

Assessment of Awareness among Physicians Regarding Gingival Overgrowth Induced by Anticonvulsant, Calcium Channel Blocker, and Immunosuppressant Therapy

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ABSTRACT

Introduction: Drug-Induced Gingival Overgrowth (DIGO) is caused due to prolonged use of anti convulsants, immunosuppressant, and calcium channel blockers given for non dental purpose. It affects the maintenance of oral hygiene and may cause speech, mastication, tooth eruption and aesthetic problems. General physicians can play a key role as they can inform the patient about gingival overgrowth as an adverse effect of these drugs.

Aim: To evaluate the awareness regarding drug-induced gingival overgrowth and to know the impact of educational qualification on their awareness among physicians.

Materials and Methods: This cross-sectional questionnaire survey was conducted from January 2019 to June 2019 in Latur district of Maharashtra, India. A total of 196 practicing physicians were approached with self-structured questionnaire and answers were collected in the presence of the investigator. Survey responses were divided into two groups based on educational qualification as group A: physicians educationally qualified to practice Allopathy, group B: physicians educationally qualified to practice alternative medicine (Ayurveda, Homeopathy etc.). Comparison of responses for qualitative variables was carried among groups using Chi-square test with p-value set as $p < 0.05$ significant.

Results: Total 167 (85.20%) general physicians responded willingly and completed the questionnaire. A total of 129 participants were male and 38 were female with age ranging from 27 to 61 years. Among total 88.62%, 34.73%, 43.11% of the physicians knew about adverse effect of antiepileptic, antihypertensive, immunosuppressant drug as gingival overgrowth respectively. Around 50.89% physicians' check the gingival status of their patients and 21.56% refer their patients to dental practitioners for signs and treatment of gingival overgrowth. Overall, 77.25% of participants said that surgical excision with drug substitution should be the line of treatment for these cases. Statistically significant difference was seen on comparative analysis of responses between group A and group B ($p < 0.05$).

Conclusion: The findings of the present study showed that even though physicians know about DIGO they were unable to mention the accountable drug. Only few of them check gingival status of patients taking these drugs during follow-up visits and refer such patients to dental practitioners. Although physicians qualified in Allopathy have more knowledge about these drugs, their approach towards this condition was somewhat similar to the physicians qualified in alternative medicine.

Keywords: Cyclosporine, Epilepsy, Gingival enlargement, Nifedipine, Phenytoin sodium

INTRODUCTION

An increase in the size of gingiva is commonly known as gingival overgrowth or gingival hyperplasia or gingival enlargement, which is a common clinical feature of gingival diseases [1]. It can be classified on the basis of underlying causes as inflammatory, drug-induced, conditioned, neoplastic and false. Drug-induced gingival overgrowth is a known side-effect of anti convulsants, immunosuppressant's and calcium channel blockers [2-4] given for non dental uses that is where the gingival tissue is not the intended target organ [5]. In spite of having dissimilar pharmacology, they have common side-effects seen on gingival tissue in the form of overgrowth [2]. Patients show variable gingival response ranging from minimal to severe gingival overgrowth affecting all teeth with predilection for maxillary and mandibular anterior teeth within a few months of starting the medication [6-8]. It begins as painless, beadlike enlargement of interdental papilla that may progress to marginal tissue and may unite to form a massive tissue fold, creating speech, mastication, tooth eruption, and esthetic problems [9]. [Table/Fig-1] shows amlodipine induced gingival enlargement covering crown portions of the teeth causing esthetic problems which impedes oral hygiene resulting in secondary inflammatory process and progression of gingivitis to periodontitis [10]. [Table/Fig-2] shows the

dilantin sodium=induced gingival enlargement resulting in severe periodontitis. Histologically, gingival overgrowth is characterised by accumulation of collagenous component with varying degree of inflammation in gingival connective tissue [11]. The pathogenesis of DIGO is considered as multifactorial with associated risk factors like age and sex of the patient, type of medication, genetic factors, and the inflammatory status of the periodontal tissues [12,13]. Among the drugs accounting for gingival overgrowth, phenytoin sodium is the most commonly prescribed medication to treat epilepsy, neuralgias and cardiac arrhythmias [14]. The prevalence of epilepsy was mentioned as 7.5% by Goel et al., 3% by Sureka et al., across different regions in India [15-17] while, incidence of DIGO in children



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

[Table/Fig-2]: Gingival overgrowth due to antiepileptic drugs. (Images from left to right)

was mentioned around 57% [15-18]. Approximately, 40 to 50% of patients treated with phenytoin show signs of gingival overgrowth [19,20]. The cases of gingival changes with other antiepileptic drugs such as valproic acid, carbamazepine, phenobarbital and vigabatrin in adult patients have been rarely reported [21-23].

Other drugs that commence gingival overgrowth are calcium channel blockers like nifedipine, nitrendipine, felodipine, amlodipine, nisoldipine, verapamil, and diltiazem. They have been widely used to treat hypertension, angina pectoris, including peripheral vascular diseases [6]. The great India blood pressure survey revealed that the prevalence of hypertension in India is 30.7% [24]. The frequency of gingival overgrowth in patients on calcium channel blockers was found to be 75% for nifedipine and 31.4% for amlodipine [25,26].

The occurrence of cyclosporine-induced gingival overgrowth seems to be around 30% [9]. In renal transplant cases, calcium channel blockers are given in addition to immunosuppressants, which increases the intensity of gingival overgrowth. The physicians as well as patients should be concerned about DIGO. If it remained unnoticed in the early phase, it may get combined with inflammatory component due to accumulation of local factors (microbial plaque) and further progress to periodontitis. In some cases the patient has to pay a penalty in the form of gingival recontouring with a blade or laser [27-29].

General physicians being primary healthcare providers can play an essential role in preventing DIGO by informing their patients about adverse drug reactions. They can advise patients to report back in case of increase in gingival size. Even physicians could evaluate their patients during follow-up visits for gingival overgrowth and if needed can substitute the medications with other agents, causing no or relatively fewer side-effects on the gingiva. Dental practitioner's consultation in time would be advantageous to the patients in controlling the progression of gingival overgrowth. As far as literature is concerned, minimal attention is given to this issue; thus, our study aimed to determine integrated knowledge and understanding of general physicians regarding drugs causing gingival overgrowth and their outlook based on their educational qualification towards it.

MATERIALS AND METHODS

A cross-sectional questionnaire survey was carried out from January 2019 to June 2019 in the Latur district of Maharashtra, India. Ethical approval was obtained from the Institutional Review Board of MIDSR Dental College and Hospital Latur, Maharashtra, India (Approval no-MIDSR/STU/837/08/2018).

Sample size calculation: All practicing general physicians from the district were considered as potential participants. The required sample size was determined on the basis of results of pilot study. By doing calculations (using formula $n = \frac{Z^2 \cdot P(1-P)}{d^2}$) minimum required sample was 98 for this study. Considering percentage of non-participation, authors tried to include maximum participants from the district in the study. List of practicing physicians were obtained from respective local body associations. A second list was prepared for those who practice Allopathy general medicine. A total of 196 practicing general physicians were approached for participation in the survey.

Inclusion criteria: General physicians serving in government institutions, running their own private hospitals in Latur district were considered for inclusion in the study. More number of physicians in rural area of the district is practicing Allopathy irrespective of their educational qualification in alternative medicine (Ayurveda/Homeopathy/Unani), so the present study included them too. The study samples were divided in two groups.

- Group A- responses of physicians educationally qualified to practice Allopathy medicine (bachelor/masters in allopathic medicine).

- Group B- responses of physicians educationally qualified in alternative medicine practicing Allopathy (Ayurveda/Homeopathy/Unani/Naturopathy).

Exclusion criteria: Incompletely filled questionnaire responses were excluded from the study. The doctors who had specialised in other fields of allopathic medicine and doing specialty practice (Orthopaedics, Gynaecology, General surgery, Skin, Psychiatric), postgraduates, Interns, and Undergraduates were excluded from the study.

Questionnaire Design

A specially designed questionnaire was prepared by authors for the present study. The basic idea of questionnaire design was referred from similar study [30] and questions were designed as per the objectives of study. The first part acquired the general information, which includes: study participant's name (optional), age/sex, qualification, designation, the experience of practice in years. The second part consisted of nine questions; the initial six questions were related to recognition and the role of mentioned drugs in inducing gingival overgrowth. The remaining questions were related to their attitude towards the gingival examination, referral of such cases to a dental practitioner, and treatment plan. At the end, one has to write a comment about the study, which was optional. A pilot study was conducted before starting the survey with 10 potential study participants to assess the understanding of the questionnaire and the time required to complete it. In order to make it simple and doubtless, we made necessary changes (related to terminology) in the questionnaire and shared with the same participants again for their opinion. The responses recorded were included in the study.

All potential respondents were visited by investigators personally and explained about the purpose of the study, making it clear that participation is voluntary and revealing one's own identity is optional. Also, they were assured about maintaining the confidentiality of their responses. After taking consent, questionnaires were given to physicians by investigator in person. The filled questionnaire were collected immediately by investigator. The collected survey responses were divided into two groups based on the educational qualification of participants.

STATISTICAL ANALYSIS

The responses collected for the questionnaire were statistically analysed using SPSS 24.0 version, IBM, USA. Qualitative data was expressed in terms of percentage and proportion. Comparison of responses for qualitative variables was carried among groups using Chi-square test with p-value set as $p < 0.001$ as highly significant and $p < 0.05$ as significant.

RESULTS

General information of study: A total of 196 practicing general physicians were approached for participation in the survey. In that 167 (84%) willingly participated and filled the questionnaire completely. Among 29 non participants, nine had not completed the questionnaire, others were unable to return the questionnaire. Among 167 general physicians, 129 were male, and 38 were female, with age ranging from 27 to 61 years (with mean age of 49 years). Amongst those who participated willingly in the study, 107 (64.07%) responses included in group A (physicians educated and qualified to practice allopathic medicine), and 60 (35.92%) responses in group B (physicians educated and qualified to practice Alternative medicine Ayurveda, Homeopathy, and Unani).

Analysis of responses: A total of 88.62% of general physicians knew that antiepileptic drugs could induce gingival overgrowth, and almost all of them were able to mention its name. Around 34.73% of the physicians knew about antihypertensive drugs, which can induce gingival overgrowth; however, 31.73% of them could name the drug. Approximately, 43.11% of the general physician recognised

that immunosuppressant drugs could induce gingival overgrowth, but just 27.54% could name the drug that induces it. In all 50.89% of the general physician checks the gingival status of their patients during follow-up visits after prescribing the drugs that cause gingival overgrowth. Only 21.56% of the physicians refer gingival overgrowth patients to dental practitioners for their further treatment plan. Regarding the line of treatment, 17.96% said surgical excision of excess gingiva should be the option, and 77.25% of participants opined that surgical excision with drug substitution should be the line of treatment for these cases [Table/Fig-3].

Variables	Frequency	%
Gender		
Male	129	77.26
Female	38	22.74
Does intake of antiepileptic drug lead to gingival overgrowth?		
Yes	148	88.62
No	19	11.38
Whether antihypertensive drugs can induce gingival overgrowth as a side-effect?		
Yes	58	34.73
No	109	65.27
Do you know that intake of immunosuppressant agents can induce gingival overgrowth?		
Yes	58	34.73
No	109	56.89
Percentage of respondents who check the gingival status of patients on antiepileptic/antihypertensive/immunosuppressant drugs which can induce gingival overgrowth?		
Yes	85	50.89
No	82	49.10
Do you refer gingival overgrowth patients to dental practitioner?		
Yes	36	21.56
No	131	78.44
Line of treatment for drug-induced gingival overgrowth		
Surgical excision	30	17.96
Drug substitution	08	4.79
Both	129	77.25

[Table/Fig-3]: Demographic profile and responses of all participants to the questionnaire.

Comparative analysis of responses between groups [Table/

Fig-4]: Around 96.26% of physicians from group A and 75% from group B knew that the use of antiepileptic drugs could lead to gingival overgrowth (p-value=0.00003, highly significant). Out of that, 95.32% from group A and 43.33% from group B could mention the name of the drug. Around 42.05% of physicians from group A and 21.66% from group B knew that antihypertensive drugs could lead to gingival overgrowth (p-value=0.0079, significant). However, 37.39% from group A and 21.66% from group B could name the accountable drug. When participants were asked about the use of immunosuppressants, which can lead to gingival overgrowth, 42.05% from group A and 21.66% from group B knew about it (p-value=0.001, highly significant). Out of that, 30.84% from group A and 21.67% from group B could name it. Approximately, 45.79% from group A and 60% from group B check the gingival status of their patients during follow-ups after starting any of this drug therapy to their patients for treatment of particular systemic diseases (p-value=0.078, not significant). A total of 26.17% of general physicians from group A, 13.33% from group B refer their patients to the dentist regarding the sign of gingival overgrowth (p-value=0.052, not significant). About 76.64% from group A, 78.33% from group B, thought that these cases need to be treated with drug substitution and surgical excision of excess gingival tissue so, the difference in opinion was not statistically significant.

Question	Response	Group A n (%)		Group B n (%)		Chi-square value (χ^2)
Does intake of antiepileptic drug lead to gingival overgrowth?	Yes	103	96.26	45	75	17.23 p-value=0.0003**
	No	4	3.74	15	25	
Name of antiepileptic drugs which induces gingival overgrowth	Able to name the drug	102	95.32	26	43.33	p-value=58.6 p-value<0.0001**
	Unable to name	5	4.68	34	56.67	
Whether antihypertensive drugs can induce gingival overgrowth as a side-effect?	Yes	45	42.05	13	21.66	p-value=7.05 p-value=0.007*
	No	62	57.95	47	78.34	
Name of antiepileptic drugs which induces gingival overgrowth	Able to name the drug	40	37.39	37.39	21.66	p-value=3.68 p-value=0.054
	Unable to name	67	62.61	62.61	78.34	
Can intake of immunosuppressant agents induce gingival overgrowth	Yes	45	42.05	13	21.66	10.32 p-value=0.001**
	No	62	57.95	47	78.34	
Name of immunosuppressant drugs which induces gingival overgrowth	Able to name the drug	33	30.84	13	21.67	p-value=1.62 p-value=0.2
	Unable to name	74	69.16	47	78.33	
Respondents who check the gingival status of patients on drugs which can induce gingival overgrowth?	Yes	49	45.79	36	60	p-value=3.1 p-value=0.078
	No	58	54.21	24	40	
Percentage of respondents refers gingival overgrowth patients to dental practitioner	Yes	28	26.17	8	13.33	p-value=3.74 p-value=0.052
	No	79	73.83	52	86.67	
Respondent's opinion on the line of treatment for drug induced gingival overgrowth?	Surgical excision	20	18.79	10	16.67	p-value=0.07 p-value=0.098
	Drug substitution	5	4.67	3	5	
	Both treatment	82	76.64	47	78.33	

[Table/Fig-4]: Responses of participants to the questionnaire according to groups.
*Significant, **highly significant

DISCUSSION

Advancement in the field of medicine leads to an increased life expectancy of the population. As a result, the older age group population is usually subjected to chronic intake of medications for various systemic diseases [31]. The drugs mentioned above are routinely prescribed by general physicians to the patients affected by systemic diseases like hypertension, epilepsy, and conditions where immunosuppressant drugs are required. Because of high prevalence rate of DIGO, the current study was undertaken to assess the awareness among the general physicians about the drugs which can lead to gingival overgrowth.

Comparative Analysis of responses between the groups showed that physicians from group A had more information regarding adverse effects of above mentioned drugs than other group. This may be because of the scientific knowledge which they pursued during their academic curriculum. However, few of them could not name the specific drug that induces gingival overgrowth. Similar results were seen in the study where 53.3% of general practitioners knew about DIGO, yet they failed to answer the drugs that can induce it [32]. In a study by Pralhad S and Thomas B, most of the participants answered in assertive that drugs cause gingival enlargement, but the responses were not uniform when asked to indicate the drugs that would cause gingival enlargement [33].

Although some of the general physicians were aware of drug-induced gingival overgrowth, only 50.89% of them examine the gingival tissue status of their patients during follow-up visits after prescribing these drugs. When responses were analysed for the same question as per the groups, lesser physicians from group A check the gingival tissue of their patients than that of group B. General physician examine mucosal surfaces of lips, tongue, and anterior tonsillar pillars as the protocol of oral cavity examination. However, the gingival examination is not a routine part of it. In a study, 70 general practitioners were interviewed, where 85.9% of the practitioners routinely examine the patient's oral cavity, but they have not mentioned about gingival examination [34].

Among all the participants, only 21.56% refer these patients to dental practitioners. When compared among the groups, more physicians from group A refer such cases to dental practitioners than that of group B. All the physicians agreed that these cases need to be treated. Total of 76.64% from group A and 78.33% from group B thought these cases need to be treated with drug substitution and surgical excision of excess gingival tissue. Long-standing DIGO often requires surgical intervention. Drug withdrawal may not be possible in all cases, so the general physician plays a crucial role in substituting the drug without hampering the patient's systemic health. A study suggested that wherever possible gingival overgrowth should be treated with a non surgical technique like drug substitution and scaling and root planning, which helps reduce plaque-induced gingival inflammation; however, surgical excision of gingiva is the most reliable option [35].

The overall results suggest that awareness about gingival overgrowth due to antiepileptic drugs was higher in all participants than other antihypertensive and immunosuppressant drugs. However, some of them could not recognise the drug which leads to gingival overgrowth. Around half of the participant physicians check the gingival status of their patients taking above mentioned drugs during follow-ups. A small number of physicians refer the patients on these drugs to dental practitioners for the checkup of gingival condition. Physicians educated and qualified to practice Allopathy showed better knowledge than physicians educated and qualified to practice alternative medicine. Still, only some of them examine their patients' gingival status during follow-up. Also, there was no difference in the awareness among both the groups regarding referral of these patients to dental practitioner.

The vital theme which arises from this study was that all the participants felt a need to know more information about the drugs causing gingival overgrowth since dental practitioners frequently come across such gingival conditions in their practice than that of a physician. The principal investigator explained the related information about DIGO to every participant personally, and a sheet of information was distributed. This study helped increase awareness and revise the knowledge of many physicians which would be beneficial to the patients.

Limitation(s)

There are some limitations to the study that responses were recorded from the participants were not categorised on basis of their experience in clinical practice. The study was restricted to single district place so, the result may not be applicable to other areas due to variation in awareness among physicians. In future, the studies can be conducted with large sample size from other geographical locations to know the responses of general physicians.

CONCLUSION(S)

The result of our survey concluded that knowledge about the drugs causing gingival overgrowth was there among most of the general physicians but they were not keen to check gingival status of these patients and to refer to the dentist. Majority of the general physicians are not as aware as they should be in detection, prevention and

treatment about DIGO. Also, educational qualification in Allopathy does have impact on awareness of physician regarding drug-induced gingival overgrowth. This awareness can be created by conducting combined dental and medical educational programs and organising conferences at regional as well as national level on such topics. By encouraging multispecialty clinics which include dental as well as medical practitioners so that the interdisciplinary comprehensive treatment plan can be decided for patients benefit.

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