Vol: 8 Issue: 1

EDJ

The Effect of Cyclosporine and Tacrolimus Systemic Therapy on Gingival Overgrowth in Renal Transplant Patients Aged Between 18-70 Years in Erbil City-Iraq

Aveen A. Jalal[(1)]

ABSTRACT

Background: Gingival overgrowth has been linked to systemic therapy with Cyclosporine and Tacrolimus in Renal transplanted cases.

Aim: The prevalence and characteristics of gingival overgrowth and periodontal treatment will be examined in patients taking cyclosporine and tacrolimus after renal transplantation in patients aged 18-70 in Erbil city.

Patients and Methods: In this study, sixty kidney transplanted patients on immunosuppressive maintenance therapy in the renal transplant unit of Hawler teaching hospital in Erbil city, Kurdistan region/ Iraq were randomly selected and retrospectively examined All patients aged over 18 years old. In medical records information regarding: drug use duration; oral hygiene index; bleeding index; and clinical gingival overgrowth index were transported into a specific data file made for research purpose. Clinical evaluations were done at baseline and three months after periodontal treatment. Using SPSS version 24.0, descriptive statistics were used to assess demographics and periodontal parameters at a significance level of $p < 0.05$.

Results: The trial comprised 56.66% cyclosporine and 43.33% tacrolimus. The cyclosporine group included 61.76% male while the tacrolimus group included 73.07% female. The average treatment duration was 79.69±10.27 days in cyclosporine and 67.11±9.79 in tacrolimus. The majority of individuals brushed twice daily (52.94% cyclosporine, 46.15% tacrolimus) and had acceptable oral hygiene (70.58%, 73.07%) respectively. Cyclosporine caused grade 2 gingival overgrowth in 55.88% compared to 11.53% in tacrolimus. Both groups had lower plaque and bleeding indices after scaling and polishing. The tacrolimus group showed more improvement.

Conclusion: Compared to cyclosporine, the Tacrolimus group showed less prevalence and severity of gingival overgrowth and better response to periodontal therapy.

Keywords: Cyclosporine, Tacrolimus, Gingival overgrowth, Periodontal treatment, Renal transplant.

Article Information

Submission Date: 14/7/2024
Revision date: 21/7/2024
Acceptance date: 13/8/2024
Publishing date: Jun 2025

Affiliation Info

[(1)]College of Dentistry, Hawler Medical University, Kurdistan Region, Iraq.
Corresponding Author: Aveen A. Jalal.
Email: aveen.ajeel@hmu.edu.krd.

DOI: doi.org/10.15218/edj.2025.5

INTRODUCTION

Renal transplantation is regarded to be the best therapeutic option for people with end-stage renal illness. Improved surgical and tissue matching processes, as well as discoveries in anti-rejection pharmaceutical treatment, have resulted in a significant improvement in patient survival after kidney transplantation during the last two decades.[1, 2] Gingival enlargement, also known as hyperplasia, is an abnormal condition in which the gingiva changes volume. It may vary from a mild hyperplasia of the interdental papillae to a development in which the dental crowns are fully covered by the changed tissue. Gingival hyperplasia is not necessarily connected to the variation of the number of tissue cells, which may be a result of the volume of the cellular elements or the extracellular matrix.[3] Gingival hyperplasia can occur in some patients but not in others taking the same medication. The characteristic inflammatory response of gingival fibroblasts and the ensuing proliferation of connective tissue matrix highlight the different ways in which each person's gingival fibroblasts react to the inciting medicines. It appears that inhibition of cation influx, specifically calcium and sodium ions, is the mechanism of action shared by these three distinct classes of drugs at the cellular level. There are numerous causes of gingival hyperplasia.4 Cyclosporin is the more frequently encountered immunosuppressant associated with gingival enlargement, alongside tacrolimus. After organ transplantation, immune suppressants are often prescribed for the treatment of certain autoimmune diseases, including rheumatoid arthritis, and renal transplants.[4] Nearly 53% of patients undergoing renal transplants and receiving cyclosporin have been identified as having gingival hypertrophy.[5] The hepatic and renal toxicity, as well as the severity of gingival proliferation, are all diminished in comparison to cyclosporin and tacrolimus.[6;7] Tacrolimus has emerged as a viable substitute for cyclosporine and is being used as a life-saving treatment for individuals experiencing organ transplant rejection and cyclosporine A-induced nephrotoxicity. Tacrolimus did not contribute to the gingival hyperplasia that was found with cyclosporine.[8] Researching the periodontal health of immunosuppressed medication recipients who have achieved medical stability after a kidney transplant is the primary goal of this study. This study will use the oral hygiene index, the gingival index, and the gingival overgrowth index to determine the frequency of gingival overgrowth and the degree to which gingival health is compromised. The study will also look at how periodontal health is correlated with pharmacological factors like the kind and length of time that renal transplant patients are on immunosuppressive medication. Also, how often these people wash their teeth relates to their periodontal health, which will be investigated in the study .

PATIENTS AND METHODS

Study design

Sixty kidney transplant recipients who were receiving immunosuppressive maintenance therapy were the subjects of this retrospective analysis. This research was conducted at Erbil Teaching Hospital's Renal Transplant Clinic in Erbil. Before beginning their involvement in the research, every participant received a signed informed permission form and was duly told of the study's aims. The rights of the subjects were continuously upheld. A sample of candidates was recruited and selected from the organ transplant unit. Regular patient visits were conducted at the designated hospitals in order to assess the progress of drug therapy and graft survival. Throughout the data collection phase spanning from July 2021 to July 2023, individuals who fulfilled the specified inclusion criteria were invited at random to partake in the research. The subjects' availability and accessibility were determined by their regular post-transplant maintenance regimen. Under this methodology, each suitable participant had examination and was then enrolled in the research groups based on the primary immunosuppressive agent. The inclusion requirements consist of individuals aged 18-70 years old, who have been taking immunosuppressive medication for a minimum of 3 months, and have at least 10 teeth. The research excluded pregnant and breastfeeding women, patients who had taken other medications, and those with disorders that impact gingival tissues, such as diabetes mellitus and leukemia. The College of Dentistry/Hawler Medical University's academic ethics committee reviewed and accepted the study protocol. Patients who satisfied the eligibility parameters were invited to participate in the trial after giving their informed consent. medical conditions, drug use, and how

long medications were used for. A periodontal probe and mouth mirror were used for the bedside clinical evaluation. The oral hygiene index,[9] bleeding index,[10] and clinical gingival overgrowth index,[11] and frequency of tooth brushing[12] were documented as periodontal parameters. A solitary examiner who had undergone calibration conducted the clinical examination using a manual probe (UNC-15, Hu-Friedy Manufacturing Company, Inc., Chicago, IL, USA). Both ultrasonic and manual tools were used to treat periodontal disease. At three months and at baseline, clinical assessments were evaluated.

Medical and pharmacological variables

The medical records of every participant were consulted for medical and pharmacological information. Regular screenings were conducted for transplant patients as part of long-term care. The most current assessment's data, which are typically gathered at the most recent medical checkup (0 –30 days), were noted. Age, gender, length of primary immunosuppressive medication, and time since transplant.

Oral Hygiene Status

Observing the following teeth's soft debris and mineralized deposits allows one to estimate the state of oral hygiene index.[9] Teeth that are missing cannot be replaced. A score between zero and three is assigned to each of the four dental surfaces: buccal, lingual, mesial, and distal. After tallying up the scores from each of the four dental regions, divide the total by four to get the tooth's plaque index. There is no microbial plaque (0), a thin layer of plaque (1), considerable accumulation of plaque (2), and a large amount of plaque (3), in the sulcus or pocket along the free gingival edge. The plaque score index, which is re- ported as a percentage, was determined for each patient by adding up all the tooth surfaces that had plaque and dividing it by the total number of checked tooth surfaces. This leads to the classification of oral hygiene status as mild (PS <30%), fair (PS 30 -<60%), or poor (PS≥60%). The frequency of tooth brushing must be recorded. The frequencies of tooth brushing are classified in to (Baban 2003):[12] 1: no brushing; 2: some times; 3: once a day; 4: twice daily;5: more than twice in a day.

Bleeding index

The index in question is utilized to assess all four surfaces of the teeth, and it is documented according to the presence or absence of bleeding.10 If there is no bleeding, it was recorded as '-' on the chart, but if there is bleeding, it was recorded as '+'. The presence of a minus sign implies a gingival bleeding index score of 0 or 1, whereas a plus sign suggests a gingival bleeding score of 2 or 3, as determined by the following scores: Gingiva in a normal state. Up to 1-Mild inflammation, absence of blood upon probing, alteration in color, and swelling; The symptoms of up to 2-Moderate inflammation include bleeding on probing, redness, oedema, and glazing. Severe inflammation, spontaneous bleeding, pronounced redness, and swelling can occur, with a maxi- mum of three instances.

Clinical Index for Drug-induced Gingival Overgrowth

The severity of drug-induced gingival overgrowth[11] was evaluated using the clinical index specifically designed for this purpose. This index is easy to use and needs no diagnostic casts or graphs. It offers a measure of the severity of the lesions and helps determine the most suitable therapy method. The evaluation is determined by the subsequent criteria: Grade 0 indicates the absence of excessive growth and a strong connection between the gum tissue and the underlying bone. There is either no or a minimal amount of stippling, as well as no or only a slight granular look. A sharp-edged papilla is located at the biting surface and there is no change in the density or size of the gum tissue. • Grade 1 - Initial excessive development, characterized by a significant rise in the thickness of the gum tissue with noticeable stippling and a granular texture. The apex of the papilla is spherical. • Grade 2 - Moderate overgrowth, characterized by enlarged papilla and/or curled edges. The shape of the gingival edge remains concave or straight. The gingival enlargement extends up to 2 mm in the buccolingual direction, starting from the tip of the papilla and moving outward. The papilla has a degree of retractability. • Grade 3 - Excessive development, indicated by the gingiva extending onto the visible part of the tooth. The shape of the gingival margin is convex, not concave. The gingival overgrowth has a buccolingual diameter
of at least 3 mm, measured from the tip of the papilla towards the outside. The papilla is easily capable of being pulled back. • Grade 4 - Severe

DOI: doi.org/10.15218/edj.2025.5

overgrowth, marked by a significant increase in the thickness of the gingiva. A significant proportion of the clinical crown is obscured. In grade 3, the papilla is capable of being retracted. The buccolingual dimension measures around 3 mm.

Statistical analysis

Data analysis was conducted using SPSS version 24.0, which is a Statistical Package for the Social Sciences. An analysis of the demographic data, oral hygiene components, and periodontal indicators was conducted using descriptive statistics. The relationship between gingival overgrowth and demographic and periodontal variables was analyzed using a crosstabulation and a t- test. A p-value below 0.05 was considered to indicate statistical significance.

RESULTS

Out of a sample size of 60 individuals, approximately 56.66% of the subjects received cyclosporine medication, whereas 43.33% reported being treated with tacrolimus. The majority of individuals in the cyclosporine treated group were males (61.76%) and had a higher degree of education (76.47%). Conversely, the majority of subjects in the tacrolimus treated group were females (73.07%) and also had a higher level of education (76.47%). The mean duration of treatment in months for the study groups was (79.69±10.27) and (67.11±9.79) correspondingly, as indicated in Table 1.

Table 1. Characteristics of sample group of Cyclosporine and Tacrolimus study groups

Variables		CsA group	Tcr group
Total samples (n=60)		34(56.66%)	26(43.33%)
Age (years)		58.11±52.64	56.32±62
Male		21 (61.76%)	17(65.38%)
Female		13(38.23%)	19(73.07%)
Education	School	8(23.52%)	6(23.07%)
	University	26(76.47%)	20(76.92%)
Duration of treatment/ months		79.69±10.27	67.11±9.79

Medications that suppress the immune system that patients take after a kidney transplant. Regarding oral hygiene, the majority of subjects in the cyclosporine group cleaned their teeth twice a day (52.94%), while in the tacrolimus group it was 46.15%. Additionally, the majority of sub- jects in the cyclosporine group had their last dental appointment within the last 6-12 months (47.05%), while in the tacrolimus group it was 53.84%. Both the cyclosporine and tacrolimus groups had relatively high rates of good oral hygiene (70.58% and 73.17%, respectively) and a fair bleeding index (50.82% and 61.53%, respectively). Eleven individuals (32.35% of the total) had a clinical gingival overgrowth index score of 1, nineteen (55.68%) had a grade 2, and four (11.76% of the total) had a grade 3. Also, as indicated in the table2, 17(65.38%) of the 26 participants treated with tacrolimus had a clinical gingival overgrowth index score of 1, 7(11.53%) had a grade 2, and 2 (17.69%) had a grade 3.

Table 2. Distribution of participants for each of oral hygiene factors, periodontal parameters with clinical gingival overgrowth in Cyclosporine and Tacrolimus groups (study subjects n=60)

Variables		CsA group	Tcr group
Frequency of toothbrush-ing	Some times	2(5.88%)	3(11.53%)
	1 time per day or less	4(11.76%)	5(19.23%)
	2 times per day	18(52.94%)	12(46.15%)
	More than 2 times per day	10(29.41%)	6(23.07%)
Last dental visit	Less than 6 months	3(8.82%)	2(7.69%)
	6-12 months	16(47.05%)	14(53.84%)
	2-5 years	10(29.41%)	8(30.76%)
	More than 5 years	5(14.70%)	2(7.69%)
oral hygiene index	Good (<30%)	3(8.82%)	4(15.38%)
	Fair	24(70.58%)	19(73.07%)
	Poor	7(20.58%)	3(11.53%)
Bleeding index	Mild (<30%)	6(17.64%)	5(19.23%)
	Fair	20(58.82%)	16(61.53%)
	Poor	8(23.52%)	5(19.23%)
Clinical gingi-val overgrowth index	Grade 0	0(0.00%)	0(0.00%)
	Grade 1	11(32.35%)	17(65.38%)
	Grade 2	19(55.88%)	7(11.53%)
	Grade 3	4(11.76%)	2(7.69%)

Among patients presented with gingival over-growth, analysis of the clinical periodontal pa-rameters (plaque score index and bleeding index) in response to scaling and polishing after 3 months of periodontal treatment are shown in Table 3 and figure 1.

DOI: doi.org/10.15218/edj.2025.5

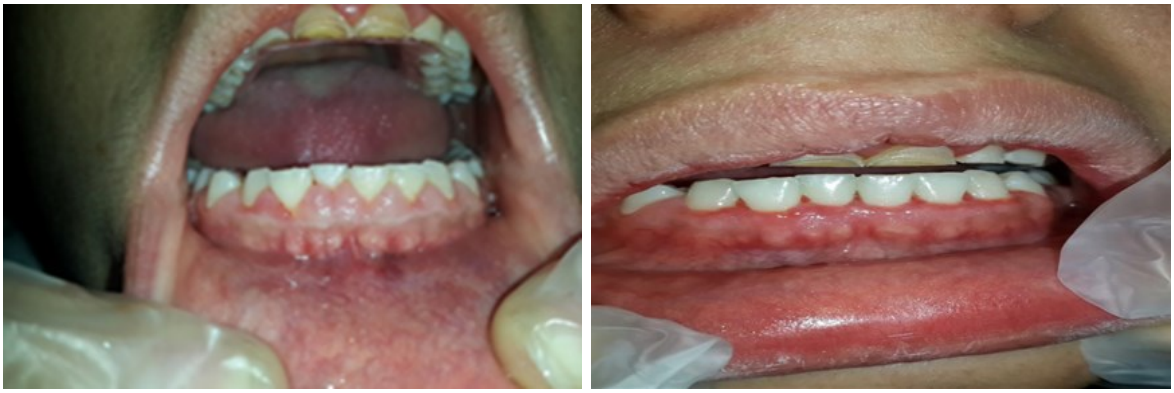

Fig1. Patient with gingival overgrowth in response to scaling and polishing after 3 months of periodontal treatment

Table 3. Association between periodontal parameters with clinical gingival overgrowth in response to scaling and polishing

Variables		Cyclosporine group/ Gingival overgrowth Mean ± SD		p-value	Tacrolimus group/ Gingival overgrowth		p-value
oral hygiene Score Index	Good	1.68±0.43	1.14±1.53	0.02	1.74±2.02	1.04±0.36	< 0.01
	Fair and	2.57±1.0	1.78±4.11	< 0.01	2.15±1.3	1.20±2.4	< 0.01
Bleeding Index	Mild	62.23±1.1	48.24±0.65	0.04	56.12±1.76	32.13±5.63	< 0.01
	Fair and poor	87.69±53	68.18±1.23	0.033	76.20±9.22	45.14±1.93	< 0.01

Table4. Comparisons of results between Cyclosporine and Tacrolimus groups with clinical gingival overgrowth, n = 60

Variables		CsA group Mean ± SD	Tcr group Mean ± SD	t-test	p-value
oral hygiene Score Index	Good	1.14±1.53	1.04±0.36	0.53	0.54
	Fair and poor	1.78±4.11	1.20±2.47	1.64	< 0.01
Bleeding Index	Mild	48.24±0.65	32.13±5.63	2.73	0.03
	Fair and poor	68.18±1.23	45.14±1.93	3.26	< 0.01

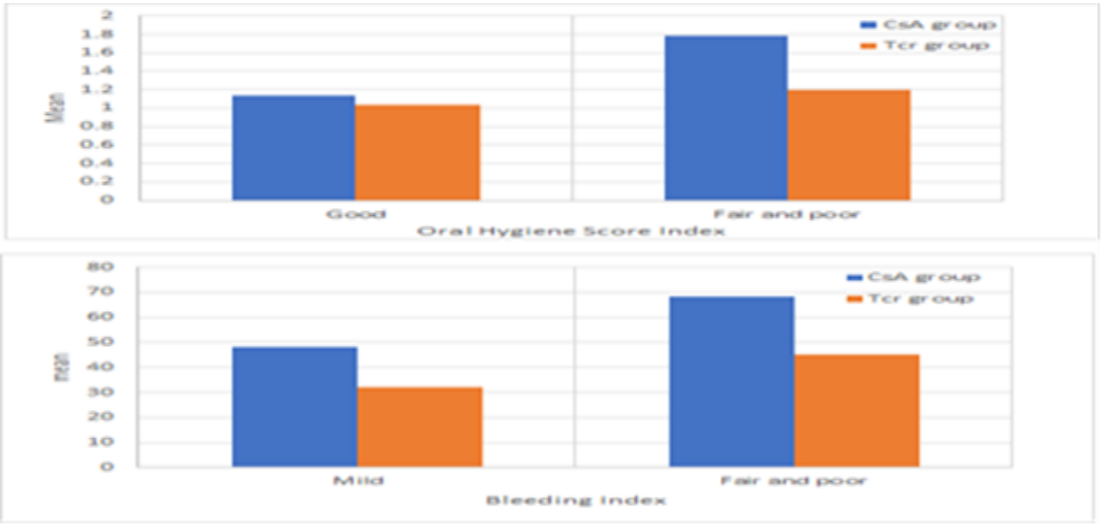

Fig 2. Comparisons of results between Cyclosporine and Tacrolimus groups with clinical gingival overgrowth, n = 60.

All the results for cyclosporine treated group showed significant reduction after 3 months of treatment, while, for tacrolimus treated group, showed highly significant differences after 3 months from treatment when $P < 0.01$. The comparison of results after 3 months of treatment with scaling and polishing in patients presented with gingival overgrowth treated by cyclosporine and tacrolimus were shown in table 4 and figure 2. Patients with fair and poor for both plaque score index and bleeding index showed statistically highly significant differences regarding the clinical parameters after the treatment period with significant difference in mild bleeding index, in addition to all that, the mean value of good plaque score index showed no statistical differences between the two groups.

DISCUSSION

Many medications, including cyclosporine, may cause gingival enlargement directly, but they can also often exacerbate their effects on gingival tissues via secondary inflammatory processes brought on by dental plaque buildup and other local variables.[13] In fact, a mixed etiology accounts for the majority of gingival enlargements.

There was no information available on gingival overgrowth (GO) in patients receiving renal transplants who were on regimens based on tacrolimus and cyclosporine. The results of the research shed important light on the treatment and demographic variations between patients receiving tacrolimus and cyclosporine. According to the sample, a minority of individuals received tacrolimus treatment, whereas a majority were received cyclosporine treatment. This distribution is representative of clinical settings where both medications are often prescribed, albeit the patient's individual needs and the doctor's choice may influence the drug selection. As calcineurin inhibitors, tacrolimus and cyclosporine are mainly used to treat certain autoimmune illnesses and prevent organ rejection after transplantation.[14] A clear gender disparity was observed; with a majority of individuals in the cyclosporine-treated group being male, while a majority of individuals in the tacrolimus-treated group were female. These trends may be influenced by gender disparities in pharmacological responsiveness and adverse effects. Studies indicate that women may have more favorable results with tacrolimus as a result of its pharmacokinetic characteristics and reduced occurrence of certain adverse effects like as hypertension and hyperlipidemia, which are more common with cy- closporine.[15] Males may be administered cyclosporine more often than females owing to previous prescription patterns or distinct clinical reactions. Both groups had a high level of education, indicating a potential link between greater education and involvement in sophisticated medical procedures. Higher educa-

DOI: doi.org/10.15218/edj.2025.5

tion is often associated with increased health literacy, which may enhance treatment adherence and results.[16] Educated patients are typically more adept at managing their health, understanding medical advice, and adhering to treatment regimens, which is crucial for the effectiveness of immunosuppressive therapies. When considering the tacrolimus group, the mean treatment duration was shorter than that of the cyclosporine group. This difference could reflect the historical context of cyclosporine being one of the first widely used calcineurin inhibitors, with tacrolimus being adopted more recently due to its superior efficacy and safety profile in some contexts. Recent studies
have highlighted tacrolimus's advantages, including lower rates of acute rejection and better overall graft survival rates, which might explain its increasing preference.[17] This study shows cyclosporine and tacrolimus are commonly used immunosuppressive agents in kidney transplant recipients to prevent organ rejection. While effective, these medications are associated with several side effects, including gingival over- growth, particularly cyclosporine.[18] Tacrolimus, although still linked to gingival overgrowth, generally presents a lower incidence and severity compared to cyclosporine (Muris et al., 2016). In the study, most subjects reported brushing their teeth twice daily in the cyclosporine group and the tacrolimus group. Regular tooth brushing is crucial for maintaining oral health and preventing periodontal diseases, which is especially important for immunocompromised patients.[19] Additionally, a substantial portion of subjects had dental visits within the last 6-12 months for cyclosporine and tacrolimus-treated patients. Regular dental visits allow for early detection and management of oral complications, including drug-induced gingival overgrowth.[19] The study found that most subjects had fair oral hygiene in cyclosporine group and tacrolimus group. Similarly, the fair bleeding index was reported for cyclosporine-treated and tacrolimus-treated subjects. Fair oral hygiene and bleeding indices suggest a moderate level of plaque control and gingival health, but also indicate that there is room for improve- ment.[20] The prevalence and severity of gingival overgrowth differed significantly between the two groups. Among cyclosporine-treated patients, the largest proportion of participants was score 2. In contrast, among tacrolimus-treated patients had a score of 1. Gingival overgrowth is a known side effect of cyclosporine, affecting up to 70% of patients on this medication. The mechanism involves increased collagen production and reduced degradation in the gingival tis- sues.18 Tacrolimus, although associated with gingival overgrowth, does so less frequently and severely, likely due to its different pharmacological properties.[21] The results in the present study evaluates the impact of periodontal treatment, specifically scaling and polishing, on gingival overgrowth and associated clinical periodontal

parameters in patients treated with cyclosporine and tacrolimus. The plaque scores significantly improved in cyclosporine-treated patients ($p=0.02$) and tacrolimus-treated group ($p<0.01$) after scaling and polishing in good plaque score. While; there was a notable reduction ($p<0.01$) and ($p<0.01$) in fair and poor plaque score of cyclosporine and tacrolimus group respectively. The potential mechanism of scaling and polishing effectively reduce plaque accumulation, as evidenced by the significant decreases in plaque scores across both treatment groups. These findings align with recent literature that emphasizes the role of professional dental cleanings in managing drug-induced gingival overgrowth by reducing plaque-induced inflammation.[19] The bleeding index improvements reflect reduced gingival inflammation post-treatment. Professional scaling and polishing are critical in managing gingival overgrowth, as they help to reduce bleeding and improve overall gingival health.[22] The scores of mild bleeding index showed decreased from ($p=0.04$) and significant improved ($p<0.01$), while; a reduction was noted ($p=0.033$) and a significant decrease ($p<0.01$) in fair and poor bleeding index of cyclosporine and tacrolimus group respectively. The bleeding index improvements reflect reduced gingival inflammation post-treatment. Professional scaling and polishing are critical in managing gingival overgrowth, as they help to reduce bleeding and improve overall gingival health.[22] The study clearly demonstrates that scaling and polishing have a positive impact on gingival health in kidney transplant patients treated with cyclosporine and tacrolimus. These findings are crucial for clinical practice, as they highlight the need for

regular periodontal care in managing side effects of immunosuppressive therapy. Patients receiving cyclosporine tend to experience more severe gingival overgrowth compared to those on tacrolimus, which is consistent with existing research indicating higher prevalence and severity of gingival overgrowth with cyclosporine.[18] Regular periodontal maintenance, including scaling and polishing, should be a cornerstone of care for transplant patients to mitigate the oral side-effects of immunosuppressive drugs. This approach not only improves oral health outcomes but also enhances overall patient quality of life.[19] The comparison of results after three months of
treatment with scaling and polishing in patients presented with gingival overgrowth treated by cyclosporine and tacrolimus reveals significant improvements in clinical parameters. Results showing notable reductions in plaque score index and bleeding index for both groups. The results suggest that both cyclosporine and tacrolimus groups experienced improvements in plaque control after three months of treatment, with statistically significant reductions observed in patients with fair and poor plaque score index. However, there was no statistically significant difference in the mean value of good plaque score index between the two groups. Both cyclosporine and tacrolimus groups exhibited significant improvements in bleeding index after the treatment period, with tacrolimus showing a highly significant reduction compared to cyclosporine. The study demonstrates the efficacy of scaling and polishing in improving periodontal parameters in patients with gingival overgrowth treated with cyclosporine and tacrolimus. While both groups experienced reductions in plaque score index and bleeding index, the tacrolimus group showed more significant improvements in bleeding index compared to the cyclosporine group. These findings are consistent with recent research high-lighting the importance of periodontal treatments in managing drug-induced gingival overgrowth and improving overall oral health outcomes.[22] The results underscore the need for regular periodontal maintenance in transplant patients to mitigate the adverse effects of immunosuppressive therapy on oral health. The findings underscore the importance of regular periodontal care, including scaling and polishing, for kidney trans- plant patients on immunosuppressive therapy. Such care is essential to mitigate the oral side effects of drugs like cyclosporine and tacrolimus, ultimately improving patients' overall quality of life. The highlights on the critical role of periodontal maintenance in managing the side effects of immunosuppressive therapy, particularly in preventing and treating gingival overgrowth, thereby enhancing the overall health and well- being of transplant patients.

CONCLUSION

Both cyclosporine and tacrolimus, commonly used immunosuppressive agents in kidney transplant recipients, can cause gingival overgrowth

(GO). However, cyclosporine is associated with a higher prevalence and severity of GO compared to tacrolimus. Regular tooth brushing and professional dental cleanings may contribute to better management of periodontal health. These improvements indicate that professional dental care is effective in managing drug-induced gingival overgrowth by reducing plaque accumulation and gingival inflammation.

REFERENCES

1. Robin W. M. Vernooij, Way Law, Sanne A. E. Peters, Bernard Canaud, Andrew Davenpor, Muriel P. C. Grooteman, Fatih Kircelli, Francesco Locatelli, Francisco Maduell, Marion Morena, Menso J. Nubé, Ercan Ok, Ferran Torres, Mark Woodward, Peter J. Blankestijn1, Michiel L. Bots. The probability of receiving a kidney transplantation in end-stage kidney disease patients who are treated with hemodiafiltration or hemodialysis: a pooled individual participant data from four randomized controlled trials. BMC Nephrology 2021; 22:70.
2. Gaetano LM, Capelli I, Gasperoni L, Comai G, Ravaioli M, et al. Long Term Outcomes of Kidney Transplant: Characteristics of Recipients with 20 or More Years of Graft Survival. J Med Surg Pathol 2016; 1: 109.
3. Souza DF, Chiapinotto GA, Martos J. Induction of gingival hyperplasia associated with the use of calcium channel blockers. South Braz Dent J. 2009; 6:447-53
4. Dongari-Bagtzoglou A., Research, Science and Therapy Committee, American Academy of Periodontology. Drug-associated gingival enlargement. J Periodontol. 2004;75 (10):1424-31.
5. Greenberg KV, Armitage GC, Shiboski CH. Gingival enlargement among renal transplant recipients in the era of new-generation immunosuppressants. J Periodontol. 2008;79 (3):453-60.

DOI: doi.org/10.15218/edj.2025.5

6. Sekiguchi RT, Paixão CG, Saraiva L, Romito GA, Pannuti CM, Lotufo RF. Incidence of tacrolimus-induced gingival overgrowth in the absence of calcium channel blockers: a short-term study. J Clin Periodontol. 2007;34(7):545-50.
7. Nassar CA, Nassar PO, Andia DC, Guimarães MR, Spolidorio LC. The effects of up to 240 days of tacrolimus therapy on the gingival tissues of rats--a morphological evaluation. Oral Dis. 2008;14(1):67-72.
8. James JA, Boomer S, Maxwell AP, et al. Reduction in gingival over growth associated with conversion from cyclosporine A to tacrolimus[review]. J Clin Periodontol 2000; 27(2):144-148.
9. Silness J, Loe H. Periodontal disease in pregnancy. Correlation between oral hygiene and periodontal condition. Acta Odontol Scand,1964;24:747-759.
10. Loe H, Silness J. Periodontal disease in pregnancy. Acta Odonto Scand 1963; 21: 533-551.
11. Wan Mohamad WM, Mat Zaid SI, Taib H, Husin A. Assessment of gingival status and gingival overgrowth among immunosuppressed patients in University Sains Malaysia Hospital. J Dent Indones. 2021;28(1):27-32.
12. Baban DA. Prevalence and severity of periodontal diseases in pregnant women. 2003, Salaheddin University, Master's thesis.
13. Malek R, El Houari B, and Kissa J. Periodontal Management of Cyclosporin A-Induced Gingival Overgrowth: A Nonsurgical Approach. Case Reports in Dentistry 2019; Article ID 8609547, 8 pages.
14. Vincenti, F., & Kirk, A. D. (2008). What's Next in Immunosuppression for Kidney Transplantation. American Journal of Transplantation 2008; 8: 1972–1981.
15. Kovarik, J. M., Hoyer, P. F., & Mueller, E. A. Gender-related differences in the pharmacokinetics of immunosuppressants: clinical implications. Clinical Pharmacokinetics2001; 40(2), 97-112.
16. Rosenberger, J., Dew, M. A., DiMartini, A. F., Dabbs, A. D., Myaskovsky, L., & Steel, J. L. Impact of education on kidney transplant outcomes. Clinical Transplantation2020; 34(4), e13841.
17. Lamb, K. E., Lodhi, S., & Meier-Kriesche, H. U. Long-term renal allograft survival in the United States: A critical reappraisal. American Journal of Transplantation 2011; 11(3), 450-462.
18. Thomson, W. M., & Francis, D. R. "Drug-Induced Gingival Overgrowth: Current Concepts in Pathogenesis." Journal of Clinical Periodontology 2020; 47(5), 559-571.
19. Chapple, I. L. C., Genco, R., & working group 2 of the joint EFP/AAP workshop. Periodontal health and systemic conditions: A consensus report. Journal of Clinical Periodontology 2018; 45(S20), S138-S149.
20. Nishida, N., Yamamoto, Y., Tanaka, K., & Shimizu, A. Oral hygiene practices and their impact on periodontal health among kidney transplant patients. Journal of Periodontal Research2019; 54(3), 231-238.
21. Muris, J., Reinders, M. E., Heemskerk, M. B., & ten Berge, I. J. (2016). Comparative study of tacrolimus and cyclosporine on gingival overgrowth in renal transplant patients. Clinical Transplantation 2016; 30(5), 584-590.
22. Heitz-Mayfield, L. J. A., Needleman, I., Lang, N. P., & Young, T. Effectiveness of non-surgical periodontal therapy in managing drug-induced gingival overgrowth: A systematic review. Journal of Clinical Periodontology 2020; 47(2), 134-149.