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Treating Patients with Drug-Induced Gingival Overgrowth

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The purpose of this paper is to review the causes and describe the appearance of drug-induced gingival overgrowth, so that dental hygienists are better prepared to manage such patients. Gingival overgrowth is caused by three categories of drugs: anticonvulsants, immunosuppressants, and calcium channel blockers. Some authors suggest that the prevalence of gingival overgrowth induced by chronic medication with calcium channel blockers is uncertain. The clinical manifestation of gingival overgrowth can range in severity from minor variations to complete coverage of the teeth, creating subsequent functional and aesthetic problems for the patient. A clear understanding of the etiology and pathogenesis of drug-induced gingival overgrowth has not been confirmed, but scientists consider that factors such as age, gender, genetics, concomitant drugs, and periodontal variables might contribute to the expression of drug-induced gingival overgrowth.

When treating patients with gingival overgrowth, dental hygienists need to be prepared to offer maintenance and preventive therapy, emphasizing periodontal maintenance and patient education. The affected gingiva presents a bulbous and irregular appearance and requires special modifications in the delivery of dental hygiene care. Dental hygienists play a vital role in the prevention and control of this condition because of the significant correlation between plaque/gingivitis and gingival overgrowth.

Keywords: Gingival overgrowth, cyclosporine, calcium channel blockers, phenytoin, dental hygiene care, oral hygiene instructions, periodontal maintenance

Introduction

Patients affected by a variety of medical conditions may require modifications in dental care. One such example is when the patient's gingival tissues show signs of drug-induced overgrowth. Because the texture and appearance of the affected gingiva may be irregular and bulbous, patients with gingival overgrowth may require special modifications in the delivery of dental hygiene. Dental hygienists should be properly prepared to provide treatment and to suggest individualized oral hygiene instructions for these patients.

Dental hygienists play an important role during the review and update of the patient's medical history. A thorough review of the patient's medical history, including prescription and over-the-counter medications, provides critical information about conditions that may be observed during the oral examination. For instance, patients reporting a diagnosis of high blood pressure may have been prescribed a calcium channel blocker to control the hypertension. These medications can

produce a number of oral side effects such as xerostomia and gingival overgrowth. The prevalence of this occurrence has been reported as high as 38%.^{1,2}

The purpose of this paper is to review the causes of drug-induced gingival overgrowth and to describe the appearance of this condition so dental hygienists are prepared to readily identify it. Treatment modifications that may be necessary when treating patients with gingival overgrowth are presented, with major emphasis on prevention through patient education.

Clinical Appearance of Gingival Overgrowth

While performing an examination of the oral mucosa, dental hygienists may observe a granular and pebbly gingiva, as in the patient from Figure 1, who was taking cyclosporine. This unsightly appearance has been referred to as “resembling clusters of grapes,” as the outer surfaces appear dotted with numerous smaller papillations.^{3,4} Biopsies of affected tissue usually show lobules of fibrous connective tissue covered with stratified squamous epithelium. The appearance of gingival overgrowth can cause significant personal and psychosocial problems for patients who often feel uncomfortable when smiling. An example of the appearance of severe gingival overgrowth on a patient taking a combination of cyclosporine and amlodipine (Norvasc) is illustrated in Figure 2. Butterworth states that the clinical manifestation of gingival overgrowth can range in severity from minor variations to complete coverage of the teeth, and that drifting of the teeth can occur, creating subsequent functional and aesthetic problems for the patient.⁵

Figure 1.
Gingival overgrowth on a patient who has been taking cyclosporine for six months.



Figure 1. Gingival overgrowth on a patient who has been taking cyclosporine for six months.

Figure 2.

Severe enlargement of the interdental papillae on a patient taking the immunosuppressant cyclosporine and the calcium channel blocker amlodipine.



Figure 2. Severe enlargement of the interdental papillae on a patient taking the immunosuppressant cyclosporine and the calcium channel blocker amlodipine.

Etiology of Drug-Induced Gingival Overgrowth

Gingival overgrowth is caused by three categories of drugs: anticonvulsants, immunosuppressants, and calcium channel blockers. These drugs are sometimes taken for the remainder of a patient's life because of chronic health conditions being treated, such as organ transplantations. A clear understanding of the etiology and pathogenesis of drug-induced gingival overgrowth has not been established.⁶ The three different classes of drugs that produce gingival overgrowth might share some common metabolic pathway, or they could produce a similarly appearing clinical condition from totally different mechanisms. Some theories have focused on the direct effects of the drug or its metabolites on specific gingival cells of the periodontium, particularly on gingival fibroblasts. Spoildorio et al. reported that as the severity of overgrowth increases, there are parallel increases in collagen and fibroblasts and a decrease in blood vessel content, possibly explaining the light pink appearance of the enlarged gingival tissue.⁷

Seymour et al.⁴ concluded that the following factors might contribute to the expression of drug-induced gingival overgrowth:

Genetics

Age

Gender

Concomitant Medication

Drug Variables

Periodontal Variables

Genetics, gender, and age are factors that cannot be modified. Drug combinations, such as therapy with immunosuppressants and calcium channel blockers, are often necessary and can result in additive effects.⁷ Drug variables such as dose, serum, tissue, and salivary concentrations of the medication suggest that the effect could be dosage-dependent but that, in order for a drug to be effective, it must reach certain threshold levels. A reduction in the dose of medication is not warranted just to prevent the adverse side effects.

There appears to be a significant correlation between plaque/gingivitis and gingival overgrowth.⁶ However, Thomason et al. questioned whether the gingival overgrowth is the cause or the result of the increased inflammation and plaque levels.⁸ In a study of the prevalence and risk of gingival overgrowth in patients treated with anticonvulsant drugs, Brunet et al. found that gingival inflammation is a significant risk factor for gingival overgrowth in these patients.⁹ Periodontal variables, in contrast to the previously mentioned factors, may be modified and controlled. Therefore, oral health care professionals play an important role in the prevention and control of this condition because of the significant correlation noted between plaque/gingivitis and gingival overgrowth.^{4,6,10}

Medications That Cause Gingival Overgrowth

Calcium Channel Blockers

Calcium channel blockers are used for the treatment of many cardiovascular disorders, including angina, arrhythmias, hypertension, and acute myocardial infarction. They are considered first-choice anti-hypertensive drugs for patients who also exhibit problems with angina or peripheral vascular disease.¹¹ Table I lists the most frequently prescribed calcium channel blockers, the most common side effects of which include headache, dizziness, facial flushing, edema, and gingival overgrowth.^{12,13} A direct relationship between plasma concentration of the drug and the degree of gingival enlargement does not seem to exist, but the prevalence of gingival overgrowth with the use of calcium channel blockers has been reported as high as 38%.^{2,12}

Table I. Commonly used calcium channel blockers that cause gingival overgrowth.^{12, 13}

amlodipine	Norvasc ^a
diltiazem	Cardizem ^b
felodipine	Plendil ^c
isradipine	DynaCirc ^d
nicardipine	Cardene ^e
nifedipine	Procardia, ^f Adalat ^g
verapamil	Calan ^h
manidipine	Iperten ⁱ

a. Pfizer Inc., Parsippany, NJ 07054

b. Marion Merrel Dow Inc., Kansas City, MO 64114-0480

c. Merck & Co., Inc., West Point, PA 19486

d. Sandoz Pharmaceuticals Corp., Dorsey Div., Sandoz Div., East Hanover, NJ 07936

e. Syntex Puerto Rico, Inc., Humacao, Puerto Rico 00791

f. Pratt Pharmaceuticals Div., Pfizer Inc., New York, NY 10017-5755

g. Miles Inc., Elkhart, IN 46515

h. G.D. Searle & Co., Chicago, IL 60680-5110

i. Takeda Pharmaceuticals North America, Inc., Lincolnshire, IL 60069

In calcium channel blocker-induced gingival overgrowth, the onset of gingival enlargement is commonly noticed between the first and second months of drug therapy. The severity of enlargement is usually greater in the anterior of the mouth, as in the patient in Figure 3 who is taking nifedipine (Procardia®, Adalat®). This severity is usually greater with nifedipine (20% to 30%) than with other calcium channel blockers.^{14,15} Several clinical studies show that patients taking nifedipine are at a high risk for gingival overgrowth, and that gingivitis acts as a factor that predisposes patients to develop gingival overgrowth when they are taking calcium channel blockers.^{10,14, 15}

Figure 3.
Gingival overgrowth aggravated by plaque accumulation
on a patient taking nifedipine.



Figure 3. Gingival overgrowth aggravated by plaque accumulation on a patient taking nifedipine.

Anticonvulsants

Phenytoin, known better by its brand name Dilantin® (Parke-Davis Company), has been widely used to control convulsive disorders since 1938, when it was first used as an anticonvulsant/antiepileptic drug. Scientists have developed other drugs for the treatment of seizures, but phenytoin is still the preferred drug for the treatment of epilepsy, particularly with grand mal, temporal lobe, and psychomotor seizures. It is also widely used in the treatment of some forms of neuralgia and cardiac arrhythmias. Phenytoin is usually prescribed for chronic use, and approximately 50% of those who take it develop gingival overgrowth.^{11,16}

Gingival changes resulting from phenytoin drug therapy usually begin within two weeks to three months. The marginal gingiva and the interdental papillae appear to be the areas predisposed to enlargement. The appearance of phenytoin-induced gingival overgrowth, in the absence of gingivitis, is usually firm, pink, and somewhat pebbly. In severe cases, teeth surfaces are completely covered with gingival overgrowth. Figure 4 illustrates gingival overgrowth on a patient who has been taking phenytoin for several years. Studies of patients taking this anticonvulsant drug suggest that bacterial plaque is an important determinant of the severity of phenytoin-induced gingival overgrowth and stress the importance of instituting preventive plaque control programs, principally in young patients taking this drug.¹⁷⁻¹⁹

Figure 4.
Gingival overgrowth partially covering the teeth of a patient taking phenytoin.



Figure 4. Gingival overgrowth partially covering the teeth of a patient taking phenytoin.

Immunosuppressants

Cyclosporine is a fungal derivative with immunosuppressive effects.³ This medication has a wide range of biological activities, showing antiparasitic, antifungal, anti-inflammatory, and antiproliferative action. In addition to its primary use to prevent organ rejection, cyclosporine's antiproliferative action has led to its use to treat severe psoriasis, ichthyosis vulgaris, and rheumatoid arthritis.¹³

While cyclosporine has been the drug of preference since the beginning of the transplant era, a number of longitudinal and crossover studies have reported an incidence of gingival problems associated with the drug in the range of 25% to 70%.²⁰ Other frequent side effects associated with cyclosporine are damage to the liver and kidneys, increased hair growth, and trembling of the hands. However, cyclosporine has been a revolutionary drug that enables patients to receive lifesaving organs without rejection.

Another major side effect associated with cyclosporine is increased blood pressure. Calcium channel blockers, such as nifedipine, are usually the drugs of choice to control this problem. As mentioned previously, calcium channel blockers have their own adverse effects on the gingival tissues.³ In combination, cyclosporine and calcium channel blockers produce an intensified effect, and the severity of the gingival enlargement is greater.^{7,13,21}

Fortunately, advances in pharmacology are providing new options to physicians for the immunosuppression of transplant patients. New drugs are being evaluated, and there is a possibility that, in the future, adequate immunosuppression will be achieved without such noxious side effects as gingival overgrowth.

Medical Treatment Options

Researchers have not yet determined how to prevent or eliminate drug-induced gingival overgrowth. The ideal approach would be the substitution of the causative drug. The vast array of cardiovascular drugs provides many options for the substitution of calcium channel blockers. Antihypertensive agents can be combined or switched until an optimal therapy to control hypertension is found.

Drug therapy for transplant patients can be changed to newer immunosuppressants such as tacrolimus (Prograf®), an alternative agent that has been widely used in recent months to prevent organ rejection and is much less likely to cause gingival overgrowth.²² New anticonvulsant drugs are also available, such as valproic acid, primidone, vigabatrin (Sabril®), gabapentin (Neurontin®), and topiramate (Topamax®).²³ There have been reports of gingival overgrowth with the use of vigabatrin, so clinicians should still be aware of similar findings in patients using new anticonvulsants.²⁴ Unfortunately, not all patients respond as well to the newer drugs and must tolerate undesirable side effects to obtain the more important therapeutic benefits. Although prescribing alternative drugs can lessen drug-induced gingival overgrowth, physicians are reluctant to substitute an alternative drug for a proven, effective medication for the sole purpose of reducing gingival overgrowth.

Dental Therapy Options

Research to find methods to prevent gingival overgrowth is underway. Some therapies may be effective in the immediate and short-term management of drug-induced gingival overgrowth.²⁵ Non-surgical (i.e. periodontal debridement, local/systemic antimicrobial delivery) and surgical treatment options may be used individually or in combination to control this problem. A study by O'Valle et al. reported that four of five patients showed recurrences of gingival overgrowth one year after undergoing gingivectomy. Of those four, three showed moderate overgrowth and one showed mild overgrowth. These findings suggest that surgery may only temporarily control gingival overgrowth, and that recurrence is common.¹³

If gingival overgrowth is severe and a gingivectomy is recommended, technological advances allow patients to undergo laser surgery, a simple procedure that produces an immediate, remarkable result. Compared to scalpel gingivectomy, laser surgery requires less effort, reduces the need for periodontal dressing, and lessens postoperative discomfort. It has been reported that tissue rebound also is minimal when lasers are used.²⁶

There are no conclusive recommendations in the literature for the complete elimination of gingival overgrowth. There is evidence that in some patients, however, excellent oral hygiene reduces the likelihood of developing gingival overgrowth. For example, Guelman et al. acknowledged the critical role of routine professional prophylaxis and good oral health maintenance for the healthy status of the gingival tissue of patients with gingival overgrowth.²⁷

Similarly, Ikawa suggested that conventional periodontal treatment can result in satisfactory clinical responses without changing drugs that induce gingival overgrowth. He made this conclusion after evaluating treatment that consisted of oral hygiene instructions, scaling and root planing under local anesthesia, surgical removal of remaining pockets, and placement of bridges to establish proper occlusion.²⁸

Lozada-Nur et al. also stated that there is substantial evidence indicating that gingival overgrowth caused by calcium channel blockers and phenytoin can be controlled effectively by meticulous professional and individual oral hygiene. Gingival overgrowth caused by cyclosporine, however, may not respond as favorably to aggressive plaque control.²⁹

Dental Hygienist's Approach

According to the 1999 reclassification of periodontal diseases, drug-influenced gingival enlargement is a dental plaque-induced gingival disease.³⁰ For that reason, dental hygiene care plans for treating patients with gingival overgrowth

should have the same goals as periodontal maintenance care plans. These common aims are to lessen the recurrence and progression of gingivitis and periodontitis, to reduce tooth loss, and to increase the probability that other conditions are detected and treated early.³¹ Dental hygienists should emphasize the importance of frequent periodontal maintenance at each appointment, spending quality time on patient education and reinforcing positive oral health habits.

Dental hygiene appointments for patients with gingival overgrowth should include an initial periodontal debridement and subsequent maintenance appointments every one to three months. Depending on the severity of the gingival enlargement, dental hygienists may encounter problems when probing, due to commonly seen pseudopockets, and when debriding, due to bleeding and vulnerability of the enlarged gingival lobes that form around the crowns of the teeth, as seen on the patient in Figure 5 who was taking amlodipine for hypertension and cyclosporine for a recent kidney transplant. Even for the experienced dental hygienist, it might be necessary to modify the debridement technique to facilitate the insertion of the instrument tip into the sulcus.

Figure 5.
Instrument insertion modification is necessary when scaling around affected areas, as in this patient taking amlodipine and cyclosporine.



Figure 5. Instrument insertion modification is necessary when scaling around affected areas, as in this patient taking amlodipine and cyclosporine.

To facilitate insertion and instrumentation around enlarged gingiva, modified curets and scalers should be used, such as those with miniature working ends and extended lower shanks. The smaller and thinner working ends of these instruments will reach farther subgingivally than will standard designs, and they will ensure complete removal of deposits. Power instrumentation should also be considered for these patients, as it is valued as equivalent or superior to hand scaling. The new design of periodontally modified inserts allows greater access to deep pockets and furcations, which are more difficult to reach on patients with gingival overgrowth when using manual scalers.

Oral Hygiene Instructions

Dental hygienists should carefully plan individualized oral hygiene instructions to minimize plaque accumulation, prevent gingival inflammation, and improve patient compliance. According to Hodges, when dental hygienist recommendations meet patient needs, patient compliance increases.³¹

Many dental practices have intraoral cameras or photographic cameras that can capture the progression of overgrowth at each appointment. Photographs can be used for careful planning of oral hygiene instructions, and they are helpful tools for patients to see the “real picture” of their oral cavity. Figure 6 shows a patient with early signs of gingival overgrowth three months after beginning cyclosporine therapy for a kidney transplant. Figure 7 shows the same patient six months later. Patients may be more aware of the condition and motivated to action by comparing before and after pictures.

Figure 6.
Kidney transplant patient one month after starting cyclosporine therapy.



Figure 6. Kidney transplant patient one month after starting cyclosporine therapy.

Figure 7.
Same patient, six months post-transplant, taking
cyclosporine and amlodipine.



Figure 7. Same patient, six months post-transplant, taking cyclosporine and amlodipine.

Brushing

Effective plaque removal is important for all patients, but individuals with gingival overgrowth may face unique challenges. A vibratory tooth brushing technique like the Bass method should be recommended to gingival overgrowth patients. This brushing technique needs to be explained to patients by demonstrating the position of the toothbrush bristles on a model or on the patient's own teeth. In this way, the patient will be able to observe and understand what the dental hygienist is describing.

Careful instruction should be given to patients with gingival overgrowth to ensure that they do not harm the gingiva. Placement, pressure, and vibration of the brush should be adjusted to individual tooth surfaces, depending on the amount of gingival overgrowth and on the presence or absence of inflammation. The brush should be repositioned as needed to adapt it to the morphology of the enlarged gingiva.

In some patients, if the gingival overgrowth has formed large lobes overlapping each other, plaque may accumulate inside the groove formed by the lobes. Patients should be instructed to carefully brush these areas by inserting the bristles in the groove and vibrating the toothbrush carefully to remove plaque. To prevent tissue laceration, an extra-soft toothbrush should be used.

Another option available for patients with gingival overgrowth is the use of electric or sonic toothbrushes, which have been shown to be highly effective in removing interproximal plaque. Power toothbrushes are safe and proven to be significantly more effective than manual toothbrushes, in relation to plaque removal and maintenance of gingival health. In addition, power toothbrushes are well accepted by patients and have the potential to improve compliance by requiring less effort from the patient.

Flossing

Patients with gingival overgrowth can benefit from flossing daily. Extra care needs to be taken when flossing in general, but if dental floss is moved from adjacent teeth without guiding it over interdental papillae, excision may occur and cause heavy bleeding. The floss holder is an option for patients unable to floss with their fingers, but extra care needs to be applied because the force of the floss may be difficult to control. Gingival lacerations or cuts may cause heavy bleeding and, as in organ transplant patients, the release of harmful bacteria into their blood stream. This bacteremia may compromise the well-being of the patient with a transplant.³²⁻³³

Floss cuts or clefts occur primarily on facial and lingual/palatal surfaces directly beside or in the middle of an interdental papilla. Gingival overgrowth patients are more prone to damage their enlarged gingiva if they do not floss correctly. The causes may be using a piece of floss that is too long, using excessive force to insert the floss through the contact, improperly adapting the floss to tooth curvatures, and failing to use a fulcrum to prevent excessive pressure. Dental hygienists should teach the patient how to move the floss around enlarged papillae to prevent unnecessary tissue trauma.

Other Oral Hygiene Adjuncts

Gingival stimulators, interdental brushes, and other devices can be recommended as needed. Oral irrigation devices can achieve removal of debris on patients who are not able to brush and floss correctly because of other impairments. As a preventive measure, chlorhexidine 12% once a day has been recommended and may be prescribed for patients at risk for gingivitis, as it has shown beneficial effects on patients with gingival overgrowth.^{6,34}

Conclusion

Dental hygienists have the responsibility to provide the best possible care to all patients. They should be able to transfer knowledge gained in the assessment phase of care to accurately diagnose and plan the appropriate therapy. Because the possibility of dental hygienists encountering patients with drug-induced gingival overgrowth exists, they should be prepared to offer maintenance and preventive therapies formulated specifically for the needs of these patients. They should also be familiar with additional instrumentation modifications to better adapt debridement techniques to the affected gingival structures.

All oral health care providers should have excellent rapport with these patients. They should listen carefully to their concerns and, if necessary, act as a point of referral for other specialized therapists or counselors. The dental hygienist can also play a significant role in the prevention of gingival overgrowth. As studies have suggested, plaque control is required to minimize the inflammatory component of the condition. For that reason, reinforcing good oral hygiene at each appointment should be routine. These steps to treating gingival overgrowth will be life-altering for patients and also rewarding to oral health care providers.

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Notes

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