

Role of Calcium Channel Blockers in Inducing Gingival Enlargement - A Cross Sectional Study

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ABSTRACT

Background

Calcium channel blockers (CCB) are the widely prescribed drugs for the management of hypertension. Gingival enlargement (GE) due to calcium channel blockers (CCB) accounts for a prevalence rate of 14.7%-83%. Literature reveals that the most frequently encountered CCB causing GE is nifedipine being 83%, and the least common is amlodipine being 3.3%. Amlodipine prescription is increasing in the recent years, attributed to its high patient compliance and cost effectiveness. The study was conducted with an aim to determine the association between GE and the use of different Calcium channel blockers and with an objective to assess the status of gingiva in patients on CCB, as well as to assess the relationship between dosage and duration of intake of CCB on the status of GE.

Material and Methods

The present study included 30 hypertensive subjects on calcium channel blockers and 30 healthy controls who were not on any of the drugs causing gingival enlargement. Written consent was obtained and history recorded for all the study subjects, Oral hygiene was assessed by Green and Vermillion index, gingival condition by Loe and Sillness index and the gingival enlargement was recorded using the Ingles index.

Results

20(66%) subjects out of 30 had gingival enlargement among whom 12(40%) subjects had Grade II GE and 5(16%) had Grade III GE. This when compared to controls was statistically significant with p value of < 0.001.

Conclusion

Slightest of the local factors trigger the gingival response to the drugs causing gingival enlargement. GE provides new niches for growth of microorganisms, resulting in tooth loss. Clinicians should and must pay attention to patients oral hygiene prior to prescription of CCB and stress on need of regular dental visits.

Key words: Gingival enlargement, calcium channel blockers, gingivitis, duration.

INTRODUCTION

Rapid advances in the field of technology, has lead to early diagnosis, treatment and prevention of diseases, at the same time there is also a rise in incidence of stress induced health problems.

As per the Global Burden of disease, hypertension is the major contributing factor for growing rate of cardiovascular diseases in India.

Hypertension being the most prevailing stress related disorder prevails in India with a rate of 24.9%¹. Hypertension is treated by various groups of drugs and one among them are the calcium channel blockers (CCB). These CCB are well documented as a cause of GE in these patients. Till date nifedipine induced GE has prevalence rate of 83%^{2,3,4}.

Amlodipine, one of the third generation dihydropyridine is the most commonly prescribed

CCB in the recent years due to its effectiveness and increased patient compliance in terms of single dose and cost⁵. Amlodipine has side effects like constipation, drowsiness, of concern to the dentist is the gingival enlargement caused by it which is comparatively less prevalent. Literature reports few studies and cases regarding amlodipine induced gingival enlargement having a prevalence rate of 3.3%^{6,7,8,9,16,17}.

As per Jorgensen et al (1997)⁹, there was no significant evidence of GE following use of amlodipine in 150 cardiac subjects examined by him and amlodipine was suggested to be a viable alternative to nifedipine. Seymour RA (1994)⁶ was first to document a case of amlodipine induced gingival enlargement.

In the light of above information, this study was conducted to determine the type of CCB causing GE, so that these patients are counseled to maintain good oral hygiene or drug substitution would be advised in consultation with the physician, and thereby improving the gingival health.

MATERIAL AND METHODS

The study included 30 study subjects & 30 control subjects both being age and sex matched, reporting as outpatients to the Department of Oral Medicine and Radiology at our Institute. Subjects taking CCB as antihypertensives for atleast 6 months and having atleast 12 natural teeth and subjects with no periodontal treatment within the previous 6 months were included in the study. However patients on polymedication for hypertension as well as other systemic diseases, patients unwilling to participate and patients on other drugs associated with GE were excluded.

A written consent was obtained from all the study subjects, and the demographic as well as medical history regarding hypertension in terms of duration, type of medication and dose in mg was noted. Ethical clearance from the Institutional Review Board was obtained. History of oral hygiene was recorded in terms of brushing habit, which revealed whether the subject brushed using brush or finger, with paste or abrasive, frequency and method.

Oral hygiene was assessed by Green and Vermillion index, gingival condition using Loe and Sillness index and gingival enlargement by Ingles index¹⁰. Gingival enlargement was measured using periodontal probe placing it perpendicular to the gingiva labially or buccally. (Fig 1)

Statistical analysis

The study parameters were tabulated and subjected for analysis using student't' test, Chi-Square test. The intergroup comparison (between study and control groups) was done using ANOVA test.

RESULTS

The study subjects ranged from 36-68 years with mean of 50.53±9 and 30 control subjects ranged from 32-63 years with mean of 49.37±8 (Table 1). The study comprised of 25(83%) females and 5(17%) males affirming the higher prevalence of hypertension among females, both groups being age and sex matched.

Distinctively almost all the subjects i.e 28(93%) in our study were taking amlodipine for more than 6 months with exception of one each on nifedipine and felodipine. This clearly revealed higher prescription of amlodipine.

Further 24 patients were on less than 5mg of amlodipine and 4 patients on greater than 5mg.

As per the duration, 20 patients were on amlodipine for less than 5 years and 10 patients for greater than 5 years.

Brushing technique was more or less similar in both the study and control subjects, where maximum subjects used horizontal brushing

Table 1: Distribution of age of study and control subjects

Age groups in years	Study	Control
31-40	5	4
41-50	12	13
51-60	8	9
61-70	6	4

method. In the present study, fair oral hygiene was present in 16(53%) study subjects and 20 (66%) had moderate gingivitis which was not significantly different from the controls(Table 2).

Regarding GE, 20(66%) subjects in study group had GE among which 12(40%) subjects had Grade II GE, 5(16%) had Grade III and 3(10%) had Grade I GE, as compared to controls where none had Grade II GE, which was statistically significant with p value < 0.001. (Graph 1, Table 3)

10(42%) patients taking amlodipine less

than 5 mg had Grade II GE and 4(17%) had Grade III GE, whereas 2(50%) patients taking greater than 5 mg had Grade II and 1(25%) had grade III GE (Graph 2), suggesting that dose does not affect the severity of GE as the differences were statistically insignificant.

8(40%) patients taking amlodipine for duration less than 5 yrs , had Grade II GE and 4(40%) patients taking amlodipine for duration greater than 5 yrs, had Grade II GE, revealing lack of significant correlation between duration of intake of drug and GE (Graph 3, Table 4)

Table 2: Distribution of type of gingivitis amongst the study and control groups

Groups	Mild	Moderate	Severe	X ₁ ² and p value
Study subjects	6	20	-	3.2 and 0.073 NS
Control subjects	13	14	1	

NS : Non significant

Table 3: No. of subjects showing different grades of GE in study and control groups

Groups	Grade 0	Grade I	Grade II	Grade III	X ₁ ² and p value
Study subjects	10	3	12	5	
Control subjects	11	19	0	0	28.6 and <0.001Sig

Sig: Significant

Table 4: Correlation between duration of CCB intake and gingival enlargement

Duration	Gingival enlargement				X ₁ ² and p value
	Grade 0	Grade I	Grade II	Grade III	
≤5 years	6	3	8	3	0.018 and >0.05NS
≥5 years	4	-	4	2	

NS : Non significant

DISCUSSION

In the present study, the study subjects had a mean age of 50.5years which is similar to reports of Seymour RA et al (1994)⁶, Barclay (1992)³

and Amit Kumar et al(2010)¹⁷ who reported cases between 35-66years with hypertension but in contrast to study by Jorgensen G M(1997)⁹ who had patients in age range of 33-87 years which could be due to differing prevalence of hypertension

among Indians, most common being the third decade.

Higher prevalence of hypertension among the females was observed, in the present study which is similar to that reported by Seymour RA et al (1994)⁶, Amit Kumar et al (2010)¹⁷ where all the patients affected were females, but in contrast to Barclay (1992)³ where 90% of males had reported.

Maximum subjects were on amlodipine which is due to its long duration of action and increased patient compliance as evaluated in a community survey¹ and is similar to all the patients on amlodipine as reported in different case series^{7,8,16,17}.

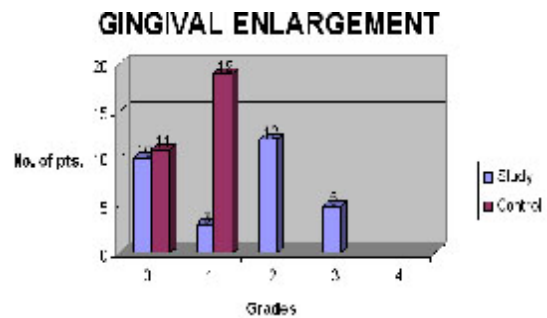
Fair oral hygiene was observed with moderate gingivitis which was in compliance with fair to poor oral hygiene as previously reported^{9,17,18}.

Gingival enlargement increases in presence of poor oral hygiene and pre-existing gingival inflammation. Inflammation develops due to direct toxic effects of drug in GCF leading to upregulation of cytokines such as TGF β 1 promoting tissue overgrowth^{13,15}. However it is also stated that individual susceptibility to develop fibrogenic response to the CCB is also variable. On the contrary Barclay et al³ and Jorgensen⁹ reported no relationship between gingival changes and plaque scores in their studies. Few authors have reported that evidence exists wherein oral hygiene procedures have reduced extent of GE and prevented its occurrence^{11,12}.

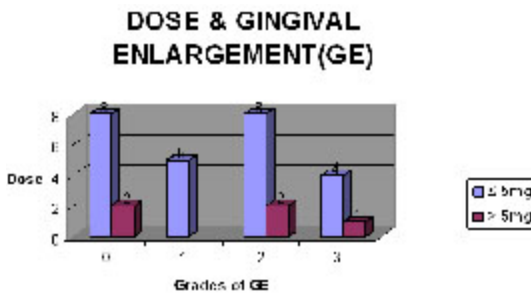
Regarding GE, maximum study subjects had Grade II GE which is in accordance to that reported by Lafzi (2006)¹³ who identified a patient with severe GE taking 10 mg amlodipine for 2 months, Seymour RA (1994)⁶, Abirmani K et al (2004)⁸, Vishaka(2007)¹⁶ and Amit Kumar et



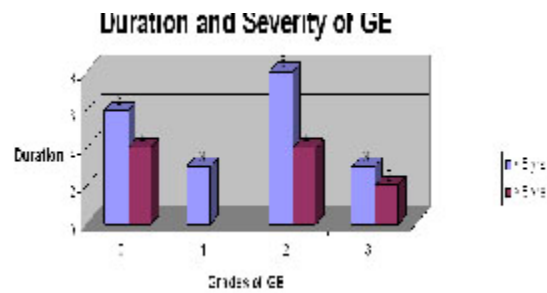
Fig. 1: Showing measurement of GE using periodontal probe



Graph 1: Gingival enlargement among study and control subjects



Graph 2: Showing relationship between dose of amlodipine intake and gingival enlargement



Graph 3: Showing relationship between duration of amlodipine intake and GE

al(2010)¹⁷, but contrast to Jorgensen(1997)⁹ who reported a prevalence of 3.3% of GE in 150 cardiac subjects on amlodipine(Graph I). This variation could be attributed to dosage variation, different population groups studied, different oral hygiene practices followed and varying individual susceptibility to GE.

Further dosage, duration of drug intake did not have any significant effect on severity of GE, which holds right for the fact that, patients on 5mgm of amlodipine for 6 months did not show GE⁹ when compared to patient on amlodipine only for 2 months had remarkable GE¹³, suggesting GE due to CCB to be multifactorial.

Our study subjects were referred to Department of Periodontology where they were subjected to periodontal therapy based on severity of GE. Mild to moderate GE subjects underwent scaling followed by root planning and curettage.

Severe enlargement subjects were referred to their physicians and drug substitution was advised followed by surgical intervention.

GE provides susceptible sites for growth of microorganisms, reduces effectiveness of brushing, resulting in periodontitis. By the year 2025, it is estimated that 213.5 million people would be affected by HTN, with an expected increase in prescription of CCB. GE gets exacerbated in the presence of local factors.

Hence the general physicians should and must pay attention to patients oral hygiene while prescribing CCB and inform them regarding GE associated with these drugs. The oral physicians should emphasize on educating patients taking CCB to maintain good oral hygiene thus preventing GE, provided in cases where oral hygiene methods fail, drug substitution should be advised after consultation with the patient's physician.

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