DRUGS AND PERIODONTIUM A REVIEW

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ABSTRACT

Effective periodontal therapy involves a comprehensive mechanical therapy and specific antimicrobial coverage. Use of various chemotherapeutic agents in conjunction with mechanical instrumentation provides an additional beneficial effect, offering an increased opportunity to control disease. Host modulation is an emerging avenue in the use of chemotherapeutic agents.

Medications such as the anticonvulsants, antihypertensives, NSAIDs, immunosuppressants etc which have become quite common in the treatment of the multitude of lifestyle associated diseases have a profound influence on the periodontium and this influence should be understood and appropriate care has to be taken while administering these drugs. Finally, the recognition of the beneficial activity of several groups of commensal species such as probiotics might open new strategies for periodontal therapy.

This article gives an overview of the various drugs that are used in our day today lives and their influence on periodontium.

Key words: Drugs, Periodontium, antimicrobial.

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INTRODUCTION

The adult population is living longer and retaining their teeth in old age. A major part of this increase in life expectancy is attributed to an expansion in our understanding of disease processes and the subsequent explosion in drug treatments. Some of these drugs will have an impact on the periodontium and its response to bacterial plaque.

Effective periodontal prevention and therapy includes professional debridement, supragingival and subgingival antiseptics, adequate oral hygiene, specific antimicrobial coverage. However, it seems necessary to employ additional or alternative antimicrobial strategies or surgical access to effectively debride deep periodontal lesions. Incorporation of an appropriate chemotherapeutic agent in conjunction with mechanical instrumentation provides an additional antimicrobial effect offering increased opportunity to control disease. This paper reviews the various possible interactions between a patient's medication and their periodontium in both health and disease.[1]

Common Drugs Influencing the Periodontium

The effect of systemic drug therapy on the periodontium can cause an adverse effect on the periodontal tissues or afford some degree of protection against periodontal breakdown or can lead to an increased risk of periodontal breakdown. The different types of drugs that affect the periodontium include Antihypertensives, Immunosuppressants, Anticonvulsants, Non Steroidal Anti Inflammatory Drugs, Antibiotics, Corticosteroids and Hormonal replacement therapy.

Anticonvulsants, Antihypertensives, Immunosuppressants

A number of medications may cause gingival enlargement. In addition, fibrotic gingival enlargement has been reported and is believed to be the result of a genetic predisposition. Of the predisposing factors associated with gingival overgrowth, selected anticonvulsant drugs, calcium channel blockers and a potent immunosuppressant (cyclosporine A) have generated the most investigative attention in the scientific community.

These agents may reduce cytosolic calcium levels in gingival fibroblasts and T cells, thus interfering with T cell proliferation or activation and collagen synthesis by gingival fibroblasts. The gingival overgrowth results from overproduction of extracellular ground substance characterized by increased presence of sulphated-mucopolysaccharides and collagen, and abundant active fibroblast[2].

Dill et al.[3] have proposed that phenytoin increases the production of platelet-derived growth factor, and that excessive platelet-derived growth factor production would mediate gingival overgrowth. Also it may interfere with folic acid absorption and metabolism. As a result of its role in DNA synthesis, tissues with higher turnover rates are often affected first. In summary, evidence suggests a direct effect on specific subpopulations of fibroblasts, genetic predisposition, intracellular calcium metabolism exchange, molecular mechanisms (cytokines such as epidermal growth factor, platelet-derived growth factor- P), inactivation of collagenase and inflammation induced by bacterial plaque.

Phenytoin-induced gingival overgrowth is characterized by initial enlargement of the interdental papillae, and is less frequently accompanied by increased thickening of the marginal tissue. Affected tissues typically present a granular or pebbly surface, with the enlarged papillae extending facially and or lingually, obscuring the adjacent tissue and tooth surfaces.

Affected papillae may become enlarged to the point that they contact, resulting in the clinical presence of pseudoclefts. Gingival enlargement has also been associated with a number of calcium channel blockers, including nifedipine, verapamil, diltiazem, amlodipine and, to a lesser extent, isradipine. This research supports the concept that alteration of the intracellular calcium level in gingival cells by nifedipine, in combination with appropriate local inflammatory factors, is important in eliciting gingival enlargement.

It also has been shown that in patients unable to discontinue nifedipine use, gingival enlargement did not recur after gingivectomy when thorough plaque control was carried out – again supporting earlier

findings of the role of inflammation and plaque. The interdental papillae are initially affected, becoming enlarged and resulting in a lobulated or nodular morphology. These effects are limited to the attached and marginal gingiva, and are more frequently observed anteriorly, especially on the facial surfaces. The enlarged gingival tissues are often accompanied by inflammatory changes associated with poor plaque control. The gingival overgrowth results from overproduction of extracellular ground substance characterized by increased presence of sulphated-mucopolysaccharides and collagen, and abundant active fibroblasts [2].

Gingival enlargement also has been reported with cyclosporine, with an incidence of approximately 25%. In reviewing cases of patients with gingival enlargement from the above medications, it has been noted that enlargement is most severe in plaque retention areas and in tissue around periodontal pockets. The enlarged gingival tissues were soft, red or bluish-red, extremely fragile and bleed easily upon probing.

These enlarged tissues are generally more hyperaemic than the gingival tissues associated with phenytoin-induced overgrowth. Synergistic effects have been reported when cyclosporine A is administered concurrently with calcium channel blockers of the dihydropyridine derivatives (such as nifedipine)[2] . Pernu et al [4] found that patients who expressed HLA-DR1 appeared to have a protective role against gingival overgrowth from cyclosporine A, whereas those expressing HLA-DR2 showed an increased risk for overgrowth. However, many aspects of connective tissue homeostasis may serve as targets for drug-induced gingival overgrowth, and the response of the connective tissue may be the main cause of this diseased condition. [5]

Non Steroidal Anti Inflammatory Drugs

Non steroidal anti-inflammatory drugs are drugs with analgesic and antipyretic effects and anti inflammatory effects. NSAIDS inhibit the formation of prostaglandins, including PGE2, which is produced by neutrophils, macrophages, fibroblasts & gingival epithelial cells in response to the presence of lipopolysaccharide. Research shows that the periodontal benefits of taking long term NSAIDs are lost when patients stop taking the drugs, with a return to, or even an acceleration of, the rate of bone loss seen before NSAID therapy which is known as the "Rebound Effect"[6] .

The new COX-2 inhibitors have all the attributes of NSAIDs with a reduced risk of unwanted effects. These drugs have been evaluated as an adjunct to root surface instrumentation in patients with chronic periodontitis [7]. The results showed little clinical benefit of COX-2 inhibitors in the management of such patients, but significant reductions in gingival tissue levels of PGE2 and PGF2 [8]. Since bleeding on probing is considered to be indicative of periodontal disease, a false-positive may occur in patients taking oral anti-coagulants, antithrombic agents, non-steroidal anti-inflammatory drugs, or those taking aspirin daily in doses as low as 81mg [9].

ANTIBIOTICS

Selection of an appropriate antibiotic follows a diagnosis and clinician's decision to incorporate chemotherapeutics into treatment. Studies enrolling patients characterized as having refractory or recurrent periodontitis found systemic tetracycline and doxycycline, in conjunction with scaling and root planing, significantly reduced probing pocket depth and resulted in increased attachment gain relative to scaling and root planing and placebo[10]. Such improvements were likely due to the elimination or severe repression of A. actinomycetemcomitans in the infected site.

Hence, systemic administration of the tetracyclines may yield benefits in patients with localized aggressive periodontitis and in some patients refractory to previous mechanical therapy. However, there currently seem to be better choices of an antibiotic for systemic use. Amoxicillin, a semisynthetic penicillin is absorbed well following oral administration, and penetrates into the gingival crevicular fluid. Unfortunately, amoxicillin is highly susceptible to bacterial b-lactamases which hydrolyzes the b-lactam ring, thus destroying all antimicrobial activity of the penicillin.

As a result, amoxicillin's use as an adjunct to periodontal therapy has been limited. Augmentin, combines the antibiotic amoxicillin with a b-lactamase inhibitor, clavulanic acid which can be used as an adjunct to periodontal therapy. Azithromycin demonstrates good in vitro activity against Aggregatibacter actinomycetemcomitans and Porphyromonas gingivalis[11]. The fact that metronidazole specifically targets obligate anaerobic bacteria makes it an attractive antibiotic for use as an adjunct to periodontal therapy. Metronidazole readily penetrates into the gingival crevicular fluid[12] and achieves concentrations in excess of the minimum inhibitory concentrations established in vitro for most putative periodontal pathogens [13].

The adjunctive use of metronidazole/ciprofloxacin in periodontal therapy may be useful under certain circumstances. It is highly unlikely that metronidazole/ciprofloxacin would provide significant additive benefit in the treatment of periodontitis due to classical gram-negative anaerobic pathogens. The combination of metronidazole with amoxicillin /clavulanate does not offer any real advantage over metronidazole /amoxicillin in the vast majority of periodontal cases. [14]

Oral contraceptives and Hormonal replacement therapy

Hormones are specific regulatory molecules that modulate reproduction, growth and development and the maintenance of internal environments as well as energy production, utilization and storage[15].

Researchers have shown that changes in periodontal conditions may be associated with variations in sex hormones. Under the broad category of dental plaque induced gingival diseases that are modified by systemic factors, those associated with the endocrine system are classified as puberty, menstrual cycle and pregnancy associated gingivitis.

Estrogen receptors are found on periosteal fibroblasts, scattered fibroblasts of the lamina propria, and also periodontal ligament fibroblasts and osteoblasts.[16] They decrease keratinization while increasing epithelial glycogen that results in the diminution in the effectiveness of the epithelial barrier, increase cellular proliferation in blood vessels and increases the amount of gingival inflammation with no increase of plaque. Menopause usually begins between 45 and 55 years of age unless accelerated by hysterectomy and/or ovariectomy.

The levels of estrogen that have inhibitory effects on osteoclastic function begin to drop mainly during the late follicular and luteal phase of the menstrual cycle when women approach menopause. The effects of reduced estrogen levels on epithelial keratinisation along with decreased salivary gland flow may have other significant effects on the periodontium. Women may demonstrate menopausal gingivostomatitis and the clinical signs of this disease are drying of the oral tissues, abnormal paleness of the gingival tissues, redness and bleeding on probing and brushing. Oral discomfort is also commonly reported by postmenopausal women with burning sensation, xerostomia and bad taste.

The postmenopausal period is associated with an increased risk of osteoporotic fractures, myocardial infarction, menstrual cycle disorders, hot flushes, night sweats, vaginal dryness. The most significant problem that develops during menopause is osteoporosis[7]. The incidence of periodontitis also correlates with signs of generalized osteoporosis. It is also reported that skeletal bone mineral density is related to interproximal alveolar bone loss and, to a lesser extent, to clinical attachment loss.

CORTICOSTEROIDS

Long-term use of corticosteroids, such as methyl prednisolone and prednisone, may result in osteoporosis, which is seen mainly in long bones but also can occur in alveolar bone. Prolonged therapy with corticosteroids may favor osteoporosis, which is now regarded as a risk factor for periodontal disease. When steroids are injected directly into the gingival tissue, they cause a histological reduction in capillary permeability, a reduction in plasma cells and granulation tissue, an inhibition of collagen synthesis and a clinical improvement in hemorrhagic and hypoplastic gingivitis. When steroids are injected directly into the gingival tissue, they cause a

histological reduction in capillary permeability, a reduction in plasma cells and granulation tissue, an inhibition of collagen synthesis and a clinical improvement in hemorrhagic and hypoplastic gingivitis.[1]

Drugs affecting oral hygiene

As salivary flow decreases, these patients accumulate excessive amounts of plaque biofilm on their teeth which contain not only periodontal pathogens, but also caries pathogens[13]. Some of the more common groups of medications that cause xerostomia are cardiovascular medications (antihypertensives, diuretics, angiotensin-converting enzyme inhibitors, calcium channel blockers); antidepressants; sedatives; centrally acting analgesics; anti-Parkinson medications; and anti-allergy medications.

Xerostomia is a concern because saliva plays a major antimicrobial role in protecting both the soft and hard oral tissues. Because of their tendency to accumulate excess plaque biofilm, patients with xerostomia require not only frequent recall intervals but also careful evaluation of the occurrence of root surface and recurrent caries. Detection of these forms of caries can easily be incorporated into the scaling and root planning phase of periodontal therapy as well as periodic recall visits. [17]

CONCLUSION

Mechanical debridement with scaling and root planning can reduce total supragingival and subgingival bacterial masses but the major periodontal pathogens may persist. Systemic antibiotic therapy is administered to reinforce the mechanical periodontal treatment and support the host defense system in overcoming the infection by killing subgingival pathogens that remain after conventional mechanical therapy.

In reviewing cases of patients with gingival enlargement, the author has noted that enlargement is more severe in plaque retention areas and in tissue around periodontal pockets. Therefore, elimination of plaque retention areas is essential in these patients. The pathogenesis of periodontal disease involves a complex interplay between bacterial pathogens and the host tissues. Adjunctive host modulation, although only an emerging area of interest may prove to be promising in the treatment of patients with aggressive periodontitis as well as periodontitis that is refractory to treatment. Finally the recognition of the beneficial activity of several groups of commensal species such as probiotics, might open new strategies for periodontal therapy.[18]

Clinical Significance

It is evident that periodontal tissue is susceptible to a range of systemic medications. Such drug therapy can produce unwanted effects (e.g. gingival overgrowth), and reduce or increase the expression of periodontal disease. As far as antibiotics are concerned the increasing resistance of the periodontal pocket microbiota must remind clinicians to restrict the use of antibiotics to exceptional cases.

Local antibiotics may be of significance when relapse of periodontitis occurs and/or when surgical reintervention conflicts with the patient's emotions. The periodontium may also be the target of adverse reactions. This emphasizes the importance of regular medical and drug histories and thorough oral and periodontal screening for all patients.

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