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Scientific Research

Pattern of Gingival Overgrowth among Patients on Antihypertensive Pharmacotherapy at a Nairobi Hospital in Kenya

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Abstract

The objective of the study was to describe the prevalence and severity of gingival overgrowth (GO) among patients on anti-hypertensive pharmacotherapy at a Nairobi hospital in Kenya and to evaluate the relationship between GO and associated risk factors among these patients. The study design was a cross-sectional survey using a consecutive convenient sampling method. All the patients were examined for gingival enlargement by the method described by Seymour, *et al.* and modified by the authors to allow for measurement in millimetres. Gingival inflammatory status and plaque scores were also evaluated. The results showed that of the 164 hypertensive patients recruited, 20.7% had gingival overgrowth. Slightly over half (56.1%) of these patients were on calcium channel blockers (CCB). Patients on CCB had a higher prevalence (31.5%) of GO compared to those on non-CCB (7%). This difference was statistically significant (Yates χ^2 = 13.39: 1 df: P = 0.000) with an odds ratio of 6.17 (95% CI 0.21 - 19.45). There was no statistically significant association between gender, drug dosage, plaque levels and gingivitis with GO. In conclusion, usage of CCB pharmacotherapy showed a significant association with GO.

Keywords

Gingival Overgrowth; Hypertension; Calcium Channel Blockers

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1. Introduction

Gingival overgrowth (GO) is an excessive growth of the gingiva which may occur as a side-effect of systemic medications, mainly anticonvulsants, immunosuppressants and antihypertensives [1]. Hypertension is a common disease in Sub-Saharan Africa with a reported prevalence of about 10% to 20% [2]. Calcium channel blockers (CCB) are extensively used in the management of hypertension. The mechanism by which CCB induce GO is not well understood. The proposed mechanism is that CCB alter transmembrane calcium flux in gingival fibroblasts, producing an inactive form of collagenase enzyme which reduces the degradation of collagen. This effect is compounded by increased production of collagen associated with growth factors including the basic fibroblast growth factor and transforming growth factor-β [3]. Some studies indicate that plaque is a prerequisite for CCB-induced gingival enlargement to occur [4].

While there are numerous internationally executed studies on nifedipine-induced GO, they present highly variable prevalence rates ranging from 21% to 38%, with a high of 83% reported [5]-[7]. However, in a community based study, a lower prevalence of 6.3% was reported [8]. Few African [9] and indeed no Kenyan published studies on GO further compound this problem, in view of such factors as, genetic background, environmental peculiarities, variability in pattern and response to medication and oral hygiene habits. This dearth of information on the subject from the Sub-Saharan region necessitates this study that aims to determine the prevalence and severity of GO among hypertensive patients as well as to evaluate the relationship between GO and associated risk factors**.**

2. Study Population

All patients aged 18 years and above, with a confirmed chart diagnosis of hypertension who were on regular doses of antihypertensive drugs for a minimum of 3 months prior to the study, were included. The presence of at least 6 of the 8 most anterior teeth in the upper and lower jaws (1st premolar on the right side to the 1st premolar on the left side) was required. The excluded patients were those who had had periodontal treatment within the last 6 months prior to the initiation of the study, those with systemic disorders known to affect the gingiva (diabetes and connective tissue diseases), pregnant women, patients using partial denture prostheses and those taking anticonvulsant drugs or cyclosporine A. The comparative group comprised of patients treated with other types of antihypertensive drugs other than CCB, who fulfilled the same inclusion and exclusion criteria as indicated above. All patients gave a written informed consent to participate in the study.

3. Materials and Methods

A cross-sectional study was carried out at the Kenyatta National Hospital (KNH) medical outpatient clinic, Nairobi, Kenya. The University of Nairobi and KNH Ethics and Research Committee granted ethical approval for the study.

GO was graded on study models on the buccal and lingual/palatal papillae associated with the six most anterior upper and lower teeth, based on the method originally described by Seymour *et al*. [10] and modified by the authors to allow for measurement in millimetres (mm) as follows; Gingival encroachment on adjacent tooth surfaces was measured from the proximal surface to the free gingival margin and graded from 0 to 3 as illustrated in **Figure 1**: Grade 0, normal gingiva, Grade 1, less than 2 mm increase in size, Grade 2, 2 - 4 mm increase in

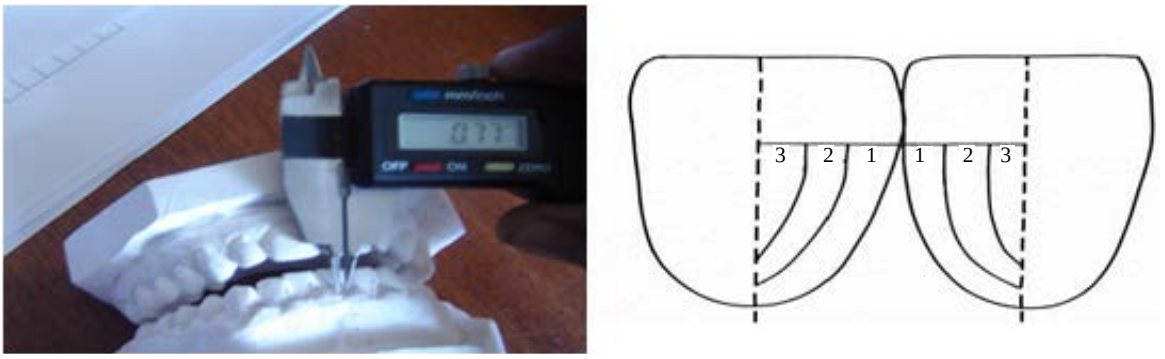

Figure 1. Criteria used for assessing gingival encroachment on adjacent tooth surfaces for a gingival unit.

size, Grade 3, nodular growth greater than 4 mm. Where a discrepancy existed between the adjacent teeth, the highest score was awarded. The horizontal enlargement was measured in the buccal-lingual direction from the enamel surface, at the inter-dental contact point, to the outer papillary surface and graded from 0 to 2 as shown in **Figure 2**: Grade 0, papillary thickness of less than 1 mm, Grade 1, papillary thickness between 1 and 2 mm, Grade 2, papillary thickness greater than 2 mm. Depending on the amount of vertical encroachment and horizontal enlargement, two scores were obtained between 0 and 5, one for the buccal papilla and the other for the lingual/palatal papilla. A score of ≥30 was considered to be a clinically significant overgrowth [11]. Gingival inflammatory status using the gingival index (GI) as described by Loe & Silness (1963) and plaque scores using the Turesky modification of plaque index (PS) by Quigley & Hein (1962) were also measured on the buccal and lingual surfaces of the same teeth. The GI and PS measurements were done directly on the patient. The same examiner (W.A.), unaware of the drug status of the subjects, did all the measurements.

4. Statistical Analysis

The statistical analysis was directed at comparing either CCB-treated patients with those on non-CCB, using the Chi-square (χ^2) test or Fisher's exact test for category variables and the Mann-Whitney test for continuous ones. The influence of associated risk factors on GO was explored by the χ^2 test with Yates correction and calculated using Epi info 3.3.2 version 2005.

5. Results

The study included 164 patients, among whom 40 (24.4%) were male while 124 (75.6%) were female. Slightly more than half of the patients (56.1%) were on CCB while 43.9% were on non-CCB antihypertensive drug regimens. Among the patients on CCB, all were using the dihydropyridines class of CCB with 73.9% of the patients being on nifedipine while 26.1% of them were on amlodipine pharmacotherapy.

GO occurred in 34 (20.7%) of the patients, with only 3 (8.8%) of these having a clinically significant overgrowth. The mean plaque and gingivitis scores were higher in patients with GO (PS 2.35 ± 0.54, GI 1.32 ± 0.45) than those without GO (PS 2.13 ± 0.50 GI 1.23 ± 0.40), but this was not statistically significant with p values of 0.061 and 0.275 for PS and GI respectively.

The prevalence of GO was higher in the patients taking CCB at 31.5%, compared to a prevalence of 6.9% in patients on non-CCB antihypertensive pharmacotherapy. This difference was statistically significant (P = 0.000) with an odds ratio of 6.17 (95% CI 0.21 - 19.45) (**Table 1**). The mean plaque and gingivitis scores were similar for those on CCB (PS 2.2 ± 0.5, GI 1.25 ± 0.4) compared to those on non-CCB drugs (PS 2.1 ± 0.5, GI 1.24 ± 0.4).

The patients in the nifedipine-treated group used doses of 20 and 40 mg/day for a mean period of 30.9 ± 20.9 months (range 4 - 120 months) while those treated with amlodipine were using doses of 5 and 10 mg/day for a mean period of 12 ± 8.8 (range = 6 - 36 months). The relationship between the drug dosage of nifedipine and amlodipine with the prevalence of GO was not statistically significant (P = 0.117) (**Table 2**). On the association of GO with gender, out of the 40 male participants, 13 (32.5%) had GO compared to 21 (16.9%) of the 124 female participants. This difference appeared to have been stastically significant (P = 0.035), but when Yates correction was done, gender influence on GO was no longer statistically significant (P = 0.59)) (**Table 3**). Male

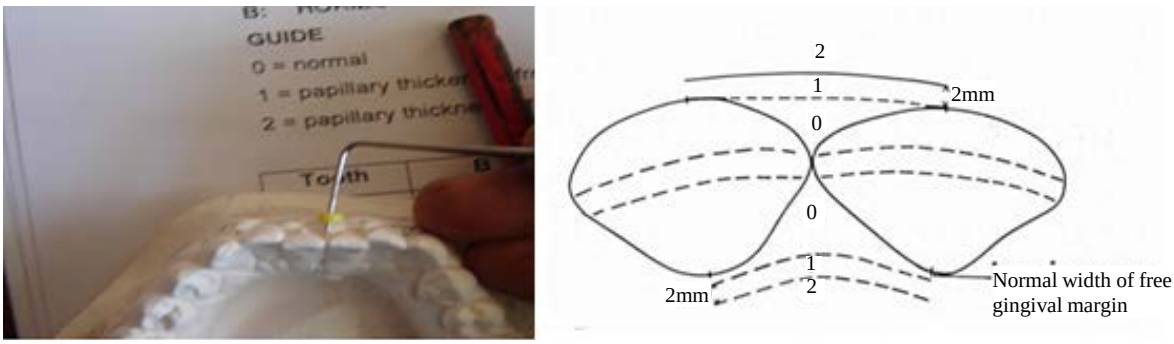

Figure 2. Criteria used for assessing gingival thickness in a labio-lingual direction for a gingival unit.

Table 1. Gingival overgrowth prevalence by CCB and Non CCB antihypertensive drugs.

Presence of GO	Type of drug		
	CCB	Non CCB	Statistical test-Chi-square
GO present	29 (31.5%)	5 (6.9%)	χ^2 yates = 13.39: 1 df: P = 0.000**
GO absent	63 (68.5%)	67 (93.1%)	**OR = 6.17** (95% CI 0.21 - 19.45)

Table 2. Association between Calcium Channel Blockers dosages and prevalence of Gingival Overgrowth.

CCB DRUG	GO PRESENT	GO ABSENT	Statistical test-Fischer Exact
Nifedipine (n = 68)			
20 mg	22 (39.3%)	34 (60.7%)	χ^2 = 0.868: 1 df:
40 mg	3 (25.0%)	9 (75.0%)	P = 0.352 (>0.05)
Amlodipine (n = 24)			
5 mg	2 (11.8%)	15 (88.2%)	χ^2 = 1.008: 1 df:
10 mg	2 (28.6%)	5 (71.4%)	P = 0.315 (>0.05)

Table 3. Association of gingival overgrowth prevalence by Gender.

Presence of GO	Gender		Statistical test-Chi-square
	Male	Female	
GO present	13 (32.5%)	21 (16.9%)	χ^2 = 4.5: 1 df: P = 0.035 (p < 0.05)
GO absent	27 (67.5%)	103 (83.1%)	χ^2 yates = 3.56: 1 df: P = 0.59 (p > 0.05)

participants, had slightly higher periodontal variables, i.e., mean plaque and gingivitis scores (PS 2.4 ± 0.4, GI 1.4 ± 0.43) when compared to the females (PS 2.2 ± 0.5, GI 1.2 ± 0.38).

6. Discussion

There were significantly more females than males examined, which may be a reflection of better health seeking behaviour by females, since a similar overall prevalence of hypertension has been reported [2]. More than half of the patients (56.1%) were on CCB. This could have been because that CCB have been reported to be effective in controlling hypertension among patients of African descent [12] and are readily available at KNH.

The prevalence of GO was significantly higher in those patients who used CCB. Due to the cross-sectional study design used, preexisting GO could not be assessed and controlled for as patients were not examined before they received their antihypertensive therapy. However, since the two groups were similar in age, gender, mean plaque and gingivitis scores, suggests that the higher prevalence of GO observed was possibly as a result of CCB usage. As previously reported in other studies [1] [5], drug dosage was not identified as a significant risk indicator for GO in the present study. This may be because drug dosage tends to be a poor predictor of gingival changes as it is influenced by pharmacokinetics and pharmacodynamics.

Though statistically insignificant, higher PS and GI scores were observed in patients with GO, it was difficult to establish whether this was the consequence of the enlarged gingival tissues or the cause of the GO due to the nature of the cross-sectional study design. Male patients had a higher prevalence of GO which could be related to periodontal variables, suggesting that a patient's oral hygiene may play a role in the expression of drug-induced GO. In a previously reported case by Hancock and Swan, nifedipine-induced GO was treated by controlling plaque [13].

In conclusion, Calcium channel blockers were the predominantly utilised antihypertensive pharmacotherapy with the prevalence of GO among the patients using CCB being significantly higher than those on non-CCB.

7. Recommendations

With the continued use of CCB to manage hypertension, it should be anticipated that drug-induced GO will continue to be a problem. Therefore, newly diagnosed hypertensive patients whose CCB drugs have been recommended should be informed of the possibility of GO as a side effect.

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