A REVIEW ON RECENT ADVANCEMENTS IN TREATMENT OF PERIODONTITIS

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ABSTRACT

Periodontitis is considered as a chronic localized inflammatory disease related to teeth and its supporting structures. The disease is initiated by subgingival periopathogenic bacteria followed by inflammation of gums, degeneration of the periodontal ligament and alveolar bone loss. In this outlook scaling and root planing was considered as the basic treatment approaches to treat periodontitis which have severe shortcomings like unable to reach the deep pockets and inhibiting the progression of the bacterial infection. In order to overcome the shortcomings of scaling and root planing various novel preventive treatment modalities like host modulation, anti-microbial therapy, and full mouth disinfection can be used as either adjunctive treatments or stand-alone treatment options. These novel treatment modalities had shown significant improvement in blocking the growth of bacteria when compared with the traditional approaches of treatment. This review will cover an update on the past and the recent advancements in the various treatment modalities for periodontal diseases.

KEYWORDS: Periodontitis; Periodontal therapy; Oral hygiene; Host modulators; Anti-microbial.

INTRODUCTION

Periodontitis (PDT) disease was known to mankind from ancient times. Physicians and researchers have established different forms of this disease, clinical symptoms, and the rate at which disease progression happens.[1-3] Chronic periodontitis is termed as a progressive disease where gingival periodontal ligament and alveolar bone will be affected and as a result
of this infection, there will be a change in tooth structure leading to alveolar bone resorption.\textsuperscript{[4-6]}

Periodontitis can be diagnosed by understanding the anatomy of healthy gums. A healthy gum will be in pink color stippled firmly to the underlying tissue, scalloped at cemento-enamel junction with a gingival crevice of 1-3 mm without any bleeding and this attached gingival extends from gingival groove to mucogingival junction by tightly binding to the underlying bone and resists any kind of injury.\textsuperscript{[7]} Further, any kind of deviations from this condition will lead to either gingivitis or periodontitis. Gingivitis is considered as an acute and a reversible condition where inflammation is restricted to only marginal and surrounding connective tissue without any loss of attachment. Whereas, periodontitis is considered as a chronic and irreversible condition which occurs when the inflammation reaches the periodontal ligament and alveolar bone.\textsuperscript{[8-10]}

The pocket formation between tooth surface and gingiva occurs due to apical displacement of the epithelium at the junctions which can be termed as a primary indicator for periodontitis. However, it is known that not all cases of gingivitis will lead to periodontitis. Similarly Loes et al.\textsuperscript{[11]} has done a study on the initiation and progression of periodontal disease in the Srilankan population. From the study, it was evident that 8% of the population had rapid progression of the disease, while 81% had moderate progression and for 11% of the population there is no progression of the disease from gingivitis.

Periodontitis is associated with the incidence of coronary heart disease, pneumonia, rheumatoid arthritis, preterm birth, head and neck squamous cell carcinoma (HNSCC) and risk of developing lung, kidney, pancreas and hematological cancer.\textsuperscript{[12]} An understanding of the latest trends in the treatment options is essential to treat periodontitis.

**ETIOLOGY**

By the mid-1960s, several researchers had come to the conclusion that initiation and progression of periodontal disease are caused by the supra and subgingival dental plaque which is now called the microbial biofilm. The identification and characterization of these “periodontal pathogens” have been a major driving factor of periodontal research for the past 5 decades. Periodontitis is termed as a chronic inflammatory disease, in which severe forms of the disease are associated with specific bacteria that have colonized the subgingival area regardless of the host’s protective mechanisms. In recent times focus on the etiology of
periodontal disease has changed markedly with a emphasis on specific anaerobic microorganisms like porphyromonas gingivalis (p. Gingivalis), tanneralla forsythia, treponema denticola, aggregatibacter actinomycetemcomitans (previously known as actinobacillus actinomycetemcomitans), prevotella intermedia, and others including fusobacterium nucleatum, wolinella recta, and spirochetes as the initiating factors which are also considered as primary etiologic factors.\[^{13, 14}\] Further, in more aggressive (and rare) forms of periodontal disease microorganisms like aggregatibacter actinomycetemcomitans have been observed.\[^{15, 16}\] Furthermore, a group of pathogens not typically present in the oral cavity has also been linked to periodontal diseases, such as enterobacteracea, pseudomonadacea, and acinetobacter.\[^{17}\]

**SIGNS AND SYMPTOMS**\[^{18}\]
- Swollen or puffy gums
- Bright red, dusky red or purplish gums
- Gums that feel tender when touched
- Gums that bleed easily
- Gums that pull away from your teeth (recede), making your teeth look longer than normal
- New spaces developing between your teeth
- Pus between your teeth and gums
- Painful chewing
- A change in the way your teeth fit together when you bite
- Halitosis, or bad breath, and a persistent metallic taste in the mouth
- Deep pockets between the teeth and the gums (pockets are sites where the attachment has been gradually destroyed by collagen-destroying enzymes, known as collagenases).
- Loose teeth, in the later stages (though this may occur for other reasons, as well) People should realize gingival inflammation and bone destruction are largely painless. Hence, people may wrongly assume painless bleeding after teeth cleaning is insignificant, although this may be a symptom of progressing periodontitis in that person.

**PATHOPHYSIOLOGY**
Besides dental caries, periodontal disease is considered as one of the most prevalent diseases in the world. The milder, reversible form of the disease, gingivitis, comprises inflammation of the gingival tissue. In disease-susceptible individuals, gingivitis may progress to periodontitis, which is a chronic inflammatory state of the gingiva causing destruction of
connective tissue as well as of alveolar bone resulting in reduced support for the teeth and ultimately tooth loss as shown in Fig. 1.\textsuperscript{[19-21]} The pathogenesis of periodontitis has been gradually elucidated during the latter half of the 20th century. In the 1960s and 1970s, research on humans and animals showed that bacteria play a critical role in initiating gingivitis and periodontitis.\textsuperscript{[22]} Leading up to the 1980s, there were further advances within the field and the pivotal role of the host inflammatory response in disease progression began to emerge.\textsuperscript{[23]} Further, systemic conditions and environmental factors such as smoking were also shown to greatly affect the disease onset and progress.\textsuperscript{[24]} For over a decade now, the concept of periodontitis has been considered to be a complex interaction between the microbial challenge and the host response, which alters the physiology of both connective tissue and the bone as depicted in Fig. 2.\textsuperscript{[25]}
CURRENT TREATMENT APPROACHES OF PERIODONTITIS

The initiation of periodontitis is generally caused by bacterial infections. Further, treating periodontitis is considered a great challenge due to the formation of bacterial biofilm which is hugely resistant to antimicrobials and host response modulators. Bacteria continue to remain in the oral cavity even after the removal. Various approaches can be used to treat periodontitis like Surgical, non-surgical and pharmacological therapies which are explained in detail in the below section.

Nonsurgical treatments

Scaling

Scaling removes tartar and bacteria from your tooth surfaces and beneath your gums. It may be performed using instruments, a laser or an ultrasonic device.

Root planing

Root planing smoothes the root surfaces and inhibit the further build-up of tartar and bacteria, and removes bacterial by-products that contribute to inflammation and delay healing or reattachment of the gum to the tooth surfaces as shown in Fig 3.

Fig. 2. Schematic overview of the pathogenesis of periodontitis.
Surgical treatments
Surgical approach to treat periodontitis is required when the progress of the infection is way too advanced and different surgical options were discussed below in detail.

Flap surgery (pocket reduction surgery)
Flap surgery will be initiated by making a tiny incision on the gum so that it can be lifted by exposing the roots. Further, more effective scaling and root planing can be performed as periodontitis causes considerable loss of bone as shown in Fig 4. Post scaling and root planing the gum tissue is sutured back in place and proper care should be taken to keep the gum tissue healthy and to avoid relapse of bacterial infection.\textsuperscript{29}

Fig. 3: Root planning.

Fig. 4: Pictorial view of flap surgery.
Soft tissue grafts
Gum tissue damage in periodontitis leads to changes in the gumline which should be replaced. A typical procedure involves removing a small segment of tissue either from the upper portion of the mouth or from a donor and attached to the affected site as shown in Fig 5. Further, this tissue grafts can reduce the recession of gums, coverage of exposed roots and gives a pleasing appearance to the teeth.\[30\]

![Fig. 5: Pictorial view of a soft tissue graft.](image)

Bone grafting
A typical bone grafting procedure will be performed when the bacterial infection has completely destroyed the bone surrounding the teeth. Further, the procedure involves placing a graft consisting of either bone from the patient or from a donor or it can also be of synthetic origin as depicted in Fig 6. The placed graft gives strength to hold the teeth in place and serves as a platform for the regrowth of damaged bone.\[31\]

![Fig. 6: Pictorial representation of a bone graft.](image)
Guided tissue regeneration

Tissue regeneration technique is employed to treat periodontitis when the bacterial infection is in an advanced stage. A typical procedure involves placing a piece of biocompatible fabric between damaged bone and teeth. The grafted material will prevent the entry of unwanted tissues and allow the damaged bone to grow back.[32] Similarly to treat the infected bone a special gel containing tissue simulating proteins is applied to the infected root.[33]

Pharmacological therapies

The systemic antimicrobial approach in the treatment of periodontitis

Traditional antimicrobial approach to treat periodontitis involves mechanical debridement of root surfaces to disrupt the formed bacterial biofilm.[34] Further, this approach blocks the only progression of biofilm attachment but if the disease is caused by invasive periopathogenic bacteria like (Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis or Prevotella intermedia) mechanical debridement is not sufficient to treat the disease. In order to overcome the above drawback systemic anti-microbial approach can be used. Wherein, the systemic anti-microbial approach includes the administration of drugs like amoxicillin, metronidazole, tetracyclines (doxycycline), clindamycin, azithromycin, clarithromycin and ciprofloxacin (Table 1) as an adjunct to mechanical debridement. As reported earlier periodontal lesions to occur due to a mixture of pathogenic bacteria where a combination of prescribed antibiotics would be necessary.[35] Further, when a periodontal infection is caused by enteric rods, pseudomonas or A. actinomycetemcomitans a combination of metronidazole and ciprofloxacin can be used and in another case, a combination of amoxicillin and clavulanic acid can also be used to treat periodontal infections.[36] Research data also suggested that given antibiotics are within the therapeutic range to treat the infection effectively. However, disadvantages include inadequate drug concentration in the periodontal pocket, a rapid decline of the plasma antibiotic concentration to sub-therapeutic levels and high peak plasma concentration that might be associated with side effects that can be overcome by formulating novel micro and nano-drug carriers.
Table 1: Antibiotics used in the treatment of periodontal diseases.

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Dosage in adult periodontitis</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metronidazole</td>
<td>500 mg three times daily</td>
<td>[37]</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>150 mg three times daily for eight days</td>
<td>[38]</td>
</tr>
<tr>
<td>Penicillins (amoxicillin)</td>
<td>250-500 mg three times daily</td>
<td>[39]</td>
</tr>
<tr>
<td>Tetracyclines (doxycycline)</td>
<td>200 mg initially, 100 mg for seven days</td>
<td>[40]</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>250-500 mg for three days</td>
<td>[41]</td>
</tr>
<tr>
<td>Claritromycin</td>
<td>500 mg 2 x daily for three days</td>
<td>[41]</td>
</tr>
<tr>
<td>Fluoroquinolones (ciprofloxacin)</td>
<td>500 mg twice a day for eight days</td>
<td>[42]</td>
</tr>
<tr>
<td>Amoxicillin/Metronidazole</td>
<td>250-375 mg of each 3 x daily for 8 days</td>
<td>[43]</td>
</tr>
<tr>
<td>Metronidazole/Ciprofloxacin</td>
<td>250 mg of each 2 x daily for 8 days</td>
<td>[44]</td>
</tr>
<tr>
<td>Amoxicillin + clavulanic acid/metronidazole</td>
<td>250 mg 3 x daily for 8 days</td>
<td>[45]</td>
</tr>
</tbody>
</table>

The local antimicrobial approach in the treatment of periodontitis

Delivery devices intended to cure periodontal infections locally are fibers, strips, films, injectable gels, micro/nanoparticulate systems or vesicular systems. Further, various drugs like tetracycline-hydrochloride, doxycycline, minocycline, metronidazole, chlorhexidine, and ofloxacin were used to load in the above-mentioned carriers to treat periodontal infections. Some of the commercially available local delivery systems for periodontal treatment and their characteristics are given in Table 2.

Table 2: Commercially available local delivery systems for periodontal treatment

<table>
<thead>
<tr>
<th>Commercial product</th>
<th>Local drug delivery system</th>
<th>Therapeutic compound</th>
<th>Applications</th>
<th>Advantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actisite™</td>
<td>Nonabsorbable Fiber</td>
<td>25% tetracycline HCl</td>
<td>1 application 7-day treatment Chairside</td>
<td>Bactericidal High levels of tetracycline in GCF</td>
</tr>
<tr>
<td>Atridox™</td>
<td>Gel</td>
<td>10% doxycycline hyclate</td>
<td>1 application 7-day treatment Chairside</td>
<td>Forms solid implant Biodegradable bactericidal</td>
</tr>
<tr>
<td>Arestin™</td>
<td>Microspheres</td>
<td>1 mg minocycline HCl</td>
<td>1 application 14-day treatment Chairside</td>
<td>Bioadhesive Biodegradable Bactericidal</td>
</tr>
<tr>
<td>Periocline® Dentomycin®</td>
<td>Gel</td>
<td>2% minocycline HCl</td>
<td>1 application 14-day treatment Chairside</td>
<td>Bioadhesive Biodegradable bactericidal</td>
</tr>
<tr>
<td>Periochip®</td>
<td>Thin, solid, chip</td>
<td>2.5 mg chlorhexidine digluconate</td>
<td>1 application 7-day treatment Chairside</td>
<td>Biodegradable bactericidal</td>
</tr>
<tr>
<td>Elyzol®</td>
<td>Gel</td>
<td>25% metronidazole benzoate</td>
<td>2 applications 7-day treatment Chairside</td>
<td>Biodegradable bactericidal</td>
</tr>
</tbody>
</table>
Topical antiseptics

Povidone-iodine
The broad-spectrum antibacterial properties of povidone-iodine are well known in medicine. This compound is effective against various periodontopathic bacteria and cytomegalovirus activity (herpes virus implicated in the pathogenesis of periodontitis). Povidone-iodine does not exhibit adverse side effects such as discoloration of teeth and tongue or change in taste as seen with the usage of chlorhexidine. It has a low potential for developing resistance and adverse effects. Further, a solution containing a 10% concentration of povidone-iodine is considered as an effective concentration for subgingival irrigation. A typical procedure involves applying the above-said concentration with the help of an endodontic syringe up to 5 min. Different researchers have reported a favorable clinical outcome after treating advanced periodontitis with subgingival povidone-iodine and systemic antibiotics.[47]

Sodium hypochlorite
Sodium hypochlorite has been used as an endodontic irrigant for more than 75 years. Sodium hypochlorite poses various advantages like broad antimicrobial activity; rapid bactericidal action; relatively non-toxic; no color or staining; ease of access; and economical. Various research works suggested that using sodium hypochlorite as a treatment option improved periodontal histological healing.[48]

Corticosteroids for local application on the periodontium
Corticosteroids are a class of drugs that were used for various biomedical applications because of their potent anti-inflammatory and immunosuppressant properties.[49] Topically, their predominant anti-inflammatory action appears to be on eicosanoid formation. Corticosteroids stimulate the production of various polypeptides, collectively called lipocortin that inhibits phospholipase A2 activity. Further, another corticosteroid induced-complex, vasocortin has been found to inhibit oedema formation. Corticosteroids are thought to in some ways stabilize lysosomal membranes, thus suppressing the release of lytic enzymes.[50] Literature suggested that budesonide which is a new generation corticosteroid with potent local anti-inflammatory effect could be used in the treatment of periodontal disease. Further, in vivo studies have shown that inhaled budesonide could not modulate periodontal breakdown, this might be due to inappropriate formulation and dosage. Additional studies are needed to estimate the effects of budesonide on the oral mucosa and the periodontium.[51] While a topical application of corticosteroids for skin disorders is well
documented, there is considerably less critical information available for lesions of the oral mucosa, including periodontal disease. Therefore, there is a need for further research into therapeutic systems that improve local delivery of corticosteroids to oral mucosa and periodontium as well as controlled clinical studies in order to evaluate the clinical effectiveness of these formulations attended for treatment of periodontal lesions.\[52\]

**Host modulatory therapies**

Host Modulatory Therapies (HMT) can be used to reduce the progression of infection and allows to treat the infection and can also be used as preventive agents against the periodontal infection. In the last two decades, scientists have investigated various host modulating strategies in both animal and human experimental models and prescribed a set of modulations like regulation of production of arachidonic acid metabolites; regulation of bone remodeling; regulation of matrix metalloproteinase (MMPs) activity; regulation of nitric oxide synthase activity.\[53\]

**Nonsteroidal anti-inflammatory drugs (NSAIDs)**

The non-steroidal anti-inflammatory drugs are a group of pharmacological agents that have been well studied as an inhibitor of the host response in periodontal disease. These agents have been shown to prevent the formation of arachidonic acid metabolites, especially prostaglandins which have an important role in the pathogenesis of periodontitis.\[54\] *In vitro* and *in vivo* preclinical studies using NSAIDs have suggested their ability to reduce prostanoid formation by inhibiting COX enzymes.\[55\]

**Biphosphonates**

Biphosphonates are the therapeutic agents used to slow down the alveolar bone loss and increase mineral bone density. In recent times research works have suggested that a significant clinical improvement was observed. These results encourage the use of biphosphonates as adjunctive agents to periodontal therapy. However, additional studies are further needed in order to evaluate the relative risk-benefit ratio of biphosphonate therapy.\[56\]

**Regulation of matrix metalloproteinase activity**

Matrix metalloproteinases (MMPs) represent a family of zinc-dependent membrane-bound and secreted proteolytic enzymes that catalyze the breakdown of proteins in the cell plasma membrane or within the extracellular matrix.\[57\] Deregulation of MMPs activity is required in
different conditions such as rheumatoid arthritis, tumor cell metastasis, and periodontal disease.\textsuperscript{[58]} The ability of anti-microbials like tetracycline and doxycycline to inhibit MMP activity was first identified in the early 1980s. Tetracyclines block the active enzyme and inhibit reactive oxygen species involved in the activation of these enzymes.\textsuperscript{[59]}

RECENT ADVANCEMENT IN TREATMENT OF PERIODONTITIS

There are many advancements introduced in the probing system which helps in knowing the correct measurements of pocket depth and clinical attachment loss. The various advancements in the treatment of periodontal disease are as follows.

1. Vaccine for the disease.
8. Newer drugs developed for treating periodontal disease.

Vaccine for disease

The vaccination process gives immunity to the body by producing antibodies against the antigens. The vaccination concept for periodontitis was introduced because the origin of the disease is due to bacteria with some other factors. Vaccination work on three principles 1. Active immunization in which entire bacteria cells are introduced in a host as an antigen, 2. Passive immunization in which monoclonal antibodies are introduced in host and 3. Genetic immunization where the live and viral vaccine is introduced. In the 20\textsuperscript{th} century, the periodontal vaccine came into existence with Vancott's vaccine and the Inava endocarp vaccine. Bacterias like P. Gingivalis, Aggregatibacter actinomycetemcomitan and T. Forsythia are responsible for periodontal infection. This vaccination process has the potential to stop the progress of infection and improve quality of life.\textsuperscript{[60]}

Laser in treatment of periodontal disease

Albert Einstein has given the concept of Laser. Nowadays laser is being used for various purposes in the field of periodontology, like de-epithelialization, incision, curettage, sulcular debridement frenectomy, second stage implant surgery etc., Laser-Assisted New Attachment
Procedure (LANAP) with ultrasonic root debridement was done for immediate post-treatment effects on putative bacterial pathogens in deep human periodontal pockets. A typical procedure involves selecting 26 systemically-healthy adults with severe periodontitis. LANAP surgery was performed using, pulsed Nd: YAG laser, with laser energy (4.0W, 150-µs pulse duration, 20-Hz) directed circumferentially around teeth parallel to root surfaces in a coronal-apical direction to probing depth. After ultrasonic root debridement and gingival flap advancement to the alveolar bone crest, a second laser pass (4.0 W, 650-µs pulse duration, 20-Hz) was similarly performed in an apical-coronal direction to thermally initiate a fibrin clot at the tooth-gingival flap junction. Another laser system SiroLaser Blue has been introduced that works at three wavelengths that is at 970, 660 and 445nm. This system has been newly introduced in the United States in September 2018 and promoted by Dr. Smon Suppelt for its cutting efficiency at 445nm. This is manufactured by Dentsply Sirona. This system emits blue light at 445nm.[61, 62]

**Probiotics in the treatment of periodontitis**

At the beginning of the 20th century, Elie Metchnikoff discovered some useful bacteria that have a positive effect on health and suggested that these bacteria can help to eliminate harmful bacteria. Probiotics are defined as “Live microorganisms that once administered in adequate amounts confer a health advantage on the host”. The mechanism of probiotics is as follows.

- They compete for space and inhibit the pathogenic bacteria or its growth that cause dental plaque.
- Compete for nutrients and inhibit the growth of the pathogen.
- They increase the production of IgA antibodies or inhibits the production of pro-inflammatory cytokines.

All these mechanisms act as antagonists to pathogenic bacteria and reduce tissue inflammation and destruction. Probiotics are used in the form of tablets, lozenges, capsules, cheese, yogurt, rinses and liquids.[63] Golfre et al. in their study used Lactobacillus reuteri Prodentis as a probiotic to treat patients with peri-implant mucositis or periimplantitis who already had periodontitis in combination with non-surgical mechanical therapy and found out that there was a significant improvement in clinical parameters both in mucositis and periimplantitis around the implant.[64]
Microsurgery for periodontal treatment

Microsurgery is defined as the surgical procedure done under the microscope for better visualization and for better healing. In the field of periodontology, microsurgery is being used for procedures like root coverage procedure, papilla reconstruction, aesthetic implant surgery, periodontal flap surgery, etc. Tibbetts and Shanelec in 1994 used the microsurgical technique for regeneration and augmentation of periodontal soft tissue. The advantage of this procedure is better and fast healing with less post-operative pain. Similarly, Cortellini and Tonetti in 2007 came with the concept of minimally invasive surgical technique and later introduced the concept of space provision for regeneration with the modified MIST (M-MIST). The procedure is done under magnification with microsurgical instruments. Loups or microscope is being used for the purpose with magnification ranging from 3.5-20. The main advantage of the procedure is less postoperative pain and better and faster healing.

Photodynamic therapy in the treatment of periodontal disease

Jodelbaner and Von Tappeiner introduced the term photodynamic in 1904. With it’s targeted action and non-invasive nature this treatment modality has been successfully used for the treatment of many precancerous and cancerous lesions. A typical procedure involves using the photosensitizer that gets localized to the site of action and upon illumination, with the light of wavelength 630-700 nm the photosensitizer turns into the excited state and leads to two types of reaction Type I and Type II reactions in photodynamic therapy. The Type I pathway involves reactions that require a transfer of an electron from the photosensitizer triplet state with the involvement of a substrate to produce radical ions that can react with oxygen to produce cytotoxic species. In Type II pathway energy transfer takes place from the photosensitizer triplet, state to the ground state molecular oxygen (triplet) to produce excited singlet oxygen species, which can lead to oxidation of biological molecules. Birang et al. In their study found that adjunctive laser therapy or photodynamic therapy showed more improvement of CAL gain compared to that of SRP alone, which shows that laser and photodynamic therapy reduces inflammatory mediators like IL-1beta and IL-17 and enhances the clinical symptoms.

Tissue engineering in the treatment of periodontal disease

Melcher introduced the concept of tissue engineering in the field of periodontology, and he introduced the cell barrier principle in 1976. Due to the introduction of guided tissue regeneration in periodontology by Nyman and Karring in 1982 using the barrier membrane...
has raised the evolution of tissue engineering. Gaubys et al. Studies showed a positive influence on periodontal tissue complex regeneration by stem cell therapy. Recent advancement has focused on the development of periodontal ligament attachment around dental implants to replace lost teeth. Similarly, gene therapy where genes are transferred to the desired site by means of vector which can be viral like Retrovirus, Lentivirus, Adenovirus, Adenoassociated virus or non-viral vectors like physical vectors consisting of Electroporation, Gene gun, Ballistic particle delivery; chemical vectors like Cationic polymer diethylamino methyl-dextran, Calcium phosphate co-precipitation, Lipid mediated types like Cationic liposomes, Lipoplexes and as Gene-editing tools like Zinc finger nucleases (ZFNs), Transcription Activator Like Effector-based Nucleases (TALENs) and Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR-Cas9) is being used for controlling the release of growth factor to the defect site so that an appropriate amount of factors are released at the appropriate time and in the production of pluripotent cells, called induced pluripotent stem cells. It is also being used to enhance host modulation to resist disease.\cite{70,71}

**Nanotechnology in the treatment of periodontal disease**

Tanaguchi introduced the term “nanotechnology”. Dr.Richard Phillips Feynman attributed the discovery of nanotechnology. “Nanotechnology is research and technology development at the atomic, molecular or macromolecular level in the length scale of approximately 1-100 nm range, to provide a basic understanding of phenomena and materials at the nanoscale and to form and use structures, devices, and systems that have novel properties and functions due to their little and/or intermediate size”. Various nanoparticles used in the field of periodontology are carbon nanoparticles, Titanium nanotubes coated dental implants, nanoceramics for bone regeneration, nanorobots for oral analgesia.\cite{72}

**New drugs for treating periodontal disease**

Newer drugs like Resolvin are used in periodontal disease, as it lowers the recruitment of neutrophils at the inflammation site and reduces the cytokines and reactive oxygen species and thus reduces inflammation. Other drugs like Adalimumab, Golimumab, anti-cytokine loke Anakinra, Tocilizumab and RANKL inhibitors like Denosumab are also preferable as they induce periodontitis but they are still under study. Reed et al. studied on amixicile a new antibiotic which is a novel inhibitor of pyruvate ferredoxin oxidoreductase. A minimal inhibitory concentration ranging from 0.5-1.5 micrograms per ml has inhibited the growth and other central processes to virulence in an *in-vitro* study.\cite{72}
Ozone therapy has a long history of research with humans along with the clinical application. Joachim Hansler and Hans Wolff developed the ozone generator for medical use. Ozone has been used for the following purposes: 1. Elimination of pathogens. 2. Restoration of proper oxygen metabolism. 3. Induction of a friendly ecologic environment. 4. Increased circulation. 5. Immune activation. 6. Simulation of the humoral anti-oxidant system. Routes of administration are Gaseous ozone, Ozonated water, Ozonized oil.[73] In 2006 Huth et al study has shown that ozone in aqueous form acts as a potential antiseptic agent and shows less cytotoxicity compared to gaseous ozone.[74] Kshitish and Laxman in 2010 performed a randomized, double-blind, split-mouth study. The results showed a higher reduction in plaque index(29%) and bleeding index(26%) using ozone irrigation. Ozone therapy was contraindicated in pregnancy, Autoimmune disorder, Gravis, Alcohol intoxication, CVD, MI, Ozone allergy and Hemorrhage.[75]  

CONCLUSION  
Periodontal diseases comprise a wide range of inflammatory conditions that affect the supporting structures of the teeth (the gingiva, bone, and periodontal ligament), which could lead to tooth loss and contribute to systemic inflammation. Chronic periodontitis predominantly affects adults, but aggressive periodontitis may occasionally occur in children. Periodontal disease initiation and propagation are through a dysbiosis of the commensal oral microbiota (dental plaque), which then interacts with the immune defenses of the host, leading to inflammation and disease. This pathophysiological situation persists through bouts of activity and quiescence until the affected tooth is extracted or the microbial biofilm is therapeutically removed and the inflammation subsides. The severity of the periodontal disease depends on environmental and host risk factors, both modifiable (for example, smoking) and non-modifiable (for example, genetic susceptibility). Prevention is achieved with daily self-performed oral hygiene and professional removal of the microbial biofilm on a quarterly or bi-Annual basis. New treatment modalities that are actively explored include antimicrobial therapy, host modulation therapy, laser therapy, and tissue engineering for tissue repair and regeneration.  

ACKNOWLEDGMENTS  
The authors express their gratitude to the Principal of Vijaya Institute of Pharmaceutical Sciences for Women for providing necessary support in due course of the work.
Conflict of Interest
The author confirms that this article content has no conflict of interest.

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