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Prevalence And Distribution Of Drug-Induced Gingival Enlargement In Urban Population - A Retrospective Cohort Study

Research Article

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Abstract

Drug-Induced gingival overgrowth is a well-recognised adverse effect of certain systemic medications. Calcium channel blockers, anticonvulsants and immunosuppressants are frequently implicated drugs in the aetiology of drug-induced gingival enlargement. The aim of the present study was to assess the prevalence and distribution of drug induced gingival enlargement in the patient population. Data were collected from the clinical record regarding, drug history and gingival enlargement.. Data were analysed to find out whether there was any significant difference in the prevalence of drug induced gingival enlargement with respect to different age groups, gender and the type of medication, using Chi-square test (SPSS software). There was a statistical significant difference in the prevalence rate of drug induced gingival enlargement in the age group < 30 years (p value-0.03). There was no statistical significant difference in the prevalence rate, between male and female patients (p value-0.37). There was a statistically significant difference in the prevalence rate among different medications (p value- 0.01). Prevalence rate of drug induced gingival enlargement was higher in patients under medication of phenytoin as compared to amlodipine and other drugs.

Keywords: Amlodipine; Cyclosporine; Drug-Induced; Gingival Enlargement; Nifedipine; Phenytoin.

Introduction

Gingival enlargement is an overgrowth or increase in size of the gingiva. It is the preferred term for all medication-related gingival lesions. Previously termed as gingival hyperplasia or gingival hypertrophy. Several causes of gingival enlargement are known and the most recognised is drug-induced gingival enlargement and it remains as a significant problem for the dentists and the periodontist.

An increasing number of medications are associated with gingival overgrowth. Currently, more than 20 prescription medications are associated with gingival enlargement [9]. Drugs associated with gingival overgrowth can be broadly divided into three categories: Anticonvulsant, calcium channel blockers and immunosuppressant.

Although the pharmacological effect of each of these drugs is different and directed towards various primary target tissues, all of them seem to act similarly on a secondary target tissue, that is, the gingival connective tissue causing common clinical and histopathological findings.

Clinical manifestations frequently appear within one to three months, after initiation of treatment with the associated medications. Gingival overgrowth normally begins at the interdental papillae and is more frequently found in the anterior segment of the labial surface. Gradually, gingival lobulations are formed that may appear inflamed or fibrotic in nature depending on the degree of local factor-induced inflammations. The fibrotic enlarge-

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ment is normally confined to the attached gingiva but may extend coronally causing the extensive disfigurement of gingiva. Among the causes of drug-induced gingival enlargement, phenytoin is the most common agent [10].

Phenytoin was first reported for causing gingival overgrowth by Hassel.et.al in 1981 [12]. Other anticonvulsants such as sodium valproate, phenobarbitone, vigabatrin and primidone have also been associated with gingival enlargement in adult patients but have been rarely reported [11].

Calcium channel blockers have been widely prescribed for the treatment of various cardiovascular diseases, mostly hypertension [6]. Calcium channel blockers were first reported in gingival enlargement in 1984 by Lederman.et.al, in patients treated with nifedipine [5].

Amlodipine was first reported for causing gingival overgrowth as a side effect by Seymour. et.al 1994 [31]. Cyclosporine induced gingival enlargement was first reported by Rateitschak. et.al 1983. [29].

The distribution of inflammatory enlargement is usually generalised or localised. Inflammatory enlargement can be plaque induced. Whereas, drug induced enlargement is usually generalised.

The difficulty in maintaining oral hygiene leads to further plaque accumulation and inflammation, the presence of previous inflammatory factors like cytokines, TNF - alpha, endothelins and IL-21 favours the action of drugs on the gingival connective tissue, perpetuating this cycle [18, 21, 34, 1, 23].

Besides gingival enlargement being an entity in periodontal disease, it may appear as a clinical feature in periodontitis. Periodontitis is a multifactorial disease with primary etiological factors being plaque and microflora [25, 26]. The treatment of periodontitis is a multidisciplinary approach, starting from synthetic drugs like antibiotics to regenerative methods [28, 30] like PRF [22], growth factors and stem cells [3, 16].

Periodontitis impedes proper dental hygiene and apart from cosmetic disfigurement, ensures painful chewing and eating, maintenance of oral hygiene and prevention of periodontal diseases can be done by using chlorhexidine, herbal mouthwashes [24-27].

Various studies have been done regarding the prevalence rate of drug induced gingival enlargement [2, 8]. This study has been undertaken to assess the prevalence and distribution of drug-induced gingival enlargement in urban populations in chennai.

The objective was (I) to assess the prevalence rate of drug induced gingival enlargement in different age groups,(II) to assess the prevalence rate of drug induced gingival enlargement in male and female patients,(III) to assess the prevalence rate of drug induced gingival enlargement with respect to different drugs.

Materials And Methods

A retrospective study was conducted in Saveetha Dental College, chennai. Before scheduling the retrospective study, the official permission was obtained from the Institutional ethical committee (ethical approval number - SDC/SIHEC/2020/DIASDATA/0619-0320).

Inclusion and Exclusion criteria

Patients with drug history and drug induced gingival enlargement were included in the study. Patients with inflammatory gingival enlargement were excluded from the study.

Data Collection

Case sheets of patients visiting a private dental institution were reviewed and 332 patients were under medication of Phenytoin, Amlodipine, Nifedipine and Cyclosporine. Among those patients under medication, 14 patients had drug induced gingival enlargement. Cross verification was done with another examiner to avoid any missing data values. Sampling bias was minimised by including all available data. Demographic details such as patient identity number(PID.No), age and sex were recorded. The grading of gingival enlargement was assessed by Bokenkamp and Bohnhorst'sclassification(1994) and entered as grade 1, 2 and 3. Data was entered in a methodological manner. Incomplete data were excluded from this study. Independent variables were age, gender and the dependent variable was drug history and prevalence of drug-induced gingival enlargement. Data were analysed to find out whether there was any significant difference in the prevalence of drug induced gingival enlargement with respect to different age groups, gender and the type of medication.

Statistical Analysis

Data was entered in Microsoft Excel sheets. The data was imported and transferred to the computer and subjected to statistical analysis using SPSS(IBM SPSS Statistics, Version 24.0, Armonk, NY: IBM Corp]. Chi-square test was performed to find the association between the variables. Null hypothesis was formulated for all the objectives. The level for a statistical significance was set at $p<0.05$. The results were demonstrated in the form of tables and bar graphs.

Results And Discussion

In the present study, Table 1 showed that 332 patients were under medication of anticonvulsant, calcium channel blockers and immunosuppressants. 33% were under medication of phenytoin, 66% were under medication of Amlodipine, 0.6% were under medication of nifedipine and 0.3% were under medication of cyclosporine. In the study done by Sowmya. et.al [8], it was reported that the distribution of patients under the medication of nifedipine and amlodipine were more.

Figure 1 showed that the prevalence of drug-induced gingival enlargement was seen more in patients in the age group of below 30 years. Our Null Hypothesis - There is no difference in the prevalence of gingival enlargement in different age groups. Chi-square test was done to check the null hypothesis. P value was 0.031 so the null hypothesis was rejected and an alternative hypothesis was accepted. There was a statistical significant difference in the prevalence rate of drug induced gingival enlargement in the age group < 30 years.

Studies by Greg. et.al [7] and Meena. et.al [19] also reported that phenytoin induced gingival enlargement was more common in children and in young adults. In the study by Jayanti. et.al [14] about Amlodipine induced gingival enlargement, it was reported that Amlodipine induced gingival enlargement was more prevalent in elderly people.

Table 2 showed that out of 332 patients under medication, 54% were females and 46% were males.

Figure 2 showed that the prevalence of drug-induced gingival enlargement was more in male patients than female patients. Our Null Hypothesis - There is no difference in the prevalence of gingival enlargement in gender. Chi-square test was done to check the null hypothesis.P value was 0.371 so null hypothesis was accepted. There was no statistical significance in the prevalence rate of drug induced gingival enlargement between male and female patients.

In the study by Greg. et.al [7] about phenytoin induced gingival enlargement, it was reported that males were more likely to develop overgrowth than females. In a similar study by Sowmya.et.al [8], it was reported that the prevalence of gingival overgrowth was higher in male patients. The studies reported by Baracketal [4], Thomson. et.al [33], Seymouretal [31], also reported that males were at a greater risk from developing drug-induced gingival enlargement than females.

Figure 3 showed that among drug induced gingival enlargement, 64.2% were phenytoin induced gingival enlargement, 21.4% were amlodipine induced gingival enlargement, 7.2% were nifedipine induced enlargement and 7.2% were cyclosporine induced enlargement. Our Null Hypothesis - There is no difference in the prevalence of gingival enlargement in various drugs used. Chi-square test was done to check the null hypothesis. P value was 0.01 so the null hypothesis was rejected and an alternative hypothesis was accepted. There was a statistically significant difference in the prevalence rate among different medications.

In the study by Jorgensen. et.al (Jorgensen, 1997), the prevalence of Amlodipine induced gingival enlargement was 3.3%. In a similar study by Sowmya. et.al [8], the frequency of occurrence of gingival overgrowth in patients under medication of antihypertensive drugs was 27.1%. Frequency of occurrence of gingival overgrowth was 75% for nifedipine, 31.4% for Amlodipine and 25% for Amlodipine and metoprolol combination. In the study done by Miranda. et.al [20], the prevalence of nifedipine induced gingival overgrowth ranged from 20 to 83%. In the study by Seymour. et.al 1994. [31], the prevalence of Amlodipine induced gingival overgrowth was 1.7%. In the study by Hernandez.et.al [13], it was reported that the prevalence of cyclosporine-induced gingival overgrowth was very less compared to other drugs. It also stated that gingival overgrowth after replacement of cyclosporine drug with tacrolimus.

Figure 4 showed that the Grade 2 of gingival enlargement was more commonly seen than grade 1 and grade 3. Among the patients with drug induced gingival enlargement, 57% belonged to Grade 2, 29% belonged to Grade 1 while the remaining 14% belonged to Grade 3 of gingival enlargement. Grading of gingival enlargement was done using Bokenkamp and Bohnhorst classification. Even in the study by Jayanti. et.al [14], it was reported that Grade 2 of gingival enlargement was more commonly seen in amlodipine induced gingival overgrowth.

The finding from the present study adds to the consensus of the

Table 1. Table depicts the percentage of drugs used in different age groups. Patients under the medication of amlodipine were more.

DRUGS USED					
AGE GROUPS	**Phenytoin**	**Amlodipine**	**Nifedipine**	**Cyclosporine**	**Total**
15-30	37 (11.4%)	2(0.60%)	0	0	39(12%)
31-45	50(15.06%)	36(10.84%)	0	0	86(26%)
46-60	15(4.52%)	118(35.54%)	0	1(0.30%)	134(40%)
61-75	9(2.71%)	62(18.67%)	2(0.60%)	0	73(22%)
	111(33.6%)	218(65.5%)	2(0.60%)	1(0.30%)	332

Figure 1. Bar chart depicts the association of gingival enlargement in different age groups. X-axis denotes age groups. Y-axis denotes the number of patients with gingival enlargement. Chi-square test was done and was found to be statistically significant (Pearson chi square, p value- 0.031;(<0.05). Drug induced gingival enlargement was more prevalent in the age group below 30 years.

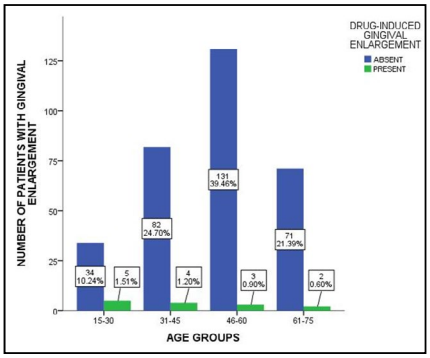


Table 2. Table depicts the percentage of drugs used in male and female patients. Females were more under medication than males.

DRUGS USED					
GENDER	Phenytoin	Amlodipine	Nifedipine	Cyclosporine	Total
Female	69(20.78%)	110(33.13%)	1(0.30%)	1(0.30%)	181(54%)
Male	42(12.65%)	108(32.53%)	1(0.30%)	0	151(46%)
	111(33.6%)	218(65.5%)	2(0.60%)	1(0.30%)	332

Figure 2. Bar chart depicts the association of gingival enlargement in male and female patients. X-axis denotes gender. Y-axis denotes the number of patients with gingival enlargement. Chi square test was done and was found to be statistically not significant (Pearson chi square, p value-0.371;(>0.05). Prevalence of drug induced gingival enlargement was more in male patients than in female patients.

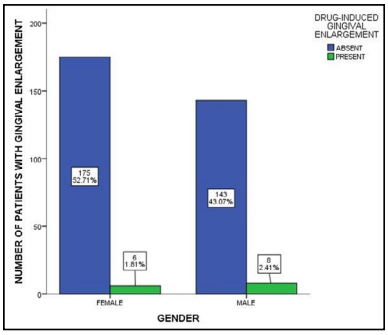


Figure 3. Bar chart depicts the prevalence of gingival enlargement in various drugs used. X-axis denotes various drugs used. Y-axis denotes the number of patients with gingival enlargement. Chi-square test was done and was found to be statistically significant (Pearson chi square, p value-0.01;(<0.05). Prevalence of drug-induced gingival enlargement was seen more in patients under the medication of phenytoin.

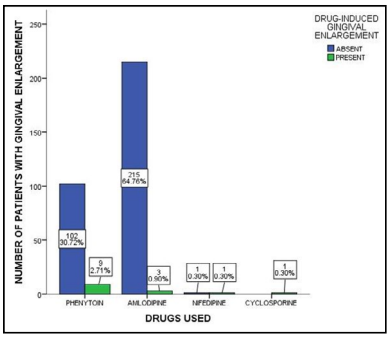
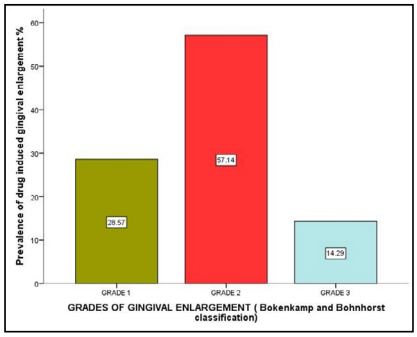


Figure 4. Bar chart depicts the prevalence of grades of gingival enlargement. X-axis denotes the grades of gingival enlargement. Y-axis denotes the prevalence of gingival enlargement. Grade 2 (Red) of gingival enlargement was seen more commonly than the Grade 1 and Grade 3.



previous studies. Limitations of the study were smaller sample size so it cannot be generalised to the whole population. Further studies can be done with a larger population and it can be a multicentered study.

Conclusion

Fromthe present study, we can conclude that there was a statistical significant difference in the prevalence rate of drug induced gingival enlargement in the age group < 35 years. There was no statistical significant difference in the prevalence rate, between male and female patients. There was a statistically significant difference in the prevalence rate among different medications. Prevalence rate of drug induced gingival enlargement was higher in patients under medication of phenytoin as compared to amlodipine and other drugs.

Author Contributions

First author (B .JohnRozar Raj) performed the analysis, interpretation and wrote the manuscript. Second author (Dr.N.D. Jayakumar) contributed to conception, data design, analysis, interpretation and critically reviewed the manuscript. Third author (Dr. Niveditha.M.S) participated in the study and reviewed the manuscript. All the three authors have discussed the results and contributed to the final manuscript.

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