

Clinical characteristics and therapeutic response in patients with Burning Mouth Syndrome: accompanying 2 years

Características clínicas e resposta terapêutica em pacientes portadores da Síndrome de Ardência Bucal: acompanhamento de 2 anos

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Resumo

Introdução: A Síndrome de Ardência Bucal (SAB) é uma condição caracterizada pelo sintoma de ardência na mucosa oral na ausência de qualquer sinal clínico. Sua etiologia ainda é desconhecida e, até o momento, não dispõe de tratamento efetivo. **Objetivo:** Avaliar o perfil do paciente portador de SAB, as terapias instituídas e seus resultados em estudo retrospectivo. **Material e método:** Foram coletados os dados clínicos e terapêuticos dos prontuários de pacientes diagnosticados com SAB, no período de janeiro de 2013 a abril de 2015, no Ambulatório da Disciplina de Estomatologia Clínica da Faculdade de Odontologia da Universidade de São Paulo. Os critérios para o diagnóstico utilizados se basearam nos estabelecidos pela *International Headache Society* em 2013 e foram observadas as terapêuticas empregadas e seus resultados. **Resultado:** Doze pacientes foram diagnosticadas com SAB neste período, todas do sexo feminino, média de idade 61,18 anos, e a principal região acometida pelo sintoma de ardor foi o ápice de língua. O tempo de duração deste sintoma variou de 6 meses a 25 anos. As terapias utilizadas para o controle de sintomas da SAB foram capsaicina, clonazepan tópico, laserterapia e homeopatia. Dentre as terapias instituídas, a capsaicina apresentou efeito imediato na redução dos sintomas. **Conclusão:** O presente estudo demonstrou que os desafios que circundam a obtenção de um tratamento efetivo para a SAB são diversos e estão principalmente relacionados ao desconhecimento da etiopatogenia da doença. O perfil demográfico dos pacientes aqui estudados foi semelhante ao descrito na literatura disponível, entretanto, as variáveis representadas por sintomas secundários (história médica, níveis de ansiedade e depressão) podem constituir fatores modificadores da resposta terapêutica e da própria etiopatogenia da doença.

Descritores: Síndrome da Ardência Bucal; tratamento; dor neuropática

Abstract

Introduction: Burning Mouth Syndrome (BMS) is a condition characterized by burning symptom of the oral mucosa in the absence of clinical signs. Its etiology is still unknown and, to date there is no effective treatment. **Purpose:** The aim of this study was to evaluate patients with BMS profile and the therapies results in a retrospective study. **Material and method:** Clinical and therapeutic data were collected from records of patients with BMS diagnosed between January 2013 to April 2015 at the Clinic of Stomatology Clinic, Faculdade de Odontologia of Universidade de São Paulo, according to the criteria established by the *International Headache Society* in 2013. The therapies used for BMS control were also evaluated. **Result:** Twelve patients were diagnosed with BMS at this period. All of them were women with a mean age of 61.18 years and the apex of the tongue was the most common affected site and the duration of the burning sensation ranged from 6 months to 25 years. Many therapies were prescribed for BMS control, such as topical capsaicin, topical clonazepan, low level laser therapy and homeopathy. Among the established therapies, capsaicin has immediate effect in reducing symptoms. **Conclusion:** The present study showed that the challenges towards an effective treatment for BMS are varied and are mainly related to the lack knowing of the pathogenesis of this disease. The demographic profile of patients studied here was similar to that described in the available literature, however, the variables represented by secondary symptoms (medical history, anxiety and depression levels) may be modifying factors of therapeutic response and the pathogenesis of the disease itself.

Descriptors: Burning Mouth Syndrome; treatment; neuropathic pain.

INTRODUCTION

Early XX century Butlin and Oppenheim characterized the Burning Mouth Syndrome (BMS) as glossodynia¹, and it was subsequently named glossopyrosis, oral dysesthesia, painful tongue, stomatodynia and stomatoprosis².

According to the current diagnostic criteria of the *International Headache Society* (IHS) de 2013³; BMS features chronic pain, spontaneous burning, with visibly intact mucosa, in addition to presenting normal clinical, dental, laboratorial and systemic findings⁴. According to IHS, BMS is a distinct nosologic entity, characterized by burning episodes lasting at least four months⁵.

Symptoms rise spontaneously and may be commonly followed by tasting changes (metallic or bitter) and xerostomia⁶. In most cases, the reports describe painful peaks during the day and these may be isolated or persistent. Symptoms rise in the morning, worsening during the day, with its peak later in the afternoon, ending at the evening, rarely interfering with the patient sleep⁷ and also vary according to the food ingested and emotional state. The most affected anatomical regions are tongue, followed by palate, lower lip and jugal mucosa⁸. Complaints are normally bilateral but it may also occur unilaterally^{9,10}.

Several factors mimic the BMS symptoms, such as non-adapted prosthesis, parafunctional factors, allergies, candida, diabetes, hypothyroidism, menopause, nutritional deficiencies (iron, folic acid, vitamin B and/or zinc), digestive disorders, Sjögren syndrome and other autoimmune diseases, antihistaminic drugs, antiepileptic, hypotensive and diuretics^{3,4,6}. These must be investigated and excluded for the BMS diagnosis.

Changes in psychological profile can be observed in addition to the mentioned symptoms, such as anxiety, depression, hypochondria, cancerophobia, and emotional instability^{11,12}.

Published prevalence data as scarce and variable (0.7 to 4.6%)¹⁰, and this variability in the numbers reflect the difficulty in establishing a criterion for the BMS diagnosis¹³.

It is seven times more common in women than men, between the 4th and 5th decade of life and the following risk factors contribute to its development: female gender, perimenopause, Parkinson disease and other chronic diseases, including gastrointestinal and urogenital diseases¹⁴.

There is no remedial protocol regarding the BMS therapy. Thus, the patients are oriented with several therapies, with results not always satisfactory that vary from tongue protectors to prescription drugs¹⁵.

The use of drugs as tricyclic antidepressants, clonazepam (benzodiazepine), gabapentin and antiepileptic is common, targeting the control of the oral burning symptoms⁴. In an attempt to minimize the adverse effects, the use of topical clonazepam was evaluated, with reduction of 70% in the burning sensation¹⁵. However, the study performed by Moraes et al.¹⁶ observed that even in topical form, some patients reported side effects, such as drowsiness, xerostomia, and increased burning sensation in the mouth in some cases.

Thus, other modalities with lower adverse effects have been evaluated and considered as first line of treatment for BMS. Petruzzi et al.¹⁷ evaluated the effect of systemic capsaicin over four weeks. The authors observed a significant reduction of the symptom and suggested that the positive results support the hypothesis of neurologic etiology. However, the treatment caused gastric pain in 32% of the patients, with symptoms starting from the second week of treatment¹⁷. The use of topical capsaicin presents the unpleasant side effect because it is derived from pepper, but has a positive effect in reducing the symptoms¹⁵.

Low level laser irradiation with wavelength between 632 and 780 nm has shown that phototherapy increases the metabolism of the injured nervous cell, stimulating the production of scar tissue in the injured region. This prevents and/or reduces the degeneration of injured fibers; stimulates the axonal growth and its remyelination. The effects produced remain the same after the irradiation period ceases¹⁸. These benefic effects were observed in the study by Kato et al.¹⁹, that investigated the low level laser effect in the BMS treatment, observing 80% reduction of the symptoms for up to 90 days.

Homeopathy is also a therapeutic alternative for BMS with no significant adverse effects. In a randomized controlled study performed by Chebel[†] in 2012, pioneer in this area, there was a 40% reduction of BMS symptoms with a homeopathic treatment using *Arsenicum album*, and a 60% reduction in individual homeopathic treatment for the patient according to the specific anamnesis for this therapy.

Purpose

The aim of this study was to evaluate patients with the profile of BMS and the therapies results in a retrospective study.

MATERIAL AND METHOD

The study was approved by the Ethics Research Committee of the Faculdade de Odontologia da Universidade de São Paulo – FOU SP (CAAE no.: 0151.0.017.000-11). All subjects signed an Informed Consent to participate in this research, according to the Declaration of Helsinki.

Records of patients with BMS seen at the Clinical Stomatology Ambulatory of the FOU SP between January 2013 to April 2015 were included in this study analysis. All diagnosis were based on the report of symptoms in agreement with BMS, according to criteria established by the *International Headache Society* de 2013³, i.e., presence of daily burning symptom for period above four months and absence of clinical changes in the affected tissues.

The exclusion criteria established for BMS diagnosis were based on local and systemic changes regarding mouth burning symptoms, such as candidosis, xerostomia/hyposalivation, anemia, nutritional deficiency, diabetes mellitus and Sjögren's Syndrome.

† Chebel OFI. Ação do tratamento homeopático na sintomatologia da síndrome da ardência bucal em duas fases: estudo duplo cego placebo controlado e estudo aberto [tese]. São Paulo: Faculdade de Odontologia, Universidade de São Paulo; 2013.

Information gathered from these records were correlated to the patients demographic data, such as gender and age, regarding mouth burning complaint, such as local, duration, intensity and therapy used.

Regarding therapy used, we annotated the therapies used and the effects reported by the patients. In this case, the protocols used for treating BMS are based on those published in the global literature^{15-19†}, and are applied to the patients according to the lower chance of important adverse effects and availability, including homeopathy, laser therapy, topical capsaicin and topical clonazepam.

In addition, we evaluated information on hematological exams (complete blood count, fasting blood glucose, serum iron, ferritin, folic acid and vitamin B12) requested to exclude the systemic changes aforementioned. As well as records of yeast research of the genre *Candida*, using the method of exfoliative cytology and sialometry at rest to evaluate the non-stimulated saliva flow, to exclude the local changes also mentioned above.

The data collected from records were organized in spreadsheets and the results were expressed in a descriptive manner and presented in tables.

RESULT

During this period of 27 months, 12 patients were diagnosed with BMS, in a total of 1625 new patients seen at the Clinical Stomatology Ambulatory of the FOUSP. Therefore, the BMS prevalence in this population was of 0.74%. Considering that BMS occurs predominantly in adults, the BMS prevalence in individuals above 50 years of age (877/1625) was of 1.37%.

It is noteworthy that other patients came to the Ambulatory with complains of burning mouth; however, they did not meet the criteria for BMS diagnosis. Those patients presented yeast infection by *Candida*, confirmed by the cytological test and, therefore, were diagnosed as oral candidiasis and treated with nistatin 1.000 IU as mouth wash during 10 days (n=2).

Other two patients that presented deficit in the hematological exam were referred to a general practitioner for evaluation and proper treatment, these cases were resolved after normalizing the blood serum levels. The case of burning due to trauma was resolved after removal/adaptation of the causing agent (n=1) and the cases with hyposalivation (n=3), proved by the sialometry test, receive a prescription for saliva stimulation and/or oral humectants, as well as orientation to moisturize the mouth.

In the casuistic of 12 patients diagnosed with BMS, all were female, aged between 48 and 71 years old, and average age of 61.18 years. According to the diagnosis criteria, the exfoliative cytology results of these patients were Papanicolau grade I or II and were negative for the yeast *Candida*. Thus, the results of the hematological tests requested to investigate nutritional deficit were within the normal range.

All denied tobacco and alcohol use, two patients had prosthesis, one bimaxilar and the other upper total.

From the 12 patients evaluated with BMS, all mentioned burning symptom in the tongue, mainly apical, and 3 reported also the

palate, gum and lips. Regarding the symptoms duration, reports varied from 6 months to 27 years according to Table 1.

Among the systemic changes (Table 2) we observed that only 2 patients did not present any systemic disease. The remaining, 5 had gastrointestinal changes (gastroesophageal reflux, gastritis and hemorrhoids), 4 had psychiatric disorders (anxiety and depression), 3 had hypothyroidism, 3 had high blood pressure, 1 had osteoporosis and 1 cardiac arrhythmia.

Regarding the drugs used to treat the systemic changes described, associated or isolated, we observed that 5 patients used proton pump inhibitors, 3 used antihypertensive, 3 used thyroid hormones, 2 antidepressive, 2 anxiolytics, 1 had hormonal replacement therapy with estrogen. Only two patients did not use any medication, as shown in Table 3.

According to the records, 12 patients were treated during this period with several therapeutic protocols previously investigated and published in the global literature^{15-19†}, as described in Table 4. The symptoms evaluation regarding therapy was performed using the Analogical Visual Scale records available in the patients' records.

Of the 12 patients with BMS, three had homeopathic therapy with 60% reduction of burning symptoms, except one patient that was referred to neurological treatment with systemic antidepressants due to the unsuccessful of this therapy.

Table 1. Anatomical region affected and time of duration of symptoms in patients with BMS, from January 2013 to April 2015

Factor (sample)	Patient n (%)	
Region	Tongue	12 (100%)
	Lips	2 (16.6%)
	Gum	2 (16.6%)
	Palate	1 (8.3%)
Duration	6 months to 1 year	6 (50%)
	2 years to 5 years	3 (25%)
	6 years to 8 years	2 (16.6%)
	9 years or more	1 (8.3%)

Table 2. Systemic diseases reported by the patients with BMS, from January 2013 to April 2015

Systemic diseases	N (%)
Gastric	5 (41.6)
Psychiatric	4 (33.3)
Hypothyroidism	3 (25)
Hypertension	3 (25)
Bone	1 (8.3)
Cardiac	1 (8.3)
None	2 (16.6)

Table 3. Drugs used by the patients with BMS, from January 2013 to April 2015

Drugs	N (%)
Proton Pump Inhibitors	5 (41.6%)
Antihypertensives	3 (25%)
Thyroid hormones	3 (25%)
Antidepressants	2 (16.6%)
Anxiolytics	2 (16.6%)
Hormonal replacement (estrogen)	1 (8.3%)
None	2 (16.6%)

Table 4. Therapy used to treat BMS, from January 2013 to April 2015

Therapy	N of patients
Capsaicin	5
Laser therapy	4
Homeopathy	3
Topical Clonazepan	2
Did not adhere to treatment	2

Four other patients underwent treatment with laser therapy, showing 60% reduction of symptoms during the therapy. However, one patient left the treatment due to inability to continue the 10 sessions of low level laser application and 1 patient showed recurrence of burning symptoms in the tongue after the end of the laser therapy, and along with other 5 new patients underwent topical treatment with capsaicin.

According to the patients' records, we observed an immediate effect in the reduction of symptoms, about 50%, with the use of topical capsaicin. However, one patient left the treatment due to local adverse effect of increase burning sensation, and also 2 cases showed loss of therapy efficacy after the period of 3 months of treatment with capsaicin, and was then treated with topical clonazepan and showed 50% of symptom control.

DISCUSSION

BMS is an important clinical condition as it causes significant problems to the patient quality of life^{4,11,20}. Due to the invisible clinical signs, the patient often feels discredited by families and health providers that do not know the BMS. Therefore, they have great difficulty in diagnosis, and are referred to several health specialties and undergo several therapies, most of the time, not efficient. Thus, the scientific investigation of therapeutic and etiologic aspects is essential.

The group of patients diagnosed with BMS consecutively included in this study was exclusively female with an average age of 61.18 years. These data agree with the findings of several epidemiological studies that designed these patients profile as predominantly female and in the peri/pos menopause^{4,9,11,14,20}.

The characterization of the burning symptom showed a pattern previously described in the literature in 100% of the patients evaluated, which shows reports of the symptom in the morning, worsening along the day, but rarely interfering with sleep^{4,7,9}. This profile also varies according to the food ingested and emotional state. Most of the patients evaluated reported great discomfort when ingesting acid food and increased intensity of burning according to the level of emotional stress in certain days.

Regarding the anatomical region of burning sensation, 58.3% of the patients reported higher frequency in the apex of tongue, even though the literature shows that the most common complaint was bilateral in the tongue sides^{9,10}.

In clinical practice we observed that xerostomy affected 33.3% of the patients; despite the complaint, the salivary flow measured was within the normal range and did not indicate hyposalivation in the evaluated patients. In addition, all patients used several drugs to treat systemic chronic diseases, which impair the diagnosis of primary BMS. The observations in this study show that the current definition of BMS may need to be revised due to the great difficulty in classifying the patient in the strict clinical criteria established, also evidenced by other researchers^{3,21,22}.

This study showed concomitantly to the difficulty in establishing the diagnosis, problems to establish a relationship with the patients since most of them present anxiety and depression, even skepticism in the cure of a disease that does not have evident lesions but is able to trigger significant social, feeding and psychological issues. In the casuistic evaluated, 33.3% of the patients already presented the anxiety and/or depression and were being treated for these behavioral disorder. The burden of suffering BMS for years was also pointed out as cause of the changes in the psychological profile, due to the loss of quality of life^{4,11,12,23,24}.

Other systemic change often reported by the patients in this study was the presence of digestive disorders such as gastritis and gastroesophageal reflux in 41.6%. This correlation was also observed in other studies^{12,14,25}.

Finally, we also observed in the patients' follow-up that the BMS treatment is challenging, even when the patients present similar complaints and age. Even though the therapies used (homeotherapy, laser, topical capsaicin and clonazepan) showed a good result in reducing symptoms, they are not curative and lose their efficacy, which lead to drug replacement and discredit by some patients. On the other hand, professional contact and welcoming also show positive result in light of the patient emotional component. This correlations were reported in the literature^{16,24}, and considering the primary BMS subtypes⁹ and that the neuropathic pain may be associated to BMS may be a mixture of peripheral or central²⁶, the proposed ideal therapy must be individual²⁷. However, new studies are needed in order to define better treatment protocols.

CONCLUSION

The present study showed that the challenges towards an effective treatment for BMS are varied and are mainly related to the lack knowing of the pathogenesis of this disease. The demographic profile of patients studied here was similar to that described in the

available literature; however, the variables represented by secondary symptoms (medical history, anxiety and depression levels) may be modifying factors of therapeutic response and the pathogenesis of the disease itself.

ACKNOWLEDGEMENTS

The authors acknowledge the dental surgeon and master Vivian Diane Pellegrini for the study initial design.

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CONFLICTS OF INTERESTS

The authors declare no conflicts of interest.

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Received: January 12, 2016
Accepted: October 17, 2016