ORAL DISEASES

Oral Diseases (2010) 16, 89–95. doi:10.1111/j.1601-0825.2009.01609.x

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ORIGINAL ARTICLE

Comparison of oral lesion prevalence in renal transplant patients under immunosuppressive therapy and healthy controls

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OBJECTIVE: The aim of this study was to analyse the prevalence of oral lesions in a group of renal transplant patients (RTPs) compared with healthy controls (HCs).
SUBJECTS AND METHODS: The study included 500 RTPs (307 men, 193 women, mean age 53.63 years) and 501 HCs (314 men, 187 women, mean age 52.25 years). Demographic and pharmacologic data were recorded for all subjects.
RESULTS: Forty percent of the RTPs presented with oral lesions compared to 23.4% of HCs. The most frequent lesion was candidiasis (7.4% in RTPs, 4.19% in HCs). Lip herpes simplex lesions were observed in 2.6% of RTPs and 2.2% of HCs; aphthae were observed in 2.2% of RTPs and 1% of HCs. Xerostomia prevalence was significantly greater in RTPs than HCs (1.4% *vs* 0.2%). Lichen planus appeared in 0.6% of RTPs, and one RTP suffered from hairy leukoplakia.
CONCLUSIONS: We report a lower prevalence of oral candidiasis and hairy leukoplakia in RTPs than previous reports and describe other oral conditions not presented before in prevalence studies of RTPs, such as xerostomia, aphthous ulcers and lichen planus. These oral lesion changes in RTPs and the risk of malignancy emphasize the importance of regular oral screening in these patients.
Oral Diseases (2010) **16**, 89–95

Keywords: oral lesions; immunosuppressive therapy; renal transplantation

Introduction

Kidney transplants have the greatest potential for offering patients with end-stage renal disease increased longevity and enhanced quality of life. However, the immunosuppressant treatments necessary for renal transplants have a series of short- and long-term side-effects such as infection, increased cardiovascular risks and neoplastic disease, which can be life-threatening for the patient (Andrés, 2005).

Immunosuppressant treatment depresses the cell-mediated immune response. For the clinician, this means a greater risk of oral infection and other associated complications. In patients treated with immunosuppressants, oral pathogens are more likely to cause local destruction and opportunistic infections because of the immune system's inability to suppress and destroy pathogens. Oral lesions may also develop as a result of side-effects and drug interactions during immunosuppressive therapy (Parisi and Glick, 2003). In renal transplant patients (RTPs), little is known about the presence of oral lesions, with the exception of gingival enlargement; only a few studies have shown an increased risk of developing oral infections such as candidiasis and herpes simplex infections, hairy leukoplakia (Tyldesley *et al*, 1979; King *et al*, 1994; Seymour *et al*, 1997; Tyrzyk *et al*, 2004; de la Rosa *et al*, 2005; Spolidorio *et al*, 2006; Al-Mohaya *et al*, 2009) or lip cancer (King *et al*, 1995; Spolidorio *et al*, 2006).

Immunosuppressive treatment has changed in recent years. There have been dramatic shifts in baseline immunosuppression with an increased use of induction agents and the nearly universal replacement of azathioprine by mycophenolate mofetil. Also, tacrolimus use has increased from 13% to 79% at discharge, whereas cyclosporine A (CsA) use has fallen from 76% to 15% (Knoll, 2008). Sirolimus, a mammalian target of the rapamycin inhibitor, is an immunosuppressant with unique anti-atherogenic and anti-neoplastic properties that is usually used (Augustine *et al*, 2007). These changes in the immunosuppressant protocol could be responsible for alterations in the prevalence of oral lesions in RTPs reported in previous studies. In fact, Spolidorio *et al* (2006) demonstrated that RTPs treated with CsA suffer more oral diseases than RTPs treated with FK-506, but there are no studies that have analysed

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Received 19 April 2009; revised 21 June 2009; accepted 03 July 2009

the presence of oral lesions in RTPs undergoing other current immunosuppressive regimens.

The aim of this study was to analyse the prevalence and clinical features of oral pathological, abnormal, unusual lesions (non-gingival enlargement) in a group of RTPs compared with a group of age and gender-matched healthy control (HC) subjects. The study also aimed to identify possible risk factors and predictable variables.

Patients and methods

Subjects

Five hundred patients who received kidney transplants between February 1989 and March 2007 were recruited from the outpatient Renal Transplant Clinic of the Hospital 12 de Octubre in Madrid (307 men, 193 women; mean age 53.63 ± 13.42 years, range 19–95 years; mean time since transplant 59.66 ± 55.81 months, range 1–330 months). The HCs were recruited from the Julio Morate Health Center in Madrid (314 men, 187 women; mean age 52.25 ± 15, range 20–93 years). Age and gender were not significantly different ($P < 0.12$ *vs* $P < 0.68$) in the RTPs and HC subjects. The study was conducted with the approval of the ethics committee at the Hospital 12 de Octubre and informed consent was obtained from the study subjects.

All HC subjects were attending the health center for routine medical treatment, such as hypertension, diabetes or weight control, and none were seeking treatment for any oral mucosal disorder. Healthy controls were excluded from the study if they had received a transplant, had been treated with immunosuppressants and/or corticosteroids or had renal disease.

Clinical assessment

The intraoral mucosa and lips of all subjects were examined clinically by a single investigator (R.M.L.P). The location, character, color and clinical diagnosis of any oral lesions were recorded. Gingival enlargement was not considered in this study. The clinical diagnosis of hairy leukoplakia was made according to the EC-Clearinghouse on Oral Problems Related to HIV Infection and WHO Collaborating Centre on Oral Manifestations of the Immunodeficiency Virus (1993) Leukoplakia was diagnosed according to the WHO Collaborating Center for Oral Precancerous Lesions (1978). The clinical diagnosis of candidiasis was based on the clinical impression, and definitive diagnosis was supported by a positive response to antifungal treatment, positive Candida culture and demonstration of candidal hyphae in stained smears. Clinically, four types of candidal lesions were recognized: pseudomembranous candidiasis, erythematous candidiasis, denture-induced candidiasis and angular cheilitis. Herpes simplex cases were established when the patient presented with erosions, ulcerations or crust preceded by blistering on the vermilion borders or the oral keratotic mucosa.

Patients were asked about xerostomia symptoms and an affirmative response to at least one of the five following questions was used to confirm the subjective manifestations of xerostomia: 'Does your mouth usually feel dry?' 'Does your mouth feel dry when eating a meal?' 'Do you have difficulty swallowing dry foods?' 'Do you sip liquids to aid in swallowing dry foods?' and 'Is the amount of saliva in your mouth too little most of the time, or do you not notice it?' To confirm the clinical signs of hyposalivation, unstimulated whole saliva was collected by the draining method, which was initiated approximately 50 min after the ingestion of served orange juice. The unstimulated whole saliva was collected in a preweighed plastic cup for a period of 10 min. A volume of less than 0.12 ml per minute confirmed a hypo-functioning salivary gland (Guggenheimer and Moore, 2003).

Cases of nodular or papillomatous-like tissue, leukoplakia and lichen planus lesions were confirmed histopathologically by biopsy. We considered like miscellanea lesions to be those with no pathologic lesions, such as saburral tongue, hairy tongue, geographical tongue, coated tongue, torus, leukoedema and macroglossia.

Subjects' variables

The RTPs and HC subjects' outpatient databases were reviewed with particular interest to gender, age, diabetic history, antidepressant treatment, smoking habits, alcohol consumption, exposure to sunlight and the presence of dentures. All findings including medical history, medications and habits were recorded. Details of the time since transplant, immunosuppressive treatment and immunosuppressive dose were reviewed only for RTPs. Hematologic studies were performed only for RTPs and included tests for blood levels of immunosuppressants, neutrophil and eosinophil counts, and hemoglobin and creatinine levels. Hematologic studies were done the same day as oral exploration.

Patients were asked about their smoking habits and current alcohol consumption. A tobacco habit was measured in cigarettes smoked per day. One cigar was assumed to be equal to four cigarettes. The intake of alcoholic beverages was expressed in units of alcohol per day (one unit was approximately 10 g of alcohol or one-half pint of beer, one small glass of wine or one measure of spirits/hard liquor). Sun exposure was assumed when a patient worked in an outdoor occupation, participated in outdoor activities more than 10 h per week or sunbathed more than 14 days per year.

Statistical analysis comprised basic descriptive statistics. Differences between continuous variables and categorical variables were assessed with the Student's *t*-test and chi-squared test respectively. To explore the association between oral lesions and selected clinical variables, a multiple logistic regression model was fitted. Variables stayed in the model if they were predictors of the outcome ($P < 0.01$). The final model included age, gender and group (RTP/HC). Significance was set at $P < 0.05$.

Results

The subject variables and differences between these two populations are presented in Table 1 In the HC subjects,

Table 1 Subject variables, risk factors and the differences between RTPs and HCs

Variables	*RTP* (n = 500)	*HC* (n = 501)	P
Gender			
Male	307 (61.4%)	314 (62.7%)	0.68
Female	193 (38.6%)	187 (37.3%)	
Age (years)	53.63 ± 13.42	52.25 ± 15	0.12
Active smokers	103 (20.6%)	142 (28.3%)	0.004
Tobacco consumption (cigarettes/day)	2.49 ± 6.06	4.03 ± 8.31	0.001
Smoking history	122 (24.4%)	49 (9.78%)	0.0001
Alcohol	72 (14.4%)	121 (24.2%)	0.0001
Alcohol consumption (dose/day)	0.23 ± 0.66	0.40 ± 0.86	0.001
Sun exposure	140 (28%)	103 (20.6%)	0.006
Diabetic patients	85 (17%)	16 (3.2%)	0.0001
Insulin-dependent diabetes	57 (11.4%)	3 (0.6%)	
Non-insulin-dependent diabetes	28 (5.6%)	13 (2.6%)	
Patients with dentures	135 (27%)	100 (20%)	0.002
Acrylic denture	82 (16.4%)	46 (9.2%)	
Metallic denture	48 (9.6%)	43 (8.6%)	
Acrylic and metallic dentures	5 (1%)	11 (2.2%)	
Antidepressant treatment	66 (13.2%)	28 (5.6%)	0.004

there was significantly more tobacco and alcohol consumption. Among RTPs, however, the number of patients with diabetes, dentures or taking antidepressants and the amount of sun exposure was significantly greater than in the HC group.

Thirty-seven per cent (37.2%) of the RTPs were taking prednisolone, FK-506 and mycophenolate mofetil; 14.4% were taking prednisolone, CsA, and mycophenolate mofetil; 9% were taking prednisolone and CsA; 6.8% were taking prednisolone and FK-506; and 37.6% were taking other combinations of different immunosuppressive drugs (Table 2).

Table 2 Immunosuppressive regimen of the RTPs

Immunosuppressive regimen	*Frequency*
Pred + FK + MMF	186 (37.2%)
Pred + CsA + MMF	72 (14.4%)
Pred + CsA	45 (9%)
Pred + FK	34 (6.8%)
Pred + FK + Aza	26 (5.2%)
Pred + CsA + Aza	23 (4.6%)
Pred + CsA + Siro	16 (3.2%)
CsA	15 (3%)
FK + MMF	13 (2.6%)
Pred + Siro	12 (2.4%)
CsA + MMF	12 (2.4%)
Pred + FK + Siro	10 (2%)
Pred + Siro + MMF	9 (1.8%)
FK	8 (1.6%)
Pred + Aza	6 (1.2%)
Pred + MMF	4 (0.8%)
MMF	3 (0.6%)
Siro + MMF	2 (0.4%)
FK + Siro	2 (0.4%)
CsA + Aza	1 (0.2%)
CsA + Siro	1 (0.2%)

Pred, prednisolone; FK, FK-506; MMF, mycophenolate mofetil; CsA, cyclosporine; A; Aza, azathioprine; Siro, sirolimus.

Table 3 shows the mean ± standard deviation immunosuppressive drug doses taken by the RTPs, the number of subjects treated with the different immunosuppressive agents and the blood levels of immunosuppressants, hemoglobin and creatinine from the laboratory tests performed the same day as the check-up.

Forty per cent (40.6%) of the RTPs presented with oral lesions compared to 23.4% of HC subjects ($P < 0.0001$). More than one lesion was found in 3.2% of the RTPs but only in 1.59% of HCs ($P < 0.0001$).

Table 4 presents a summary of the oral lesions found in the RTPs and HC subjects. The most frequent lesion was oral candidiasis with a prevalence of 7.4% in the RTPs compared to 4.19% in HCs ($P < 0.03$). One or more symptoms of xerostomia were reported by 1.4% of the RTPs and 0.2% of HC subjects ($P < 0.03$). The

Table 3 The immunosuppressive drug doses and laboratory test results for the RTPs

Variables	*Mean ± s.d.*	*Subjects*
Pred dose (mg)	6.91 ± 6.39	443
CsA dose (mg)	160.39 ± 61.79	187
FK dose (mg)	5.26 ± 2.96	279
Siro dose (mg)	2.40 ± 1.20	52
MMF dose (mg)	977.08 ± 427.99	301
Aza dose (mg)	77.23 ± 26.23	56
CsA blood level (ng ml^{-1})	154.11 ± 62.74	187
FK blood level (ng ml^{-1})	8.52 ± 2.86	279
Siro blood level (ng ml^{-1})	8.69 ± 3.06	40
MMF blood level (ng ml^{-1})	2.38 ± 2.04	112
PMN e (%)	1.64 ± 1.21	500
PMN n (%)	63.61 ± 11.05	500
Hemoglobin (g dl^{-1})	13.89 ± 1.92	500
Creatinine (ng ml^{-1})	1.58 ± 1.23	500
Time since transplant (months)	59.66 ± 55.81	500

Mean ± s.d., mean ± standard deviation; Pred, prednisolone; FK, FK-506; MMF, mycophenolate mofetil; CsA, cyclosporine A; Aza, azathioprine; Siro, sirolimus.

Table 4 Prevalence of oral lesions in the RTPs and HC subjects

Oral lesions	*RTP* (n = 500)	*HC* (n = 501)	P
Oral candidiasis infections	37 (7.4%)	21 (4.19%)	0.03
Denture candidiasis (erythematous)	27 (5.4%)	18 (3.6%)	
Angular cheilitis	8 (1.6%)	1 (0.2%)	
Pseudomembranous	2 (0.4%)	2 (0.4%)	
Fibroma	14 (2.8%)	8 (1.6%)	0.12
Lip herpes simplex infection	13 (2.6%)	11 (2.2%)	0.52
Actinic cheilitis	13 (2.6%)	7 (1.4%)	0.17
Aphthae	11 (2.2%)	5 (1%)	0.13
Leukoplakia	7 (1.4%)	3 (0.6%)	0.20
Xerostomia	7 (1.4%)	1 (0.2%)	0.03
Hyposalivation	3 (0.6%)	1 (0.2%)	0.31
Lichen planus	3 (0.6%)	4 (0.8%)	0.71
Papilloma	3 (0.6%)	1 (0.2%)	0.31
Hairy leukoplakia	1 (0.2%)	0	0.32
Pyogenic granuloma	1 (0.2%)	0	0.32
Palate overgrowth	1 (0.2%)	0	0.32
Sjögren syndrome	1 (0.2%)	0	0.32
Miscellanea lesions	107 (21.4%)	64 (12.77%)	0.0001

Table 5 Odds ratios (OR) and 95% confidence intervals (CI) for the final multiple logistic regression model

Variables	*OR*	*95% CI*	P
Group (RTP/HC)	0.45	0.34–0.59	0.0001
Age	1.02	1.01–1.03	0.0001
Gender	0.75	0.56–0.99	0.04

unique case of palate overgrowth appeared in a patient treated with CsA who suffered from severe gingival enlargement; the lesion resembled papillary hyperplasia affecting the hard palate. Miscelanea lesions were significantly greater in the RTPs (21.4%) than HC subjects (12.77%, $P < 0.0001$).

The oral lesions in RTPs occurred in 40% of men and 41% of women ($P < 0.76$), whereas oral lesions in the HCs occurred in 18.47% of men and 31.55% of women ($P < 0.001$). Patients with oral lesions were older than those without for both RTPs (mean age 55.74 ± 13.10 years *vs* 52.20 ± 13.46 years; $P < 0.004$) and HCs (mean age 56.69 ± 15.79 years *vs* 50.90 ± 14.54 years; $P < 0.0001$). We found a correlation between oral lesions and subjects who had been medicated with antidepressants in the HC group ($P < 0.003$) but not in the RTPs ($P < 0.39$). No association was found between the prevalence of oral lesions and a smoking habit, tobacco consumption, smoking history, alcohol habit, alcohol consumption, sun exposure, diabetic history and/or denture presence in the RTPs and HC subjects.

We did not find a correlation between the presence of oral lesions and the different immunosuppressive regimens ($P < 0.58$); 36% of RTPs with oral lesions were taking CsA, 55.2% were taking FK-506, 4.8% were taking sirolimus, 2% were taking azathioprine and 2% were taking mycophenolate mofetil. No association was found between the presence of oral lesions and the time since transplant and the different pharmacologic variables and blood tests.

Table 5 shows odds ratios (OR) and 95% confidence intervals (CI) for the final multiple logistic regression model. The multiple logistic regression model chose first for group, second for age and last for gender. The RTPs were more likely to have oral lesions; group (RTP/HC) was a strong predictor of oral lesions. Age was a significant predictor of oral lesions; lesions were more frequent in older patients. For gender, females were more likely to have oral lesions.

Discussion

The RTPs undergoing long-term graft-preserving immunosuppressive therapy are predisposed to a variety of oral complications. Previous studies (King *et al*, 1994; Tyrzyk *et al*, 2004; de la Rosa *et al*, 2005; Spolidorio *et al*, 2006; Al-Mohaya *et al*, 2009) have documented a wide variation in the frequency of oral lesions in these patients. King *et al* (1994) studied the oral mucosa of 159 RTPs treated with azathioprine and prednisolone, and sometimes CsA, and 160 HCs. The prevalence of oral lesions in the group of RTPs was greater than in the HC group (54.7% *vs* 19.4%). This study observed that RTPs have a significantly greater risk of suffering gingival enlargement, oral candidiasis and hairy leukoplakia. Al-Mohaya *et al* (2009) determined the prevalence of intraoral lesions in a group of 58 RTPs treated with prednisolone and CsA and 52 HC subjects. The results of this study showed that RTPs have a greater risk of suffering gingival enlargement, erythematous candidiasis and hairy leukoplakia.

Some studies (Tyrzyk *et al*, 2004; de la Rosa *et al*, 2005; Spolidorio *et al*, 2006) have shown the prevalence of oral lesions only in RTPs. Tyrzyk *et al* (2004) studied the prevalence of oral lesions in 30 RTPs treated with CsA, the more frequent oral lesions were fungal infections and leukoplakia. de la Rosa *et al* (2005) analysed the prevalence of oral lesions in 90 RTPs treated with CsA; they observed that 60% of patients suffered from oral lesions. Spolidorio *et al* (2006) studied the oral lesions present in 88 RTPs treated with CsA and 67 RTPs treated with FK-506; they found that oral lesions were more frequent in the group treated with CsA.

This study analysed the prevalence of oral lesions that presented in a wide RTP group and HC subjects. The findings of this study, like King *et al* (1994), demonstrate that RTPs have a greater prevalence of oral lesions than HC subjects (40.6% *vs* 23.4%). Despite this result, the prevalence of oral lesions in the RTPs in our study (40.6%) was lower than that found by King *et al* (1994) and de la Rosa *et al* (2005) (54.7% and 60% respectively). In our study, the mean time since transplant in the RTPs was 59.55 months, but in de la Rosa *et al*'s (2005) study the mean time since transplant was 10 months. This shorter time since transplant could be the cause of a high prevalence of oral lesions because, in the early post transplant months, the immunosuppressant doses administered to RTPs are higher, and this level of immunosuppression might have given rise to increased oral infections. In fact, the RTPs in de la Rosa *et al*'s (2005) study had CsA blood levels of 214 ± 80 ng ml^{-1}; in our study, CsA blood levels were less than 154.11 ± 62.74 ng ml^{-1}.

The RTPs of earlier studies (King *et al*, 1994; de la Rosa *et al*, 2005) used prednisolone, azathioprine and/or CsA as an immunosuppressant treatment. In our study, the RTPs were taking different immunosuppressive regimens, the most frequently used was prednisolone, FK-506 and mycophenolate mofetil or prednisolone, CsA and mycophenolate mofetil, but there was also a large group of RTPs taking azathioprine and sirolimus in combination with other immunosuppressants. Spolidorio *et al* (2006) suggested that RTPs taking CsA suffered more oral lesions than RTPs taking FK-506. In this study, no significant results were observed with regard to this topic. We think that it would be interesting to analyse the presence of oral lesions in uniform RTP groups on different immunosuppressant regimens.

Previous studies (King *et al*, 1994; Al-Mohaya *et al*, 2002, 2009; Güleç *et al*, 2003; de la Rosa *et al*, 2005) have shown that the prevalence of candidiasis in RTPs is significantly higher than in HC subjects. The prevalence of oral candidiasis in RTPs is highly variable, from 9.4% to 46.7% (King *et al*, 1994; Al-Mohaya *et al*, 2002, 2009; Güleç *et al*, 2003; Tyrzyk *et al*, 2004; de la Rosa *et al*, 2005). The clinical forms that are more frequently described are erythematous candidiasis, angular cheilitis and pseudomembranous candidiasis (King *et al*, 1994; Al-Mohaya *et al*, 2002, 2009; de la Rosa *et al*, 2005). This study showed a higher prevalence of oral candidiasis in RTPs and denture candidiasis (erythematous) was the most frequent form (73%), followed by angular cheilitis (22%) and pseudomembranous candidiasis (5%). Golecka *et al* (2006) showed that transplant patients with dentures suffer more denture candidiasis and angular cheilitis than HCs with dentures, indicating that dentures are a risk factor for oral candidiasis. Thus, adequate pre- and post transplant oral health and denture cleaning and adjustment are recommended for these subjects to prevent this infection.

Infections related to herpes simplex virus (HSV) are also common in RTPs. The reported prevalence of oral HSV lesions in RTPs is 0% to 11.3% (King *et al*, 1994; de la Rosa *et al*, 2005; Spolidorio *et al*, 2006). The prevalence of oral HSV infection in the RTPs in this study was 2.6%. Sometimes oral HSV infections are more severe in RTPs than in non-immunocompromised patients (Seymour *et al*, 1997). In this study, two RTPs suffered large herpes simplex lesions that affected the lower and upper lip and the nose.

Hairy leukoplakia is associated with immunodeficiency and Epstein–Barr virus in HIV-infected and organ transplant patients (Schmidt-Westhausen *et al*, 1991; Kanitakis *et al*, 1991; Epstein *et al*, 1993; Schmidt-Westhausen *et al*, 1993; Seymour *et al*, 1997; Ammatuna *et al*, 1998, 2001). Hairy leukoplakia has a prevalence of 0% to 13% in RTPs (King *et al*, 1994; de la Rosa *et al*, 2005; Spolidorio *et al*, 2006; Al-Mohaya *et al*, 2009). In transplant patients, hairy leukoplakia is usually a marker of increased immunosuppression (Epstein *et al*, 1988; Schmidt-Westhausen *et al*, 1991; Seymour *et al*, 1997). The prevalence of hairy leukoplakia in our study was low (0.2%, only one case). However, de la Rosa *et al* (2005) found a hairy leukoplakia prevalence of 13% in RTPs, which could be attributable to the high cyclosporine blood levels we remarked on above.

No aphthous ulcers were observed in prevalence studies of oral lesions in RTPs until now, but there have been reports of oral ulcers in transplant patients in relation to immunosuppressants, such as mycophenolate mofetil (Garrigue *et al*, 2001; Schmutz *et al*, 2003; Apostolou *et al*, 2004), sirolimus (van Gelder *et al*, 2003; Montalbano *et al*, 2004; Sundberg *et al*, 2004) and FK-506 (Hernández *et al*, 2001; Macario-Barrel *et al*, 2001). In this study, RTPs with oral ulcers were treated with prednisolone, FK-506, and mycophenolate mofetil (72.7%); prednisolone, sirolimus and mycophenolate mofetil (18.2%); or prednisolone and CsA (9.1%). Aphthous ulcers could be related to a high dose of immunosuppressants, the withdrawal of corticoids and/or pharmatoxicologic problems (Hernández *et al*, 2001; Ponticelli and Passerini, 2005). Therefore, it is important to make a good differential diagnosis to correctly treat these lesions.

Xerostomia has not been evaluated in RTPs in previous studies (King *et al*, 1994; Tyrzyk *et al*, 2004; de la Rosa *et al*, 2005; Spolidorio *et al*, 2006; Al-Mohaya *et al*, 2009). In this study, xerostomia was significantly more common in RTPs than HC subjects, which could be attributable to xerostomic medications usually used in RTPs, such as antidepressants and diuretic agents (Guggenheimer and Moore, 2003).

There are no previous studies of lichen planus in RTPs. Recent studies suggest that topical immunosuppressants are an effective and secure treatment for lichen planus (Hodgson *et al*, 2003; Conrotto *et al*, 2006; Laeijendecker *et al*, 2006; Lozada-Nur and Sroussi, 2006; Yoke *et al*, 2006). The three RTPs who presented with lichen planus had atrophic lesions at the time of their oral examinations. These patients were taking systemic immunosuppressant treatments, such as CsA, FK-506, azathioprine and mycophenolate mofetil, which are the same immunosuppressants used to treat lichen planus. This finding shows that immunosuppressant treatment might not be so effective in the treatment of lichen planus.

The incidence of malignancy has ranged from 2.3% to 31% in several large series of RTPs (de Visscher *et al*, 1997; Penn, 1999; Amado, 2005). The most frequent oral cancer in RTPs is lip cancer, making up 1.5–8% of all de novo neoplasms (Regev *et al*, 1992; King *et al*, 1995; de Visscher *et al*, 1997; Penn, 1999; Spolidorio *et al*, 2006). Lip cancer in RTPs was shown to be more frequent in males and elderly patients in a lengthy post transplant follow up (Penn, 1999; Amado, 2005). The risk factors for lip cancer are smoking, an alcohol habit and sun exposure. At the time of the oral examination, we did not find oral cancer in the RTPs, but six patients had previously suffered lip cancer and one patient had Kaposi Sarcoma of the palate (López-Pintor *et al*, 2007). Because of the significantly higher incidence of lip cancer in RTPs, it is important to periodically check their oral condition.

In summary, this study showed that the prevalence of oral lesions in the RTP group was significantly higher than in the HC group. We found a lower prevalence of some oral lesions, such as candidiasis and hairy leukoplakia, than in previous reports, and described other oral conditions such as xerostomia, aphthous ulcers and lichen planus, which had not been previously presented in prevalence studies of RTPs. These changes in oral lesion prevalence and the risk of malignancy emphasize the importance of regular oral screening in these patients.

Acknowledgement

We would like to acknowledge current financial support from the Mutua Madrileña Foundation.

Author contributions

GH designed the study and revised the paper. AA recruited the renal transplant patients and collected hematologic results. RMLP examined the patients, collected and analysed data and wrote the paper. LA discussed the results and commented on the manuscript.

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