


Need for dental treatment in patients on the waiting list for liver and simultaneous pancreas-kidney transplant at a single center.

Necessidade de tratamento odontológico em pacientes candidatos a transplante simultâneo de pâncreas-rim e fígado num centro único.

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ABSTRACT

Objective: to evaluate the oral conditions and the main predisposing factors for dental treatment of patients on the waiting list for liver and simultaneous pancreas-kidney transplantation, in a single center. **Methods:** we evaluated 100 patients in the waiting list, 50 candidates for liver transplantation and 50 for simultaneous kidney-pancreas transplantation, from August 2015 to February 2018. We correlated extra and intraoral examinations with pre-transplant demographic variables. **Results:** the main oral alteration in the pancreas-kidney and liver transplant candidates were decayed, lost and filled teeth, present in 83% and 100% of the candidates, respectively ($p=0.03$). The need for dental treatment was equal in both groups: 71% and 70%. In liver transplant candidates, the predisposing factors for dental treatment were age, color and etiological diagnosis of liver cirrhosis. We did not identify predisposing factors for dental treatment in candidates for simultaneous pancreas-kidney transplant. **Conclusion:** candidates for liver and for simultaneous pancreas-kidney transplantation had poor oral hygiene, with cavities, residual roots, gingivitis and periodontitis, revealing that dental evaluation should be part of the transplantation waiting list.

Keywords: Liver Transplantation. Pancreas Transplantation. Kidney Transplantation. Oral Manifestations. Oral Health.

INTRODUCTION

In the scenario of chronic systemic diseases, chronic kidney disease (CKD) has in its evolution the progressive and irreversible decline of renal filtration, requiring dialysis or kidney transplantation. Among the several causes of CKD, the main one is diabetes *mellitus* (DM), which also affects other organs and has a negative impact on quality of life and survival¹⁻³.

These systemic diseases also have significant repercussions on periodontitis, and DM has a great impact on oral health. Type 1 (DM1) and type 2 (DM2) DM affect the periodontium at all ages, promoting important changes in bone metabolism. Chronic hyperglycemia leads to the accumulation of advanced non-enzymatic glycosylation products, increased RANKL/OPG

(receptor activator of nuclear factor kappa-B ligand and osteoprotegerin) ratio and oxidative stress, as well as induction of proinflammatory cytokines and interleukins (IL-1 β , IL-6 and TNF- α)⁴. Such changes trigger reduced bone formation, increased osteoclastogenesis and increased apoptosis of osteoblasts of the periodontal ligament, which in turn lead to alveolar bone loss⁴.

The evolution of periodontal inflammation observed in patients with DM1 and DM2 has been associated with periodontal tissue damage triggered by bacteria that colonize tooth surfaces. An important question is whether the increase in periodontal damage in diabetic individuals is solely due to a change in host response or there is a change in bacterial pathogenicity that leads to increased inflammation and damage, or whether even both mechanisms are present⁵.

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In these patients, the most common symptoms include xerostomia, halitosis, bone lesions and greater tartar formation, among others^{6,7}.

Likewise, the main oral problems in liver disease patients are poor oral hygiene, high prevalence of periodontal disease, tooth decay and bone loss⁸. Thus, the early diagnosis of oral cavity disorders in diabetic patients with CKD and chronic liver patients who are candidates for transplantation is important, since an infectious dental focus in the pre-transplant period may lead to postoperative complications.

The objective of this study was to evaluate the oral conditions and the main risk factors for dental treatment of patients on the waiting list for simultaneous pancreas-kidney transplantation and for liver transplantation at a single center.

METHODS

This research was approved by the Ethics in Research Committee of the Federal University of São Paulo - UNIFESP-EPM, with opinion number 1,319,459, CAAE: 50334815.4.0000.5505. All patients were informed of the character of the study and all signed the Free and Informed Consent Form.

We evaluated 100 patients, 50 candidates for liver transplantation (LTx) and 50 for simultaneous pancreas-kidney transplantation (SPKT), from August 2015 to February 2018, enrolled in the transplant waiting list at UNIFESP-EPM. We used a questionnaire for the dental survey, as well as the identification form and anamnesis, and evaluation of systemic conditions, such as characteristics of the liver disease, alcoholism and smoking association,

MELD (Model for End Stage Liver Disease), presence of hepatocarcinoma, amaurosis, DM time, dialysis time. The choice of the questionnaire for the dental survey was based on the "Dental Treatment Protocol" of the Albert Einstein Hospital, electronic version updated in 2009⁹, since it is a protocol containing all the pertinent questions to the study.

In the extraoral examination, we evaluated paranasal sinuses, skin, lymph nodes, ganglion chains, muscles and joints. In the intraoral examination, we evaluated upper and lower lips, vestibule, alveolar and jugal mucosa, gingiva, labial and lingual frenuses, salivary gland, parotid gland duct, tongue, mouth floor, tongue belly, oropharynx, hard and soft palates, and occlusion.

Periodontal examination was performed using the parameters of the Periodontal Screening & Recording (PSR)¹⁰. We performed cavity evaluation using the DMFT (decayed, missing or filled teeth) index. We also evaluated endodontic, surgical, dental, prosthesis and soft tissue disease aspects. The criteria established for the need for dental treatment were decayed teeth, teeth with need for endodontic care, fractured teeth, soft or hard tissue lesions, and gum disease. All patients underwent coagulation tests and assessment of the need for prophylactic antibiotics.

To determine which traditional factors and those associated with transplantation were related to the need for dental treatment, all potential risk factors that were univariably associated with a value of $P=0.3$ were simultaneously entered into a binary linear regression model. We considered p -values <0.05 as statistically significant.

RESULTS

Among the 50 patients on the waiting list for SPKT, 33 were male (66%), 24 (49%) white, with a mean age of 39 ± 7.03 years (26-51). We identified unilateral amaurosis in 11 (22%) patients, and bilateral in five (10%) (Table 1).

Table 1. Demographic data of patients who are candidates for simultaneous pancreas-kidney transplantation.

Variables	N=50
Mean age (years) \pm SD*	39 ± 7.03
Gender (male) n(%)	33 (66%)
White color n(%)	24 (49%)
Average dialysis time (years) \pm SD*	4 ± 1.5
Mean diabetes time (years) \pm SD*	25 ± 7.2
Amaurosis (unilateral) n(%)	11 (22%)
Amaurosis (bilateral) n(%)	5 (10%)

* SD: standard deviation.

Among the 50 patients on the waiting list for LTx, 35 (70%) were male, 23 (46%) white, and the average age was 44.5 ± 12.9 years (25-69). We observed hepatocarcinoma in 20 (40%) patients; the main underlying disease was viral hepatitis (60%) and 45% of the patients had diabetes *mellitus*. The MELD score ranged from 16 to 20 (Table 2).

Table 2. Demographic data of liver transplant candidates.

Variables	N=50
Age (years), mean \pm SD*	44.5 ± 12.9
Gender (male) n(%)	35 (70%)
White color n(%)	23 (46%)
MELD <10	8 (20%)
11-15	6 (15%)
16-20	11 (27%)
21-25	8 (23%)
26-30	4 (15%)
Hepatocarcinoma, n(%)	20 (40%)
Pre-LTx diabetes <i>mellitus</i> n(%)	22 (45%)
Etiology of liver cirrhosis	
Viral hepatitis n(%)	30 (60%)
Alcoholic hepatitis n(%)	5 (10%)
Other etiologies of cirrhosis n(%)	15 (30%)

* SD = standard deviation.

Extraoral clinical aspects

In the palpation exam of ganglion chains, muscles and joints, we did not observe significant differences and the physical exam was normal in more than 75% of the studied sample.

Soft tissue evaluation

Salivary gland assessment was normal in 54% of SPKT candidates and 36% of LTx ones ($P=0.009$). Gum evaluation was normal in 77% of SPKT candidates and in 51% of LTx ones ($P=0.015$). Regarding the lips exam, it was normal in 46% ($n=23/50$) of the SPKT candidates and in 55% ($n=27/50$) of the LTx ones. Tongue examination was normal in 72% ($n=36/50$) of SPKT candidates and in 57% ($n=28/50$) of LTx ones. Examination of the parotid duct was normal in 78% ($n=38/50$) of SPKT candidates and in 70% ($n=35/50$) of LTx ones. Tongue floor examination was normal in 98% ($n=49/50$) of SPKT candidates and in 96% ($n=48/50$) of LTx ones. Hard and soft palates examination was normal in 96% ($n=48/50$) of SPKT candidates and in 88% ($n=44/50$) of LTx ones. There was no statistical significance regarding the examination of the lips, tongue, parotid duct, tongue floor and hard and soft palate between the SPKT and LTx candidates.

Dental aspects

Although the number, size and shape of teeth were normal in most LTx and SPKT candidates, fractures and wear were present in 58% and 77% and 33% and 62%, respectively, without statistical significance.

Clinical dental aspects

We noted that 42% of SPKT waiting list patients and 17% of LTx waiting list individuals required endodontic treatment ($P=<0.0001$).

The DMFT index of 6.6 for cavity prevalence, 83% and 100%, respectively, was rated as very high ($P=0.030$). During periodontal evaluation, we observed bleeding on probing, presence of supra and/or subgingival calculi and/or excess restorative margins (code 1) in 47% ($n=22/50$) of patients waiting for SPKT and in 38% ($n=19/50$) of the ones on the Ltx list, without statistical significance.

Univariate and multivariate analyzes of demographics

In assessing the predisposing factors for dental treatment in patients on the waiting list for SPKT, we found no statistical significance for age, gender, amaurosis color, diabetes *mellitus* time and dialysis time (Table 3).

In the analysis of risk factors for dental treatment in LTx candidates, we observed that younger patients, ie those with a median age below 58 years, had significantly more frequent treatment indication than those older than 58 years (84% *versus* 54%) (Table 4). As for color, both white and black ($n=34$, 75%) required dental treatment, this indication being superior to the groups of brown ($n=2$, 66%) and yellow skin ($n=0$, 0%). Regarding the etiology of liver cirrhosis, 76% ($n=23/30$) of patients diagnosed with viral hepatitis required dental treatment and this proportion was 80% ($n=4/5$) for those with alcoholic cirrhosis and 60% ($n=9/15$) for patients with cirrhosis of another etiology. Among patients with a history of hepatocellular carcinoma, the need for dental treatment was 65% ($n=13/20$).

Table 3. Univariate and multivariate analyzes of risk factors for dental treatment in patients on the waiting list for simultaneous pancreas-kidney transplantation.

Variables	Univariate analysis	Multivariate analysis
Age	0.05 (CI* - 0.05 to 8.79)	0.17
Gender	0.66 (CI* - 0.24 to 0.37)	-
Color	0.59 (IC* - 0.41 to 0.71)	-
Amaurosis	0.64 (IC* - 0.68 to 0.43)	-
Dialysis time	0.26 (CI - 0.49 to 1.72)	0.33
DM time	0.13 (CI - 1.23 to 8.57)	0.72

* CI= confidence interval.

Table 4. Univariate and multivariate analysis of dental treatment risk factors in the liver transplant waiting list.

	Univariate analysis	Multivariate analysis
Age	0.07 (CI*: -0.87 to 15.149)	0.04
Gender	0.89 (CI*: -0.27 to 0.31)	-
Color	0.07 (CI*: -0.044 to 0.92)	0.04
History of hepatocarcinoma	0.39 (CI*: -0.51 to 0.21)	-
MELD	0.54 (CI*: -3.15 to 5.89)	-
History of pre-transplant diabetes	0.13 (CI*: -1.23 to 8.57)	0.72
Etiological diagnosis of cirrhosis	0.27 (CI*: -0.26 to 0.89)	0.03

* CI= confidence interval.

DISCUSSION

Our study revealed a high need for dental treatment, around 70%, in diabetic patients with CKD and chronic liver disease candidates for SPKT and LTx. Since infections are often the cause of morbidity and mortality in patients before and after liver transplantation, preventing risk factors for these infections is of great importance, and preoperative dental evaluation is essential to reduce some of these complications⁷.

Regarding oral hygiene, most participants stated that they brushed their teeth once or twice a day, corroborating other studies^{11,12}. However, the clinical observation of the oral condition of these individuals was not consistent with that information. When evaluated the means of oral hygiene, most stated to use toothpaste, mouthwash and dental floss. These results are similar to another study¹³, in which 96% of CKD patients used toothpaste, 32% used mouthwash and most (74%) did not floss. These findings show the need for greater dental attention to encourage oral hygiene in this population.

In our study, we also analyzed the oral condition of patients waiting for SPKT and LTx by the DMFT index. In both groups of patients, the DMFT index was high (6.6), demonstrating the high prevalence of cavities in this population, as shown by another study that found a DMFT index of 7.48 in CKD patients¹⁴, indicating that cavities are worrying factors in this population.

We noticed that only 45% of the patients had unaltered salivary glands. Indeed, patients with DM1 and DM2 may develop histological changes

in the salivary glands due to complications of the disease, which may increase the risk of cavities and periodontal disease, in addition to compromising the mesenchymal stem cells and periodontal ligament of such patients¹⁵.

Regarding the PSR index, which assesses gum and periodontal conditions, we detected a score 2 in both populations, showing bleeding on probing and supra and subgingival calculi. These findings indicate the need for dental intervention, as well as oral hygiene instruction¹⁶. As for the self-perception of oral health problems, people with participants from CKD reported more often dry mouth (51.5%), followed by bad breath (30%). Among the oral manifestations, gingivitis and the presence of dental calculus were the most prevalent, with 66.2% and 56.2%, respectively.

Our results showed that 33% of patients needed endodontic treatment and pointed to care regarding dissipation of infectious foci in the periapex. Teeth with periapical alterations, such as periapical space thickening or radiolucent areas detectable on radiographic examination have surgical indication, not endodontic, due to the post-transplant immunosuppression that would make the repair of the lesion impossible, thus maintaining infection¹⁶.

In addition, type-I diabetic patients often develop diabetic retinopathy in parallel with worsening renal function, which may lead to unilateral or bilateral amaurosis¹⁷. Oral hygiene may be hampered by visual impairment. However, we did not observe the impact of visual deficit on oral hygiene of diabetic patients with CKD and candidates for SPKT, suggesting that these patients already had previous dental guidance.

The lack of complementary exams, such as panoramic X-ray at the time of screening, made it difficult to assess the actual state of the oral cavity, preventing the visualization of buried residual roots, cysts and granulomas, among others. The lack of systematic referral of the transplant team for dental evaluation in the pre-transplant period was also a limitation of the study.

We verified that the candidates for liver transplantation and simultaneous pancreas-kidney transplantation had a great need for dental treatment due to poor hygiene, presence of active

cavities, residual roots, gingivitis and periodontitis. Demographic characteristics such as age, color and etiology of cirrhosis in liver transplant candidates may require greater attention of the dental surgeon regarding the need for dental treatment. However, we did not identify demographic risk factors for this treatment in simultaneous pancreas-kidney transplant candidates. We believe that dental evaluation should be part of the preoperative care protocol for patients in the transplant waiting list, since oral health is often compromised in this population.

R E S U M O

Objetivo: avaliar as condições bucais e os principais fatores predisponentes para tratamento odontológico de pacientes em lista de espera para transplante simultâneo de pâncreas-rim e para transplante hepático, em um centro único. **Métodos:** foram avaliados 100 pacientes na fila de espera, 50 candidatos a transplante hepático e 50 a transplante simultâneo de pâncreas-rim, no período de agosto de 2015 a fevereiro de 2018. Exames extra e intrabucais foram correlacionados com variáveis demográficas pré-transplante. **Resultados:** a principal alteração bucal nos candidatos a transplante de pâncreas-rim e de transplante hepático foram dentes cariados, perdidos e obturados, presentes em 83% e 100% dos candidatos, respectivamente ($P=0,03$). A necessidade de tratamento odontológico foi igual nos dois grupos: 71% e 70%. Nos candidatos a transplante hepático, os fatores predisponentes para tratamento odontológico foram idade, cor e diagnóstico etiológico da cirrose hepática. Não identificamos fatores predisponentes para tratamento odontológico nos candidatos a transplante simultâneo pâncreas-rim. **Conclusão:** pacientes candidatos a transplante simultâneo de pâncreas-rim e transplante hepático apresentaram higiene bucal precária com presença de cárie, raízes residuais, gengivite e periodontite, revelando que a avaliação odontológica deve fazer parte do protocolo de atendimento dos pacientes em fila de espera para transplantes.

Descritores: Transplante de Fígado. Transplante de Pâncreas. Transplante de Rim. Manifestações Bucais. Saúde Bucal..

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