# Drug Induced Gingival Enlargement: Troubleshooting Dentist and Physician

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The increasing population of the developing and developed countries presents new challenges to dental professionals. At least one fourth of the general population take prescribed medications; more than 400 medications are known to have oral side effects. Treating these patients require thorough evaluation of the patient's medical and dental history and a comprehensive knowledge of the various medications that may affect oral health. Gingival hyperplasia due to the concomitant unaesthetic appearance is considered a serious adverse drug reaction. This article examines gingival hyperplasia, an abnormal growth of gingival tissues that may be caused by three main groups of medications: anticonvulsants, anti-hypertensive calcium antagonists and the immunosuppressant cyclosporine

**Drugs responsible for gingival enlargement:-**

| **Anticonvulsants** | **Calcium Channel Blockers** |
|---|---|
| Carbamazepine | Amlodiine |
| Ethosuximide | Bepridil |
| Ethotoin | Diltiazem |
| Felbamate | Felodipine |
| Mephentoin | Nicardipine |
| Methsuximide | Nifedipine |
| Phenobabital | Nimodipine |
| Phensuximide | Nitrendipine |
| Phenytoin | Verapamil |
| Pimidone | Sodium Valproate |

**Other Drugs with Potential to cause gingival enlargement**

| | |
|---|---|
| Cotrimoxazole | Phenobarbital |
| Cyclosporine | Primidone |
| Erythromycin | Sertraline |
| Ethosuximide | Sodium Valproate |
| Ketoconazole | Topiramate |
| Lamotrigine | Vigabatrin |
| Lithium | Oral Contraceptives |

**Phenytoin-induced gingival enlargement:-**

This is more likely to occur in patients with gingivitis and dental plaque.

Increased dental plaque has been suggested to induce local inflammation and to serve as a reservoir for phenytoin.

There is evidence that mast cell mediated androgen action in the gingiva in response to phenytoin could contribute to gingival overgrowth.

The incidence of phenytoin-induced gingival overgrowth is approximately 50 percent, but it is higher in both teenagers and institutionalized epileptics.

Gingival overgrowth usually becomes apparent during the first 3 months after starting phenytoin and is most rapid in the first year.

**Cyclosporine-induced gingival enlargement:-**

In susceptible patients (ie, presence of dental plaque, swollen gums, high dose of cyclosporine), enlargement may develop by the third month of therapy.

Patients with poor oral hygiene and displaced teeth tend to develop bleeding gums upon probing.

Aggressive plaque control and routine oral hygiene help in maintaining gums but may not prevent the onset in susceptible individuals.

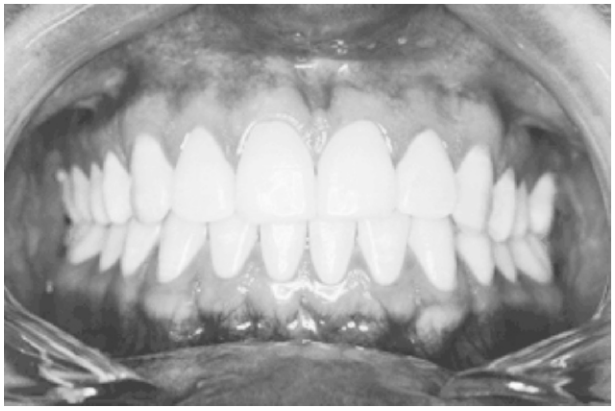
Cyclosporine-induced enlagement is reversible once therapy is discontinued or when the dose is reduced.

**Cyclosporine and nifedipine-induced gingival enlargement:**

Nifedipine potentiates the adverse effect (ie gingival enlargement) of cyclosporine.

**Nifedipine induced gingival enlargement:-**

Nifedipine, the most commonly used calcium channel

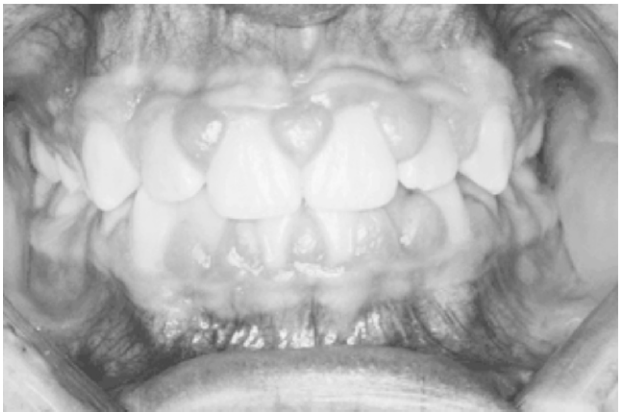


**Normal Gingival**

blocker, induces gingival enlargement in 20% of the cases.

Amlodipine, diltiazem, felodipine, nitrendipine, and verapamil also induce gingival overgrowth. The dihydropyridine derivative isradipidine does not induce gingival overgrowth. There is also evidence that nifedipine istimulates macrophage-induced death of fibroblasts which results in gingival overgrowth.

Nifedipine is frequently prescribed to organ transplant patients to reduce the nephrotoxic effects of cyclosporine and, thus, an additive effect on the gingival tissues is usually observed.



**Mild Drug induced gingival enlargement secondary to nifedipine theapy**

**Oral contraceptives induced gingival enlargement:-**

The incidence of gingival overgrowth by oral contraceptives is not rare and resolves when the drug is withdrawn. There is evidence that the accumulation of metabolic products of the naturally occurring sex hormones in gingiva is an important factor in the pathogenesis of chronic gingivitis.

**Potential risk factors for drug-induced gingival enlargement include the following**:-

Poor oral hygiene

Periodontal disease

Periodontal pocket depth

Gingival inflammation

Degree of dental plaque

Duration and dose of medication

**Pathophysiology:-**

The underlying mechanism remains to be fully understood. However, two main inflammatory and non-inflammatory pathways have already been suggested. The proposed non-inflammatory mechanisms include defective collagenase activity due to decreased uptake of folic acid and upregulation of keratinocyte growth factor (KGF).

Alternatively, inflammation may develop as a result of direct toxic effects of concentrated drug in crevicular gingival fluid (CGF) and/or bacterial plaques . This inflammation could lead to the upregulation of several cytokine factors such as TGF-ß1 .

**Differential Diagnosis:-**

1. Non drug induced gingival fibromatosis
2. Leukemia (bleeding gums)
3. Pyogenic granuloma
4. Pregnancy induced gingivitis

**Investigations:-**

Lab Studies

CBC( complete blood cell) count is indicated in patients with severe gum bleeding to rule out anemia and leukemia.

Imaging Studies

Periapical (full mouth series) or panoramic view radiographs are indicated prior to treatment to evaluate the status of the periodontal tissue or any compromised teeth.

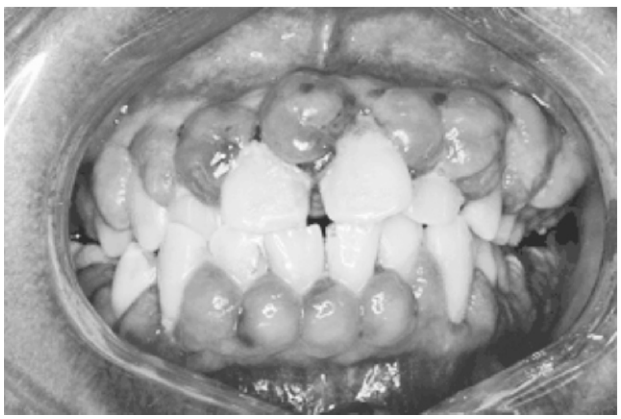
Other Tests

Culture is recommended to rule out oral candidiasis.

**Prevention:-**

Ensure healthy periodontal tissue prior to any organ transplantation or the use of phenytoin or calcium channel blocker.

Consider alternative drugs (ie, mycophenolate or



**Severe drug induced gingival enlargement secondary to nifedipine theapy**

tacrolimus in organ transplant recipients, verapamil in place of calcium channel blockers) for patients at high risk.

Educate patients about the importance of good oral hygiene and routine dental care, not only to minimize gingival enlargement but also to reduce risk of systemic complications, including organ rejection.

**Treatment:-**

1. Referral will be made to a dentist for evaluation, dental cleaning and ongoing monitoring if this has not been initiated.
2. Reduce or discontinue calcium channel antagonist.
3. Trial of Azithromycin.

   **Dose:** Azithromycin tablets 500 mg on day 1 followed by 250 mg od on days 2-5. (Tablets can be taken on either empty or full stomach. If capsules are ordered, instruct patient to take 1 hour before or 2 hours after meals)
4. Tolerance: usually well tolerated and minimal side effects
5. If no improvement, consider conversion to Tacrolimus

**Dosing:** 0.1mg-0.2mg/kg dependent on length of time since transplant

**Surgical Care:-**

Gingivectomy with carbon dioxide or YAG laser is recommended for patients who have moderate-to-severe gingival enlargement that does not resolve when the dose is reduced, proper oral hygiene is maintained, or after a short course of antibiotics.

**Conclusion:-**

Cyclosporin , nifedipine & phenytoin induced gingival hyperplasia are all similar in clinical appearance, risk factors & treatment.

The dentist has a professional responsibility to review the medical history & assess the needs of each patient.

The dentist who is aware of the clinical signs of drug induced hyperplasia & its treatment can identify patients at risk & emphasize the importance of reducing gingival inflammation through better techniques.

Physicians on the other hand also have the responsibility to prescribe medications which are less prone to cause gingival enlargement, to diagnose the condition and to change the prescribed medication if required.

*Special Acknowledgment to*
**Dr. Sankalp Verma**