

Gingival Enlargement in Antihypertensive Medication

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ABSTRACT

Introduction: Drug-induced gingival enlargement is a well documented side effect with the use of phenytoin, cyclosporine and calcium channel blockers. The prevalence of gingival enlargement induced by calcium channel blockers is uncertain. Several studies show conflicting results ranging from 20% to 83%. This study was conducted to determine the prevalence of gingival enlargement in patients taking antihypertensive medication.

Methods: All consecutive patients on antihypertensive agents attending the Dental OPD were studied. The prevalence of drug induced gingival enlargement was determined. The periodontal condition of all subjects were assessed including plaque index and probing depth.

Results: Total 81.2% of subjects taking antihypertensive were seen to have significant enlargement. Among them 71.1% were taking calcium channel blocker, 21.5% were taking ACE Inhibitors, and 7.4% were taking β -blockers.

Conclusions: Patients taking antihypertensive agents are at increased risk for gingival enlargement and inflammation is an important cofactor for the expression of this effect.

Key Words: *anti-hypertensive drugs, gingival enlargement*

INTRODUCTION

Drug induced gingival enlargement (DIGE), as a well documented side effect has been reported with systemic use of anti-convulsants, immunosuppressants and calcium channel blockers (CCBs).¹⁻⁸ It was first reported in 1939⁶ with chronic usage of phenytoin. CCBs, Angiotensin converting enzyme (ACE) inhibitors and β -blockers are the most commonly prescribed antihypertensives. It has been reported in patients treated with CCBs like nifedipine,⁹⁻¹³ nitrendipine,¹⁴ nicardipine,¹⁵ felodipine,¹⁶ and amlodipine.^{17,18}

DIGE presents with similar clinical and microscopic appearance. It begins within 3 months as a firm, nodular enlargement limited to keratinized portions of interdental papilla. Histologically, it is characterized by an increase in connective tissue component. Gingival inflammation also appears to be an important predisposing factor suggesting that the lesion is a consequence of interaction between gingival fibroblasts, cellular and biochemical mediators of inflammation and drug metabolites. The present study aims to determine the prevalence and severity of DIGE in patients taking antihypertensive drugs and their relation with oral hygiene status of the patients.

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METHODS

A cross sectional study was carried out among all consecutive patients attending the out patient department (OPD) of dental surgery, Bir Hospital, Nepal Academy of Medical Sciences (NAMS) from July 2008 to December 2008. Ethical approval and patient consent was obtained. Patients presenting with dental problems on antihypertensive agents were included. Gingival enlargement was considered to be present if visible enlargement was present in interdental papilla, marginal gingiva and/or attached gingiva and graded according to the severity into mild (only interdental papilla involved), moderate (marginal gingiva also involved) and severe (attached gingiva also involved). Patients were divided into 4 groups based on the duration of drug consumption viz. group I (0-1 yr), group II (1-5y), group III (5-10 years) and group IV (> 10 years).

Plaque index was considered as described by Quigley and Hein (1962) and divided into good, fair and poor plaque index.¹⁸ A standard periodontal probe (Michigan O probe with William markings) was used to measure the probing depth.

Prevalence rate was determined. It was analysed as per severity; oral hygiene status and duration of drugs consumption using Statistical Package for Social Sciences (SPSS) 13.0 Chi-square test was used to determine statistical significance.

RESULTS

Total 150 patients taking antihypertensive agents were included. Significant enlargement was seen in 81.2%. The prevalence of gingival enlargement was higher in patients taking CCBs (71.1%) followed by ACE inhibitor (21.5%) and β -blockers (7.4%). Mild gingival enlargement was seen in 19%, moderate in 71.9% and severe in 9.1%. Among the CCB users 18.6% had mild, 74.4% had moderate and 7.0% had severe gingival enlargement. Significant difference was not seen in patients using different antihypertensive agents ($P > 0.05$) which possibly shows the effect of poor oral hygiene on gingival enlargement (Table 1). Patients taking antihypertensive agents for 5 to 10 years showed the most severe gingival enlargement (Table 2).

Plaque index was either poor or fair in all patients. None had good plaque index. Among patients with poor oral hygiene, mild gingival enlargement was seen in 10.6%, moderate in 66.4% and severe in 7.1% ($P < 0.05$) (Table 3). Poor plaque index was seen among 73.6% using CCBs, 19.8% using ACE inhibitors and 6.6% using β -blockers (Table 4).

DISCUSSION

In the study population, prevalence of DIGE was seen in 71.1% treated with CCBs 21.5% with ACE Inhibitors

group and 7.4% with β -blockers. Most patients had moderate severity moderate severity which could be attributed to the poor oral hygiene as well. It is thus difficult to establish whether the high plaque scores observed are the cause or the consequence of the DIGE. Therefore mild enlargement may be a very important factor taken into account for early detection of DIGE in such patients.

Ellis et al in a group of 911 patients treated with CCBs, showed a prevalence lower than in previous studies, with marked differences between the different drugs like nifedipine (6.3%), amlodipine (1.7%) and diltiazem (2.2%) and with higher risk for developing clinically significant gingival enlargement in the patients treated with nifedipine, than in those taking either amlodipine or diltiazem.¹⁹

Often drug-induced gingival enlargement involves a form of combined gingival enlargement, with the effect of the drug and the inflammatory status and, therefore, it is difficult to determine the contribution of each factor. Some authors have reported a relationship of gingival enlargement with both gingival index and plaque index^{5,12,20,21} indicate that risk factors for DIGE are: drug variables, concomitant medications, periodontal variables, age, gender and genetic factors.

The results of present study suggest that gingival inflammation has a stronger effect than drug treatment itself in patients treated with antihypertensive. This study also reflects the higher tendency of physicians to prescribe calcium channel blockers for patients with hypertension. We must highlight the great number of calcium antagonists, that are being studied and that may have an effect on the gingiva, such as verapamil,²² nitrendipine,¹⁴ felodipine,¹⁶ oxodipine in rats.²³

The logical approach in the control of gingival enlargement induced by drugs should be reduction of the dose of the drug or substitution of the drug. Reduction in gingival enlargement has been reported where a different calcium channel blocker, such as Verapamil has been substituted for nifedipine,⁹ but more usually where substitution is made by a structurally different antihypertensive drug, such as the angiotensin-converting enzyme inhibitor, enalapril,²⁴ the β -blocking drug, atenolol,²⁵⁻²⁷ or thiazide diuretics.^{17,28} Change in medication should only be considered for those patients where the new medication can offer some advantage for control of their hypertension, which present with clinically significant enlargement and are at high risk from either corrective surgery or recurrence after gingivectomy.²⁹ Reduction in the size of the gingival enlargement has been reported within a week of drug withdrawal,³⁰ and may lead to full resolution.

Table 1. Severity of gingival enlargement in patients taking antihypertensive

Drugs	Severity (%)		
	Mild	Moderate	Severe
ACE inhibitors	11.5	73.1	15.4
β-blocker	44.4	44.4	11.1
Calcium channel blocker	18.6	74.4	7.0

Table 2. Relation between duration of drug consumption and severity

Duration of drug consumption (in years)	Severity (%)		
	Mild	Moderate	severe
Group I (0-1)	14.0	53.5	9.3
Group II (1-5)	15.5	59.7	6.5
Group III (5-10)	21.4	60.7	7.1
Group IV (> 10)	18.8	56.3	6.3

Table 3. Relation between plaque index and severity

Plaque index	Severity (%)		
	Mild	Moderate	Severe
Good	0	0	0
Fair	33.3	30.6	8.3
Poor	10.6	66.4	7.1

Table 4. Relation between plaque index and drugs used

Plaque index	Drugs (%)		
	ACE Inhibitors	β-blockers	Calcium channel blocker
Good	0	0	0
Fair	20.9	14.0	65.1
Poor	19.8	6.6	73.6

Prevention and treatment includes meticulous plaque control and frequent professional debridement.³¹ Furthermore, resective gingival procedures may be needed to improve function, aesthetics and access for home care. The periodontist is restricted in controlling gingival inflammation, correcting gingival contour and treating any pre-existing periodontal disease. Ideally, all patients about to be medicated with cyclosporine, phenytoin or a calcium channel blocker, should go through a full periodontal assessment and any disease present treated appropriately. Clinicians should be aware of the prevalence and risk of gingival enlargement induced by calcium channel blockers and other antihypertensive in order to implement preventive practices as well as to establish an early diagnosis of this condition.

In Nepal very few studies has been carried out till date to our knowledge and this study could significantly contribute in dealing patients with antihypertensive

drugs and create awareness among treating physicians. However, in-depth study with larger sample size to determine the actual prevalence of gingival enlargement with different types of calcium channel blockers, ACE Inhibitors and β-blockers is required.

CONCLUSIONS

Patients on CCBs had a higher prevalence of DIGE. DIGE was also seen in patients taking antihypertensive agents like ACE inhibitors and β-blockers. However, poor oral hygiene could also have contributed to develop gingival enlargement in such patients.

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