International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 3 May - June 2021, pp: 815-827 www.ijprajournal.com ISSN: 2249-7781

A Review on Periodontal Disease

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Date Of Submission: 01-06-2021 Date Of Acceptance: 14-06-2021

ABSTRACT: Periodontal disease is wide range of inflammation that affect the supporting structure of teeth (the bone, gingiva and periodontal ligament), which lead to tooth loss, with advances in understand the pathogenesis and etiology of periodontal disease. Chronic periodontitis predominantly affect in teeth and aggressive periodontitis occur in children. Periodontal disease propagation and initiation is dysbosis of commensal dental plaque which interact with immune defence of host leading to disease. In treatment has been optimized for use of drug delivery system to periodontal pocket, delivering drug in the specific site. The severity of periodontal disease depends on host risk factors and environment, both modifiable (smoking, Diabetes Mellitus, Hormonal change in females and stress) and non-modifiable (Genetic Susceptibility). Prevention is achieved with professional removal of microbial biofilm on bi-annual basis or quarterly and daily performed oral hygiene.Periodontal diseases are prevalent both in developed and developing countries and affect about 20-50% of global population. High prevalence of periodontal disease in adolescents, adults, and older individuals makes it a public health concern.

Keyword:-Periodontal Disease, Pathogenesis, Etiology, Drug delivery system.

INTRODUCTION

The periodontitis is ainflammatory disease and chronic bacterial infection that affects the gums (the soft tissue around the teeth), bone and ligament supporting the teeth caused by bacteria resulting in destruction of teeth and bone supporting to teeth. Periodontal diseases is localized inflammation of gingiva or gums that is initiated by bacterial in the dental plaque, untreated gingivitis can advances to periodontitis. With time, plaque can spread and grows below gum line. The chronic periodontitis is oral long lasting inflammatory disease affecting soft and hard tissue, bone around teeth, when it affects >10 of the 32 teeth in the human generalised and localised are involved.In this disease microbial biofilm of dental plaque, environmental and genetic factor influence the rate of disease.(1 2 4 8 17)

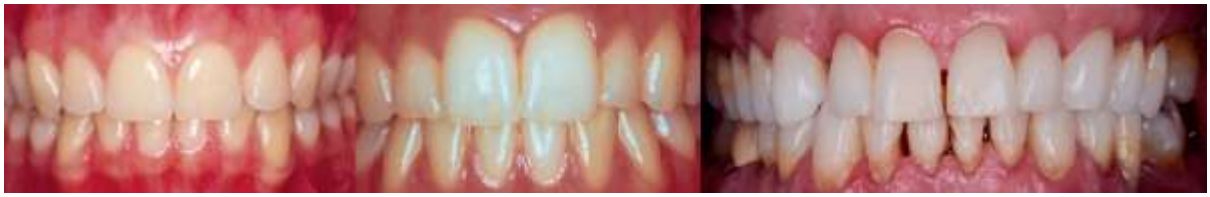

Figure 1 healthy and diseased periodontium.

Chronic periodontitis: it is chronic inflammation mostly irrversible result in loss of epithelial tissue, ligament and bone.

Gingivitis: it is reversible inflammation to the gingiva.

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Peri-implant mucositis: gingivitis occurs around dental implants.

Peri-implantitis: chronic inflammation occur around dental implants and its results in bone loss.

Aggressive periodontitis: it can present in generalized and localized forms, both are chronic periodontal inflammatory disease, typically manifesting between puberty and decade of life. No specific disease biomarkers exist that differentiate chronic periodontitis from aggressive periodontitis.

Necrotizing ulcerative gingivitis and periodontitis: necrotizing are increasingly rare and typically present in debilitated hosts, it is acute forms of periodontal disease which characterized by rapid course and associated with viruses, bacilli or spirochetes particularly anaerobic microbial biofilm.

Syndromic chronic periodontitis: A form of chronic periodontal destruction that is seen as manifestation of systemic disease, commonly associated with major gene defect that affect crucial elements of host immune defence or periodontal structure.(1 11)

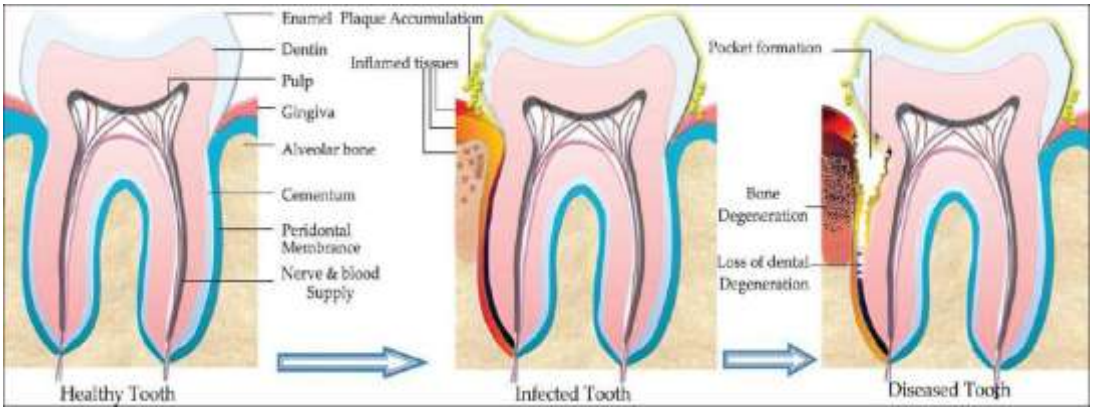

Fig 2. Healthy, infected and diseased teeth.

Prevalence

The periodontitis is oral inflammation is prevalence in children, adults and adolescents. In chronic and aggressive periodontitis vary bias, case misclassification and number of teeth and site examined. The case periodontitis depends on specific thresholds for both disease severity and disease extent are used because consistently no sets of thresholds used in the epidemiological studies. The epidemiological studies used continuous measurement of probing depth and attachment loss shown in periodontitis that result in several tooth loss affect 10-15% of population globally. The estimated prevalent range included insevere chronic periodontitis and severe aggressive in adult (35% to 70%) and overall periodontal disease affects about 20%-50% of population globally. (8 9 10 11 12 13 41).

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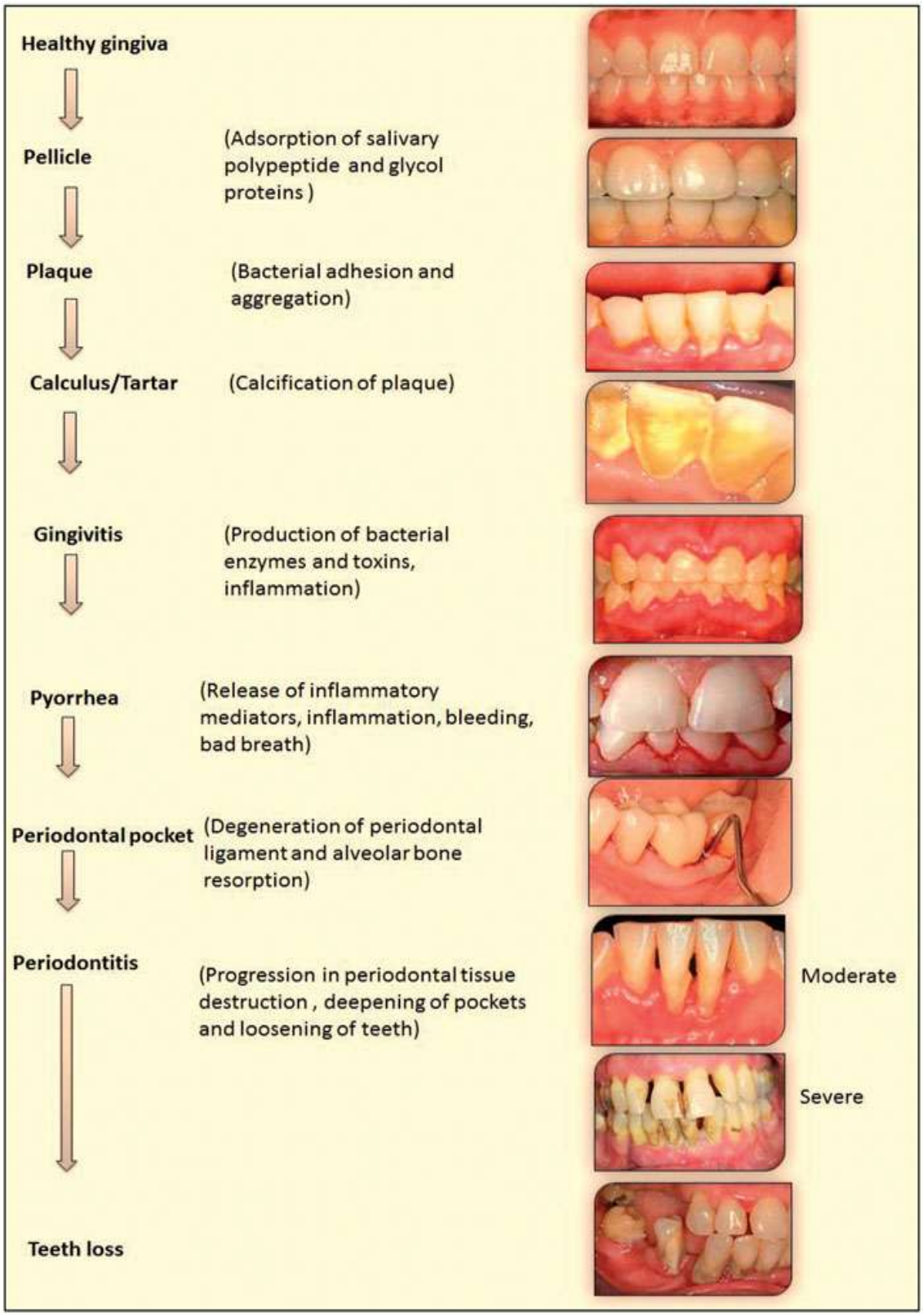

Figure 3: Various phases of periodontal disease.

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Risk factor

The periodontal disease in several risk factor that is modifiable and non-modifiable, the modifiable risk factor in included smoking, diabetes mellitus, poor oral hygiene, hormonal change changes in females, metabolic disease, stress and non-modifiable risk factor in age and hereditary.(2 3 21 35 36)

Modifiable risk factors

Smoking

The chronic periodontal disease in smoking cigarette is major modifiable risk factor and reduction in prevalence in periodontal disease is related drop smoking rate. The smoker having negative side effect of smoking cigarette, cigar, cannabis and pipe it in periodontal status in severe teeth loss and smoker also increase the damage of bone and higher prevalence tooth loss compared with non-smoker. The nicotine shows to cause breakdown of periodontal tissue, the smoking changes microbial flora and increase certain level of microorganism or group of microorganism in periodontal disease. The chronic periodontitis treatment studies shown in inferior outcomes of both in non-surgical and surgical periodontal therapy in smoker compered to non-smoker.(25 1422 28 29 30)

Diabetes mellitus

The diabetes mellitus is prevalent and systemic risk factor can play major role initiation and progression of disease.Diabetes mellitus is associated destruction of periodontal bone and ligaments which can lead tooth loss. The diabetes mellitus in periodontal treatment has been found as giving antidiabetic medication and periodontium manifest at young age affecting children negative effect of diabetes mellitus. Diabetes is leading cause of loss of limbs and diabetes in population over 65 years of age and growing public health associated its major complication.(16 23 24 31 32 33)

Hormonal changes in females

Hormonal changes in women may experience in women gingival inflammation before menstruation period and during the ovulation due to increase level of progesterone, which is block repair of collagen fibre. The estrogen deficiency reducebone density which can be bone loss and falling of teeth. A 42171 women postmenopausal stages intreatment of osteoporosis with estrogen hormonal therapy resulting reduced bone and tooth loss.(2 6 34)

Stress

The dental plaque formation is caused by stress due to clear evidence that stress reduce the flow of salivary secretion. In empirical articles indicated immune system related to stress and different stressful event occur different immunological changes. The cortisol higher concentration in gingival crevicular fluid they poorly respond to treatment of periodontitis. The stress also result in poor oral hygiene. (2 3 45)

Non-modifiable risk factors

Non-modifiable risk factors in the age and hereditary. In advancing age periodontal disease increase that is high prevalence seen in elderly population. In hereditary factors also associated with periodontitis, some people susceptible to disease than other.The complex genetic factor with demographic and environmental has been demonstrate wide variation.(2 3)

Mechanism and pathophysiology

Dental plaque

Chronic gingivitis and periodontitis are sustained and initiated by the microorganism of dental plaque, the microbial film extensively studied and comprise 150 species in a single person and 800 different species have been identified in human dental plaque. The species are particularly virulent and can drive disease onset lasted decade and is not resolved. The putative pathogen include spirochetes, bacteria and even virus but probable that no single pathogen is causative on its dysbiosis. If periodontal disease caused by few specific pathogen the therapeutic strategy targeted alternation of plaque microbiota rather than biofilm removal. (18 1926 27 56)

Microbial biofilm

Periodontal disease have associated with colonization by specific clones of aggregatibateractinomycetemocomitans in cohort studies. Other species include porphyromonasgingivalis have been associated progressive periodontits, but temporality of the microbial biofilm associated are less clearly established. A review conclude that aggressive and chronic periodontitis based on specific periodontal pathogens, a finding that suggest the causative microbial biofilm for similar disease. (18 19 2537 38 39 40)

Calcification

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Dental plaque is present in both in calcified and uncalcified forms; subgingival plaque is typically dark in colour and calcified, supragingival plaque is usually uncalcified and this calculi are more difficult to remove. Calcification of subgingival plaque caused by ions from serum transudate by inflammation in periodontal tissue, where results for supragingival calculus from salivary calcium and phosphate ions that aggregate within the plaque.(42 43 44)

Immunopathogenesis

The pathogenesis for periodontal disease might not be sufficient microbial biofilm. Disease occurs when balance between the microbial biofilm and dysbiosis, host is lost or immune over reaction of the microbial presence host. The imbalance is complex as there remarkable varience in both host genetic and dental plaque and immune system profile and result in inflammatory state lead to tissue damage is observed in periodontal disease.(1 45)

Susceptibility

In chronic periodontitis might reflect susceptibility individual progress to gingivitis in chronic periodontal disease and finding epidemiological studies, furthermore absence of gingivitis is good indicator for maintenance of periodontal on site specific basis. early studies describing experimental gingivitis in man presented evidence that severity and onset of inflammatory response of gingiva to accumulation of dental plaque. However difference attributed to different bacterial species present in microbial biofilm or different plaque accumulation rates. Later studies used same model have documented individual with qualitatively similar dental plaque present in different inflammatory response in its represent indival trail and susceptibility to periodontal disease depend in host genetic factor. The level of inflammatory mediator such as prostaglandin E2, IL-1, tumour necrosis factor correlate extent periodontal damage. High level of mediators in response to dysbiosis will more severe tissue loss, many drugs such asnifidipine, phenytoin and cyclosporine can stimulate gingival overgrowth and modulate pre-existing chronic periodontitis. (1 2 20)

Diagnosis, screening and prevention

Diagnosis

The first challenge in diagnosis treating periodontal disease is timely and accurate, as the loss of soft tissue and periodontal bone is largely irreversible and incremental. The symptoms of gingivitis is a bleeding and pain while brushing is rarely reported. The chronic periodontitis include changed texture, redness and swelling of marginal gingiva and gingival bleeding of in gingival pocket area, increased periodontal pocket depth, destruction of supporting structure of teeth, recession of marginal gingiva, increase drifting and mobility of tooth. Diagnosis of chronic periodontal disease is based on clinical measurement include bleeding in probing, probing depth, clinical attachment level. And additional more information such as family and medical history and specific clinical feature can help distinguish type of periodontitis. An accurate diagnosis require multiple parameter in different location of teeth which results in diagnostic process that depend on expertise examiner. And clinical parameter are best for measure diagnosis can assess the current extent and severity of disease. (1 7 15)

Screening and prevention

The screening for susceptibility is detection of gingivitis in periodontal disease. The prevention of gingivitis primary prevent chronic periodontitis, the prevention is achieved daily oral hygiene and bio-annual basis professional removal biofilm, the dental association recommendations for daily brushing twice in day for 2 minutes with soft toothbrush, every part of mouth cleaning using fluoride toothpaste and having maintaining diet with limited between the snacks. The prevention of disease daily maintain teeth by brushing in two to three time brushing in a day.(1 7 15)

Non-surgical therapy

The expertise removal of subgingival and supragingival dental calculus and plaque with scaling and root planning in non-surgical therapy of periodontitis. The non-surgical clinical outcome is dependent on skill of operator, skill of patient in practicing in home care and patient compliance recommended periodontal maintenance. Non-surgical therapy is effective strategy with no difference in surgical and non-surgical therapy. The root planning and scaling performed ultrasonic instruments or scaler and curettes. The sharp instrument hand scelarswth cutting edge removal of calculus, plaque, subgingival and supragingival. The crucial in periodontal disease used ultrasonic instrument its range is approximately 25000-30000 cycles per second can be used to remove adherent

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deposits from teeth, ultrasonic instrument is achieve improve in clinical parameter and it is effective in altering of subgingival. In scaling and root planning with power driven instrument require substantially less time and these instrument may cause root damage. And root planning and scaling it is completed 4-6 week period is required adequate healing of connective tissue. And non-surgical therapy depending on extent and severity of residual inflammation. (46 54 55)

Adjunctive therapies

The adjunctive therapies in enhance treatment outcomes, it in several adjuncts to non-surgical treatment periodontitis treatment have proposed it include systemic antibiotics, local drug delivery and systemic host modulation agents. (53)

Local delivery of drug

The local delivery of drug in antibiotics such as tetracycline, doxycycline, minocycline and antimicrobial drug such as chlorhexidine is directly delivered to localized treatment by using periodontal pocket like gel, film, fibre, chip, etc. in systematic review studies primary goal in using periodontal pocket for delivery of antibiotics and antimicrobial drug and maintenance therapeutic level of drug for required period of time. That kill bacteria or microorganism, without harm to the tissue. (47 48)

Systemic antibiotics

The systemic antibiotics in type, duration, dosage and timing have been proposed, a broad spectrum antibiotics is used alone or combination with antibiotics targeting gram negative bacteria. In studies evaluated different systemic antibiotics it used in treatment of chronic and aggressive periodontitis concluded that combination of antibiotics like amoxicillin and metronidazole seems to be most potent and resultant improve in clinical probing depth and clinical attachment level gain and reduction bleeding on probing than scaling and root planning. The result of these studies on systemic antibiotics are promising, several treatment aspect such drug, dosage and duration in adjunctive systemic antibiotics treatment and appropriate timing during non-surgical treatment to antibiotics use. All over studies that include tooth loss is end point in addition to the clinical measurement are needed. (47 48)

Surgical therapy

Surgical therapy in open flap procedure in which surgically separated section of gingiva from underlying tissue provide access to the lesion and visibility. Pocket reduction surgery included resection of soft and hard tissue using various technique. Regenerative surgery it includes guided tissue regeneration, grafting and use biologics. Laser assisted new attachment procedure recently introduced conservation alternative to surgical therapy. LANAP uses as Nd:YAG laser for de-epithelialization in initial pocket and final fibre clotting instead of a suture and scalpel and does not include extensive gingival flap elevation. (49 50 51)

Treatment outcome

Long term studies controlled trails evaluating different modalities of surgical and non-surgical periodontal therapy shown all effective in improving clinical diagnostics parameter. When comparing non-surgical and surgical therapy the disease progression breakdown rate was lower for surgical therapy, especially on posterior multi rooted teeth. In fact surgical access to diseased teeth enables more accurate determination of prognosis; thus teeth worse prognosis may be extracted in initial surgery, in results better long term prognosis for remaining teeth. The appropriate maintenance of teeth and patient compliance with recommended for interval periodontal maintenance session were key factor that contributed long term stability of disease and its treatment success. In the majority of surgical periodontal therapy and non-surgical, healing occur formation of long junctional epithelium or connective tissue attachment to disease root surface. The regenerative surgical procedure have potential to induce restoration of lost periodontal ligament, cementum and aloveolar bone.In systemic review guided tissue regeneration it concluded that regeneration in furcation defects and intra-bony defects is possible on previously diseases sites as an evidenced by clinical attachment gain, radiographic bone fill and probing depth reduction, these outcome better than obtained open flap debridement alone. Another systematic review on periodontal regeneration in finding and future added that intra bony defects, the use of biologics results in clinical improvement is comparable with obtained bone replacement grafts and guided tissue regeneration. LANAP has potential improve clinical outcome as shown in clinical evaluation, however randomized controlled studies are evaluate the long term efficiency of

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procedure compared current established surgical and non-surgical approaches. (52 53 54 55 56 57)

Periodontal maintenance

The periodontal therapy has control disease progression and reduce tooth loss. The successive periodontal therapy is dependent on appropriate maintenance after treatment has been completed. In periodontal maintenance consist of removal of subgingival and supragingival dental plaque and is performed regularly in life. In generally maintenance interval is 3 month in patient treated for chronic periodontitis has been shown appropriate to long term success by disturbing the microbial biofilm before it pathogenic. The maintenance interval dependent on patient susceptibility and presence and absence of patient risk factors, such as diabetes mellitus, smoking or the ability to perform adequate home care. The periodontal therapy aims to maintenance long term periodontium, occlusion, dentition, oral aesthetics and mandibular. This therapy phase is challenging as it relies again patient motivation and adherence to strict recall interval. In patient population trated in a private practice, compliance with recommended recall interval was approximately 50% patient trated for chronic periodontitis and compliance was achieved complete is <20%. (52 53 54 55 56 57)

Various Approaches to treat periodontitis

In periodontal disease tartar and plaque are removed from teeth, gingivitis can treated simply. In routine dental procedure more serious cases of periodontal disease cannot be treated.Dental surgery may be necessary to remove tartar, plaque and infected gums disease. Surgical access to mechanical instrumentation of roots has utilized to treat chronic periodontitis. Appropriate therapy for patients with extent and pattern of local anatomical variation, attachment loss, therapeutic objectives and type of periodontal disease.

1 Conventional periodontal therapy

The purpose of the periodontal treatment is reduce the number of pathogenic bacteria, cure the inflamed tissue and elimination the depth of diseased pockets and stop bone resorption. The conventional method of pocket elimination are less or more mechanical and aim to removal of supra and plaque and necrotic tissue lining the gingival wall of periodontal pocket through root planning and scaling. The ability of microorganism to penetrate deeper tissue. Re-colonization and inaccessibility of pathogen can occur in root planning and scaling with oral hygiene. The single periodontal session after pathogenic sub gingival microbial may re-establish within 42-60 days. (53 63)

2 Antibiotic systemic therapy

In periodontal disease treatment use of antibiotics helps to eliminate or reduce bacteria that cannot be removed by scaling and root planning.Fluoroquninolones, imidazole, tetracycline derivatives etc. are most favoured antibiotics. Chemotherapeutic agent can administered locally and systematically.

Antimicrobial drugs used to treat dental infection and it can be divided into two categories i.e. narrow spectrum and broad spectrum. Narrow spectrum antimicrobial drug are having limited antimicrobial efficiency, they are not effective against aerobic and anaerobic betalactamase producers as well as other specific organisms. Narrow spectrum antimicrobial include amoxicillin, penicillin, macrolides,teteracyclines and cephalexin. Systemic periodontal antimicrobial therapy based on premise that specific microorganismcause periodontal disease and antimicrobial agent in periodontal pocket can kill the pathogens. One disadvantage of systemic antibiotics is needed to treat periodontal disease is high, because the concentration that reaches the periodontal tissue after systemic ingestion is low, systemic antibiotics to treat disease has contribute to level of antibiotics resistance worldwide. (53 62 63)

3 local drug delivery

Locally applied antimicrobial agents enable targeted use antimicrobial with a lower dose than would be required given systemically and release the antimicrobial agent in controlled manner or above minimum inhibitory concentration over period of several days. In addition to effective at lower dose and no antibiotics resistance has been found use of locally applied periodontal disease or antimicrobial agents. Local application control only supra gingival microbial plaque involving pocket formation and also require high initial concentration and multiple application in order to provide sustained effectiveness.Local application in incorporating drug into different device for insertion into periodontal pocket. Many drug like tetracycline, chlorhexidine are used in mouth rinse in treatment of periodontal disease. Local drug delivery device are two types in first type the drug

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delivery system is designed to locally deliver in periodontal pocket without mechanism to prolonged period of time. Such device increase on exponential and decrease in drug concentration at site. Second type controlled release local drug delivery device which many antimicrobial effect at diseased site prolonged period of time.that can be achieved local and systemic application. These delivery system are by produced antimicrobial and antibiotic with carrier to provide controlled local release. (62 63)

4 controlled release local delivery devices

These device controlled release technologies to assure therapeutic concentration of antimicrobial agent in sub gingival area for long period following single application. A wide variety of specialized local drug delivery have been designed maintain drug concentration in gingival crevicular fluid. Drug delivery system can be classified in three categories according to mechanism of controlling the drug release.

i solvent controlled matrix system are based on macromolecular matrix permeability to small molecules after matrix swelling into hydrated medium.

iiReservoir system are controlled by drug diffusion across a polymeric membrane.

iii chemically control system in which the rate of drug release is controlled by rate of degradation of chemical bonds and erosion of polymeric matrix.

Several studies have evaluated use of antibacterial and antimicrobial agent in periodontal therapy such as sulphonamide, iodine, phenolics and antibiotics such as minocycline, doxycycline, tetracycline, chlorhexidine, metronidazole, ciprofloxacin, clindamycin, ofloxacxin and azithromycin etc. (63)

Drug delivery devices

The application methods are available intrapocket drug delivery devices for the treatment of periodontitis.

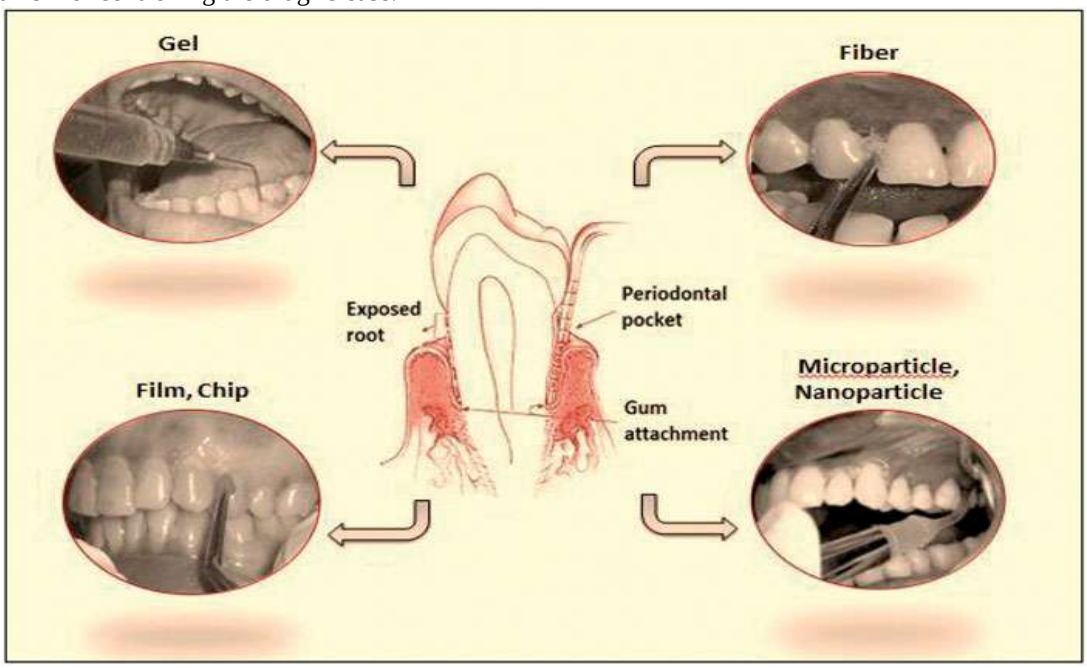

Figure 4: Application methods for intrapocket drug delivery devices.

Fiber

Fibers are reservoir-type, thread-like drug delivery systems. They are placed into the pockets using applicator and sealed in placed by applying cyanoacrylate adhesive. Theprovide sustained release entrapped drug into the pockets, the drug simply diffused out through reservoir system into the pocket. The single application of fibres helped in freeing the spirochetes and gingival sulcus effectively. Hollow fibre allowed rapid emptying of drug. The matrix type of fibre was developed by drug incorporating in polymers with spinning high temperature followed by cooling. But major disadvantage of nonbioabsorbable and replaced by new ones after exhaustion.Nonbiodegradable ethylene vinyl acetate fibres are available with actisite. Other polymers utilized so include nylon, chitosan, polycaprolactone, collagen and chitosan. Several drug loaded fibre used for treatment of periodontitis.

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In this devices improvement of clinical parameters was observed, the process of fiber insertion was time consuming. Also patients were discomforted during placement of system. The fibre placed in pocket its retention in place throughout the course and removal of weekly basis and both patient proved troublesome. (58 59 60)

Strip

Strip is thin, elongated matrix band made of flexible polymer having a securing mechanism, a wide range of interproximal spacing and drug dispersed throughout the polymer. A number of researcher worked on strips made of acrylic polymer using single or combination of drugs. But some demerits associated with acrylic strips. Pressure melt method and solvent casting method used for fabrication of stripes. The strips significant improvement in various clinical signs by effective microbial. Nonbioabsorable nature of strip removed after therapy which impair the regenerating tissue at site. The surface of strip dissolves in physical properties of acrylic strip in serum. Also material has been found to disintegrated during preparation. All factor collectively a risk of leaving injuries acrylic material in periodontal pocket during removal of strip. (58 61)

Films

Film are commonly used for drug delivery, these matrix drug delivery devices of drugs distributed throughout the polymer and drug released by matrix dissolution or diffusion or erosion. The method of preparation of films includes direct milling or solvent casting method. The film are cut into dimension are suitable to insertion to the pocket, film placed in cavity onto the surface of gingiva or mucosa. Films have many merit like less discomfort to the patient, easy insertion. Those with adequate adhesiveness and thickness less than 400 um are not easily dislodged by daily oral hygiene routine followed by patient. Films composed of water insoluble or nondegradable polymer drug release by only diffusion and water soluble or biodegradable polymer release by diffusion or dissolution or matrix erosion. Ethyl cellulose films incorporating number of drug like metronidazole, minocycline and tetracycline. Sustained release rates depending on drug load and solvent casting were obtained. Disadvantages of nonbiodegradable led to its replacement by biodegradable polymer. Several drug loaded films used for treatment of periodontitis. (62)

Gels

Gels are semisolid device that came in lie light for targeted delivery. The advantages of semisolid device is easy to prepare and administer, they have faster drug release rate and also they are more biocompatible and bioadhesive, easily adhere mucosa in dental pocket. The risk of allergic host reaction or irritating at the site of application is less in case of gels. Desirable result have been obtained number of hydrogels and oleogels for delivery of metronidazole, tetracycline. Hydrogel are hydrophilic polymeric networks consisting 3D cross linked structure of hydrogen bonding and ionic interaction.This network is nonporous, macro porous or micro porous. Various polymer like PLGA, pluronic, collagen, chitosan are used for preparation of gel dosage form. The liquid state room temperature of gel at 34-37 C. the sol obtained agreeable taste, syringability was thermo reversible and controlled drug release to gel in periodontal pocket. (58)

Micro particle

The micro particle are solid spherical polymeric structure containing drug dispersed throughout the polymeric matrix. They are free flowing powder and provide controlled and sustained drug release at target site. Many biodegradable or non-biodegradable matrials including polmers from are used. They used dental paste, chip or directly injected into the pocket. Microparicle are number of advantages like controlled drug release, improved patient compliance, sustained therapeutic effect, enhance bioavailability and decrease frequency. (58 62)

Nanoparticle

Nanoparticle made around the globe for making delivery system suitable and more effective. In micro particle based hydrogel used so far in drug release was affected by their structure. Certain factor make nanoparticle more advantageous than micro particle, microspheres delivery systems. The solid particles having size ranges 10-1000nm. The drug is dissolved, encapsulated, entrapped or attached to nanoparticle matrix. They are highly dispersible in aqueous medium, enhanced stability and controlled release rate. A uniform drug distribution for prolong period of time is obtained and decreasing dosage frequency. (58 62)

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System	Polymer matrix	Drug Incorporated
Fibers	cellulose acetate	Tetracycline HCL
		Chlorhexidine
	Ethylene vinyl acetate	Tetracycline HCL
Strip	Polyethylmetha acrylate (acrylic)	Tetracycline HCL
		Metronidazole
	Hydroxypropyl cellulose	Doxycycline, tetracycline
		Chlorhexidine
	Ethyl cellulose	chlorhexidine
Films	Ethyl cellulose	metronidazole, minocycline
	Cross linked atelocollegen	tetracycline
	Gelatin	chlorhexidinediacetate
	Cross linked gelatin + glycerine	chlorhexidinedigluconate
	Chitosan	Taurine
	Chitosan + PCL	Metronidazole
	Chitosan + PLGA	Iproflavone
	Eudragit	clindamycine
Gels	chitosan	metronidazole
	HEC + polyvinylpyrrolidone	tetracycline
	HEC + polycarbophil	metronidazole
	PLGA	tetracycline
	Poloxamer 407 + Carbopol934P	Propolis
Microparticle	Pluronic F 127	Tetracycline
	PLGA + PCL	Doxycycline
	PLGA	tetracycline
Nanoparticle	Chitosan	Antisense oligonucleotide
	PLGA	Triclosan

ACKNOWLEDGEMENT

The Authors thanks for giving support and proper direction for making successful research work and also help to find new information for making review article. We would also like to thanks Sanjivani College of Pharmaceutical Education and Research Kopargaon, Maharashtra-42363, India. For Providing required facilities to carry out this Research work.

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International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 3 May - June 2021, pp: 815-827 www.ijprajournal.com ISSN: 2249-7781

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