JIDA

Periodontology

Clinical assessment of gingival overgrowth in patients treated with anti-hypertensive drugs: A hospital based study

Supreet Kaur [1], Manpreet Kaur Behl [2], Vandana [3]

Abstract

Brief Background

Gingival overgrowth (GO) is a known side effect of calcium channel blockers. This study was conducted to determine the clinical assessment and prevalence of GO in patients treated with various antihypertensives.

Materials and Methods

A cross-sectional study of 50 patients taking antihypertensives was conducted in the department of Periodontology & Oral Implantology at Sri Guru Ram Das Institute of Dental Sciences & Research, Sri Amritsar. All patients were examined for the presence of GO using different indices: Miranda-Brunet (MB) index, Angelopoulos and Goaz (1972) (GO index). Probing depth and modified sulcus bleeding index were also measured.

Results

The frequency of GO was significantly higher in nifedipine-treated cases than other drug groups. Frequency of GO was 57.1% for nifedipine, 31.4% for amlodipine. Higher plaque and calculus were observed in patients taking calcium channel blockers.

Summary and Conclusions

Patients taking antihypertensives were having poor oral hygiene. Patients taking nifedipine showed a higher frequency of GO. Gingival inflammation may act as a risk factor.

Key Words

Calcium channel blockers, gingival overgrowth, Nifedipine, Amlodipine, Periodontitis.

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Introduction

A common feature of the gingival diseases is increase in size of the gingiva. Gingival enlargement is the proliferation and intensification of the gingiva which is a prevailing character of the diseased gingival tissues [1]. Proliferative overgrowth of the gingiva makes it more difficult for patients to maintain mouth hygiene. Changes in the gingival sizes can range from minor to complete coverage of the teeth. As per the literature "Gingival Enlargement" (GE) and "Gingival Overgrowth" (GO) are the ongoing approved clinical nomenclatures used to construe this clinical manifestation. The enlargement of the gingival tissue may occur due to many reasons such as inflammatory, conditioned, neoplastic or drug intake associated [2]. Calcium channel blockers (CCBs), as a group, have been frequently implicated as an etiologic factor for a common oral condition seen among patients seeking dental care: drug-induced gingival overgrowth (DIGO). It is characterized by an increase of the gingival mass and volume, which can range from mild to extremely severe (Fig. 1). The drug-induced gingival overgrowth could be detected clinically as early as 1–3 months following the initial dose of CCB. It affects more the anterior teeth and facial/buccal rather than the posterior teeth and lingual surfaces [3] (Fig. 2).

Materials and Methods

A cross-sectional study was carried out in the Department of Periodontology & Oral Implantology at Sri Guru Ram Das Institute of Dental Sciences & Research, Sri Amritsar.

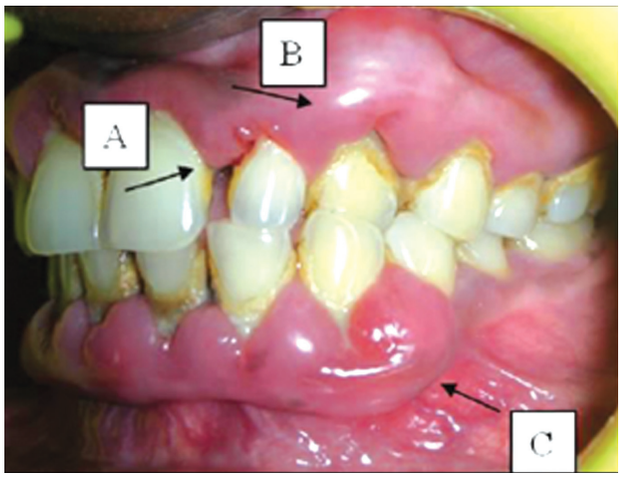


Fig.1: A. Blunting of gingival margin, B. Lateral spread of papilla across buccal tooth surface, C. Loss of normal papilla form (marked encroachment of papilla).

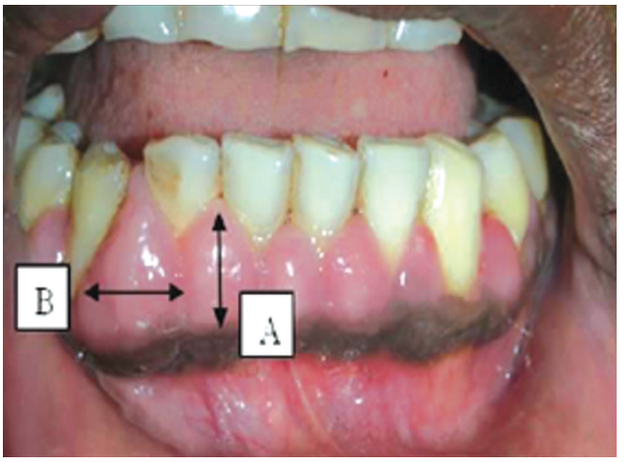


Fig.2: A. Vertical extension, B. Horizontal extension

Patients taking an antihypertensive drug for a minimum duration of 3 months and with the presence of minimum 16 permanent teeth (minimum of 10 anterior teeth) were included. Patients who had undergone periodontal treatment within 6 months prior to the initiation of the study and with systemic disorders (diabetes, or immunodeficiency conditions etc.) or any other drug medications (anticonvulsants etc.) or any other condition (such as pregnancy) that could affect the gums were excluded from the study. All the participating patients (n= 50) were made to fill the questionnaire along with written consent and were informed in advance about the detailed study.

Various researchers have described multiple indices to evaluate gingival enlargement of which the Miranda and Brunet index had a better sensitivity in evaluating the gingival enlargement [4].

Gingival enlargement was graded according to the following two indices:

1. Miranda and Brunet index (2001) (MB index)[5] described an index in which horizontal measurement of the enlargement is possible. This index is also termed as nodullary papilla index. In this index the measurement is carried out from the enamel surface of the interdental contact point to the outer papillary area (Fig. 3-5). The scores of this index are as mentioned below:

a. Score 0: Papilla thickness < 1 mm

b. Score 1: Papilla thickness 1- 2 mm

c. Score 2: Papilla thickness > 2 mm

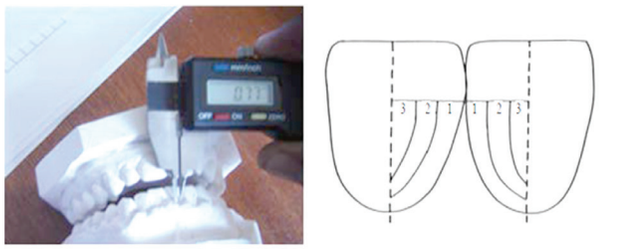


Fig.3: Criteria used for assessing gingival encroachment on adjacent tooth surfaces for a gingival unit

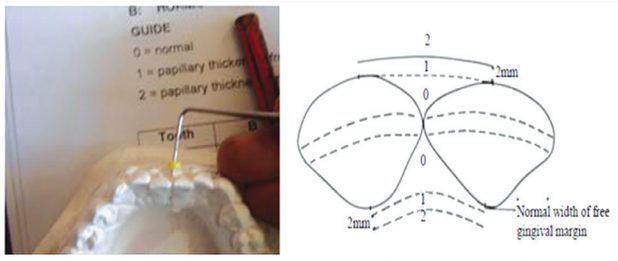


Fig.4: Criteria used for assessing gingival thickness in a labio-lingual direction for a gingival unit. (Open Journal of Stomatology, 2014, 4, 169-173)

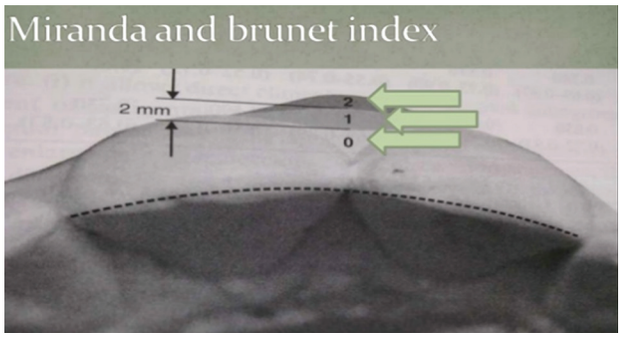


Fig.5: Gingival thickness (labio-lingual)

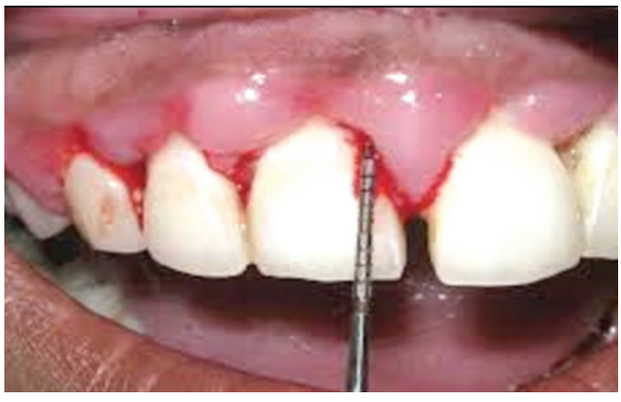


Fig.6: Gingival thickness (apico-coronal)

2. Angelopoulos and Goaz (1972) (GO index)[6] described an index for measuring the vertical component of gingival (Fig. 6). Three grades based on the enlargement covering the clinical crown were described as:

a. Grade 0: None.

b. Grade I: Not more than 1/3rd of the clinical crown covered.

c. Grade II: Any part of the middle third of the crown covered.

d. Grade III: Greater than 2/3rd of the crown covered.

For both indices an average mean was calculated for the whole mouth, anterior and posterior areas. GO was considered to be present when grades other than zero were recorded in one or in both GO and MB indices. Other measures such as modified sulcus bleeding index, mSBI, (Mombelli et al. 1987) [7] and probing pocket depth (PD) [8] were also evaluated for all the subjects.

Statistical analysis

Means were calculated for all the variables. Means of quantitative variables were calculated and the difference for means was assessed using Student's t-test. The difference in proportions was calculated using Chi-square test. Correlation analysis was done to account for confounders. The results were considered to be statistically significant if the $P < 0.05$.

Results

A total of 50 patients participated in the study. There was no significant difference for age, sex distribution ($P > 0.05$) between the drug groups (table:1, graph:1-2). The mean age of the patients was 56 years and consisted of 17 females and 33 males. Age and sex-wise distribution of GO cases among different drugs used by the study population of all the three groups were also not significant.

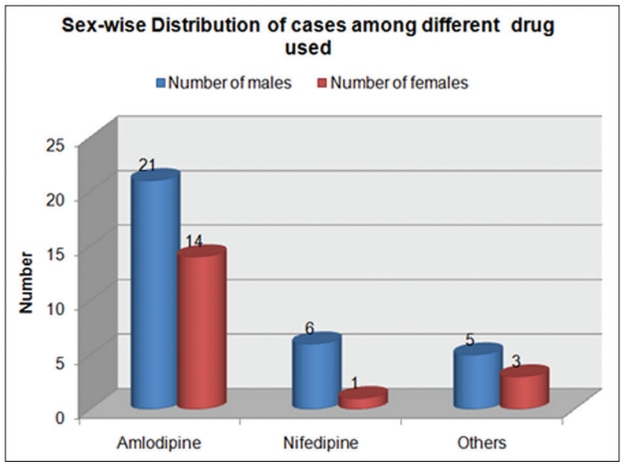
On the basis of antihypertensive drug being taken, the patients in the study population were grouped into group1(amlodipine group), group2 (nifedipine group) and group 3 (other antihypertensives such as enalapril, losartan, atenolol, metoprolol). Of the 50 patients taking antihypertensive drugs, 15 subjects manifested with GO. The frequency of occurrence of GO was 57.1% for nifedipine (group2), 31.4% for amlodipine (group1). No case was detected with GO in a total 8 patients of group 3 (table:2, graph:3).

Table 1

	Amlodipine (n=35)	Nifedipine (n=7)	Others (n=8)	P value
No of males	21	6	5	0.431
No of Females	14	1	3	
Age (years) Mean± SD	57.09 ± 6.46	55.86 ± 5.46	55.00 ± 7.43	0.682

NS:p>0.05; Not significant

Graph 1



Graph 2

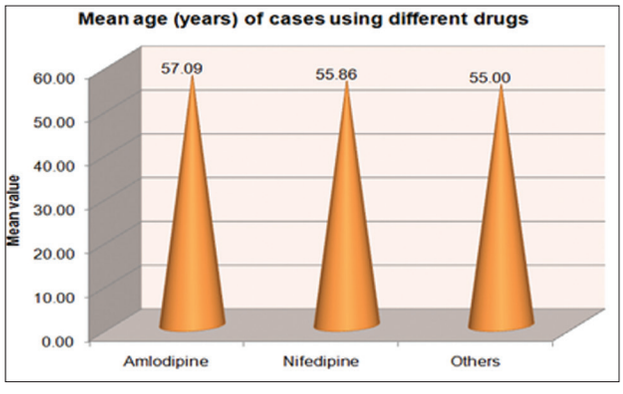


Table 2

Drug	With Go	Without Go	Total
Amlodipine	11(31.4%)	24(68.6%)	35
Nifedipine	4(57.1%)	3(42.9%)	7
Others	-	8(100%)	8
Total	15	35	50

X^2 =5.918; df=2; p=0.052; Not Significant
Amplodipine vs Nifedipine: X^2 = 1.680; df=1; p=0.195; Not significant

Graph 3

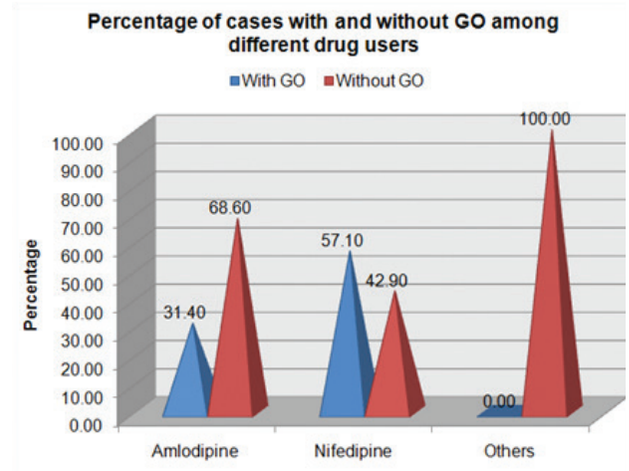


Table 3

Varibale	Amlodipine (n=35)	Nifedipine (n=7)	Others (n=8)	P value
PD	1.56 ± 0.92	2.01 ± 0.88	1.29 ± 0.25	0.260^{NS}
mSBI	0.94 ± 0.73	1.44 ± 0.82	0.46 ± 0.29	0.032*
Go Index	0.36 ± 0.61	1.07 ± 0.79	0.00 ± 0.00	0.003*
MB Index	0.47 ± 0.73	1.18 ± 0.88	0.00 ± 0.00	0.008*

NS: p>0.05; Not Significant;*p<0.05; significant

Graph 4

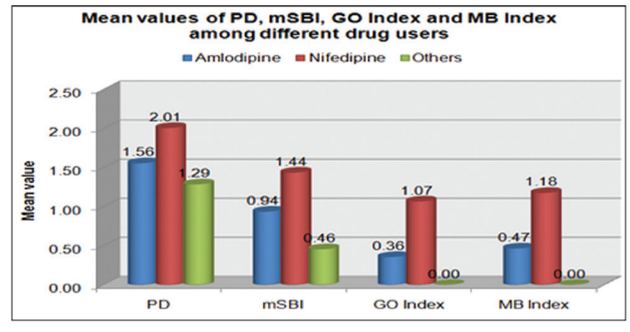
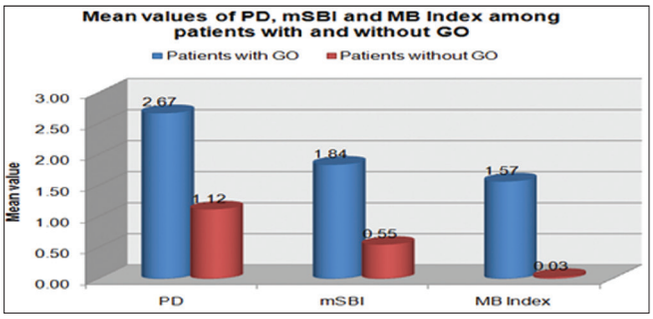


Table 4

Varibale	Patient with GO (n = 15)	Patient without Go (n = 35)	P value
PD	2.67 ± 0.71	1.12 ± 0.34	<0.001**
mSBI	1.84 ± 0.60	0.55 ± 0.33	<0.001**
MB Index	1.57 ± 0.40	0.03 ± 0.19	<0.001**

**p<0.001; Highly Significant

Graph 5



Out of the 7 patients of group2 (nifedipine group), 4 presented with GO and out of 35 of group1 subjects who were taking amlodipine, only 11 patients were seen with GO. The statistical analysis showed a significant association between 3 various groups of patients ($P < 0.05$) in respect to their gingival overgrowth measurements as well as periodontal parameter such as mSBI, whereas the comparison of GO measurement was shown to be not significant ($P > 0.05$) between amlodipine group (group1) and nifedipine group (group2).Although there was no statistically significant difference between patients with overgrowth and without overgrowth with regard to the Pocket probing depth (PD), scores were moderately high for groups of patients showing GO as compared to group3 (table:3, graph:4)

Highly significant association ($P < 0.001$) was found between patients with overgrowth and without overgrowth with regard to periodontal parameters and MB index (table:4, graph:5)

Discussion

Of the 50 patients on antihypertensive drugs, 15 were diagnosed clinically as having GO. The frequency of occurrence of GO is 30%.

GO was found in patients taking nifedipine and amlodipine that is only in patients medicated with calcium channel blockers.

The frequency of GO induced by nifedipine is in accordance with the previous studies where prevalence of nifedipine-induced GO ranged from 20% to 83% and is much lower than revealed (75%) by some studies. This may have occurred as there has been a reduction in prescription of nifedipine in the past few years which reduced the number of nifedipine-induced GO. The frequency of amlodipine induced overgrowth in the present study is 31.4% which is higher than the previous studies. Jorgensen 1997[9] reported a prevalence of 3.3%; Ellis et al. 1999 [10] reported 1.7% for amlodipine induced GO. This higher prevalence of amlodipine-induced GO was in accordance with the Intercontinental Medical Statistics Health Canada revealing amlodipine as the most frequently prescribed CCB among adults. [11]

Although amlodipine induced GO is lesser prevalent than that of nifedipine as amlodipine is more polarized and requires a complex transport mechanism to penetrate the cell membrane. In contrast, nifedipine is highly lipophilic and penetrates the cell membrane rather quickly. Since both drugs are dihydropyridines and hence structurally similar. However, the two drugs differ in their physico-chemical profile. Another possible factor that contributes to the differences between amlodipine and nifedipine is the variation in their half-lives and their volume of distribution (amlodipine: 34 h and 21 l/kg; nifedipine: 7.5 h and 0.78 l/kg). Amlodipine's higher volume indicates that the majority of amlodipine is tissue bound (hence 'inactive') and does not circulate freely in the blood. It has been suggested that a plasma threshold may exist above which drug-induced gingival changes are initiated. Amlodipine rarely achieves such threshold levels, unlike nifedipine, which tend to exhibit pronounced peak plasma levels, possibly affecting drug-induced gingival enlargement.[12]

No GO case was found in group3 patients, since there have been no reports of GO induced by other classes of antihypertensives except CCBs. According to Barclay S, 1992 CCBs affect calcium metabolism by reducing the calcium ions cell influx, leading to a reduction in the uptake of folic acid, thus limiting the production of active collagenase. As a result of the reduction in collagen degradation, increased collagen accumulation occurs, as the hallmark of the enlargement is the increase in the amount of connective tissue matrix dominated by collagen fibres.

Highly significant association was found between patients with overgrowth and without overgrowth with regard to periodontal parameters. Duncan MR,1991 [13] reviewed the Pro-inflammatory cytokines, such as interleukin-1β and interleukin- 6 seem to have a synergistic effect in the enhancement of collagen synthesis by human gingival

fibroblasts. The importance of the microbial plaque as a co-factor in the aetiology of drug-associated gingival enlargement has been recognized in a recent classification system of periodontal diseases by the American Academy of Periodontology (AAP)[14]. The overgrown tissue creates pockets that harbour pathogenic bacteria that are beyond the reach of a toothbrush or dental floss. These negative changes impair optimal oral hygiene and can lead to an increased host susceptibility to oral infection, caries and periodontal disease. Proinflammatory cytokines (IL-6) has been shown to target such as fibroblasts, both by enhancing their proliferation and by increasing collagen production and glycosaminoglycan synthesis. This highlights the role of the bacterial biofilm in inducing gingival inflammation, production of cytokines and gingival enlargement.

Department of Periodontology and Oral Implantology

Proforma

General Information

Name: Case No:

Age: OPD No:

Sex: Date:

Occupation: Tel No:

DOB: Address:

Condition Profile

1. At what age were you told you had a Hypertension ? .....

2. What prescribed medication do you take for Hypertension? Amlodipine Or Nifedipine Or Others .....

.....

3. Now taking prescribed medication ? .....

4. At what age you had started taking the prescribed medication for Hypertension? .....

5. Prescribed medication Dosage? .....

6. Frequency of prescribed medication (per day) ? .....

7. Do you take non-prescribed medications or supplements?(if yes, kindly name them).....

8. Has your treatment (type/dosage) changed within last 12 months?

a) When it was changed? b) What was changed? b) Why was it changed?

....

9. Any other Medical History ?(if yes, kindly mention in detail) ? .....

.....

10. Relevant Dental History History ? .....

11. Self-assessment of swollen gums (Gingival overgrowth)? *a) When has this condition been noticed by you* .....

b) Have you noticed this condition to be associated with any medication etc .....

c) Chief complaint associated with swollen gums? .....

d) You do anything for this condition? .....

12. Do other members of your family have Hypertension? .....

13. When was the last time you had your blood pressure checked ? (with B.P. in mm Hg) ? .....

....

Patient Signature *Doctor's Signature*

The finding that all 42 patients treated with CCBs (amlodipine group = 35 and nifedipine group = 7) does not develop gingival enlargement, leading to involvement of recent concept of fibroblasts that are susceptible to CCBs. A genetic predisposition could influence the metabolism of CCBs, as these drugs are metabolized by the hepatic cytochrome P450 enzymes. Cytochrome P450 genes exhibit considerable polymorphism, which results in inter-individual variation in enzyme activity. This inherited variation in metabolism of the offending drug may influence the patient's serum and tissue concentrations, and hence their gingival response [15]. As in our study, the family history (proforma, pg. 21) revealed the role of genetic predisposition of GO in many patient families.

Conclusion

The overall frequency of GO related to antihypertensive usage in this small sample sized study is 30% with nifedipine (57.1%) causing the most significant GO, based on our convenience sample, which would have masked the true prevalence for each drug. Since the presence of gingival inflammation is an important risk-factor in the expression of GO, regular periodic maintenance of the periodontal health is mandatory for patients taking antihypertensives.

Conflict of Interest: None

Source of Support: Nil

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