Original Article

DOI: 10.7860/JCDR/2023/58493.17613

Dentistry Section

Comparison of Three Different Calcium Channel Blockers on Gingival Overgrowth in Hypertensive Patients

KISHORE KUMAR KATURI[1], SURESH JANNU[2], APARNA DUDDU[3], SWETHA CHENNU[4], SHIVANI CHERUVU[5], RAMANARAYANA BOYAPATI[6]

ABSTRACT

Introduction: Calcium Channel Blockers (CCBs) like Nifedipine is the most widely used drug in many countries in the management of hypertension, with other drugs also in use like Amlodipine, and Felodipine. Gingival hyperplasia is the common adverse effect of the three classes of CCBs used commonly as dihydropyridine calcium antagonists.

Aim: To compare the effect of three different CBCs on gingival overgrowth in hypertensive patients.

Materials and Methods: The present cross-sectional study was carried out in the Department of Periodontics, Sibar Institute of Dental Sciences, Guntur, Andhra Pradesh, India. The study was conducted between September 2020 and February 2022. A total of 206 patients with hypertension taking CCBs, were enrolled and divided into three groups based on the patient's medication as group I (nifedipine; n=83), group II (amlodipine; n=71) and group III (felodipine; n=52). Gingival Overgrowth (GOG) was graded and periodontal parameters like Plaque Index (PI), Gingival Index (GI), and Probing Pocket Depth (PPD) were recorded. One-way analysis of variance and Tukey's post-hoc test were done to evaluate and compare between the groups.

Results: Mean age of the patients in group I was 60.81±4.13 years, in group II was 62.70±4.19 years, and in group III was 59.54±3.42 years. No significant difference in PI scores and GI scores was seen between the groups. The mean score for PPD in group I was 5.91±0.14 mm, in group II score was 5.76±0.14 mm and in group III the score was 5.13±0.22 mm. A statistically significant difference ($p<0.001$) was observed in group I when compared with group II and group III. The mean GOG scores in group I, group II, and group III were 3.49±0.22, 2.98±0.3, and 2.74±0.16, respectively. A statistically significant ($p=0.001$) increase in GOG scores was observed in group I followed by group II and group III.

Conclusion: Nifedipine was the most prescribed drug with high amount of gingival overgrowth in patients with hypertension, compared with amlodipine and felodipine.

Keywords: Blood pressure, Dihydropyridine calcium antagonists, Gingival hyperplasia

INTRODUCTION

Hypertension is one of the most frequent cardiovascular disorders affecting adults and the elder population that increases the risk of stroke, coronary heart disease, and heart failure [1]. Hypertension was defined by systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mm, in accordance with World Health Organisation (WHO) and American Heart Association recommendations [2]. The risk for cardiovascular disease problems increases at a very high percentage about >30%, with the presence of risk factors [3].

Dihydropyridinic CCBs are considered one of the first-line therapeutic options to treat hypertension and reduce hypertension related cardiovascular morbidity and mortality. These CCB have ability to interact with either cardiac or vascular (or both) L-type voltage-dependent transmembrane calcium channels. The dihydropyridinic agents are nifedipine, amlodipine, and felodipine respectively, which mostly act as dilating agents at the peripheral vessel level [4].

The prevalence of gingival overgrowth relates to genetic factors, age, dosage, duration of intake, and oral hygiene status [5]. GOG was reported as a common adverse effect with the usage of different classes of calcium channel blocker drugs due to an exuberant response by the gingival tissue to various changes between the host and environment [6,7].

The CCB drugs are commonly used in the treatment of various cardiovascular problems such as unstable angina, hypertension, arrhythmias, acute myocardial infarction, and ischaemic heart disease due to their easy availability and low cost [8,9].

Nifedipine-associated gingival overgrowth was first reported by Lederman D et al., in 1984 [10]. Histologically, gingival tissue overgrowth shows an increase in the number of cellular proliferation and intercellular actions mainly decreasing the production of matrix metalloproteinases which are responsible for collagen degradation during tissue homeostasis [11].

Later Lafzi A et al., reported amlodipine-induced gingival enlargement [12]. Lombardi T et al., reported gingival hyperplasia in a patient treated with felodipine [13]. Although such overgrowths show an inflammatory stimulus over the bacterial plaque, susceptibility to the other possible systemic factors influences the amount of gingival overgrowth in hypertensive patients [14].

Previous studies were carried out in different types of population has reported high prevelance of gingival overgrowth with the three different CCB [15,16]. Previously, published data available among Indian population was scarce with only two cross-sectional studies were published regarding the prevalence of gingival overgrowth in hypertensive patients using nifedipine and amlodipine [17,18]. To the best of our knowledge, no study has been carried out to compare the association of use of three CCBs (nifedipine, amlodipine, felodipine) with gingival overgrowth.

Thus, the present cross-sectional study was carried out to observe the prevalence of gingival overgrowth in hypertensive patients consuming three different types of CCB.

MATERIALS AND METHODS

The present cross-sectional study was carried out in the Department of Periodontics, Sibar Institute of Dental Sciences, Guntur, Andhra Pradesh, India. The study was conducted between September 2020 and February 2022. The study was approved by an Institutional

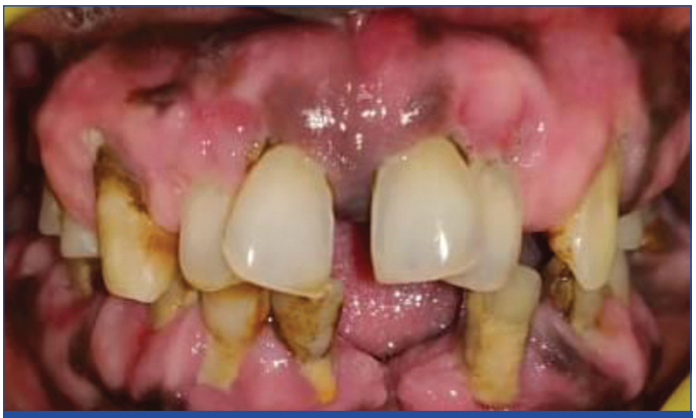
Ethical Committee (Pr.242/IEC/SIBAR/2020) and an informed consent was obtained from patients who are willing to participate in the study. Patients suffering from hypertension (systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg) according to the classification of the American heart association were included in the study [2].

Sample size calculation: Sample size was determined with an effect size of 1.7, α error of 0.05, and a power of 80% was considered [19].

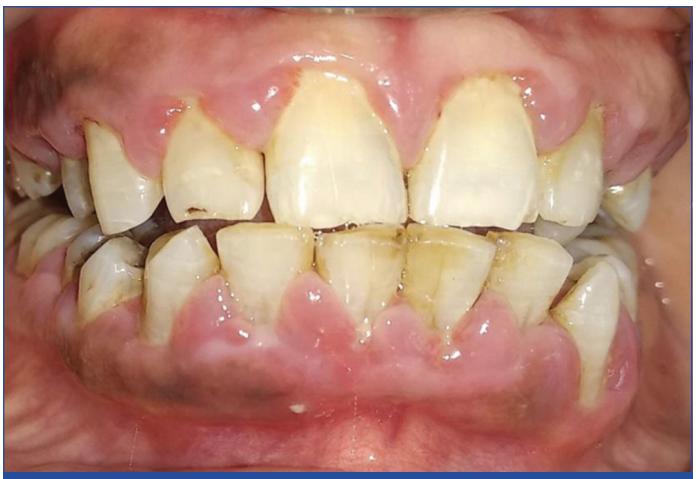
Final sample size of 206 was calculated by using the following formula:

$$n=\frac{n=2(Z_a+Z_{1-\beta})^{2\sigma 2,}}{\Delta^2}$$

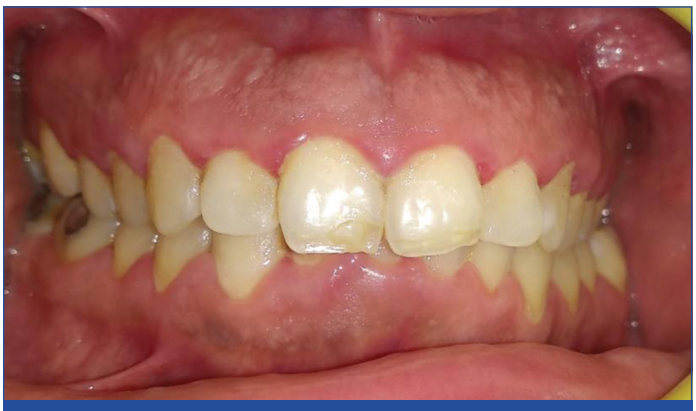
All the recruited patients were divided into three groups based on the type of CCB as group I (n=83; Nifedipine), group II (n=71; Amlodipine), and group III (n=52; Felodipine) [Table/Fig-1-3].



[Table/Fig-1]: Nifedipine induced gingival overgrowth.



[Table/Fig-2]: Amlodipine induced gingival overgrowth.



[Table/Fig-3]: Felodipine induced gingival overgrowth.

Inclusion criteria: Patients diagnosed with hypertension and under antihypertensive therapy for atleast one year, patients above 40 years of age, and those who had not undergone any form of periodontal treatment in the past six months were included in the study.

Exclusion criteria: Patients without having proper medical records for regular visits, patients having the habit of smoking or any form of tobacco use, patients who were suffering from other systemic diseases, patients who were under medication other than CCB that have an impact on the gingival tissues, pregnancy or lactation were excluded from the study.

Study Procedure

Intraoral examination was done and periodontal parameters were recorded by a single calibrated examiner. Periodontal parameters like PI, GI, and PPD were recorded by measuring from the gingival margin to the base of the sulcus using the UNC -15 periodontal probe (Hu-Friedy, Chicago, USA) [20].

The GOG was assessed by the grading index given by Eva and Ingles [21]. The buccal papilla and palatal/lingual papilla were measured separately. Grade 0: No overgrowth, firm adaptation of the attached gingiva to the underlying alveolar bone; Grade 1: early overgrowth, as evidenced by an increase in density of the gingiva with marked stippling and granular appearance; Grade 2: moderate overgrowth, manifested by an increase in the size of the papilla and/or rolled gingival margins; Grade 3: marked overgrowth, represented by the encroachment of the gingiva onto the clinical crown; Grade 4: severe overgrowth, characterised by a profound thickening of the gingiva.

The final grading score was calculated as=Total score/no. of papilla measured.

STATISTICAL ANALYSIS

The collected data was stored in Microsoft excel and analysed using windows SPSS statistics version 25.0. IBM corp, USA Kruskal-Wallis one-way analysis of variance is done for the evaluation of mean values for the PI, GI, and PPD. A pair-wise comparison between the groups was done using the Tukeys post-hoc test.

RESULTS

Patients suffering from hypertension, irrespective of gender were included and divided into three groups based on the patient's medication.

The age of the patients included in the study was between 50-70 years, with the mean age in group I being 60.81±4.13 years and in group II mean age was 62.70±4.19 years, and group III mean age was 59.54±3.42 years, respectively. No statistically significant difference (p=0.758) was observed in age between the groups. Gender distribution in group I was 57 males and 26 females, in group II there were 53 males and 18 females and in group III there were 41 males and 11 females, respectively [Table/Fig-4].

Group	n	Mean±SD (years)	SE	F-value	p-value
Nifedipine	83	60.81±4.13	0.45	0.277	0.758
Amlodipine	71	62.70±4.19	0.49		
Felodipine	52	59.54±3.42	0.47		

[Table/Fig-4]: Comparison of mean age between the study groups.
One-way Analysis of Variance; p≤0.05 considered statistically significant

The mean PI score in group I was 1.79±0.38, in group II, the score was 1.81±0.39, and in group III, the score was 1.78±0.5. When PI scores were compared between the groups, there was no statistically significant (p=0.955) difference in PI scores observed between the groups [Table/Fig-5].

Group	n	Mean±SD	SE	F-value	p-value
Nifedipine	83	1.79±0.38	0.04	0.046	0.955
Amlodipine	71	1.81±0.39	0.04		
Felodipine	52	1.78±0.5	0.07		

[Table/Fig-5]: Comparison of mean Plaque Index (PI) scores between the study groups.
One-way Analysis of Variance; p≤0.05 considered statistically significant

The mean GI score in group I, group II, and group III were 1.13±0.3, 1.05±0.3, and 0.98±0.3, respectively. There was a statistically significant difference (p=0.021) in group I when compared with group II and group III [Table/Fig-6]. Intergroup comparison of GI scores showed an increase in group I than in group II and group III, which was statistically significant (p=0.05) [Table/Fig-7].

Group	n	Mean±SD	SE	F-value	p-value
Nifedipine	83	1.13±0.3	0.03	3.948	0.021*
Amlodipine	71	1.05±0.3	0.036		
Felodipine	52	0.98±0.3	0.04		

[Table/Fig-6]: Comparison of mean gingival index scores between the study groups.
One-way Analysis of Variance; p≤0.05 considered statistically significant; *statistical significant

Reference group	Comparison group	Mean difference	p-value
Nifedipine	Amlodipine	0.08	0.05*
	Felodipine	0.15	0.05*
Amlodipine	Felodipine	0.07	0.05*

[Table/Fig-7]: Pair-wise comparisons of mean gingival index scores between the study groups.
Tukey's post-hoc tests; p≤0.05 considered statistically significant; *statistical significant

The mean score for PPD in group I was 5.91±0.14, in group II mean score was 5.76±0.14 and in group III the score was 5.13±0.22. A highly significant difference (p=0.001) in PPD was observed in group I when compared with group II and group III [Table/Fig-8]. The pair-wise comparisons of mean PPD between the study groups show that group I has a highly significant (p=0.001) PPD over group II and group III. A significant difference was also found in group II in comparison with group III which was statistically significant (p=0.001) [Table/Fig-9].

Group	n	Mean±SD (mm)	SE	F-value	p-value
Nifedipine	83	5.91±0.14	0.01	308.51	0.001*
Amlodipine	71	5.76±0.14	0.01		
Felodipine	52	5.13±0.22	0.03		

[Table/Fig-8]: Comparison of mean probing pocket depth between the study groups.
One-way Analysis of Variance; p≤0.05 considered statistically significant; *statistical significance

Reference group	Comparison group	Mean difference	p-value
Nifedipine	Amlodipine	0.15	0.001*
	Felodipine	0.78	0.001*
Amlodipine	Felodipine	0.63	0.001*

[Table/Fig-9]: Pair-wise comparisons of mean probing pocket depth between the study groups.
Tukey's post-hoc tests; p≤0.001 considered statistically significant; *Statistical significance

The mean GOG scores in group I, group II, and group III were 3.49±0.22, 2.98±0.3, and 2.74±0.16, respectively. There was a statistically significant difference (p=0.001) in GOG scores in group I was seen followed by group II and group III [Table/Fig-10]. Pair-wise comparisons of the mean GOG scores of the study groups showed that the mean difference between group I and group II was 0.51, between group I and group III was 0.75, and between group II and group III, the mean difference was 0.24 which was statistically significant (p=0.001) [Table/Fig-11].

Group	N	Mean±SD	SE	F-value	p-value
Nifedipine	83	3.49±0.22	0.02	174.12	0.001*
Amlodipine	71	2.98±0.3	0.03		
Felodipine	52	2.74±0.16	0.02		

[Table/Fig-10]: Comparison of mean gingival overgrowth scores between the study groups.
One-way Analysis of Variance; p≤0.001 considered statistically significant; *statistical significance

Reference group	Comparison group	Mean difference	p-value
Nifedipine	Amlodipine	0.51	0.001*
	Felodipine	0.75	0.001*
Amlodipine	Felodipine	0.24	0.001*

[Table/Fig-11]: Pair-wise comparisons of mean gingival overgrowth scores between the study groups.
Tukey's post-hoc tests; p≤0.001 considered statistically significant; *statistical significance

DISCUSSION

The present study has been carried out to measure the severity of gingival overgrowth associated with three different CCBs (nifedipine, amlodipine, and felodipine) in patients with hypertension. Nifedipine and amlodipine taking patients showed greater GI scores, PPD, and GOG than patients taking felodipine.

The GOG occurs predominantly due to interaction of the drug within the gingival connective tissue, although the pathogenesis was concluded as multifactorial [22].

Pathogenic pathways explained for the cause of the enlargement were due to the acceleration of intracellular fibroblast growth factor and transforming growth factor β. GOG was seen mostly after the long-term use of these drugs in the presence of plaque leading to the secretion of inflammatory cytokines such as IL-1, IL-8, and IL-6 causing increased fibroblasts proliferation leading to collagen synthesis [23,24].

Nery EB et al., first observed a high-risk of gingival hyperplasia in subjects who were under nifedipine dentate subjects than in edentulous subjects [25]. Jorgensen MG conducted a study among patients with hypertension who are using amlodipine and found that GOG was 3.3% [26]. Later, studies by Lafzi A et al., and Karnik R et al., also observed the prevalence of amlodipine induced GOG and both have reported 6.3-83% of GOG in hypertensive patients [12,17].

Miranda J et al., conducted a cross-sectional study to determine the GOG and associated risk factors in nifedipine-treated patients. The study found that GOG was higher in nifedipine-taking patients when compared with non recievers of the drug [27].

Vidal F et al., conducted a study on the association of CCB use with the prevalence of GOG and found that 34% of hypertensive patients presented GOG. Among all the three CCBs, Nifedipine was reported with 35.2% followed by amlodipine (20.4%) and felodipine (12.5%). The study also reported high plaque scores, PPD, and CAL scores were associated with GOG in patients with hypertension [28].

According to a study conducted by Karnik R et al., a high prevalence of gingival overgrowth was reported in 157 dentate patients with hypertension who were using amlodipine with a high-risk ratio due to significantly increased plaque and gingival index scores [17].

Similar findings were also reported in a hospital-based study by Gopal S et al., where they observed the prevalence of GOG in three different types of CCB and found a significantly high in nifedipine-treated patients (75%) than amlodipine and felodipine [18].

The GI scores were found to be significantly high in all the three CCB with more severe gingival inflammation observed in nifedipine and amlodipine-taking patients than felodipine. The present study is also in agreement with earlier studies where increased GOG scores were found in patients who were under nifedipine than amlodipine and felodipine [Table/Fig-12] [7,12,15-18,27,28].

Felodipine consuming patients in this study showed less amount of GOG than the other CCBs. This observation was by following the order of an earlier case reports and a cross-sectional study. Young PC et al., presented a case report on GOG in hypertensive patient after initiation of felodipine drug and later improved upon its discontinuation [29]. Another case reports by Fay AA et al., and Sun L et al., presented a clinical and histologic case of felodipine-influenced GE in an hypertensive patient with type 2 diabetes [30,31]. A cross-sectional study conducted by Vidal F et al., in hypertensive patients showed that 12.5% of felodipine-taking patients exhibited GOG compared to nifedipine (40%) and amlodipine (27.3%) and case reports [28].

S. No.	Author's name and year	Place of study	Number of subjects	Objective of the study	Parameters compared	Conclusion
1	Miranda J et al., 2001 [27]	Barcelona, Spain	n=212 (65=nifedipine and 147=healthy)	Prevalence of gingival enlargement in nifedipine treated patients.	PI, GI, PPD and GO	Patients taking nifedipine are at high-risk for gingival enlargement.
2	Kaur G et al., 2010 [7]	Netherlands	n=20,636 (patients taking CCB or RAS)	Dose and type of CCBs on the risk of gingival hyperplasia.	Symptomatic gingival hyperplasia compared with risk factors	Two-fold higher risk of gingival hyperplasia in CCB users than RAS.
3	Karnik R et al., 2012 [17]	Manipal, India	n=157 (dentate adult patients using CCB)	Prevalence of amlodipine-induced GO among elderly subjects.	PI, GI and GO	High prevalence of amlodipine-associated GO was reported.
4	Gopal S et al., 2015 [18]	Calicut, India	n=133 (hypertensive patients taking CCB)	Prevalence and risk factors for GO in patients treated with CCB.	PI, GI, PPD and GO	Patients taking nifedipine showed a higher frequency of GO.
5	Umeizudike KA et al., 2017 [16]	Nigeria	n=116 (58=CCB and 58=non CCB)	Association of CCBs with GO in hypertensive patients.	PI, GI and GO	The risk of GO is three times higher in CCB than non CCB users and twice higher in amlodipine than nifedipine.
6	Vidal F et al., 2018 [28]	Brazil	n=160 refractory (hypertensive patients using CCB)	Association between nifedipine, amlodipine and felodipine with severity of GO.	GO, PPD, CAL, PI and BOP	55 patients (34%) has GO with high percentage in nifedipine (40%) and amlodipine (27.3%) than felodipine (12.5%) was observed.
7	Ustaoglu G et al., 2020 [15]	Turkey	n=131 (hypertensive patients)	Rate of GO in patients treated with ACE inhibitors, ARBs and CCBs.	GO, PPD, CAL, PI, GI and BOP	All the three types of drugs showed with more severity in CCB (19.6%) followed by ARBs (12.5%) and ACE inhibitors (7.5%).
8	Present study	Sibar Institute of Dental Sciences, Guntur, Andhra Pradesh, India	n=206 (hypertensive patients)	Association of three types of CCB with GO in hypertensive patients.	PI, GI, PPD and GO	All the three types of CCB showed GO, with high GO in nifedipine group patients. Moderate GO was observed in amlodipine patients and less GO was observed in felodipine patients.

[Table/Fig-12]: List of previously published studies [7,12,15-18,27,28].
*=Hu-Friedy, Chicago, USA.
†=windows SPSS 25.0 version, IBM corp, USA

Genetic predisposition has been considered to be the other risk factor influenced by the metabolism of nifedipine drugs in the gingival tissues. MDR-1 gene polymorphisms are said to be associated with the modified inflammatory response of host tissues towards the drug [32]. In-vitro analysis of the drug action in host tissues is by overexpression of c-Myc and Bcl-2 oncoprotein genes in the hyperplastic gingival epithelium [33].

Another in-vitro study carried out to observe the effect of amlodipine on hyperplastic gingival tissues showed the overexpression of CCR10 and IL-1A related genes in hyperplastic connective tissue [34].

In this observational study, the predominant drug prescribed by the physicians to the patients was nifedipine or amlodipine because of their quick action and minimum adverse effects. Felodipine was prescribed to less number of patients probably due to cost-effectiveness compared to nifedipine, drug interactions, and due to mild positive inotropic effects.

Limitation(s)

Patients with different stages of hypertension and patients suffering from refractory hypertension which presented with serious effects on the cardiovascular system were not included. Based on the frequency and duration of drug intake, patients were not categorised. Personal habits like alcohol consumption, daily physical activities, diet, and oral hygiene practices were also not considered. The effect of felodipine on GOG was not found to be less significant due to less number of patients observed in this study. Future studies are recommended to be carried out in a large number of patients to address the severity of GOG based on the use of these three CCBs.

CONCLUSION(S)

The present cross-sectional study carried out in patients with hypertension to observe the association of CCB with GOG. Age and oral hygiene (PI) were similar in all the patients, although nifedipine and amlodipine taking patients showed increased GOG than the patients who are under felodipine. Felodipine can be considered as an alternative medication for hypertension to reduce GOG with periodic periodontal health maintenance.

REFERENCES

[1] Herman W, Konzelman JL Jr, Prisant LM. New national guidelines on hypertension: A summary for dentistry. J Am Dent Assoc. 2004;135:576-84.
[2] Whelton PK, Carey RM. The 2017 American College of Cardiology/American Heart Association clinical practice guideline for high blood pressure in adults. JAMA Cardiol. 2018;3(4):352-53.
[3] Lawes CM, Vander Hoorn S, Rodgers A. Global burden of blood-pressure-related disease, 2001. Lancet. 2008;371:1513-18.
[4] Tocci G, Battistoni A, Passerini J, Musumeci MB, Francia P, Ferrucci A, et al. Calcium channel blockers and hypertension. J Cardiovasc Pharmacol Ther. 2015;20(2):121-30.
[5] Seymour RA, Thomason JM, Ellis JS. The pathogenesis of drug-induced gingival overgrowth. J Clin Periodontol. 1996;23:165-75.
[6] Nishikawa S, Tada H, Hamasaki A, Kasahara S, Kido J, Nagata T, et al. Nifedipine-induced gingival hyperplasia: A clinical and in vitro study. J Periodontol. 1991;62(1):30-35.
[7] Kaur G, Verhamme KM, Dieleman JP, Vanrolleghem A, van Soest EM, Stricker BH, et al. Association between calcium channel blockers and gingival hyperplasia. J Clin Periodontol. 2010;37(7):625-30.
[8] Pontremoli R, Leoncini G, Parodi A. Use of nifedipine in the treatment of hypertension. Expert Rev Cardiovasc Ther. 2005;3(1):43-50.
[9] Fardal O, Lygre H. Management of periodontal disease in patients using calcium channel blockers-gingival overgrowth, prescribed medications, treatment responses, and added treatment costs. J Clin Periodontol. 2015;42(7):640-46.
[10] Lederman D, Lumerman H, Reuben S, Freedman PD. Gingival hyperplasia associated with nifedipine therapy. Report of a case. Oral Surg Oral Med Oral Pathol. 1984;57(6):620-22.
[11] Brown RS, Beaver WT, Bottomley WK. On the mechanism of drug-induced gingival hyperplasia. J Oral Pathol Med. 1991;20:201-09.
[12] Lafzi A, Farahani RM, Shoja MA. Amlodipine-induced gingival hyperplasia. Med Oral Patol Oral Cir Bucal. 2006;11(6):E480-82.
[13] Lombardi T, Fiore-Donno G, Belser U, Di Felice R. Felodipine-induced gingival hyperplasia: A clinical and histologic study. J Oral Pathol Med. 1991;20:89-92.

[14] Kataoka M, Kido J, Shinohara Y, Nagata T. Drug-induced gingival overgrowth--a review. Biol Pharm Bull. 2005;28(10):1817-21.
[15] Ustaoğlu G, Erdal E, Karaş Z. Influence of different anti-hypertensive drugs on gingival overgrowth: A cross-sectional study in a Turkish population. Oral Dis. 2021;27(5):1313-19.
[16] Umeizudike KA, Olawuyi AB, Umeizudike TI, Olusegun-Joseph AD, Bello BT. Effect of calcium channel blockers on gingival tissues in hypertensive patients in Lagos, Nigeria: A pilot study. Contemp Clin Dent. 2017;8:565-70.
[17] Karnik R, Bhat KM, Bhat GS. Prevalence of gingival overgrowth among elderly patients under amlodipine therapy at a large Indian teaching hospital. Gerodontology. 2012;29:209-13.
[18] Gopal S, Joseph R, Santhosh VC, Kumar VVH, Joseph S, Shete AR. Prevalence of gingival overgrowth induced by antihypertensive drugs: A hospital-based study. J Indian Soc Periodontol. 2015;19:308-11.
[19] Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods. 2007;39(2):175-91.
[20] Loe H. The gingival index, the plaque index, and the retention index system. J Periodontol. 1967;38(6):610-16.
[21] Inglés E, Rossmann JA, Caffesse RG. New clinical index for drug-induced gingival overgrowth. Quintessence Int. 1999;30(7):467-73.
[22] Ellis JS, Seymour RA, Steele JG, Robertson P, Butler TJ, Thomason JM. Prevalence of gingival overgrowth induced by calcium channel blockers: A community-based study. J Periodontol. 1999;70:63-67.
[23] Calhoun DA, Jones D, Textor S, Goff DC, Murphy TP, Toto RD, et al. Resistant hypertension: Diagnosis, evaluation, and treatment. A scientific statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research. Hypertension. 2008;51:1403-19.
[24] Dongari-Bagtzoglou A. Research, Science and Therapy Committee, American Academy of Periodontology. Drug-associated gingival enlargement. J Periodontol. 2004;75(10):1424-31.
[25] Nery EB, Edson RG, Lee KK, Pruthi VK, Watson J. Prevalence of nifedipine induced gingival hyperplasia. Journal of Periodontal. 1995;66(7):572-78.
[26] Jorgensen MG. Prevalence of amlodipine-related gingival hyperplasia. J Periodontol. 1997;68(7):676-78.
[27] Miranda J, Brunet L, Roset P, Berini L, Farré M, Mendieta C. Prevalence and risk of gingival enlargement in patients treated with nifedipine. J Periodontol. 2001;72(5):605-11.
[28] Vidal F, de Souza RC, Ferreira DC, Fischer RG, Gonçalves LS. Influence of 3 calcium channel blockers on gingival overgrowth in a population of severe refractory hypertensive patients. J Periodontal Res. 2018;53(5):721-26.
[29] Young PC, Turiansky GW, Sau P, Liebman MD, Benson PM. Felodipine-induced gingival hyperplasia. Cutis. 1998;62(1):41-43.
[30] Fay AA, Satheesh K, Gapski R. Felodipine-influenced gingival enlargement in an uncontrolled type 2 diabetic patient. J Periodontol. 2005;76(7):1217.
[31] Sun L, Wang C, Xi S, Zhou T, Wang G, Gang X. Felodipine-associated gingival overgrowth in type 2 diabetic patient: A case report and literature review. Exp Ther Med. 2019;17(5):3399-402.
[32] Meisel P, Giebel J, Kunert-Keil C, Dazert P, Kroemer HK, Kocher T. MDR1 gene polymorphisms and risk of gingival hyperplasia induced by calcium antagonists. Clin Pharmacol Ther. 2006;79:62-71.
[33] Saito K, Mori S, Tanda N, Sakamoto S. Immunolocalization of c-Myc and BCL-2 proto-oncogene products in gingival hyperplasia induced by nifedipine and phenytoin. J Periodontol. 2000;71(1):44-49.
[34] Lauritano D, Martinelli M, Baj A, Beltramini G, Candotto V, Ruggiero F, et al. Drug-induced gingival hyperplasia: An in vitro study using amlodipine and human gingival fibroblasts. Int J Immunopathol Pharmacol. 2019;33:2058738419827746.

PARTICULARS OF CONTRIBUTORS:
1. Professor, Department of Periodontics, Sibar Institute of Dental Sciences, Guntur, Andhra Pradesh, India.
2. Postgraduate, Department of Periodontics, Sibar Institute of Dental Sciences, Guntur, Andhra Pradesh, India.
3. Postgraduate, Department of Periodontics, Sibar Institute of Dental Sciences, Guntur, Andhra Pradesh, India.
4. Postgraduate, Department of Periodontics, Sibar Institute of Dental Sciences, Guntur, Andhra Pradesh, India.
5. Senior Lecturer, Department of Periodontics, Sibar Institute of Dental Sciences, Guntur, Andhra Pradesh, India.
6. Professor, Department of Periodontics, Sibar Institute of Dental Sciences, Guntur, Andhra Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Kishore Kumar Katuri,
Professor, Department of Periodontics, Sibar Institute of Dental Sciences, Takkelapadu, Guntur-522509, Andhra Pradesh, India.
E-mail: kishoreuga@yahoo.co.in

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jul 05, 2022
- Manual Googling: Sep 16, 2022
- iThenticate Software: Oct 31, 2022 (18%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Jul 04, 2022**
Date of Peer Review: **Sep 17, 2022**
Date of Acceptance: **Nov 01, 2022**
Date of Publishing: **Mar 01, 2023**