Ministry of Higher Education

And Scientific Research

University of Diyala

College of Medicine

2022-2023

Article in

(Calcium channel blockers drugs and gingival health in hypertensive patients in Iraqi population)

Submitted to the Council of the College of Medicine, Diyala University, in Partial Fulfillment of Requirements for the Bachelor Degree in medicine and general surgery.

Submitted by :Ahmed Hassan Abbass

Supervised by: Ass. Lec. Ali Hakiem Tawfieq

قال تعالى:

{شَهِدَ اللَّهُ أَنَّهُ لا إِلَهَ إِلَّا هُوَ وَالْمَلائِكَةُ وَ أُولُو الْعِلْمِ قَائِماً بِالْقِسْطِ } آل عمران :18

Dedication

To his fragrant biography, and enlightened thought; He was the first credit for my attainment of higher education(My beloved father), may God prolong his life. To the one who put me on the path of life, and made me calm,She nursed me until I was big(My dear mother), may God bless her soul.to my brothers; Those who had a great impact on many obstacles and hardships.(for my teacher) Thank you from the bottom of my heart for your constant giving, and your wonderful stances. Words of praise do not fulfill your right, and all expressions of thanks do not describe how grateful I am to you .

Table of contents

Abstract

Gingival overgrowth (GO) or enlargement is an undesirable effect of drugs that occurs on the gingiva. Hypertension is a global burden systemic ailment that is becoming more prevalent, with more individuals receiving antihypertensive medications.

Objective: The purpose of this study was to determine the prevalence of drug-induced gingival overgrowth (DIGO) and related risk variables among hypertensive patients at Baquba Teaching Hospital.

Methods:This cross-sectional study included 50 patients with an average age of 48.86 years old. Individuals were chosen if they had been using antihypertensive medications for at least 6 months. Demographic information and dental hygiene status were collected, and the existence of DIGO was determined using a clinical index for gingival overgrowth.

Results: A total of 50 patients were recruited, with a mean age of 48.86 years. All of the patients were Iraqis, with somewhat more females (48%) than males (Table 1). About half of the patients (46%) had other systemic disorders such as diabetes mellitus, and only ten (20%) were smokers.

Conclusion: We find that DIGO is common (60%) in hypertensive individuals and is mostly caused by CCB. DIGO is not substantially connected with oral hygiene status or demographic data, but it is more likely to co-occur with generalised gingivitis.

INTRODUCTION

Gingival overgrowth (GO) or enlargement is an undesirable effect of drugs that occurs on the gingiva.1 It manifests as gingival swelling and disfiguration, usually affecting the interdental papilla and resulting in a lobulated or nodular morphology.2,3 Gingiva can swell slightly, interdentally, or diffusely, impacting both anterior and posterior teeth. This disorder impairs aesthetic, mastication, speaking, and oral hygiene measures, leading to additional periodontal degeneration.4 Anticonvulsants such as phenytoin, calcium channel blockers such as

Nifedipine and amlodipine, and immunosuppressive medications such as Cyclosporin A and tacrolimus are among the most prevalent drugs that have been reported to produce GO.5 The onset usually occurs within the first three months of starting the medicine, and it predominantly affects the anterior gingivae. Unless there is pre-existing periodontal disease, it is usually not related with attachment loss or tooth mobility.2,6,7 Yet, this disease may pose a significant challenge to dental hygiene routines, increasing the risk of periodontal infection and inflammatory consequences. 8 Hypertension is a worldwide chronic systemic illness that is common in many countries.9 As a result, more individuals are using antihypertensive medications, notably calcium channel blockers (CCBs) like nifedipine or amlodipine. Unfortunately, patients are frequently ignorant of the potential negative effects of those drugs in the oral cavity, which might impair mastication, aesthetics, and social life. 4 Furthermore, many people may be unaware of the health of their gingival tissue unless they experience symptoms such as gum bleeding. As a result, patients may have drug-induced gingival overgrowth (DIGO), which can only be recognized clinically by a doctor or dentist. To avoid this unfavorable consequence, patients should get an oral examination as soon as possible. Lederman first observed calcium channel blocker-induced GO in nifedipine patients in 1984.10 CCB is a calcium antagonist, a type of medicine that is often used to treat hypertension. The overall number of prescriptions for this class of medicines has increased in recent years. These are the most common drugs used in therapy of hypertension.11 Apart from ACE inhibitors, angiotensin II receptor blockers, diuretics, and B-blockers are also used.12 This medicine is effective and has seen substantial and widespread use over the world, with approximately 20% in the United States and 6% in the United Kingdom, with amlodipine being the most prescribed drug.13,14 These medicines, however, are implicated in the gingival disease because they encourage excessive development, presumably through a biochemical process. 5 The prevalence of GO caused by CCBs was predicted to range from 6% to 83% in the Caucasian population.1,14,15

DIGO is a regular phenomenon mentioned in the literature.16,17 Unfortunately, data from the local population is limited, despite the fact that several cases have been documented.3,18,19 Information or scientific data on the incidence of GO and its related risk factors in the local community may serve as justification for physicians to advise or refer their patients to dental practitioners as soon as possible. Furthermore, by identifying patients who are 'at risk,' appropriate treatment methods and early care can be created to prevent this unpleasant side effect of their medications. As a result, the purpose of this study was to establish the

prevalence of DIGO among hypertensive patients, particularly those on CCB, and to identify the risk factors for this illness.

METHODS

A cross-sectional study was conducted at the Outpatient Clinic, Baquba Teaching Hospital involving hypertensive patients who were taking anti-hypertensive agents for at least 6 months.

Participants were chosen at random from the waiting room during their follow-up visit to the clinic using easy sampling. We included all patients above the age of 18 who had at least 6 teeth. Individuals who had received periodontal therapy during the previous 6 months, those who were taking other medications or had other systemic conditions known to influence the gingiva, and pregnant women were excluded. Patients were told about the study protocols, and informed written consent was obtained. The patient's background, medical and medication history were obtained from the patient's record, and an oral examination was conducted. During the history-taking process, oral hygiene and smoking habits were noted. Participants were advised to seek routine periodontal treatment if they showed evidence of GO, periodontal disease, or another tooth condition. The Human Research Ethics Committee authorized the study protocol.
During oral examinations, plaque score (PS), gingivitis score (GS), and Clinical Index for Drug-induced Gingival Overgrowth (CIGO) were recorded. The standardized Michigan 'O' periodontal probe was used to measure all of these parameters.

Plaque Score

PS was carried out by visually detecting plaque and also by running the probe down the gingival margin. Plaque was recorded as presence (yes) or absence (no) on the buccal, lingual, mesial, and distal surfaces of the teeth and was reported as a percentage of the number of tooth surfaces inspected in each patient.

Gingivitis Score

GS was determined by gently probing the gingival crevice for the presence of bleeding. GS, like PS, was recorded for four tooth surfaces. If bleeding occurs within 10 seconds after probing, it is graded as present (yes) or absent (no) . For each patient, GS was expressed as a percentage of hemorrhage over the entire number of tooth surfaces examined.

Clinical Index for Drug-induced Gingival Overgrowth

This score was used to detect and classify drug-induced gingival overgrowth. It is simple to use and does not need diagnostic casts, but it does provide some indications of the severity of the lesions and aids in the choice of suitable therapy interventions based on a scoring scale of 0 to 4.

Grade 0- There is no overgrowth, solid adaptation of the connected gingiva to the underlying alveolar bone, zero or just slightly granular appearance, and knife-edged papilla toward the occlusal surface. There isn't any change in gingiva density or size.

Grade 1- Early overgrown, increased gingiva density with stippling and granular texture. The interdental papilla's tip is round.

Grade 2- Moderate overgrowth is marked by a rise in papilla size and/or rolling margins. The gingival margin contour remains concave or straight. The papilla is extendable to some amount. Gingival growth can have a buccolingual thickness of as much as two mm measured from the papilla tip outward.

Grade 3- Overgrowth is noticeable as gingiva encroaching on the clinical crown. The gingival border contour is convex morerthan concave. Gingival enlargement has a buccolingual size of 3 mm or more, measured from the papilla tip outward. The papilla is obviously extendable.

Grade 4- Extreme enlargement marked by significant gingiva thickening. A considerable portion of the clinical crown is protected. The papilla, like in grade 3, is retractable. The buccolingual dimension is about 3 mm.

Table 1. Demographic characteristic of the study subjects (n=50)

Variables	Frequency, n(%)
Age, years	**48.86**
Gender	
Male	**26 (52)**
Female	**24 (48)**
Ethnicity	
Iraqi	**50 (100)**
Type of antihypertensive	
[a]CCB	**50 (100)**
Other systemic diseases	
Yes	**23 (46)**
No	**27(54)**
Smoking habit	
Non-smokers	**40 (80)**
Smokers	**10 (20)**

HPT= hypertension CCB= calcium channel blockers
[a]47.6% Amlodipine

DIGO was detected in 20 (40%) of the patients. However there is no significant relationship between GO and antihypentensive medication kinds. Because As amlodipine is the most CCB taken, 12 (60%) of them had GO, with the majority having a clinical index of GO grade 1. (mild in severity).

Table 2. The prevalence of gingival overgrowth among hypertensive patients (n=50)

Variables	n (%)	CCB n (%)
Gingival overgrowth		
Present	20 (40)	**20 (40)**
Absent	**30 (60)**	**30 (60)**

[a]95%CI (38%, 73%); [b]Fisher's exact test; CCB=calcium channel blockers

M 44 sd yes smoker +

1. M 65 sd no smoker+
2. M 47 sd no smoker
3. M 66 sd yes smoker
4. M 45 sd no smoker +
5. F 60 sd yes smoker +
6. F 30 sd yes smoker
7. F 38 sd no smoker +
8. F 41 sd yes smoker

Data analysis

The Statistical Software for Social Sciences (SPSS) version 24 was used to analyze the data. Prior to analysis, data was checked and cleaned. The frequency (%) was calculated using descriptive analysis. The factors related were examined using the Chi-square test or the Fisher exact test, as appropriate.

RESULTS

A total of 50 patients were selected, with an average age of 48.86 years. Each of the patients were Iraqis, with somewhat less females (48%) than males (Table 1).Fewer than half of the patients (46%) had additional systemic disorders such as diabetes, and just ten (20%) were smokers. Almost 20% of the patients had been diagnosed as having hypertension for more than ten years, and 100percent were using CCB. Amlodipine was the most commonly given antihypertensive medication.

DISCUSSION

Twenty of the 50 patients on antihypertensive medication were clinically diagnosed with GO. The occurrence rate of GO is 40%. GO was discovered in patients using nifedipine and amlodipine. It was discovered that GO only was identified in patients who were using calcium channel blockers.

The prevalence of GO caused by nifedipine is substantially greater than in earlier research, where the prevalence of GO caused by nifedipine ranged from 20% to 83%.[3,5,11] The increased frequency of GO caused by nifedipine in this study may be related to the very tiny sample size because it was a hospital-based study and not a real reflection of the community. The decrease in nifedipine prescriptions over the last few years may have contributed to the small sample size.

In the current study, the frequency of amlodipine-induced overgrowth is 47.6%, which is greater than in earlier studies. Jorgensen 1997[14] reported a prevalence of 3.3%; Ellis *et al*. 1999[4] reported 1.7% for amlodipine induced GO. Patients taking amlodipine (47.6%) were more numerous than other drug users, as were those who presented with GO. According to the findings of this investigation, amlodipine can cause GO.

Four patients were given a combination of amlodipine and β blocker, one of whom developed GO. There is no report of GO caused by this drug combination in the literature. Because there have been no instances of GO caused by β blockers, this patient's overgrowth could have been caused by amlodipine.

Although there are reports of GO induced by diltiazem,[7,13] there are no reports for β blockers or losartan. The findings of previous studies[5,9,15] suggest that the dihydropyridines are more frequently cited as a cause of drug-induced GO than other types of calcium channel blockers. The nonsignificant effect of these drugs couldAlthough there are reports of GO induced by diltiazem,[7,13] there are no reports for β blockers or losartan. The findings of previous studies[5,9,15] suggest that the dihydropyridines are more frequently cited as a cause of drug-induced GO than other types of calcium channel blockers. The nonsignificant effect of these drugs could be because of a lack of statistical power in relation to a small sample size and reduced prescription of these drugs for cardiovascular treatment.

The number of males in the present study who presented with GO is 26 (52%) and that for females 24 (48%). Even though, the number of males is higher than females, the difference is not statistically significant. Case reports and previous prevalence studies on calcium channel blocker induced GO have had a strong male bias since men have a higher incidence of cardiovascular disease than women. A link to androgen metabolism has been suggested, since nifedipine increases the conversion of testosterone to 5α dihydrotestosterone when added to gingival fibroblasts in culture. It was hypothesized that there was a serum level at which overgrowth occurred, and that this amount was lower in males.The incidence of GO was observed to be highest for nifedipine, followed by amlodipine.Those consuming nifedipine appeared to be more likely than those taking amlodipine to have clinically significant overgrowth. The distinction between nifedipine and amlodipine is important because both medications are dihydropyridines and hence structurally identical. In addition, both are found in gingival crevicular fluid.Even though, the physicochemical profiles of the two medicines differ. While the mechanism of drug-induced GO is thought to be multifactorial,[16] the drug/cellular contact plays an important role in the pathophysiology of this effect.It might be suggested that the physicochemical nature of nifedipine facilitates such a drug/cellular interaction within gingival tissues.This does not happen as much with amlodipine. Because the sample size for nifedipine is substantially smaller than that for amlodipine, the current study cannot provide a real frequency for nifedipine-induced GO.

CONCLUSION

We find that DIGO is common (60%) in hypertensive individuals and is mostly caused by CCB. DIGO is not substantially connected with oral hygiene status or demographic information, but it is more likely to co-occur with generalized gingivitis. High blood pressure patients, specially those on CCB, should be recommended to have regular dental checkups to avoid and/or treat this unwelcome condition.Partnership with medical peers is also important in raising patient awareness.

REFERENCES

1. Andrew W, Evelyn W, Francis M, Mark J, Mark C. Pattern of gingival overgrowth among patients on antihypertensive pharmacotherapy at a Nairobi hospital in Kenya. Open J Stomatol. 2014;4:169-73.

2. Hassell TM, Hefti AF. Drug-induced gingival overgrowth: old problem, new problem. Crit Rev Oral Biol Med 1991;2:103-37.

3. Taib H, Ali TBT, Kamin S. Amlodipine-induced gingival overgrowth: a case report. Arch Orofac Sci. 2007;2:61-4.

4. Amit B, Shalu B. Gingival enlargement induced by anticonvulsants, calcium channel blockers and immunosuppressants: a review. IRJP. 2012;3:116-9.

5. Brown RS, Arany PR. Mechanism of drug-induced gingival overgrowth revisited: a unifying hypothesis. Oral Dis. 2015;21:e51-61.

6. Ellis J, Seymour R, Monkman S, Idle J. Disposition of nifedipine in plasma and gingival crevicular fluid in relation to drug-induced gingival overgrowth. J Periodont Res. 1993;28:373-8.

7. Kataoka M, Kido J-i, Shinohara Y, Nagata T. Drug-induced gingival overgrowth—a review. Biol Pharm Bull. 2005;28:1817-21.

8. Trackman PC, Kantarci A. Molecular and clinical aspects of drug-induced gingival overgrowth. J Dent Res. 2015;94:540-6.

9. Chia YC, Kario K. Asian management of hypertension: Cur rent status, home blood pressure, and specific concerns in Malaysia. J Clin Hypertens. 2020;22:497-500.

10. Seymour RA, Thomason JM, Ellis JS. The pathogenesis of drug-induced gingival overgrowth. J Clin Periodontol. 1996;23:165-75.

11. Seymour RA. Effects of medications on the periodontal tissues in health and disease. Periodontol 2000. 2006;40:120-9.

12. MOH. Clinical Practice Guidelines Management of Hypertension. 2018; http://www.acadmed.org. my/view_file.cfm?fileid=894. Accessed 27 April 2020.

13. Hughes A. Calcium Channel Blockers. Hypertension: A Companion to Braunwald's Heart Disease E-Book. 2017:242.

14. Beaumont J, Chesterman J, Kellett M, Durey K. Gingival overgrowth: Part 1: aetiology and clinical diagnosis. Br Dent J. 2017;222:85-91.

15. 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- 7.

16. Golob Deeb J, Lyons DJ, Laskin DM, Deeb GR. Severe drug-induced gingival enlargement and periodontitis: A case series with clinical presentation and management. Oral Maxillofac Surg Cases. 2020;6:100143.

17. 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.

18. Asari ASM. The expert says. Current concept in gingival overgrowth. Malays Dent J. 2007;28:107- 11.

19. Mason YKS, Rath A, Hesarghatta PR, Sidhu P, Fernandes B, Halasagundi V. Non-surgical management of amlodipine induced gingival

overgrowth: A short review and a case report. Asia Pac J Health Sci Res. 2017;2:9.