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Burning Mouth Syndrome: Clinical Profile of Brazilian Patients and Oral Carriage of *Candida* Species

Desirée Rosa CAVALCANTI
Esther Goldenberg BIRMAN
Dante Antonio MIGLIARI
Fernando Ricardo Xavier da SILVEIRA

Department of Oral Diagnosis, University of São Paulo, School of Dentistry, São Paulo, SP, Brazil

Burning mouth syndrome (BMS) is a complex disease of unknown cause. It is characterized by a burning sensation in the oral mucosa, notwithstanding its clinical normal aspect. BMS is particularly seen in postmenopausal women. The purpose of this study was to investigate this syndrome on a clinical basis and, in addition, to analyze its possible relation to the frequency of *Candida* species. Thirty-one patients (28 women and 3 men; 13 Caucasians and 18 non-Caucasians; mean age = 61.3, range 30-85 years) were evaluated. Most patients (80.6%) were under long-term medication, antihypertensive, ansiolitic and antidepressant drugs being the most used. Burning mouth complaint was associated with other secondary oral complaints in 83.8% of the cases. Tongue was the most commonly affected site (70.9%), followed by the vermillion border of the lower lip (38.7%) and hard palate (32.2%). The association of the burning sensation with oral cancer (cancer phobia) was reported by 67.7% of the patients. Haematologic examination (hematocrit, haemoglobin and fasting blood glucose level) revealed 2 cases each of anemia and type 2 diabetes. Local factors, tooth extractions and dentures wearing, were associated with the onset of symptoms in 35.5% of the cases. Daily activities were changed as a consequence of BMS in 29% of the patients. Among the species of the genus *Candida*, *C. albicans* was the most frequent in BMS patients (9 - 29.03%) and controls (12 - 38.70%), followed respectively by *C. parapsilosis* (2 - 6.45% and 0 - 0%); *C. tropicalis* (1 - 3.22% and 2 - 6.45%); *C. krusei* and *C. kefyr* (1 - 3.22% and 0 - 0%). Therefore, such difference did not reach valuable results. In conclusion, these data were similar to those reported in other studies. The highlights of the present findings were the possible relation of BMS with chronic drug use, depression, menopause and cancer phobia. No association was found between BMS and the prevalence of *Candida* species.

Key Words: Burning mouth syndrome, long-term medication, *Candida species.*

INTRODUCTION

Burning mouth syndrome (BMS) is caractherized by a burning sensation in a normal oral mucosa and occurs particularly in postmenopausal women (1,2). The tongue is the most commonly affected site, but the burning sensation can be diffused in any area of oral mucosa, being variable in intensity and has a chronic course (3,4). Several studies indicate that BMS is fairly common, wich explains the increased attention that the condition has received in the recent literature (5). The etiology is poorly understood and considered multifactorial, being associated to different local, sistemic, psychogenic and neurologic causes (6,7). Therapy is empiric and without evidence of efficacy, leaving the condition with no recognised treatment (8,9).

Little information about the variations of BMS in the different population in the world is available, the same applies to its prevalence. The wide range of prevalence values, from 0.01 to 0.7% in general population (10) or 26% in the elderly, reflects the lack of any accurate definition (11).

The candidal infection has been investigated for some authors as a possible local associate factor, but

Correspondence: Profa. Desirée Rosa Cavalcanti, Departamento de Estomatologia, Disciplina de Semiologia, Faculdade de Odontologia, Universidade de São Paulo, Avenida Prof. Lineu Prestes, 2227, Cidade Universitária, 05508-900 São Paulo, SP, Brasil. Tel/Fax: +55-11-3091-7883. e-mail: dcavalcanti@usp.br

there are few studies related to BMS microbiota and the present data were not enough conclusive to evaluate its importance as a factor in the etiology of this condition (7,11).

The aim of this study was to characterize the clinical profile of Brazilian BMS patients and to investigate the prevalence of *Candida* species by means of comparison to control group.

MATERIAL AND METHODS

This study involved patients from the Oral Medicine Service of Stomatology Department of the Dentistry School, University of São Paulo, Brazil and was approved by the Ethics in Research Committee and each involved patient signed an informed consent form.

The study group was formed by 31 patients that had burning sensation for over 6 months, without any clinical change that could explain the symptoms (12), being 28 women (90.3%) and 3 men (9.7%); 13 Caucasians and 18 non-Caucasians, mean age of 61.3 years (range 30 to 95 years). The data were obtained from a single examinator. In all cases, a previously designed protocol was completed, including health status and oral examination. Haematologic data (hematocrit, haemoglobin and fasting blood glucose level) and non-stimulated salivary rates were performed. Hyposalivation was considered to levels under 0.1 mL/min (13). A visual analogue scale (VAS) ranging from 0 to 10 was used for the measurement of burning sensation.

For mycological examination, samples of oral washes were obtained by Samaranayake method (11) (10 mL of saline for 1 min) in the BMS patients and in 31 sex and age matched individuals without oral lesions and without burning complaints (control group), enrolled after being examined and granting informed consent, among the individuals that were searching for dental and/or prosthetic care at our School Dental Clinic. The samples were inoculated in agar Sabouraud-dextrose plus Chloranphenicol, followed by count of colony-forming units (CFU) *per* mL, identified by microcultive, germ tube formation, sugar assimilation and fermentation techniques.

RESULTS

The main clinical data of the patients are presented on Table 1. Climacteric changes were present in 71% of the women (22/31), with mean duration of 157 months and the burning arose after 44 months. Systemic drugs were used for 80.6% of the patients; the most common being the benzodiazepines (35.5%), antidepressants (19.35%) and the antihypertensives (38.7%). Sixteen patients were under two or more kind of drugs. Two patients suffered from anemia and type 2 diabetes and received adequate treatment, with reduction of burning in only one case of anemia.

The mean duration of BMS was 9.3 years (range 6 months to 20 years) and the mean intensity, evaluated by VAS was 50.6 (± 26.7) mm (range 4 to 95 mm), being the tongue and the lower lip the most affected areas. The use of removable prosthesis was found in 19 patients (61.3%), whom presented inadequacies in their dentures in 14 cases (73.6%). After improvement or replacement, 13 patients (68.4%) did not observe any relief of their complaints and one patient did not return for follow up. Secondary oral complaints, such as dry mouth, dry lips and dysgeusia were observed in 26 patients (83.8%). The mean non-stimulated salivary flow rate was 0.319 (± 0.198) mL/min and two patients had rates under 0.1 mL/min.

The foremost factors associated with the onset of the symptoms were: exodontias and dentures, associated in 11 patients (35.48%); emotional conditions in

Table 1. Clinical profile of BMS patients (n = 31).

Characteristics	Patients
Men	3 (9.67%)
Women	28 (90.32%)
Mean age	61.3 years
Systemic diseases	
Hypertension	14 (45.16%)
Depression	15 (48.38%)
Digestive diseases	5 (16.12%)
Anemia	2 (6.45%)
Thyroid dysfunctions	3 (9.67%)
Type 2 Diabetes	2 (6.45%)
Osteoporosis	4 (12.9%)
Habits	
Tobacco/alcohol	2 (6.45%)
Oral conditions	
Dentate	9 (29.03%)
Removable prosthesis wearers	19 (61.29%)

6 cases (19.35%); drugs, climacteric changes and systemic diseases in 4 cases (12.9%). Seven patients (22.58%) did not associate the onset to any special event. Citric and spicy foods (87%) and psychological distress (57%) were the main worsening features. In 1 case, burning worsened by smells.

In relation to an interference of BMS in the patients' life, the burning did not affect the daily activities in 70.9% (22/31) of the patients, but 29% (9/31) reported to upset due to the burning sensation or changes in feeding habits and some patients reported to avoid social contacts. Twenty-one patients (67.7%) associated BMS with oral cancer (cancer phobia) (Table 2).

Positive cultures for *Candida* were observed in 45.16% (14/31) of the samples for both, test and control group (Table 3). *C. albicans* was the most prevalent species in both groups (9 - 29.03% and 12 - 38.70%), followed, respectively, by *C. parapsilosis* (2 - 6.45% and 0 - 0%), *C. tropicalis* (1 - 3.22% and 2 - 6.45%) and *C. krusei* and *C. kefyr* (1 - 3.22% and 0 - 0%). The mean count was 113.8 (± 46) CFU/mL in the test group and 95.2 (± 40.8) CFU/mL in the control group.

Table 2. Characteristics of BMS symptoms (n = 31).

Simptomatology	Patients/Data
Chief complaint	
burning	26 (83.87%)
burning + pain	3 (9.67%)
burning + numb	2 (6.45%)
Secondary oral complaints	
Dry mouth	17 (54.83%)
Dry lips	17 (54.83%)
Persistent taste (dysgeusia)	10 (32.25%)
Mean duration of symptoms (years)	9.33
BMS Subtypes	
Type 1	15 (48.38%)
Type 2	11 (35.48%)
Type 3	5 (16.12%)
Mean VAS	50.60 mm
Cancer phobia	21 (67.74%)
Interference of BMS in social and oral functions	9 (29.03%)

DISCUSSION

In accordance with other studies, BMS subjects were primarily postmenopausal women. The use of systemic drugs was observed in 80.6% of the patients, especially antihypertensives and antidepressants. Other studies found similar chronic use of drugs as a significative factor in BMS (2). Antidepressants (tricycles and benzodiazepines) are widely prescribed by the professionals that try treating these patients. Our group did not observe relief of symptoms after the use of these drugs, but it could not be evaluated if the doses were in accordance to those utilized by Grushka (4), that recommend low doses and association between tricycles and benzodiazepines as most effective in BMS control. These data suggest that the chronic drug use by BMS patients should be better investigated.

The role of anemia in BMS is still controversial. Grushka (4) did not consider anemia as an important factor in BMS. Two cases of anemia were observed in our study and the treatment for relief burning symptoms in just one patient. Our results are in accordance with those of Grushka (4), but we agree that hematological examination should be performed in BMS patients.

Adjustment and/or replacement of prostheses were not important in the relief of burning symptoms in

Table 3. Frequency of *Candida* species in BMS patients and in the control group.

Patients	BMS (n = 31)	Control (n = 31)
Yeasts	25(80.64%)	20(64.51%)
Men	2	4
Women	23	16
Mean age (range)	63 (53-80) yrs	63 (30-85) yrs
Removable prosthesis	17 (54.83%)	19 (61.29%)
Candida species	14 (45.16%)	14 (45.16%)
Candida albicans	9 (29.03%)	12 (38.70%)
Candida parapsilosis	2 (6.45%)	0 (0%)
Candida tropicalis	1 (3.22%)	2 (6.45%)
Candida krusei	1 (3.22%)	0 (0%)
Candida kefyr	1 (3.22%)	0 (0%)
Other yeasts	11 (35.48%)	6 (19.35%)
CFU (median)	113.8 ± 46.0	95.2 ± 40.8
Variation (CFU/mL)	6 to 597	4 to 390

the present study. The mean VAS in the group was considered as moderate in intensity and secondary complaints, such as dry mouth, dry lips and dysgeusia were observed in 83.8% of the cases. In this aspect, it is important to note that studies showed that BMS is commonly accompanied by complaints of xerostomia and persistent or altered taste (4,14-17). The results of the present study are in accordance with these. The association of BMS and dry mouth was very evident in the present study, but only 2 patients had salivary flow rates under 0.1 mL/min. These data suggest a possible role of salivary composition in the underlying mechanism related to xerostomia, dysgeusia and burning sensation, like those observed by Sreebny (13) and by Nagler and Hershkovich (18).

The onset of symptoms was associated to prior causes in 77.4% of the patients, the most common being exodontias and denture use. Similar data have been found (4) and suggest an interdisciplinary investigation.

The spontaneous association between burning sensation and oral cancer was very evident in our patients (67.7%) and higher than that found by Lamey and Lamb (12). This psychological behavior due to BMS shows the importance of the orientation to these patients, who's generally did not receive it on their prior visits to several clinicians and dentists.

In relation to daily activities, BMS did not affect the majority of the patients, despite of some diet and social restrictions. In 29% of them, the changes on alimentary habits carried on important annoyance, even in relation to wearing prosthesis and changes in social behavior. Similar results were observed by other authors (3,4).

This study was proposed to investigate a possible relation to yeasts from *Candida* genus as an associated etiologic factor in BMS, as published elsewhere (7,11). In this study, found positive cultures for *Candida* species were found in 45.16% of the patients, a higher prevalence than that observed by Samaranayake et al. (11), but in our study the difference to the control group did not reach valuable results. A possible explanation for these divergences could be related to regional differences between Brazilian population and individuals of other countries mainly because of the increased use of prostheses (most of them with inadequacies) in the Brazilian population, which is an important factor for the presence of species from the genus *Candida* in the oral mucosa. In fact, the control group, which had a higher frequency of removable prosthesis wearers, presented also a higher frequency of *C. albicans* than the study group, despite the mean count, which was higher in the test group (113.8 ± 46.0 CFU/mL) than in the control group (95.2 ± 40.8 CFU/mL). For these reasons, it could not be confirmed the presence of *C. albicans* as an associated factor in the role of BMS etiology.

It was also observed that the chief complaint of burning was frequently associated to secondary oral complaints. The disease occurred predominantly in women in the postmenopausal period. The continuous use of medications associated to the pre-existing chronic diseases, such as hypertension, depression and anxiety, in addition to cancer phobia constituted important aspects of patient profile. Yeasts from the genus *Candida* did not play a role in BMS symptoms.

RESUMO

A Síndrome de ardência bucal (SAB) é uma doença complexa, de etiologia desconhecida. Caracteriza-se por uma sensação de queimação na mucosa bucal, não obstante seu aspecto clínico normal, sendo bastante freqüente em mulheres após a menopausa. O propósito deste estudo foi o de investigar a SAB em bases clínicas e, em adição, analisar sua possível relação com a freqüência de espécies do gênero *Candida* isoladas da cavidade bucal desses indivíduos. Foram estudados trinta e um pacientes, 28 mulheres e 3 homens, 13 caucasianos e 18 não caucasianos, média de idade 61,3 (faixa dos 30 - 85 anos). A maioria deles (80,6%) estava sob medicação por longo período. Anti-hipertensivos, ansioliticos e antidepressivos foram as drogas mais utilizadas. A ardência bucal estava associada a outras queixas secundárias em 83,8% dos pacientes. A língua foi o sítio mais afetado (70,9%), seguida pelo vermelhão do lábio inferior (38,7%) e palato duro (32,2%). A associação de sensação de ardência com câncer bucal (cancerofobia) foi referida por 67,7% dos pacientes. Exames hematológicos (hematócrito, hemoglobina e glicemia em jejum) revelaram dois casos cada, de anemia e diabetes tipo 2. Fatores locais, exodontias, e uso de próteses estavam associados com o conjunto de sintomas em 35,5% dos casos. Foram referidas alterações importantes nas atividades cotidianas, em conseqüência da SAB, em 29% dos pacientes. Leveduras do gênero *Candida* foram isoladas da cavidade bucal de 45,16% dos indivíduos com SAB e igualmente do grupo-controle, não constituindo dado qualitativamente importante. Dentre as espécies do Gênero *Candida*, *C. albicans* foi a mais freqüente (9 - 29,03% e 12 - 38,70%), seguida de *C. parapsilosis* (2 - 6,45% e 0 - 0%), *C. tropicalis* (1 - 3,22% e 2 - 6,45%), *C. krusei* e *C. kefyr* (1 - 3,22% e 0 - 0%). Em conclusão, nossos resultados mostraram a importância de uma possível relação da SAB com o uso crônico de medicamentos, depressão, menopausa e cancerofobia. Não foi observada associação entre SAB e prevalência de leveduras do gênero *Candida*.

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