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Evaluation of periodontal parameters in kidney transplant patients using immunosuppressive medications: a cross-sectional study

Avaliação de parâmetros periodontais em pacientes transplantados renais que usam medicações imunossupressoras: estudo transversal

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ABSTRACT

Objective: The aim of this study was to evaluate periodontal parameters in renal transplant patients compared to a control group, due to the possible interference caused by the use of immunosuppressive medication. **Methods**: This was a cross-sectional observational epidemiological study of 80 patients. The transplant patients

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consisted of 40 patients, in whom the plaque index, clinical probing depth, clinical attachment level, bleeding on probing and the presence of gingival hyperplasia were analyzed. The control group, made up of 40 patients, was assessed according to the same indices. **Results**: No statistically significant difference was found between the groups with regard to the presence of plaque (p = 0.279), bleeding (p = 0.262), severity (p = 0.707) and location (p = 0.949) of periodontitis, only in relation to the grade (p = 0.041), where grade C was more present in transplant patients, with transplant time being a contributing factor. The presence of hyperplasia (p = 0.021), the gingival bleeding index (p = 0.011) and the plaque index (p = 0.031) were significantly higher in patients taking Ciclosporin. transplant patients had rapidly progressing periodontitis. **Conclusion**: Increased gingival volume, bleeding and plaque index were more associated with Ciclosporin use.

Indexing terms: Gingival hyperplasia. Kidney transplantation. Immunosuppressive agents. Periodontal disease. Renal insufficiency, chronic.

RESUMO

Objetivo: O objetivo desse trabalho foi avaliar parâmetros periodontais em transplantados renais comparados a um grupo controle, devido às possíveis interferências ocasionadas após uso de medicações imunossupressoras. **Métodos**: Estudo epidemiológico observacional transversal, composto por 80 pacientes. Os transplantados renais, composto por 40 pacientes, nos quais analisou-se o índice de placa, a profundidade clínica de sondagem, o nível de inserção clínica, sangramento à sondagem e a presença de hiperplasia gengival. E o grupo controle, composto por 40 pacientes, avaliados de acordo com os mesmos índices. **Resultados**: Não foi encontrada diferença estatisticamente significativa entre os grupos quanto à presença de placa (p=0,279), sangramento (p=0,262), severidade (p=0,707) e localização (p=0,949) da periodontite, somente em relação ao grau (p=0,041), onde o grau C foi mais presente em transplantados renais, sendo o tempo de transplante um fator contribuinte. A presença de hiperplasia (p=0,021), o índice de sangramento gengival (p=0,011) e o índice de placa (p=0,031) foram significativamente maiores em pacientes que faziam uso da Ciclosporina. Pacientes transplantados renais apresentaram periodontite com progressão rápida. **Conclusão**: O aumento do volume gengival, sangramento e índice de placa estavam mais associados ao uso de Ciclosporina.

Termos de indexação: Hiperplasia gengival. Transplante de rim. Imunossupressores. Doença periodontal. Insuficiência renal crônica.

INTRODUCTION

Chronic kidney disease (CKD) is a public health problem, with morbidity and mortality as a result [1]. It is characterized as a clinical syndrome resulting from the slow, progressive and irreversible loss of glomerular filtration rate, requiring permanent replacement therapy [2,3].

The most common etiologies of CKD are diabetes mellitus, hypertension, glomerulonephritis, tubulo-intestinal nephropathies, and polycystic kidney disease [1,4,5]. Patient care should be multi-professional, and there are four methods: conservative treatment (pre-dialysis), peritoneal dialysis, hemodialysis and, finally, kidney transplantation [2]. When kidney failure reaches stage 5, the best procedure is kidney transplantation, which improves survival [6], as well as eliminating constant trips to hospital for dialysis sessions [7].

Immunosuppressive treatment, which is necessary to prevent organ rejection, depresses the cell-mediated immune response. However, the treatment brings disadvantages such as infections,

hypertension, and chronic transplant nephropathy [8]. For the dental surgeon, this suggests an increased risk of oral infection and other odontogenic complications [7].

Due to the amount of medication ingested, some systemic and metabolic changes also occur, which can affect the oral cavity, causing mucosal pallor, gingival inflammation, loss of insertion, xerostomia, changes in saliva composition, enamel hypoplasia, and dental erosion [9]. In addition, oral candidiasis, hairy leukoplakia, herpes- simplex type 1 infection, and gingival hyperplasia have also been reported in the literature [7].

Gingival hyperplasia is usually induced by the use of antihypertensive drugs (Calcium Channel Blockers) to reduce blood pressure, and immunosuppressive drugs (Cyclosporine), used mainly by individuals who are going to undergo a TR or who are in the terminal stage of the disease, associated with poor hygiene. This alteration can delay eruption or lead to teeth erupting in an abnormal position and also difficulty with oral hygiene [10] and, when it extends to the crown of the tooth, it can interfere with the patient's occlusion, chewing and phonetics [4].

Because of this, the pathogenesis of gingival growth caused by the use of immunosuppressive medications has been investigated in relation to some factors: dosage of the drug, duration of therapy, age of the patient, genetic predisposition and the presence of inflammatory factors such as plaque and calculus [11]. Tacrolimus, which can reduce this gingival growth [12]. This macrolide antibiotic has been shown to be an effective immunosuppressant and is an alternative to Ciclosporin (CsA), as well as reducing the side effects caused by it, related to immunosuppression [4,13]

Around 60% of patients with advanced renal failure or who have low immunity due to TR will present at least one oral alteration [14], it is important to be monitored by a qualified dental surgeon to maintain the oral health of pre-transplant and transplant patients.

The occurrence of infections is a concern post-RT, especially in the early stages, when the risk of rejection is higher and the doses of immunosuppressants are still being adjusted [15]. Therefore, in patients who are candidates for RR, a dental consultation and assessment is necessary, as all infectious foci must be removed [16].

Periodontitis is a multifactorial chronic inflammatory disease associated with dysbiotic plaque biofilms and characterized by destruction of the dental support apparatus [17]. The accumulation of bacteria between the gingival tissue and the tooth acts as a stimulus for the host's immunoinflammatory response which, added to the virulence of the periodontopathogens, is crucial for both the onset and progression of inflammation and loss of periodontal tissue [18]. In more susceptible individuals, this initial acute inflammatory response fails and leads to deregulated chronic inflammation that destroys the supporting tissues of the teeth [19].

Bacterial plaque and subgingival biofilm, in contact with the ulcerated epithelium of periodontal pockets, can act as a reservoir of bacteria, bacterial derivatives, proteins and pro-inflammatory cytokines, which constantly flood the bloodstream, affecting more distant sites. Likewise, CKD promotes a permanent systemic inflammatory state, even in the absence of a specific infection, justifying the idea that the inflammatory response induced by periodontal disease (PD) could increase the total inflammatory burden in these patients [18].

It is possible that CKD leads to increased susceptibility to PD or that the chronic infectious and inflammatory environment of PD may increase susceptibility to develop CKD [1,18,20,21]. And, in the long term, it is possible to notice a decrease in the immune system response of these patients, making them

more susceptible to infections [7]. Thus, PD can be considered a new and potentially modifying risk factor for CKD, while CKD is associated with an increased systemic inflammatory burden [19,20,22].

Studies point to a positive effect of periodontal treatment on renal function, leading to a decrease in inflammatory markers such as C-reactive protein, interleukin 6, cystatin C (a renal marker), an increase in glomerular filtration rate and also contributing to an increase in vasodilation, since periodontal disease can also cause endothelial and cardiovascular dysfunction [23].

Oral health plays an important role in the preparation of health plans in TRs and cannot and should not be forgotten. Medical and dental follow-up is essential, both in the pre-surgical plan and during the post-surgical period, which is the most delicate phase due to the possible rejection of the transplant and, even after this phase, due to the mandatory immunosuppression of these patients [24]. It is therefore essential to study the relationship between periodontal disease in chronic kidney disease and kidney transplant patients, as well as to identify the prevalence of periodontal alterations, such as gingival growth, in kidney transplant patients compared to a control group, due to the use of immunosuppressive medication.

METHODS

Study design, sample division and location

This is an epidemiological, cross-sectional, observational study, made up of a convenience sample of 80 individuals over the age of 18, of both sexes and divided into 2 groups. Group 1 is made up of 40 kidney transplant patients using immunosuppressive medication, all from the Nephrology Service of the Hospital das Clínicas da UFPE (HC-UFPE) and seen at the UFPE Stomatology Service. Group 2, the control group, is made up of 40 individuals without CKD, from the UFPE Stomatology Service itself.

This study was approved by the UFPE Research Ethics Committee under number 5.266.352. All the patients underwent a clinical assessment, after signing the Informed Consent Form (ICF), where probing was carried out for periodontal analysis, and a clinical form was filled out to identify the patient, containing medical data and a history of the current disease.

Eligibility criteria

Group 1

– Inclusion criteria

Individuals of both sexes, aged 18 or over, who had undergone a kidney transplant, were using immunosuppressive medication and had signed an informed consent form to take part in the study.

– Exclusion criteria

Individuals who have fewer than 8 teeth, positive serology for HIV, CKD still undergoing hemodialysis treatment, alcohol or tobacco users, pregnant or breastfeeding women or those taking anticoagulants, Nifedipine, Diltiazen, Verapamil, Phenytoin, Sodium Valproate and Azithromycin.

Group 2

- *Inclusion criteria*

Individuals of both sexes, aged 18 or over, without CKD, who had never undergone hemodialysis or organ transplantation and who signed the informed consent form for their participation in the study.

- *Exclusion* criteria

Individuals with fewer than 8 teeth, positive HIV serology, carriers of any autoimmune disorder, alcohol or tobacco users, pregnant or breastfeeding women or those taking immunosuppressive drugs, anticoagulants, Nifedipine, Diltiazem, Verapamil, Phenytoin, Sodium Valproate and Azithromycin.

Data collection and clinical examination

The individuals who met the inclusion criteria and agreed to take part, after signing the informed consent form, answered a structured questionnaire to obtain dental and medical data and underwent a careful clinical intraoral examination, carried out in the office of the UFPE Stomatology department, by a single previously calibrated examiner. The records were kept by a note-taker who was also calibrated. The instruments used for the examination were a clinical mirror (Duflex®) and a University of North Carolina-type millimeter periodontal probe (Trinity®).

A periogram was completed for each patient in the 2 groups, assessing: visible plaque index (VPI), probing depth (PD), probing bleeding (PB), clinical attachment level (CAL) and the presence or absence of gingival growth. The SP was carried out on all permanent teeth, circumferentially, on the 6 surfaces (mid-vestibular, mid-vestibular, disto-vestibular, mid-lingual, mid-lingual and disto-lingual). The CIN was read from the amelocementary boundary to the bottom of the periodontal pocket.

Gingivitis was classified when the patient had bleeding on probing in more than 10% of the sites, PS of up to 3mm, without loss of insertion. Those with clinical attachment loss (CIL) were classified as Periodontitis in terms of severity: I mild (1 to 2mm interproximal attachment loss at the worst site, no tooth loss due to periodontitis, PS up to 4mm), II moderate (ICP 3 to 4mm, no tooth loss due to periodontitis, PS up to 5mm), III severe (ICP ≥ 5mm, loss of up to 4 teeth due to periodontitis, PS ≥ 6mm) and IV advanced (ICP ≥ 5mm, loss of 5 or more teeth due to periodontitis, less than 20 teeth remaining); for the risk of progression into: A (slow) when the amount of plaque deposition was incompatible with the degree of periodontal destruction, B (moderate) when the amount of plaque deposition was equivalent to periodontal destruction and C (rapid) when the amount of plaque deposition was less than the degree of periodontal destruction. As for extent, it was classified as: localized (≤ 30% of affected teeth) and generalized (> 30%).

We used as a parameter the new periodontal classification carried out according to the criteria of the Proceedings of the World Workshop for the Classification of Periodontal and Peri-Implant Diseases and Conditions, which took place from November 9 to 11, 2017 in Chicago, United States, published by the American Academy of Periodontology and the European Federation of Periodontology in 2018 [25].

Statistical analysis

Data were expressed as means, standard deviations and absolute and relative frequency distributions. Continuous variables were compared using the Mann-Whitney non-parametric test to compare two

categories and the Kruskal-Wallis test to compare more than two groups because the continuous data did not follow a normal distribution, while the comparison of proportions was carried out using the likelihood ratio test when Pearson's chi-square test was not possible because it violated its assumption of expected values below 20% in most cases, and Fisher's exact test was carried out for 2x2 tables. The significance level adopted was 5%, i.e. p-value < 0.05. The software used was IBM SPSS 25.0 and the data was entered into Microsoft Excel.

Research Ethics Committee

The study was approved by the UFPE Research Ethics Committee, opinion no. 4.728.265, CAAE no. 54535421.6.0000.5208, version 2, and there were no conflicts of interest on the part of the authors. The study was carried out in accordance with the principles of the Declaration of Helsinki and the World Medical Association. Patient participation was voluntary, by means of a Free and Informed Consent Form, and the confidentiality of individual data was guaranteed.

RESULTS

The validated sample that took part in this study was made up of 80 patients, divided into 2 groups, each made up of 40 individuals: Renal Transplanted (Group 1) and Control (Group 2), in which 51.2% of the patients were male, with an average age of 46.2± 11.2 years, ranging from 25 to 73 years. With regard to schooling, 61.3% had completed primary school and, of this sample, 50% were from the case group (transplant patients) and 50% from the control group.

Regarding the distribution of patients according to gender, there were no statistically significant differences (p = 0.371). As for schooling, there was a statistically significant difference (p = 0.029), and it is worth noting that the majority of kidney transplant patients had only an incomplete primary education (57.5%), while in the control group this percentage was 30.0%.

With regard to the presence of systemic diseases, such as diabetes and hypertension, there was a statistically significant difference (p = 0.002) between the groups, where 67.5% of the HTs had some comorbidity, while in the CG only 30.0% had some systemic alteration. The use of medication was present in 100.0% of the transplant patients and 25.0% in the control group, and this difference was also significant (p < 0.001). There were no significant differences in gingivitis (p=1.000), as shown in table 1.

The presence of periodontitis in the entire sample was 83.8% and, in terms of severity and location, there was a total average of 47.5% in stage IV and 47.5% generalized in both groups, with no statistically significant differences between them (p>0.05). With regard to the degree of periodontitis, there was a significant difference (p=0.041), with grade B (moderate) being 15% for the kidney transplant group and 40% for the control group, and grade C (rapid) being 47.5% for the transplant group and 22.5% for the control group, as shown in table 2.

As can be seen in table 3, only the degree of periodontitis (p = 0.022) showed a statistically significant difference with the time since transplantation, where 63.6% of those transplanted over 10 years had grade C (rapid), compared to 27.3% between 5 and 10 years of transplantation and 28.6% up to 5 years of transplantation. The severity of periodontitis (p = 0.583) and location (p = 0.485) were not statistically significant in relation to time since transplantation.

Table 1. Absolute and relative frequency of the variables use of medication, systemic disease and gingivitis according to the groups studied.

Variables	Group				Total		p-value
	Kidney transplant patients		Control				
	n	%	n	%	n	%	
Uses Medicines							<0.001[1*]
Yes	40	100.0	10	25.0	50	62.5	
No	0	0.0	30	75.0	30	37.5	
Systemic disease							0.002[1*]
Yes	27	67.5	12	30.0	39	48.8	
No	13	32.5	28	70.0	41	51.2	
Gingivitis							1.000[1]
Yes	38	95.0	39	97.5	77	96.3	
No	2	5.0	1	2.5	3	3.8	
Total	**40**	**100.0**	**40**	**100.0%**	**80**	**100.0**	

Note: [1] Fisher's exact test; [*]Statistically significant.

Table 2. Absolute and relative frequency of periodontitis variables, severity, degree and location according to the groups.

Variables	Group				Total		p-value
	Kidney transplant patients		Control				
	n	%	n	%	n	%	
Periodontitis							
Yes	34	85.0	33	82.5	67	83.8	1.000[2]
No	6	15.0	7	17.5	13	16.3	
Severity Periodontitis							
Without Periodontitis	6	15.0	7	17.5	13	16.3	0.707[1]
Internship II	9	22.5	5	12.5	14	17.5	
Internship III	7	17.5	8	20.0	15	18.8	
Internship IV	18	45.0	20	50.0	38	47.5	
Degree of Periodontitis							
Without Periodontitis	6	15.0	7	17.5	13	16.3	0.041[1*]
A (Light)	9	22.5	8	20.0	17	21.3	
B (Moderate)	6	15.0	16	40.0	22	27.5	
C (Fast)	19	47.5	9	22.5	28	35.0	
Localization Periodontitis							
Without Periodontitis	8	20.0	7	17.5	15	18.8	0.949[1]
Localized	13	32.5	14	35.0	27	33.8	
Generalized	19	47.5	19	47.5	38	47.5	
Total	**40**	**100.0**	**40**	**100.0**	**80**	**100.0**	

Note: [1]Likelihood Ratio Test; 2 Fisher's Exact Test; [*]Statistically significant.
Case Group (renal transplant patients).

Table 3. Absolute and relative frequency of periodontitis variables (severity, degree and location) according to transplant time.

Periodontitis	Transplant time						Total		p-value[1]
	Up to 5 years		From 5 to 10 years		Over 10 years old				
	n	%	n	%	n	%	n	%	
Severity Periodontitis									
Without Periodontitis	2	28.6	3	27.3	1	4.5	6	15.0	0.583
Internship II	1	14.3	2	18.2	6	27.3	9	22.5	
Internship III	1	14.3	2	18.2	4	18.2	7	17.5	
Internship IV	3	42.9	4	36.4	11	50.0	18	45.0	
Degree of Periodontitis									
Without Periodontitis	2	28.6	3	27.3	1	4.5	6	15.0	0.022*
A (Light)	0	0.0	3	27.3	6	27.3	9	22.5	
B (Moderate)	3	42.9	2	18.2	1	4.5	6	15.0	
C (Fast)	2	28.6	3	27.3	14	63.6	19	47.5	
Localization Periodontitis									
Without Periodontitis	2	28.6	3	27.3	3	13.6	8	20.0	0.485
Localized	2	28.6	5	45.5	6	27.3	13	32.5	
Generalized	3	42.9	3	27.3	13	59.1	19	47.5	
Total	**7**	**100.0**	**11**	**100.0**	**22**	**100.0**	**40**	**100.0**	

Note: [1]Likelihood Ratio Test; *Statistically significant.

The average percentage of bleeding cheeks in those transplanted up to 5 years was 10.0 ± 8.1%, between 5 and 10 years 14.7 ± 18.9% and over 10 years 29.6 ± 30.1%, and this difference was not statistically significant (p = 0.262). The average percentage of faces with plaque in relation to the time since transplantation was 19.1 ± 15.0% in patients up to 5 years, 13.8 ± 13.6% between 5 and 10 years and 18.9 ± 21.3% for those over 10 years since transplantation, and this difference was also not statistically significant (p = 0.829).

Table 4 shows that the type of measurement used presented statistically significant differences p = 0.021 with the presence of hyperplasia, with a percentage of 44.4% for those using Ciclosporin, while only 21.4% for those using Tacrolimus. None of the patients using other drugs showed hyperplasia.

Table 4. Absolute and relative frequency of the hyperplasia variable with the type of medication used.

Hyperplasia	Types of medication						Total		p-value[1]
	Cyclosporine		Tacrolimus		Others				
	n	%	n	%	n	%	n	%	
Yes	8	44.4	3	21.4	0	0.0	11	27.5	0.021*
No	10	55.6	11	78.6	8	100.0	29	72.5	
Total	**18**	**100.0**	**14**	**100.0**	**8**	**100.0**	**40**	**100.0**	

Note: [1]Likelihood Ratio Test; *Statistically significant.

In relation to the percentage of bleeding cheeks according to the type of medication, the average % of bleeding cheeks in patients using Cyclosporine was 36.6 ± 31.4% and Tacrolimus was 11.6 ± 11.5%, while those using other medications was 7.8 ± 8.3%, this difference being statistically significant (p=0.011), where the difference was greater in those using Cyclosporine. The average percentage of plaque faces in relation to the type of medication was 22.8 ± 22.0% in those using Cyclosporine, 9.1 ± 7.5% Tacrolimus and 20.5 ± 18.3% for other medications, and this difference was also statistically significant p = 0.031, where the use of Tacrolimus had the lowest average, as shown in table 5.

The presence of systemic diseases in TR patients, such as hypertension and diabetes mellitus, when related to the severity of periodontitis, did not show statistically significant differences (p = 0.494).

Table 5. Descriptive measures of the variables percentage of faces with bleeding and plaque according to type of medication.

Variables	Type of medication	n	Mean ± Standard deviation	Median	Minimum	Maximum	p-value[1]
% bleeding faces	Cyclosporine	18	36.6 ± 31.4	26.0	0.0	100.0	0.011*
	Tacrolimus	14	11.6 ± 11.5	9.0	0.0	36.3	
	Others	8	7.8 ± 8.3	5.6	0.0	25.0	
	Total	40	22.1 ± 25.8	10.8	0.0	100.0	
% faces with plate	Cyclosporine	18	22.8 ± 22.0	16.8	3.1	88.9	0.031*
	Tacrolimus	14	9.1 ± 7.5	9.0	0.0	25.0	
	Others	8	20.5 ± 18.3	11.8	4.6	51.4	
	Total	40	17.5 ± 18.2	10.4	0.0	88.9	

Note: [1]Kruskal Wallis non-parametric test; Post-Hoc with Mann-Whitney test (equal letters do not differ statistically); *Statistically significant.

DISCUSSION

By encouraging an increase in toxic metabolites in the blood, CKD triggers a series of systemic and immunological changes that can lead to the development of various systemic and oral problems. Some of these oral alterations include: increased deposition of dental calculus, gingival enlargement and xerostomia, which are predisposing factors to a serious and highly prevalent condition in these patients, periodontal disease [26].

PD continues to be a major public health problem due to its high prevalence and burden. Its pathophysiological systems represent a complex action between the host's immune system and periodontopathogenic bacteria, leading to inflammation and disease. In addition, poor clinical control of PD leads to an increase in serum inflammatory markers due to the systemic impact. It is therefore extremely important to understand its systemic impact through inflammatory mechanisms, especially in immunocompromised patients such as kidney transplant patients [27].

It is responsible not only for damaging the tissues that support the teeth, but also for increasing the levels of inflammatory mediators that can aggravate CKD, such as prostaglandins, IL-1, IL-6, TNF-α and interferon. These mediators can contribute to the severity of periodontal disease, since they act on the

metabolism of bone tissue, interfering with its remodeling and promoting greater bone resorption [28]. Therefore, the need for assessment, treatment and control of the periodontal condition in both patients with chronic kidney disease and transplant patients is essential for maintaining general health [29].

It's worth pointing out that not only the presence of CKD, but also the length of treatment prior to transplantation, could lead to a higher prevalence of periodontal alterations, since the length of time patients undergo treatment is closely related to the condition of their oral health, given that the longer the treatment, the poorer their oral health. Patients with CKD have a very stressful general health care routine, with the condition worsening over time and, as a result, oral health is not prioritized as it should be, affecting the quality of life of this population [30].

On the other hand, in the post-transplant period, as the patient has fewer visits to hospital, they may have more time to look after their oral health. In our study, the TR group was divided into 3 subgroups according to the time since transplantation: up to 5 years, 5 to 10 years and more than 10 years. No statistically significant difference was found between the groups in terms of the percentage of faces with plaque and bleeding, severity and location of PD. It is important to know that after successful transplantation, uremia tends to decrease, reducing the inflammatory condition of the periodontal tissues, however the loss of insertion and gingival recession that occurred previously remain [29].

When comparing the two groups, only a statistically significant difference was found in the grade, with a total of 47.5% in grade C for the TR versus 22.5% for the CG. The same was not achieved when comparing the severity and location of the periodontitis of the kidney transplant groups with a control group without CKD, where a total of 45% was found for stage IV severity for the TR group and 50% for the C group, as well as 47.5% in the generalized situation in both groups.

In our study, the high prevalence of periodontitis in the control group may be related to these patients' greater need for dental treatment, since they all went to the UFPE Stomatology Clinic for an assessment due to some complaint about their oral health, while all the patients in the transplant group, no longer suffering from CKD, were in hospital for medical assessments and were invited by our team to take part in the research. It is also necessary to understand that transplant patients can present systemic alterations, mainly due to the use of medication, which can favor this condition.

Despite all the advances in dialysis techniques, these are only a temporary way of controlling CKD, with RT being the gold standard of treatment, as it rescues a better quality of life for chronic kidney patients, since it reduces the constant trips to hospital for long hemodialysis sessions, replacing kidney functions, regardless of congenital origin, infectious or chronic-degenerative diseases [6, 31].

One of the factors for post-transplant success is immunosuppressive therapy. However, despite ensuring the maintenance of the transplanted organs, some of these medications can predispose to a higher prevalence of gingival bleeding and hyperplasia [31]. The main immunosuppressive drugs used in patients undergoing kidney transplantation are: prednisolone, mycophenolate mofetil, tacrolimus, azathioprine, sirolimus and also cyclosporine A [32].

CsA is already well known in the literature for causing gingival hyperplasia and a greater chance of bleeding. In our study, this was confirmed, as patients using Cyclosporine had a significant percentage of bleeding on probing (36.6%) and hyperplasia (44.4%) compared to transplant patients using other drugs, such as Tacrolimus (11.6% and 21.4%, respectively), which has less adverse effects on periodontal tissues, is effective and capable of suppressing humoral and cellular immune responses, making it an interesting alternative to CsA [4,13].

Therefore, it is interesting to look for alternatives to prevent gingival growth since the impairment of quality of life in patients who develop gingival hyperplasia during immunosuppressive therapy is relevant, as it interferes not only with aesthetics, but also compromises oral hygiene, creating the possibility of a

primary focus of gingival infection 13 and this can affect general health, bringing more complications both pre and post kidney transplant [1].

In the study by Liu et al. [33], it was shown that Tacrolimus reduced risks after HT, such as patient mortality, transplant rejection and hypercholesterolemia. However, it increased the risk of diabetes. Regarding the pharmacoeconomic analysis, it represented a more cost-effective treatment than CsA for the prevention of adverse effects after RR [33].

Socioeconomic status and level of education are other aspects that could be related to the high prevalence of periodontitis in the groups studied. In our study, more than half of the patients (total average of 61.3%) had only completed elementary school at most in both groups. This is an important finding, as it may be associated with poor oral hygiene habits, as seen in the study by Petersen & Ogawa [34], in which many of these patients did not have access to basic oral health care guidelines.

Therefore, efficient dental treatment with good oral hygiene is essential in the pre- and post-transplant phase to prevent the occurrence of serious infections and favor the survival of the transplanted organ. In addition to knowledge of general health aspects, dentists must know the correct practical approach and operative sequences to follow when treating kidney patients. From the first appointment, it is essential to instill in the patient the importance of proper oral health, explaining the possible complications arising from untreated oral foci [35].

CONCLUSION

Based on the data collected and the statistical analysis, we can conclude that the TR patients had periodontitis with a rapid progression characteristic, which showed an influence directly proportional to the time of transplantation. In addition, the increase in gingival volume, bleeding and plaque index was more associated with the use of Ciclosporin, compared to patients using Tacrolimus.

The aim of dental treatment in these patients is to detect infectious foci and carry out conservative treatment. Therefore, basic periodontal therapy and oral health monitoring are necessary in the pre- and post-kidney transplant period, leading to a satisfactory overall health outcome.

Collaborators

GP Menezes contributed to the conception, work design, data collection and analysis. FS Dantas, KH Pessôa and JJ Souza wrote the article and critically reviewed it. MM Perez was responsible for the conception, work design, data collection and analysis. JC Leão and AA Carvalho out the critical review and defined the final approval of the version to be published.

REFERENCES

1. Spezzia S. Chronic kidney disease and periodontal diseases. Odonto. 2021;29(56):1-8. https://doi.org/10.15603/2176-1000/odonto.v29n56p1-8
2. Castro DS, Herculano AB, Gaetti-Jardim EC, Costa DC. Oral changes and the dental management of patients with chronic kidney disease. Arch Health Invest. 2017;6(7):308-3015. http://dx.doi.org/10.21270/archi.v6i7.2084
3. Silva GD, Acurcio FA, Cherchiglia ML, Guerra Junior AA, Andrade EI. Exceptional drugs for chronic kidney disease: expenditure and utilization profile in Minas Gerais.

Cad Saúde Pública. 2011;27(2):357-68. https://doi.org/10.1590/S0102-311X2011000200017

4. James JA, Boomer S, Maxwell AP, Hull PS, Short CD, Campbell BA, et al. Reduction in gingival overgrowth associated with conversion from Cyclosporin A to Tacrolimus. J Clin Periodontol. 2000;27(2):144-8. https://doi.org/10.1034/j.1600-051x.2000.027002144.x
5. Ziebolz D, Fischer P, Hornecker E, Mausberg RF. Oral health of hemodialysis patients: A cross-sectional study at two German dialysis centers. Hemodialysis Int. 2012;16(1):69-75. https://doi.org/10.1111/j.1542-4758.2011.00606.x
6. Santos DL. Periodontal conditions and treatment in kidney transplant patients. Single volume. São Luís: Postgraduate Program in Dentistry, Federal University of Maranhão; 2019
7. Rezvani G, Davarmanesh M, Azar MR, Salehipour M, Sedagaht R, Karimi F, et al. Oral manifestations of allograft recipients before and after renal transplantation. Saudi J Kidney Dis Transpl. 2014;25(2):278. https://doi.org/10.4103/1319-2442.128505
8. Proctor R, Kumar N, Stein A, Moles D, Porter S. Oral and dental aspects of chronic renal failure. J Dent Res. 2005;84(3):199-208. https://doi.org/10.1177/154405910508400301
9. Araújo LF, Branco CM, Rodrigues MT, Cabral GM, Diniz MB. Oral manifestations and use of dental services by individuals with chronic kidney disease. Rev Assoc Paul Cir Dent. 2016;70:30-36.
10. Ojo AO, Morales JM, González-Molina M, Steffick DE, Luan FL, Merion RM. Comparison of the long-term outcomes of kidney transplantation: USA versus Spain. Nephrol Dial Transplant. 2013;28(1):213-20. https://doi.org/10.1093/ndt/gfs287
11. Paixão CG. Longitudinal evaluation of gingival growth induced by Ciclosporin A (CsA) and Tacrolimus, in the absence of sodium channel blockers, in renal transplant patients. Master's thesis. São Paulo; 2010.
12. Spolidorio LC, Spolidorio DM, Massucato EM, Neppelenbroek KH, Campanha NH, Sanches MH. Oral health in renal transplant recipients administered cyclosporine A or tacrolimus. Oral Dis. 2006;12(3):309-14. https://doi.org/10.1111/j.1601-0825.2005.01200.x
13. Muduma G, Saunders R, Odeyemi I, Pollock R. Systematic review and meta-analysis of tacrolimus versus ciclosporin as primary immunosuppression after liver transplant. PLoS One. 2016 Nov 3;11(11):e0160421. https://doi.org/10.1371/journal.pone.0160421
14. Cerveró AJ, Bagan JV, Soriano YJ, Roda RP. Dental management in renal failure: patients on dialysis. Med Oral Pathol Oral Cir Bucal. 2008;13(7):E419-26.
15. Antunes RSCC. Oral Alterations in Renal Transplant Recipients [dissertation]. São Paulo: Universidade de São Paulo; 2019. https://doi.org/10.11606/D.23.2019.tde-30042019-162744
16. Raimundo MC, Machado ÉR, Figueiredo AL, Beanes G. Dental management of the chronic renal patient: a literature review. Rev Fac Odontol Univ Fed Bahia. https://doi.org/10.9771/revfo.v47i1.29423
17. Papapanou PN, Sanz M, Buduneli N, Dietrich T, Feres M, Fine DH, et al. Periodontitis: Consensus Report of Workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. J Clin Periodontol. 2018;45:S162-S170. https://doi.org/10.1002/JPER.17-0721
18. Ismail FB, Ismail G, Dumitriu AS, Baston C, Berbecar V, Jurubita R, et al. Association with the severity of periodontitis in patients with chronic kidney diseases: A cross-sectional study. BioMed Res Int. 2015 [cited 2022 Nov 18] ;7. https://doi.org/10.1155/2015/370314
19. Sharma P, Cockwell P, Dietrich T, Ferro C, Ives N, Chapple ILC. Influence of Successful Periodontal Intervention in Renal Disease (INSPIRED): study protocol for a randomized controlled pilot clinical Trial. Trials. 2017;18(1):535. https://doi.org/10.1186/s13063-017-2236-5
20. Ricardo AC, Athavale A, Chen J, Hampole H, Garside D, Marucha P, Lash JP. Periodontal disease, chronic kidney disease and mortality: results from the third national health and nutrition examination survey. BMC Nephrology. 2015;16:97. https://doi.org/10.1186/s12882-015-0101-x
21. Cholewa M, Madziarska K, Radwan-Oczko M. The association between periodontal conditions, inflammation, nutritional status and calcium-phosphate metabolism disorders in hemodialysis patients. J Appl Oral Sci. 2018;26:e20170495. https://doi.org/10.1590/1678-7757-2017-0495
22. Lertpimonchai A, Rattanasiri S, Tamsailom S, Champaiboon C, Ingsathit A, Kitiyakara C, et al. Periodontitis as the risk factor of chronic kidney disease: Mediation analysis. J Clin Periodontol. 2019;46:631-639. https://doi.org/10.1111/jcpe.13114
23. Almeida S, Figueredo CM, Lemos C, Bregman R, Fischer RG. Periodontal treatment in patients with chronic kidney disease: a pilot study. J Periodont Res. 2016;52(2):262-7. https://doi.org/10.1111/jre.12390
24. Georgakopoulou E, Achtari M, Afetoulide N. Dental management of patients before and after renal transplantation. Stomatologija. 2011;13:107-112.
25. Steffens JP, Marcantonio RAC. Classification of periodontal and peri-implant diseases and conditions 2018: Practical guide and key points. Rev Odontol UNESP. 2018;47(4):189-197. https://doi.org/10.1590/1807-2577.04704
26. Weinert E, Heck MP. Oral implications of chronic renal failure. Int J Dent. 2011;10(4):259-67. https://doi.org/10.1177/154405910508400301

27. Machado V, Botelho J, Lopes J, Patrão M, Alves R, Chambrone L, et al. Impact of periodontitis on serum interleukin-6 levels in solid organ transplant patients: a systematic review and meta-analysis. Diagnostics (Basel). 2020;10(4):184. https://doi.org/10.3390/diagnostics10040184

28. Machowska A, Carrero JJ, Lindholm B, Stenvinkel P. Therapeutics targeting persistent inflammation in chronic kidney disease. Trad Res. 2016;167:204-13. https://doi.org/10.1016/j.trsl.2015.06.012

29. Schmalz G, Kauffels A, Kollmar O, Slotta JE, Vasko R, Müller GA, et al. Oral behavior, dental, periodontal and microbiological findings in patients undergoing hemodialysis and after kidney transplantation. BMC Oral Health. 2016;16(1):72. https://doi.org/10.1186/s12903-016-0274-0

30. Gonçalves JLA, Ribeiro EO, Prestes GR, Soares. Evaluation of the oral condition of patients with chronic kidney disease being treated at the Adriano Jorge Hospital Foundation - AM. Arq Odontol. 2019;55-60.

31. Ioannidou E, Shaqman M, Burleson J, Dongari-Bagtzoglou A. Periodontitis case definition affects the association with renal function in kidney transplant recipients. Oral Dis. 2010;16(7):636-42. https://doi.org/10.1111/j.1601-0825.2010.01665.x

32. Ikuta CRS, Castro RC, Rubira CM, Santos OS. Medicated gingival hyperplasia associated with the use of Cyclosporin-A after kidney transplantation. Rev Bras Med. 2016;L1:11-15.

33. Liu J, You RX, Guo M, Zeng L, Zhou P, Zhu L, et al. Tacrolimus versus cyclosporine as primary immunosuppressant after renal transplantation: a meta-analysis and economics evaluation. Am J Ther. 2016;23:e810-e824. https://doi.org/10.1097/MJT.0000000000000150

34. Petersen PE, Ogawa H. The global burden of periodontal disease: towards integration with chronic disease prevention and control. Periodontology 2000. 2012;60(1):15-39. https://doi.org/10.1111/j.1600-0757.2011.00425.x

35. Constantinides F, Castronovo G, Vettori E, Frattini C, Artero ML, Bevilacqua L, et al. Dental Care for Patients with End-Stage Renal Disease and on Hemodialysis. Int J Dent. 2018; 2018:9610892. https://doi.org/10.1155/2018/9610892

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