol or chloroform solution into molds and allowing the solvent to evaporate. The appropriate drug and plasticizing agent were incorporated into the solution prior to casting. The dried films (200–300 μm thick) were then cut into the required shapes.[16]

A number of biodegradable polymers have been investigated for the delivery of antimicrobial agents in the treatment of periodontal diseases, including hydroxypropyl cellulose, polyesters[17] and cross-linked collagens and protein films.[18]

A Sustained release biodegradable device composed of hydrolyzed gelatin matrix, cross linked with gluteraldehyde, glycerin and water into which 2.5 mg chlorhexidine gluconate has been incorporated named PERIOCHIP have been developed in 1998. It is a small, orange-brown, tombstone-shaped chip (4.0x 0.5x 0.35 mm) and has been approved by FDA[19] The adjunctive use of the chlorhexidine chip results in a significant reduction of pocket depth when compared with both scaling root planing alone and the adjunctive use of a placebo chip.[20-22] Perio Chip releases chlorhexidine in a biphasic manner, initially releasing approximately 40% of the chlorhexidine within the first 24 hours, and then releasing the remaining chlorhexidine in an almost linear fashion for 7–10 days.[20]

GELS

Gel is applied sublingually with the help of blunt cannula and syringe. The safety profile, longer-term retention, antimicrobial activity suggests that tetracycline containing copolymer gels represents a safe and effective therapy for periodontitis. Comparative analysis of tetracycline containing dental gels: poloxamer and monoglyceride based formulations have been done which shows that when applied subgingivally produce a significant improved outcome in moderate to deep periodontal pockets.[23]

Together with the solid devices, semisolid formulations also receive reasonable attention for the localised delivery of antibiotics. Semisolid gel formulations can indeed have some advantages. In spite of the relatively faster release of the incorporated drug, gels can be more easily prepared and administered. Moreover, they possess a higher biocompatibility and bioadhesivity allowing adhesion to the mucosa in the dental pocket and finally, they can be rapidly eliminated through normal catabolic pathways decreasing the risk of allergic host reactions at the application site.[24] Various oleogels and hydrogels for the delivery of tetracycline (2.5%), metronidazole (25%-Elyzol dental gel),[25-27] metronidazole benzoate (40%), have been tested with satisfactory results. Elyzol have been applied in viscous consistency to the pocket, where it is liquidized by the body heat and then hardens again forming crystal in contacts with water. After application of Elyzol 25% dental gel, metronidazole concentrations of above100 μ/ml were measurable in the periodontal pocket for at least 8 hours and concentrations above 1 μ/ml were found at 36 hours.[28]

2% minocycline HCL in a matrix of 20 mg hydroxyethyl cellulose, 25 mg magnesium chloride, 10 mg eudragit, 60 mg triacetine, and 0.5 gm glycerine available as yellow coloured ointment Dentomycin in European Union. In Japan it is commercially available with name Periocline. The concentration of minocycline in the periodontal pocket is about 1300 μg/ml, 1 hr after single topical application of 0.05 ml ointment (1 mg of minocycline) and is reduced to 90 μg/ml after 7 hrs. Results have shown that the

combination of ointment with scaling and root planing was significantly better than scaling and root planning.[29]

The only FDA approved gel system is 8.5% Doxycycline w/w (42.5 mg Doxycycline) dissolved in 37% poly (DL-lactide) (PLA)+63% N-methyl-2-pyrrolidon (NMP) ATRIDOX available as 2 syringe mixing system. Doxycycline levels in GCF peaked to 1,500-2000 μg/ml in 2 hours following treatment with ATRIDOX. These levels remained above 1000 μg/ml through 18 hours, at which time the levels began to decline gradually. Local levels of Doxycycline have been found to remain well above the minimum inhibitory concentration for periodontal pathogens (6.0 μg/ml) through Day 7 and show significant improvement in chronic periodontitis.[30-32] Approximately 95% of the polymer is bio absorbed or expelled from the pocket naturally within 28 days.[33]

BIOADHESIVE GEL SYSTEM

Bioadhesive delivery systems may improve oral therapeutics for periodontal disease and mucosal lesions.[34] Jones and coworkers[35] developed a bioadhesive semi-solid, polymeric systems based upon hydroxyethylcellulose (HEC) and polyvinylpyrrolidone (PVP) containing tetracycline for the treatment of periodontal diseases.

Chitosan, xanthan gum and poly (ethylene oxide) were selected as potential bioadhesive vehicles. xanthan gum gave the most prolonged adhesion time on the oral mucosa (153·5 min), followed by poly(ethylene oxide) (89·3 min) and chitosan (42·6 min), and these times were all significantly different from each other. Chlosite is an agent containing 1.5% chlorhexidine of xanthan type. Xanthan gel is a saccharide polymer, which constitutes of a three-dimensional mesh mechanism, which is biocompatible with chlorhexidine. The gel gets vanished from the pocket within l0-30 days of injection and effective concentration of chlorhexidine against microorganisms is established for at least 15 days in the region. Both chlorhexidine and gel matrix are mucoadhesive so that they stick inside the pockets and are not easily washed out by gingival fluid or saliva.[36]

A 20% wt/wt pluronic gel (3% wt/wt tetracycline, 1.0% wt/wt Aerosol, and 0.5% wt/wt serratiopeptidase) was prepared on a weight basis using the cold method.[37] Viscosity and bioadhesivity increased with an increase in the concentration of Aerosol. Release of tetracycline was sustained as the concentration of Aerosol increased. Various clinical parameters confirmed the acceptability and efficiency of this gel system.[38]

VESICULAR SYSTEM

Liposomal system was designed to mimic the bio-membranes in terms of structure and behaviour and hence investigated intensively for targeting periodontal biofilms. The targeting of vesicles to adsorbed films of bacteria was thought to be due to the interaction of the surface polymers of the bacterial 'glyco-calyx' with vesicles incorporating lipids with polyhydroxy head groups. The adsorption of cationic vesicles over biofilms of skin associated bacteria Staphylococcus epidermidis, having negative charge succcinylated Con A-bearing liposomes (proteoliposomes) have been found[39] to be effective for the delivery of triclosan. Triclosan is a very effective bactericide, which is only sparingly soluble in water but it is capable of being trapped in the liposomal bilayers. Even after very short exposures the succinylated Con A-bearing vesicles are retained by the bacteria eventually delivering triclosan in the cellular interiors to cause selective targeting of the invading pathogens.[40]

MICROPARTICLE SYSTEM

These are dissolution-controlled polymeric reservoir devices, which may deliver their contents with a prolonged release profile in the salivary or crevicular fluid. Microcapsules prepared from lactic acid/glycolic acid copolymers have been proposed for delivery of tetracycline and minocycline. PLGA microspheres containing minocycline have been formulated and have been used for the elimination of Porphyromonas gingivalis from the periodontal pocket and lesd to reduction in periodontal pocket depth in chronic periodontiits.[41-43] Microparticles of poly (dl-lactic-coglycolic acid) (PLGA) containing chlorhexidine free base, chlorhexidine di gluconate and their association or inclusion complex with methylated-beta-cyclodextrin (HPBCD) were prepared with single emulsion, solvent evaporation technique.[44]

A local drug delivery system (PT-01) containing Ofloxacin base on swelling controlled system was developed. This comprised Hydroxypropyl Cellulose (HPC) and Methacrylic Acid Copolymer S (MACS) as its base material and ofloxacin, a superior pyridone quinolone derivative as a drug to be delivered. This product acts in bi-phasic manner, first rapid release of ofloxacin from HPC and followed by slow release from MACS.[45] Recently to regenerate periodontal tissues, a sandwich membrane composed of a collagen sponge scaffold and gelatin microspheres containing basic fibroblast growth factor (bFGF) in a controlled-release system was developed.[46]

NANOPARTICLE SYSTEM

Nanoparticles (including nanospheres and nanocapsules of size 10-200 nm) are in the solid state and are either amorphous or crystalline. They are able to adsorb and/or encapsulate a drug, thus protecting it against chemical and enzymatic degradation. The nanoparticulate system provides several advantages as compared with microspheres, microparticles and emulsion-based delivery systems, including high dispersibility in an aqueous medium, controlled release rate and increased stability. These systems reduce the frequency of administration and further provide a uniform distribution of the active agent over an extended period of time. Biocompatible nanoparticles composed of 2-hydroxyethyl methacrylate (HEMA) and polyethyleneglycol dimethacrylate (PEGDMA) could be used as a drug delivery system for dental applications. Various studies have assessed efficacy of nanoparticles in periodontal diseases. Dung et al used Antisense oligonucleotide- loaded chitosantripolyphosphate (TPP) nanoparticles and showed the sustained release of oligonucleotides which is suitable for the local therapeutic application in periodontal diseases.[18]

HERBAL PRODUCTS

Various herbal formulations like aloevera, neem, tulsi, propolis, cocoa husk, pomegranate, cranberry etc. are being used widely these days. These products have shown promising results with no side effects and are economical as well.[47] Moulari *et al*, showed improved bactericidal activity of the Harungana madagascariensis leaf extract (HLE) on the oral bacterial strains implicated in dental caries and gingivitis infections.

MISCELLANEOUS NEWER DRUGS

Statins like simvastatin (SMV), lovastatin, are specific competitive inhibitors of 3-hydroxy-2-methyl-glutaryl coenzyme A (HMGCoA) reductase, widely used to lower cholesterol, and for treating hyperlipidemia and arteriosclerosis. Statins modulate bone formation by increasing the expression of bone morphogenetic protein-2, inflammation, and angiogenesis. Various studies showed that SMV assists in bone regeneration as well as the anti-inflammatory effect when delivered or applied locally.[48]

An interesting effect of low-dose antibiotics is that they not only kill the bacteria that may cause periodontal disease but also reduce the body's production of collagenase, an enzyme that destroys gingival tissues. The antibiotic doxycycline was found to combat these enzymes, even in doses so small that there was no antibiotic effect. Periostat is a capsule of 20 mg of doxycycline, and clinical studies have shown that patients who take two capsules daily have a reduction in clinical inflammation.[7]

CLINICAL APPLICATION OF LDD SYSTEMS

Eradication of microorganisms from the periodontal pocket is the most important step in treating periodontitis. The requirements for treating periodontal disease include a means for targeting an anti-infective agent to infection sites and sustaining its localized concentration at effective levels for a sufficient time while concurrently evoking minimal or no side effects.[49] The limitation of mouth washes and oral irrigations prompted the practitioner to favor a professional application of Tetracycline, Chlorhexidine, Doxicycline, Minocycline and Metronidazole as an adjunct to treat chronic periodontitis. (Table 1) Selecting the system to use will depend on its efficacy, user friendliness and cost.[50] Insertion of tetracycline-containing fibers is time consuming and two applications are recommended for 25% metronidazole gel, whereas a chlorhexidine chip placement is fast. In order to combat dentomicrobial infections, different antimicrobials at a variety of concentrations need to be tested against a panel of suspected pathogens. Currently, the best way to determine the ideal drug concentrations is to compare *in vitro* and *in vivo* results of various research work has been done till date (Table 2).

RESULTS

Mentioned studies employing a variety of local delivery systems incorporating drugs and have addressed the utility of these devices for the treatment of periodontitis and following results were obtained

- LDD system as a monotherapy did not show improved results as compared to SRP alone. (Goodson *et al* 1985-Tetracycline fibres,[10] Ainamo *et al* 1992-Metronidazole gel,[25] Jalavi *et al* 2012-Doxycycline polymer[32])
- LDD 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.(Jeffcot M *et al* 1998,[19] Grover V *et al* 2012-Periochip[21], Garrett *et al*-Doxycycline,[30] Pandit *et al*-Elyzol[27]).
- These systems may be used as an adjunct to SRP to treat localized non–responding sites to scaling,

Table 2: Commercial Local Drug Delivery Systems: Randomized Controlled Trials as an adjunct to SRP

Drug	Trade Name	Physical Form	Reference Study	Treatm-ent Design	Treatment	P D reduction	CAL Gain
Tetracycline	ACTISITE (0.25%w/v tetracycline)	Non-Resorbable Fibre	**Goodson** *et al* (1991)	Split	Untreated, SRP + Fibres SRP	0.46 0.67 1.02	0.38 0.40 0.65
			Newman *et al* (1994)	Split 6 month	SRP SRP + Fibre	1.08 1.81	1.08 1.56
			Sadaf *et al* (2012)	Split 3 months	SRP SRP + Fibre	2.33 ± 0.88 2.63± 0.96	-
Doxycycline	ATRIDOX (8.5% Doxycline)	Biodegradable Polymer In syringe	**Garrett** *et al* (1999)	Parallel 9 month	DOXY SRP	1.1 0.9	0.8 0.7
			Wennstrom *et al* (2004)	Parallel 6 month	SRP + 8.5% DOXY Debride + DOXY Debride	-	-
			Javali *et al* (2012)	Split 3 month	SRP alone SRP + DOXY DOXY	-	0.39 ± 0.420. 0.57 ± 1.23 0.27 ± 0.87
Metrnidazole	ELYZOL dental gel (25% gel)	Biodegradable gel	**Ainamo** *et al* (1992)	Split	2x MTZ gel 1x SRP	1.3 1.5	-
			Stelzel *et al* (2000)	Split 259 Days	SRP + 25% MTZ SRP	1.37 mm 1.17 mm	-
			Pandit *et al* (2013)	Split 1 month, 3 month	SRP+ MINO SRP + MTZ SRP	2.10 3.20 1.70 2.70 0.95 1.65	-
Minocycline	ARESTIN (2%)	Biodegradable mix in syringe	**Hellstrom** *et al* (2006)	Split 25 weeks	Surgery + MINO gel Surgical tretment	2.51 mm 2.18 mm	-
			Williams *et al* (2001)	Parallel 9 months	SRP SRP + Vehicle SRP + MINO	1.08 1.0 1.32	-
			Jhinger N *et al* (2015)	Parallel 3 months	SRP + CHX Chip SRP + MINO	2.95 ± 0.89 2.6 ± 0.89	
Chlorhexidine	PERIOCHI-P (2.5 mg)	Biodegradable device	**Jeffcoat** *et al* (1998)	Parallel 9 month	SRP SRP + Chip	0.65 0.95	0.58 0.75
			Azmak *et al* (2002)	Split 6 month	SRP + Placeb SRP + CHX chip	-	-
			Grover V *et al* (2011)	Parallel 3 months	SRP SRP ± CHX chip	0.42105 1.26316	0.47368 1.15789
			Kondred-dy *et al* (2012)	Parallel 3 month, 6 months	SRP SRP+ CHX chip	1.4 2.8 1.6 3.2	1.3 2.7 1.8 3.2

for recurrent periodontitis sites during supportive periodontal therapy. (Stelzel M *et al* 1996-Metronidazole gel[26])

- Individual dose for LDD is convenient for the treatment of single pocket or a limited number of infected sites.(Azmak N *et al*-Periochip)
- There are insufficient data to indicate the local drug delivery induces bacterial resistance to antimicrobial agents. Long term studies are needed to address this important issue.

DISCUSSION

Subgingival application of LDD is considered as primary treatment in patients of untreated or recurrent periodontitis and in pockets with probing pocket depth (PPD) of 4-5 mm and used as an adjunct to scaling and root planning.[10,29] The mean improvement in PPD resulting from the adjunctive effect compared with the scaling and root planing (SRP) controls ranged between 0.67 mm with tetracycline fibre[12] to 3.2 mm using Periochip[22] mm over a clinical follow-up time of 3-6 months.

These drugs can be placed subgingivally as an alternative to SRP. This approach has been used with the injectable gel formulation such as metronidazole (Elyzol) and chlorhexidine (Chlosite gel) as the effective agent.[25,26] Some studies has shown that these drug application to be as good as SRP and moreover challenge this routine, proven and highly effective treatment of SRP.

However, they explained that extraordinary results may be due to the minimal response obtained in the SRP group only and emphasized that this should not be interpreted as detracting from the importance of SRP.

These drugs can be placed as part of maintenance therapy for chronic periodontits patients on recall after definitive therapy. Two different clinical approaches that have been used includes either significant improvements in both PPD and clinical attachment levels (CAL) and absence of bleding on probing over the entire study period. Garrett *et al*[30] showed that doxycycline delivered subgingivally in a bioresorbable polymer, at baseline and 4 months, produced significantly better CAL, PPD, and bleeding on probing (BOP) results than a placebo polymer over a six-month period. No comparison was made with routine maintenance therapy, however. Killoy *et al*[30] reported that the subgingival placement of tetracycline fibers either at baseline only, or at baseline and 6 months, also gave significantly better results in PPD, CAL, and BOP than routine mechanical maintenance therapy.

There are other clinical situations in which LDD may prove to beclinical but for which no clinical studies are yet available. These include the treatment of furcation involvement, pericoronitis, and dry sockets. Another area of possible application is their use in periodontal surgery to reduce infection, particularly when guided tissueregenerative procedures are used.

CONCLUSION

Current data suggest that local delivery of antimicrobials into a periodontal pocket can improve the periodontal health. However these drug systems do not provide a superior result when compared to scaling and root planing or as therapy for aggressive forms of periodontitis that may require systemic antibiotics to eradicate the disease. Thus the benefits of using these systems as a monotherapy are questionable. (Table 2) In conjunction with scaling and root planing, the adjunctive use of local drug delivery may enhance the results in sites that don't respond to conventional therapy. A few localised persistent lesions in otherwise well controlled patients may offer the greatest potential for success with this treatment modality. Local delivery has the advantage over systemic therapy of possibly achieving higher concentrations of drug at the intended site of action using a lower dosage with an associated reduction in side- and toxic effects. These delivery systems 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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ABBREVIATION

LDD: Local Drug Delivery Systems

PPD: Periodontal Pocket depth

CAL: Clinical Attachment level

BOP: Bleeding on Probing

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