Depressive disorders associated with the recurrence of periodontitis in periodontal maintenance

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Abstract

Objective: The aim of this study was to evaluate the association between depressive disorders and periodontal condition and the recurrence of periodontitis, during periodontal maintenance therapy (PMT).

Methods: From a 6-year prospective cohort study with 268 individuals under PMT, 124 individuals had complete periodontal clinical data recorded between T1 (baseline) and T2 (final data at the last PMT appointment). Individuals were divided into two groups, being 35 individuals with depressive disorders (DD) and 89 individuals without DD (NDD). Full-mouth periodontal examination was evaluated at T1 and T2.

Results: The periodontal status of NDD was significantly better then DD at T2. In the NDD group, the recurrence of periodontitis was 50.6% whereas in the DD group was 62.8%. Moreover, the following variables were significantly associated with recurrence of periodontitis in final multivariate logistic regression model: DD, age, co-habitation status without companion, smoking and the interaction between DD and smoking.

Conclusion: Individuals with DD undergoing PMT presented higher rates of recurrence of periodontitis and tooth loss when compared to individuals without DD. Additionally, the interaction between DD and smoking significantly increased the risk for the recurrence of periodontitis.

Keywords: Antidepressants; depressive disorders; epidemiology; maintenance; periodontitis.

Introduction

Depressive disorders (DD) are the most commonly diagnosed conditions in psychiatry. They are conditions that might occur on their own or in association with other diseases (Cartwright *et al.* 2016). The epidemiological pattern of depressive disorders in late life represents an important public health problem (Warren *et al.* 2014, Araújo *et al.* 2016).

Periodontitis, a bacterially mediated inflammatory disease of the gingiva and the adjacent periodontal attachment apparatus, represents one of the leading causes of tooth loss among adults in developed countries due to the destruction of the periodontal ligament and alveolar bone (Dumitrescu, 2016). The presence of inflammatory mediators in the pathogenesis of periodontitis highlight the potential for a systemic impact of periodontitis and its potential association with other systemic conditions (Araújo *et al.* 2016).

The association between depression and periodontitis reported in several clinical observational studies are contradictory and have been recently discussed in three systematic reviews and meta-analyzes (Araújo *et al.* 2016, Cademartori *et al.* 2018, Liu *et al.* 2018). Araújo *et al.* (2016)

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reported a non-significant association (OR = 1.03, 95% CI = 0.75-1.41) based on seven cross-sectional studies. Cademartori *et al.* (2018) reported that depression was associated with periodontitis (HR = 1.73; 95% CI 1.58-1.89) based on data from cohort studies and Liu *et al.* (2018) reported that emotional disorders were associated with chronic periodontitis (OR = 1.54, 95% CI = 1.27-1.86).

The global use of psychoactive medications, mainly antidepressants, has grown in recent decades at a rate of around 30%, (Schmitt *et al.* 2005, Cartwright *et al.* 2016, Cademartori *et al.* 2018). This increase in the consumption may be related to the growth in the diagnosis of DD and the emergence of new medicaments for its management (Schmitt *et al.* 2005, Cartwright *et al.* 2016).

Several studies have emphasized the benefits of periodontal maintenance therapy (PMT) in preserving the homeostasis of periodontal tissues achieved after active periodontal therapy (Rósen *et al.* 1999, Axelsson *et al.* 2004, Matuliene *et al.* 2010, Lorentz *et al.* 2009, Costa *et al.* 2015, Farooqi *et al.* 2015, McCraken *et al.* 2017, Martinez-Canut *et al.* 2017, Manresa *et al.* 2018). However, without establishing a regular program of clinical re-evaluation, adequate biofilm control, and reinforcement of oral hygiene instructions, the benefits of PMT cannot be maintained over time (Axelsson *et al.* 2004, Lorentz *et al.* 2009, Costa *et al.* 2014 and 2015, Martinez-Canut *et al.* 2017) and this results in a higher risk for future recurrence of periodontitis (Lorentz *et al.* 2009, Costa *et al.* 2014 and 2015) and tooth loss (Axelsson *et al.* 2004, Costa *et al.* 2014, Manresa *et al.* 2018).

However, no prospective PMT study has evaluated the effects of antidepressants on periodontal condition and recurrence of periodontitis. We hypothesized that individuals in continuous use of antidepressant agents have greater recurrence of periodontitis, tooth loss and worse periodontal clinical condition during PMT. Therefore, the present study followed individuals in PMT over 6 years and longitudinally evaluated the effects of antidepressant agents use on periodontal condition and recurrence of periodontitis.

Materials and Methods

Study Design and Sampling Strategy

Participants for the present prospective study were selected from an open cohort study with 268 individuals under a PMT program, who were monitored in a private dental clinic in the city of Belo Horizontee – Brazil, over 6 years of consecutive recall visits (from August 2006 to February 2016). The study was approved by the local Ethical Research Committee (protocol #060/05) and informed consent was obtained from all participants.

Individuals that underwent active periodontal therapy (comprised of non-surgical and/or surgical procedures) were included in the study sample according to the following criteria: (a) diagnosis of moderate to advanced chronic periodontitis (Armitage, 1999), updated for periodontitis stage II, III and IV according to Tonetti *et al.* 2018), prior to active periodontal therapy; (b) the presence of least 4 sites with probing depth (PD) greater/equal 5mm and clinical attachment loss (CAL) greater/equal 3mm, bleeding on probing (BOP), and radiographic evidence of bone loss; (c) completion of active periodontal therapy in a period of less than 4 months prior to entry into the PMT program; and (d) at least 14 teeth.

Hence, from a 6-year prospective cohort study with 268 individuals under PMT, 126 individuals who attended at least one PMT visit within 12 months during 6 years between T1 (data was recorded after the first PMT appointment) and T2 (final data at the last PMT appointment, e.g., after 6 years in PMT) were determined to be eligible. This represents a convenience sample. According to the diagnosis of depressive disorders (DD), participants were categorized into 2 groups: 35 individuals with DD diagnosis, and 89 individuals with no diagnosis of DD (NDD). The diagnosis of DD was performed by a psychiatrist according to the American Psychiatric Association criteria (2013), as well as determined from the prescription for the continuous use of antidepressant agents. Two individuals without this diagnosis confirmation (no medical diagnosis and no continuous use of antidepressant agents) were excluded (final sample n = 124).

In order to verify the power of the sample in each subgroup, a sample size calculation was performed considering PD changes (>4mm) as the primary outcome for the recurrence of periodontitis. Considering a significance level of 5%, power of 80%, medium effect size (0.50) and 15% minimum difference between groups in relation to PD changes (mean values), a calculated number of ~23 individuals per group was determined to be necessary.

Data Collection and periodontal monitoring

In the present study, baseline data were recorded after the first PMT appointment (T1) and final data at the last PMT appointment, i.e., after 6 years in PMT (T2). Parameters of plaque index (PI) (Turesk *et al.*, 1970), PD, CAL, BOP and suppuration were recorded for all present teeth at 4 periodontal sites (mesial, distal, buccal, and lingual) with a manual periodontal probe (PCPUNC-15 Hu-Friedy®, Chicago, USA). Description of data collection and periodontal clinical procedures during all PMT visits has been reported previously by Lorentz *et al.* (2009).

The following variable data were also collected: oral hygiene habits (frequency of tooth brushing and dental flossing), sex, age, family income, co-habitation status, educational level, smoking (Tomar and Asma, 2000), alcohol use, and diabetes [fasting glicemia ≥ 126 mg/dL (American Diabetes Association 2015)].

Determination of the recurrence of periodontitis (RP) and retreatment needs

Sites determined as having retreatment needs were those with recurrence of periodontitis: PD >4mm and CAL ≥3mm together with the persistence and/or presence of BOP and/or suppuration, during any of the subsequent recall evaluations (Matuliene *et al*. 2010; Costa *et al*. 2015). PD changes were first re-treated with non-surgical procedures through mechanical subgingival debridement. After periodontal re-evaluation (45 to 60 days), sites with persistent PD ≥5mm and CAL ≥3mm underwent surgical procedures performed by Widman modified flap surgery (Costa *et al*. 2015).

Inter- and intra-examiner agreement

Two trained and calibrated periodontists performed all the interviews, examinations, and clinical periodontal procedures. Evaluations of PD and CAL were performed and repeated within a 1-week interval for 10 individuals randomly selected from study groups at T1 and at T2. Kappa coefficients for intra- and inter-examiner agreement, as well as intra-class correlation coefficients, were greater than 0.87.

Statistical analysis

Statistical analysis included a descriptive characterization of the sample according to variables of interest. Group comparisons by means of the Chi-squared and Student *t* tests were performed when appropriate. Multiple comparisons were adjusted by Bonferroni correction post-hoc test. Logistic regression analysis was performed to investigate the association between the recurrence of periodontitis and the all independent predictor variables. Individuals were considered the unity of analysis for the recurrence of periodontitis . Odds ratio (OR) estimates and their 95% confidence interval (CI) were calculated and reported. The quality of the model was determined by measures of sensitivity, specificity, and area under the ROC (Receiver Operating Characteristic) curve. All tests were performed using R Statistical Software.

Results

The study sample comprised 124 individuals under PMT over 6 years, being 35 individuals with DD diagnosis and 89 individuals with no DD diagnosis. Group characteristics regarding variables of interest are presented in *Table 1*. Significant differences were reported for sex, co-habitation status, smoking (no significant differences between FS and NS), diabetes, alcohol use, and frequency of toothbrushing and dental flossing. Important variables such as time since active periodontal therapy and number of PMT visits were not significanty different between study groups.

Periodontal status of the sample at T1 and T2 is presented in Table 2. Overall, no significant differences were observed in relation to PI, PD, CAL and sits with RP among groups at T1, except from BOP. As a result, groups were determined to be homogeneous after active periodontal therapy. Nevertheless, significant differences between groups were observed at T2. DD group showed higher mean BOP, PD, CAL, tooth loss and sites with RP. However, no differences regarding PI were observed.

Characteristics of the sample demonstrating recurrence of periodontitis at T2 are presented in Table 3. The recurrence of periodontitis was 50.6% (n = 45) in the NDD group and 62.8% (n = 22) in the DD group. These differences were determined to be significant (DD *vs* NDD: OR = 3.3; 95% CI 1.5-7.2; p<0.001). Moreover, age, co-habitation status, alcohol use, and smoking were also significantly different.

The final multivariate logistic regression model for the recurrence of periodontitis, adjusted for all variables of interest, is shown in Table 4. Depressive disorders (DD), co-habitations status without companion; age >50years, current smoking and interaction the between DD and current smoking were retained in the model as significant variables associated with the recurrence of periodontitis.

Table 5 shows non-surgical or surgical procedures performed during PMT (full-mouth procedures) in the study groups. Surgical procedures were significantly higher in individuals, teeth and sites in the DD group when compared to the NDD group. Conversely, non-surgical procedures were higher in the NDD group.

Discussion

The present study demonstrated that the recurrence of periodontitis was significantly higher among DD individuals (62.8%) in relation to NDD individuals (50.6%) under PMT over 6 years. Moreover, DD individuals presented with poorer periodontal clinical parameters (except for plaque index) and greater recurrence of periodontitis and tooth loss then NDD individuals. After adjusting for other periodontal risk variables, the OR for the recurrence of periodontitis at T2 was 3.1 (95% CI 1.2-6.7; p = 0.001) in the DD group.

Due to the absence of differences in PI at T2, we hypothesized that the poorer clinical parameters seen in the DD group could be associated with a negative effect of depressive disorders and adverse side effects of antidepressants. It is important to stress that xerostomia was self-reported by 94.3% of the individuals in the DD group. Additionally, surgical procedures were significantly higher in individuals, teeth and sites in the DD group when compared to the NDD group, revealing greater severity of periodontal clinical parameters in sites with recurrence of periodontitis.

Table 1. Characterization of the sample regarding variables of interest at T2.

Variables	Total sample	DD group	NDD group	p
N	**124**	**35**	**89**	
Sex				
Women	64 (51.6%)	24 (51.6%)	40 (46.2%)	
Man	60 (48.4%)	11 (48.4%)	49 (53.8%)	0.018*
Age				
£ 50 years	51 (41.1%)	13 (41.1%)	38 (42.0%)	
> 50 years	73 (58.9%)	22 (58.9%)	51 (58.0%)	0.317*
Family income				
< 5 BMS	50 (40.3%)	15 (40.3%)	36 (64.0%)	
≥ 5 BMS	74 (59.7%)	20 (59.7%)	54 (36.0%)	0.084*
Educational level				
< 8 years	59 (47.6%)	16 (47.6%)	43 (44.0%)	
≥ 8 years	65 (52.4%)	19 (52.4%)	46 (56.0%)	0.067*
Co-habitational status				
With companion (family/friends)	80 (64.5%)	14 (64.5%)	66 (71.2%)	
Without companion	44 (35.5%)	21 (35.5%)	17 (28.8%)	<0.001*
Smoking status				0.004
Current smoker	22 (17.8%)	14 (17.8%)	8 (22.2%)	
Former smoker	17 (13.7%)	5 (14.3%)	12 (13.5%)	
Non smoker	85 (68.5%)	16 (45.7%)	69 (77.5%)	
Diabetes				
No	114 (92.0%)	29 (82.8%)	85 (95.5%)	
Yes	10 (8.0%)	6 (7.2%)	4 (4.5%)	0.020*
Alcohol use				
Yes	91 (73.4%)	25 (71.4%)	66 (74.1%)	
No / occasional	33 (26.6%)	10 (28.6%)	23 (35.9%)	0.213*
Frequency of toothbrushing and dental flossing / daily (mean±s.d.)	3.2 (±0.4)	2.9 (±0.4)	3.5 (±0.5)	<0.001†
Time since active periodontal therapy [months (mean±s.d.)]	73.6 (±2.8)	72.5 (±2.8)	73.7 (±3.2)	0.384†
Number of PMT visits (mean±s.d.)	5.7 (±0.5)	5.6 (±0.5)	5.8 (±0.6)	0.232†

*Chi-squared test, †Student test for independent samples; BMS= Brazilian minimum salary (~250 Euros).

An extensive body of clinical research (Maes 2001; Ng *et al.* 2008; Rosania *et al.* 2009; Abahneh *et al.* 2010; Khambaty and Stewart 2013, Mendes *et al.* 2013, Solis *et al.* 2014) has reported the causal relationships between periodontitis and depressive disorders. In general, the evidence is consistent with the hypothesis that stress can modify the host immune defense and lead to the progression of periodontal infections in periodontally susceptible individuals (Warren *et al.* 2014, Dumitrescu 2016).

It has been previously noted that clinical depression and psychosocial factors can have a negative effect on periodontal treatment outcomes (Elter *et al.*2002, Bhatia *et al.* 2015). Furthermore, animal studies (Gurgel *et al.* 2013; Muniz *et al.* 2018) have shown a possible beneficial effect of the use of antidepressant agents in reducing inflammatory processes. These agents may be able to regulate the humoral and cellular immune responses and reduce the production of pro-inflammatory cytokines (Maes 2001; Muniz *et al.* 2018).

On the other hand, it has been stated that individuals with DD present with poorer oral health conditions than individuals without DD and that xerostomia caused by the use of antidepressant agents aggravates this deterioration in the oral condition (Warren *et al.* 2014). To date, data from prospective studies studying the continuous use of antidepressants and periodontal condition have not been reported. In this sense, evidence of the association between depression and periodontitis are contradictory in the literature.

Table 2. Periodontal status of DD and NDD groups at T1 and T2.

Periodontal Parameters	Examination time			
	T1		T2	
	DD (n = 35)	NDD (n = 89)	DD (n = 35)	NDD (n = 89)
Probing depth				
Mean ±s.d.(mm)	2.4 ± 0.7	2.5 ± 0.5	4.1 ± 3.8	3.5 ± 4.1
Sites with PD ≥5mm	1.7 ± 0.6	1.8 ± 0.7	5.2 ± 0.8	4.2 ± 0.5
Clinical attachment loss				
Mean ±s.d.(mm)	3.5 ± 0.5	3.6 ± 0.7	4.4 ± 2.2	3.8 ± 0.8
Sites with CAL ≥5mm	9.8 ± 1.8	9.9 ± 1.7	11.6 ± 2.3	8.2 ± 1.7
Bleeding on probing (mean±s.d)	26.3 ± 9.3	26.5 ± 6.1	30.3 ± 6.7	28.4 ± 5.1
Plaque Index (% ±s.d)	36.6 ± 6.5	37.4 ± 7.2	42.1 ± 5.5	40.1 ± 5.2
Sites with PD ≥ 4mm and CAL > 3mm concomitant with BOP and/or SU(% ±s.d)	0.31 ±0.15	0.28 ±0.12	4.9±0.9	2.7±0.6
Mean number of lost teeth (±s.d)	3.8±0.4	4.0±0.6	4.7±1.5	4.2 ±0.9

T1 – comparisons between DD and NDD: significant difference only on bleeding on probing ($p < 0.05$; Student-t test for independent samples);
T2 – comparisons between DD and NDD: significant difference on all variables, except plaque index ($p < 0.05$; Student-t test for independent samples);
DD comparisons between T1 and final T2: significant difference on all variables ($p < 0.05$; Student-t test for dependent samples).
NDD comparisons between T1 and T2: significant difference on all variables ($p < 0.05$; Student-t test for dependent samples).
Multiple comparisons adjusted by Bonferroni correction ($p = 0.026$).

In the present study, a positive association was reported between DD and the continuous use of antidepressants with a poorer periodontal condition and greater recurrence of periodontitis among patients under PMT. Thus, a beneficial effect of the use of antidepressant agents in immune-mediated processes reducing inflammation or minimizing the progression of periodontitis was not evidenced in our study. Findings from the present study corroborate the negative effect of clinical depression on periodontal condition (Ng *et al.* 2008; Abahneh *et al.* 2010; Liu *et al.* 2018).

It is generally agreed that PMT is important to maintain periodontal health (Lorentz *et al.* 2009; Costa *et al.* 2015; Martinez-Cnut *et al.* 2017). However, data to support a specific PMT frequency of recall visits for the best possible outcomes are not well established (McCraken *et al.* 2017). Some important studies (Rósen *et al.* 1999; Axelsson *et al.* 2004; Matuliene *et al.* 2010; Farooqi *et al.* 2015; Costa *et al.* 2015) have indirectly approached the issue of optimum PMT recall intervals without adequately comparing PM interval times. Hence, recent systematic reviews (McCraken *et al.* 2017; Manresa *et al.* 2018) have concluded that there is weak evidence for setting a particular fixed recall interval for PMT visits.

Compliance with PMT care is clearly an essential prerequisite for long-term periodontal stability and maintenance of a functional dentition, yet the levels of compliance are often below 50% (Lorentz *et al.* 2009; Farooqi *et al.* 2015). Based on our previous PMT studies (Lorentz *et al.* 2009; Costa *et al.* 2014; Costa *et al.*, 2015), we believe that recall visits at short interval times may compromise adherence to maintenance therapy over the years for different reasons. Considering this assumption, interval times for recall visits up to 12 months were the one in which the majority of our cohort individuals followed during PMT without further worsening their periodontal clinical condition. Consequently, it was determined to be reasonable in clinical practice. Moreover, Rosén *et al.* (1999) suggested that recall intervals extended to a year might be acceptable for the purpose of reducing periodontal disease progression in individuals with a history of limited or moderate susceptibility to the disease.

Nevertheless, the high rates of recurrence of periodontitis noted in the present study may indicate that this interval time may be sufficient for patients not previously diagnosed with and treated for periodontitis but may be an insufficient recall schedule for periodontitis patients on PMT. Thus, periodontal maintenance was not successful in reducing the recurrence of periodontitis in both groups, probably because of the longer intervals between recall visits, reflecting insufficient compliance with the PMT program.

The present study also showed that, in addition to the presence of DD, co-habitation status without companion, age >50years, current smoking and the interaction between antidepressants use and current smoking were associated with the recurrence of periodontitis.

Table 3. Distribution of independent variables by the recurrence of periodontitis at T2.

Variables (n = 124)	Recurrence of periodontitis (n = 67; 54.2%)		No recurrence of periodontitis (n = 57, 45.8%)		Crude OR (95% CI)	p*
	n	%	n	%		
Study groups						
DD (n = 35)	22	62.8	13	37.1	3.3 (1.5-7.2)	0.001
NDD (n = 89)	45	50.6	44	49.4		-
Sex						
Female (n = 64)	36	56.2	28	43.8	-	
Male (n = 60)	31	51.6	29	48.4	0.8 (0.4-1.7)	0.610
Age						
≤50 years (n = 51)	17	33.3	34	66.7	-	
>50 years (n = 73)	50	68.5	23	31.5	4.3 (2.0-9.3)	<0.001
Family income						
<5 BSM (n = 50)	22	44.0	28	56.0	-	
≥5 BSM (n = 74)	45	60.8	29	39.2	0.5 (0.2-1.04)	0.066
Educational level						
≥8 years (n = 65)	32	54.2	27	45.8	-	
	35	53.8	30	46.2	1.01 (0.5-2.0)	0.965
Co-habitation status						
With companion (n = 87)	30	81.1	7	18.9	-	
	37	42.5	50	57.5	5.7 (2.2-14.6)	<0.001
Diabetes						
Yes (n = 10)	8	80.0	2	20.0	-	
No (n = 114)	59	51.8	55	48.2	3.7 (0.7-18.3)	0.086
Alcohol use						
No/occasional (n = 33)	10	30.3	23	69.7	-	-
Yes (n = 91)	57	62.6	34	37.4	3.8 (1.6-9.0)	0.001
Smoking		77.3				
Non-smokers (n=85)	40		45	53.9	-	-
Former smokers (n = 17)	10		7	41.2	1.6 (0.5-4.8)	0.196
Current smokers (n = 22)	17		5	22.7	3.7 (1.3-12.4)	0.006

*Chi-square test; BMS = Brazilian minimum salary (~250 Euros).

Table 4. Final logistic regression model for the recurrence of periodontitis at T2.

Variables	Odds ratio (95% IC)	p
Depressive disorders	3.1 (1.2-6.7)	0.001
Co-habitations status		
Without companion	5.2 (1.9-13.8)	<0.001
Age >50years	3.6 (1.2-7.5)	0.001
Current smoking	4.1 (1.1-7.3)	0.001
Interaction between depressive disorders and current smoking	6.4 (1.41-14.3)	0.011

A detrimental effect of isolation or loneliness on health has been demonstrated previously (Courtin *et al.* 2017). However, causal and linking mechanisms are difficult to demonstrate and further investigation is warranted. A recent study evaluating the longitudinal association of combined healthy lifestyle factors with the incidence or progression of periodontitis and tooth loss in older adults concluded that simultaneous adherence to multiple healthy lifestyle factors (such as no cigarette smoking, physical activity, relative weight and dietary quality) significantly lowered the risk of the incidence or progression of periodontitis and tooth loss (Iwasaki *et al.* 2018).

Age may also be a risk indicator for periodontal disease in some populations. However, aging may be related to increased clinical attachment loss but not to periodontitis itself (Costa *et al.* 2015; Courtin *et al.* 2017).

Table 5. Recurrence of periodontitis and non-surgical or surgical procedures performed during PMT (full-mouth procedures) in NDD and DD groups.

Variables	n (%)	n (%)	p*
Recurrence of periodontitis			
Individuals	45 (50.6)	22 (62.8)	0.224
Teeth	81 (3.9)	50 (6.8)	0.001
Sites	221 (2.7)	144 (4.9)	<0.001
Surgical treatment in the recurrence of periodontitis (full-mouth)			
Individuals	20 (44.4)	13 (59.1)	0.002
Teeth	33 (40.7)	30 (60.0)	0.017
Sites	103 (46.6)	89 (61.8)	0.001
Non-surgical treatment in the recurrence of periodontitis (full-mouth)			
Individuals	25 (55.6)	9 (40.9)	0.043
Teeth	48 (59.2)	22 (44.0)	0.041
Sites	118 (53.4)	56 (38.9)	0.003

*Chi-square test.

In periodontally susceptible older adults, age may also be correlated with greater deficiencies in oral hygiene and less access to health resources (Costa *et al.* 2015; Courtin *et al.* 2017). Therefore, these individuals may experience increased recurrence of periodontitis and tooth loss.

Many studies have demonstrated that smoking is associated with an increased risk for attachment loss, bone loss, and tooth loss (Tomar and Asma 2000; Axelsson *et al.* 2004, Chaiton *et al.* 2009; Nociti *et al.* 2015). Furthermore, it has been demonstrated that smokers respond less favorably to all forms of periodontal treatment (Nociti *et al.* 2015) and demonstrate less improvement in PD and CAL, even when PMT is performed (Ramseier *et al.* 2014, Costa *et al.* 2014).

A systematic review (Fluharty *et al.* 2017) has reported a positive association between smoking and DD, with increased rates of smoking related to the severity of the disease. Currently, several hypotheses have been proposed to explain the high rates of smoking among individuals with depression and anxiety. The self-medication hypothesis postulates that individuals turn to smoking to alleviate their symptoms and therefore suggests that symptoms of depression and anxiety may lead to smoking (Chaiton *et al.* 2009).

Some limitations of the present study should be noted such as the small sample of individuals with recurrence of periodontitis for the final multivariate analysis and the profile of the studied sample (highly educated subjects from mid-high economic strata and private dental clinic). However, the 6-year follow-up monitoring period, the prospective design, the homogeneous sample regarding time since active periodontal therapy and the number of recall visits, as well the standardization of periodontal procedures during PMT can minimize the impact of these limitations.

Further studies with representative samples, different populations and different study designs may contribute to the external validation of our findings. Longitudinal monitoring is necessary to confirm if depressive disorders could influence the occurrence, the recurrence and the severity of the periodontitis. Moreover, it could be argued that clinicians need to consider depression as a risk factor for periodontal disease progression and ponder this when recommending a recall frequency to patients in order to prevent the recurrence of periodontitis.

In conclusion, DD individuals undergoing PMT presented higher rates of recurrence of periodontitis and tooth loss when compared to NDD individuals. Additionally, the interaction between DD and smoking significantly increased the risk for the recurrence of peridontitis. This finding points to the strong influence of these two modifiable variables in the imbalance of the periodontal homeostasis during PMT, and demonstrates the need for greater attention from clinicians and health policymakers regarding these variables.

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