Original Article

Gingival Status of Kidney Transplanted Patients Referred to Shariati General Hospital, Tehran

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Abstract:

Objective: The aim of the present study was to investigate the level of gingival overgrowth (GO) in patients with kidney transplant.

Materials and Methods: The target group of the study was the patients recently received kidney transplant and cyclosporine-A therapy. By a systematic case selection method, a total of 131 cases were included in the study, of whom 80 (61.6%) patients were male. The data was collected through interview with the patients as well as clinical assessment of their dental and periodontal indices. Gingival enlargement was recorded in terms of a 4-point scale from absence of enlargement to sever enlargement. Gilmore and Glickman plaque index was also recorded. Chi-square test served for statistical analysis.

Results: The mean dose of the drug received was 203 mg (SD=75), with 191 mg (SD=71) in females and 209 mg (SD=77) in male individuals. GO was found in one-third of the patients receiving CSA. Incidence of GO was found to be roughly equal in upper and lower jaw with no significant difference ($P>0.05$). Gingival enlargement was also found to be more prominent at the anterior region. Difference between two age groups was statistically significant ($P<0.05$). No Statistically significant difference was found between groups taking different doses of the drug.

Conclusion: Gingival overgrowth among the patients receiving kidney transplant and CSA therapy seems to vary according to such factors as age and gender, but not the dose of the drug taken.

Key Words: Gingival Overgrowth; Cyclosporine; Kidney Transplantation; Nifedipine; Periodontal Index

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INTRODUCTION

Gingival health is a matter of concern among the patients suffering from a general medical condition. Among these patients, those undergoing organ transplantation are more prone to gingival conditions as use of immunosuppressive drugs have shown to be indirectly influential on gingival status. Certain drugs such as cyclosporine-A (CSA), administered routinely to suppress immune system in cases with kidney transplant, could induce gingival overgrowth (GO), which will make oral health maintenance difficult [1-3]. In literature, the severity of GO resulted from this drug has been reported to be from 25% to 80% [2-4].

CSA was found in 1980's while scientists

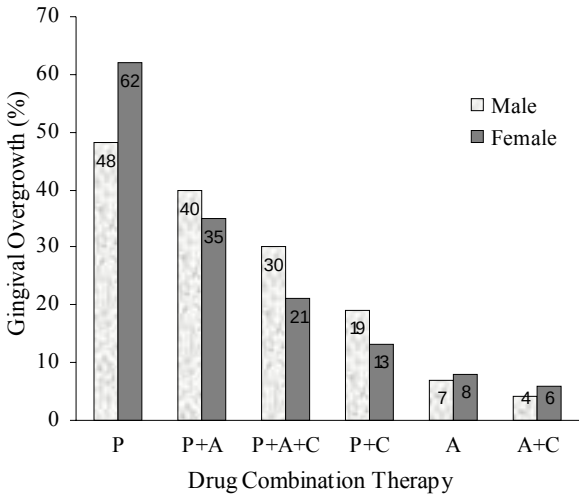

Fig 1. Distribution of gingival hyperplasia induced by cyclosporine-A among a study group (n=131) receiving kidney transplant according to gender. P=Prednizolone, A=Azaiyrocine, C=Cortisol.

were looking for anti fungal agents [4]. This hydrophobic lipophyllic cyclic protein with molecular weight of 1202 M consists of two amino acids [5]. The drug is administered 4-24 hours prior to transplantation with 15 mg/kg and is continued up to two weeks to prevent any rejection of the new organ and also any renal failure [6]. In addition to this indication, CSA is also administered in autoimmune diseases, rheumatoid arthritis, actinomyces vulgaris, pemphigus, and diabetes mellitus type I [3]. CSA is operating through three major routs of: activating macrophages to prevent interleukin 1 (IL1) synthesis; preventing the production of IL1 receptors on thalamus resulting in prevention of IL2 production; and preventing IL2 receptors production on undifferentiated cells [2].

Although cyclosporine is a very effective medication its side effects including nephrotoxicity, lymphoma, and bronchial; cardiac; and kidney fibrosis in addition to gingival hyperplasia are of major concern [3]. An over growth of gingiva is seen following 4-6 weeks of cyclosporine intake representing an inflamed, bled and edematous gingival appearance [7]. This hyperplasia is starting from interdental papilla and then extended to anterior and posterior segments mainly in labial surfaces [8].

Although the gingival effects of CSA are well known, there have been controversies over its incidence rate and its severity among the patients [9-14]. For example, in literature, the severity of GO resulted from this drug has been reported to be from 25% to 80% [2-4].

The present study was designed to evaluate the rate and severity of GO among a group of kidney transplant receivers who were under a cyclosporine regimen during 2005 at Shariati Hospital, Tehran.

MATERIALS AND METHODS

The target group of the study was the patients recently received kidney transplant and CSA therapy. By a systematic case selection method (assessing all attended), a total of 131 cases

Table 1. Gingival hyperplasia induced by cyclosporine-A among study group (n=131) receiving kidney transplant

Hyperplasia Condition			Nil n (%)	Mild n (%)	Moderate n (%)	Severe n (%)
Upper	**Buccal**	Anterior	87 (65.3)	4 (3.1)	20 (15.3)	20 (15.3)
		Posterior	91 (69.4)	20 (15.3)	16 (12.2)	4 (3.1)
	Lingual	Anterior	96 (73.4)	14 (10.6)	19 (14.5)	2 (1.5)
		Posterior	107 (81.7)	6 (4.6)	18 (13.7)	0 (0.0)
Lower	**Buccal**	Anterior	89 (68.0)	21 (16)	19 (14.5)	2 (1.5)
		Posterior	89 (68.0)	21 (16)	19 (14.5)	2 (1.5)
	Lingual	Anterior	99 (75.5)	11 (8.5)	19 (14.5)	2 (1.5)
		Posterior	109 (83.2)	3 (2.3)	19 (14.5)	0 (0.0)

were included in the study, of which 80 (61.6%) patients were male. Attempts were made to ensure a minimum of three months drug use. It was also tied to select the patients with at least four anterior and three posterior teeth present in each quadrant. Patients with other medical conditions than transplanted kidney were excluded in order to eliminate crossing effects.

The data was collected through interview with the patients as well as clinical assessment of their dental and periodontal indices. Periodontal assessment was performed using a mouth mirror, a periodontal probe, S shape probe and disclosing tablets. Periodontal index (PI) on facial surface was measured followed by gingival index (GI) on facial and palatal surfaces. Gingival enlargement was measured using McGaw index [9]. Both palatal and buccal gingival surfaces were assessed at midpoint mesial to distal papilla in terms of a 0-3 point scale as follows: 0=Nil, 1=mild enlargement, 2=moderate enlargement 3=sever enlargement [9]. PI was also recorded for each case based on scoring system introduced by Turesky et al [3]. Statistical analysis was performed using Chi-square test.

RESULTS

Based on the data collected from this sample, patients who participated had an average period of 53.5 months of CSA drug use. The mean dose of the drug used was 203 mg (SD=75) with 191 mg (SD=71) in females and 209 mg (SD=77) in males.

Assessing the gingival enlargement level showed that a group of 43 (32.8%) patients had signs of gingival hyperplasia associated with the use of CSA medication. Twenty-four out of 43 (18.3% of total) had only mild gingival hyperplasia. Fig 1 shows the differences among patients taking varying types of the drug. Incidence of GO was found to be roughly equal in upper and lower jaw with no significant difference ($P>0.05$). Gingival enlargement was also found to be more prominent at the anterior region in comparison with posterior segment ($P<0.001$). The enlargement was also much more evident at buccal compared to lingual sides (Table 1).

Although male cases had a higher rate (16.2%) of GO than female (11.8%), the difference was not significant. As observed in Table 2, patients with an age of more than 50 years showed a lower involvement rate (19.2%) in comparison with individuals younger than 27 years of age (50%). This difference was statistically significant ($P<0.05$). No Statistically significant difference was found between groups taking different doses of the drug.

DISCUSSION

Gingival enlargement resulted from drugs is a well-known phenomena in which the dose and the period are believed to play implant roles on the severity of the condition. Patients who are

Table 2. Distribution of gingival hyperplasia induced by cyclosporine-A among study group (n=131) receiving kidney transplant according to age and gender.

Gender	Age (years)	Gingival Overgrowth		Total n (%)
		Not Detectable n (%)	Detectable n (%)	
Male	≤27	4 (57.1)	3 (42.9)	7 (100.0)
	27-50	39 (65.0)	21 (35.0)	60 (100.0)
	≥50	11 (84.5)	2 (15.5)	13 (100.0)
Female	≤27	4 (45.0)	5 (55.0)	9 (100.0)
	27-50	20 (68.0)	9 (32.0)	29 (100.0)
	≥50	10 (77.0)	3 (23.0)	13 (100.0)

under such influential drugs are always concerned with their oral health and are referred to the periodontists by other medical professions. The use of CSA following kidney transplant has long been noted as being effective in GO to some degrees.

Results of the current study revealed that 32% of the patients evaluated represented signs of GO. Seymour and Jacobs [2] stated that this rate is between 25-30% following the use of CSA in similar patients of UK resident [1,2]. McGaw et al [9] reported similar results examining kidney-transplanted cases who had received CSA therapy. A rate of 27% was also reported for GO by O'Valle et al [15]. Somacarrera et al [14] reported a 43% rate for such GO conditions following CSA consumption.

The mechanism of CSA action in GO is not clear. Some believe that it could be a cofactor similar to Phenytoin [2]. Schincalgia et al [16] reported a direct effect of CSA on gingival fibroblasts by an increase in protein and collagen. CSA reduces free calcium elements and subsequently collagenase production and release. This would affect the balance between production and destruction of collagen, resulting in gingival over growth [11]. Seizure of CSA usage for 6 month has shown to completely eliminate signs of GO particularly in children in absence of any surgical intervention [5,11]. In agreement to an earlier report by Cebeci et al [17], findings of the present study revealed that the drug dosage had no direct effect on the GO condition. CSA serum level and its dose have no clear effect on GO severity [9].

A further finding of this investigation centered on the age relevancy of the CSA and GO with lower age group representing a higher effect. Daly et al [7] had looked at type I Diabetes and the use of CSA in children and adolescents showing some degree of GO. In addition, the higher effect of CSA on fibroblasts of young individuals has been proved positive [3]. Tyldesley and Rotter [11] reported a higher rate in female individuals (38%) compared to male cases (17%), which disagrees our and other's findings. However, due to small number of cases, such findings could not be referred to as clear-cut; and further investigations in various communities and conditions are required to clarify causes of such differences.

CONCLUSION

GO among the patients receiving kidney transplant and CSA therapy seems to vary according to such factors as age and gender, but not the dose of the drug taken.

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REFERENCES

1-Seymour RA, Heasman PA. Drugs and the periodontium. J Clin Periodontol 1988 Jan; 15(1):1-16.

2-Seymour RA, Jacobs DJ. Cyclosporin and the gingival tissues. J Clin Periodontol 1992 Jan;19(1): 1-11.

3-Turesky S, Gilmore ND, Glickman I. Reduced plaque formation by the chloromethyl analogue of victamine C. J Periodontol 1970 Jan;41(1):41-3.

4-Borel JF. Pharmacology of cyclosporine (sandimmune). IV. Pharmacological properties in vivo. Pharmacol Rev 1990 Sep; 41(3):259-371.

5-Williamson MS, Miller EK, Plemons J, Rees T, Iacopino AM. Cyclosporine A upregulates interleukin-6 gene expression in human gingiva: possible mechanism for gingival overgrowth. J Periodontol 1994 Oct; 65(10):895-903.

6-Barber MT, Savage NW, Seymour GJ. The effect of cyclosporin and lipopolysaccharide on fibroblasts: implications for cyclosporin-induced gingival overgrowth. J Periodontol 1992 May; 63(5):397-404.

7-Daly CG. Resolution of cyclosporin A (CsA)-

induced gingival enlargement following reduction in CsA dosage. J Clin Periodontol 1992 Feb;19(2): 143-5.

8-Thomason JM, Seymour RA, Rice N. The prevalence and severity of cyclosporin and nifedipine-induced gingival overgrowth. J Clin Periodontol 1993 Jan;20(1):37-40.

9-McGaw T, Lam S, Coates J. Cyclosporin-induced gingival overgrowth: correlation with dental plaque scores, gingivitis scores, and cyclosporin levels in serum and saliva. Oral Surg Oral Med Oral Pathol 1987 Sep;64(3):293-7.

10-Butler RT, Kalkwarf KL, Kaldahl WB. Drug-induced gingival hyperplasia: phenytoin, cyclosporine, and nifedipine. J Am Dent Assoc 1987 Jan; 114(1):56-60.

11-Tyldesley WR, Rotter E. Gingival hyperplasia induced by cyclosporin-A. Br Dent J 1984 Nov 10;157(9):305-9.

12-Mariani G, Calastrini C, Carinci F, Bergamini L, Calastrini F, Stabellini G. Ultrastructural and histochemical features of the ground substance in cyclosporin A-induced gingival overgrowth. J Periodontol 1996 Jan; 67(1):21-7.

13-Brunton LL, Lazo JS, Parker KL. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 8th ed. New York: McGraw-Hill; 1991. pp. 12-67.

14-Somacarrera ML, Hernández G, Acero J, Moskow BS. Factors related to the incidence and severity of cyclosporin-induced gingival overgrowth in transplant patients. A longitudinal study. J Periodontol 1994 Jul; 65(7):671-5.

15-O'Valle F, Mesa F, Aneiros J, Gómez-Morales M, Lucena MA, Ramírez C, et al. Gingival overgrowth induced by nifedipine and cyclosporin A. Clinical and morphometric study with image analysis. J Clin Periodontol 1995 Aug;22(8):591-7.

16-Schincaglia GP, Forniti F, Cavallini R, Piva R, Calura G, del Senno L. Cyclosporin-A increases type I procollagen production and mRNA level in human gingival fibroblasts in vitro. J Oral Pathol Med 1992 Apr;21(4):181-5.

17-Cebeci I, Kantarci A, Firatli E, Carin M, Tuncer O. The effect of verapamil on the prevalence and severity of cyclosporine-induced gingival overgrowth in renal allograft recipients. J Periodontol 1996 Nov;67(11):1201-5.