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WHAT YOU NEED TO KNOW ABOUT BURNING MOUTH SYNDROME

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ABSTRACT

Introduction: Burning mouth syndrome is a chronic and idiopathic condition characterized by a burning sensation in the oral mucosa mainly affecting the tongue without any clinical lesion or associated systemic disease. **Material and Methods**: It was performed a literature review concerning of epidemiology, classification, diagnosis, etiopathogenesis and treatment of the syndrome. **Results and Discussion:** This syndrome commonly affects postmenopausal women with emotional disorders or at least a psychological component to the symptoms. **Conclusion:** There is a lack of consensus in the literature regarding the most appropriate criteria for the classification of the Burning Mouth Syndrome.

KEYWORDS: Burning Mouth Syndrome; Stomatodynia; Dysgeusia.

INTRODUCTION

The etiology of burning mouth syndrome (BMS) has not been fully clarified and there is no universal consensus regarding the most appropriate criteria for the classification of this condition.[1] The main characteristic of BMS is a burning sensation in the oral mucosa mainly affecting the tongue without the presence of any clinical lesion or associated systemic disease.[2-4] BMS generally occurs bilaterally,[5] but is unilateral in some cases. This condition commonly affects postmenopausal women.[6] Other symptoms include dry mouth (xerostomia) and taste disorders (dysgeusia).[7]

a- Synonyms: While BMS is the most widely accepted term, synonyms include glossopyrosis (burning tongue), glossodynia (painful tongue), sore tongue and glossalgia (when the burning sensation is located in the tongue) and stomatodynia, stomatopyrosis, sore mouth and oral dysesthesia (when symptoms also appear in other locations of the oral cavity).[3]

b- Epidemiology

Prevalence: The prevalence of BMS in the general population is estimated to range from 0.7% to 15%.[3,8,9] However, the actual prevalence is difficult to establish due to the lack of rigorous criteria for the diagnosis of this condition.[8,9]

Age and Sex: BMS is more common among women over the age of 50 years,[1,10,11] and predominantly occurs in the pre-menopause and post-menopause periods.[2,5,6,11-16] This syndrome is rarely found in patients less than 30 years of age and never occurs in children or adolescents.[17] Among 150 patients with BMS, Brailo et al.[1] found that most (82%) were women over 60 years of age. Among 91 patients with symptoms of BMS, Rivera-Campillo; López-López,[11] found that the proportion of women to men was nearly 14:1 and mean age was 69.9 years. Silvestre-Rangil et al.[18] found a 10:1 proportion of women to men. In a systematic review of the literature, Patton et al.[19] found that 70% of 645 patients with BMS in the articles analyzed were women. Nasri et al.[2] also found a higher prevalence rate of BMS among women (ratio: 5.6:1) in the post-menopause period (mean age: 62.35 years), the majority of whom had low levels of estrogen (92%). Palacios-Sánchez et al.[20] found an age range of 65 to 74 years (mean: 71.2 years) and women accounted for 96.4% of patients with BMS. Silvestre et al.[21] found a mean age of 72.65 ± 12.1 years among 23 patients with BMS.

***Affected sites and duration of symptoms*:** The main symptom is a burning sensation of moderate to severe intensity,[10,22] commonly on the tongue, especially the sides and tip bilaterally.[5,18,20] However, any oral mucosa can be affected, with burning predominantly on the tongue, followed by the lips,[13,15] especially the lower lip.[5,6] The anterior portion of the hard palate, alveolar ridge and gingival tissue are also commonly affected, whereas the buccal mucosa and floor of the mouth are rarely involved.[5,22]

The symptoms tend to be chronic,[3] and multiple, such as pain and dysgeusia or pain and xerostomia, or pain alone.[7] Pain intensity can increase throughout the day as well as at times of tension, fatigue, excessive speaking and the ingestion of spicy and/or hot food, whereas cold foods, work and distraction offer some relief.[22]

The symptoms can persist for months or even years.[11,22] Patients with chronic BMS (more than six months) experience greater pain intensity and exhibit less favorable psychological characteristics in comparison to those with acute BMS (less than six months).[23] According to the International Association for the Study of Pain (IASP), half of patients exhibit spontaneous regression within six to seven years.[5]

BMS exerts a negative impact on quality of life, as demonstrated by patients responding to the Short-Form Health Survey (SF-36) and Oral Health Impact Profile (OHIP-49). Symptoms for more than three years and a high pain intensity score on the VAS are contributing factors to the high OHIP-49 score.[24]

c- Classification: Lamey et al.[25] proposed the following classification based on pain symptoms:
Type 1: Daily and progressive pain; the patient wakes up without symptoms and pain increases in severity throughout the day. This type is unrelated to psychiatric conditions and affects approximately 35% of patients. It may be associated with a systemic condition, such as a nutritional deficiency.
Type 2: Pain is constant day and night; this type affects 55% of patients, who have difficulty getting to sleeping and often present psychological disorders.
Type 3: Intermittent symptoms, with pain-free intervals as well as atypical location of pain (such as the floor of the mouth and posterior oropharynx); this type affects 10% of patients and there is a relationship between pain and the type of food ingested (preservatives and additives) and as well as allergens.

Scala et al.[7] proposed a different classification: **Primary or Essential/Idiopathic BMS**, in which the causes cannot be identified and there is an absence of clinical and laboratory signs, which is considered the true syndrome, and **Secondary BMS** resulting from local or systemic factors that cause a burning sensation.

True BMS is diagnosed by exclusion, with the absence of clinical and laboratory abnormalities.[1,17]

D- Diagnosis: The recognition of two distinct situations is needed for the diagnosis – one related to a burning sensation of the oral mucosa stemming from a systemic condition or local aggressor and one in which the symptoms have a close relationship with factors of an emotional nature, which is known as true BMS.[26,27] BMS generally presents a triad of symptoms: unremitting oral pain, altered sense of taste (dysgeusia) and dry mouth (xerostomia). However, these three symptoms are rarely found simultaneously in a single patient.[7]

Scala et al.[7] proposed the following criteria for the classification of BMS: daily intense burning sensation in some site of the oral mucosa bilaterally; persistence of burning sensation for at least four to six months; constant intensity or increase in intensity throughout the day; relief of the symptoms with certain foods and the ingestion of liquids; and no interference with sleep. Additional symptoms include dysgeusia and/or xerostomia, sensory or chemosensory alterations, mood swings and/or specific disruptions in personality traits. The altered sense of taste is most commonly bitter, metallic or both.[28] Xerostomia is related to true BMS,[1,14,22,29-31] with a change in salivary composition, but generally without hyposalivation.[5,13]

As burning mouth has a multifactor etiology, a careful clinical history, detailed general physical exams and a local examination of the mouth and oropharanyx are essential to avoiding errors regarding the diagnosis and treatment of BMS. The history of pain should be determined first, including duration, intensity using a pain scale, such as the VAS, sites and factors that alleviate or exacerbate the pain. An investigation should be made into harmful habits, vices (cigarettes and alcoholic beverages), diet, the use of antiseptic mouthwashes, type of toothpaste and denture use. The psychological history is extremely relevant and should include an investigation into anxiety, depression and cancerophobia; such patients should be sent to a psychiatrist.[22] The past medical history should involve information on a change in the sense of taste, xerostomia, current or past hypertension and diabetes and the use of medications with the potential to cause xerostomia.[22,32,34]

The physical exam should include palpation of the masticatory muscles, examination of the temporomandibular joint and examination of the hard and soft tissues of the oral cavity.[22,32-34] An oral examination involving an inspection of the oral mucosa and tongue should be performed to evaluate and rule out erythema, glossitis, atrophy of the lingual papillae, infections, benign migratory glossitis (geographic tongue), lichen planus and hyposalivation as well as the evaluation of dental status.[22]

Laboratory exams should include blood tests (complete blood count, glycemia, thyroid hormones such as TSH and T4 levels, levels of iron, ferritin, transferrin, vitamin B complex and folic acid), microbiological cultures, allergy tests, salivary tests and imaging tests, such as magnetic resonance and computed tomography, for the evaluation of diseases and systemic disorders.[22,32-34]

The different aspects related to a burning sensation in the mouth are divided into local, systemic and psychological factors.[3]

A- Local factors: (physical, chemical or biological) Physical factors are related to trauma or microtraumas in the mucosa and parafunctional habits, such as bruxism (grinding/clenching one's teeth) and the habit of pressing the tongue against the teeth.[1,14,22] Chemical factors may be related to allergic reactions to toothpaste, antiseptic mouthwash or the monomers in removable dentures as well as oral galvanism (electrochemical potential between different metals in the oral cavity).[1,22] Biological factors are related to oral infections, especially candidiasis.[1,17,29]

Dysgeusia (sometimes a metallic taste) has been described in BMS. The sense of taste is directly dependent on chemoreceptors of the taste buds on the dorsum of the tongue.[31] Cerchiari et al.[22] found that orthodontic appliances often cause a metallic taste in the mouth and the metal in the appliance can also cause an allergic reaction. Moreover, trauma to the buccal mucosa stemming from malocclusion can cause local pain and parafunctional habits should also be considered.

B- Systemic factors: Blood screening should be performed for vitamin deficiencies (vitamin B complex such as B6 and B12, vitamin C, folic acid), anemia (pernicious and iron deficiency) and low levels of zinc, iron and ferritin. Other aspects should also be investigated, such as hormonal conditions (hypoestrogenemia in climacterium, diabetes and hypothyroidism),[1,12,35] immunological diseases,[32] paraneoplastic syndrome,[1] and the use of antihypertensive drugs.[1,22,30,32] Xerostomia and/or hyposalivation may be associated with Sjögren's syndrome, anxiety or the use of medications.[1,22,30]

Diabetes mellitus (DM) has often been related to BMS.[1,12,35] However, studies comparing individuals with DM and BMS to those with DM alone have shown that the former group was predominantly female and presented peripheral neuropathy related to DM, denominated distal symmetric polyneuropathy, which was considered the cause of BMS in these patients.[35,36]

The side effects of some medications have been associated with the occurrence of burning mouth,[1,14,17,37] especially efavirenz, which is an antiretroviral agent used to fight HIV that can induce hyposalivation, affect one's appetite and alter the sense of taste.[22] Other medications can cause a burning sensation in the mouth, such as hormone replacement agents, antidepressants (fluoxetine, sertraline and venlafaxine), clonazepam, diuretics and, especially, antihypertensive drugs that act on the renin-angiotensin system, such as captopril and enalapril,[32] as well as lisinopril, eprosartan and candesartan.[32,37,38] Sulfonamides, antibiotics (cephalosporin, chloramphenicol, penicillin and gabapentin) and non-steroidal anti-inflammatory drugs can cause allergic reactions resulting in a burning sensation in the mouth.[22]

According to Silva et al.,[39] antidepressants and antihypertensive drugs are significantly associated with xerostomia ($p = 0.007$), but not hyposalivation ($p = 0.338$). However, the authors did not analyze the dosage of the medications, which is an important aspect to consider, as high doses of antidepressants cause hyposalivation.

C – Psychological factors: Many patients with BMS and symptoms of anxiety, depression and personality disorders have a tendency toward somatization and other psychiatric symptoms.[17] Indeed, the prevalence of psychiatric disorders is high among individuals with BMS and psychometric scales may be used to identify such disorders as well as evaluate the results of treatment.[40]

The psychogenic factors that can cause BMS include anxiety,[13] depression,[18] stress, difficult life events, personality disorders, cancerophobia and hypochondria.[1,6,14,29,35,41,42] Psychological elements, such as stress, anxiety or depression, play a significant role in BMS,[22,23,40,43] especially in postmenopausal women.[42]

Souza et al.[40] evaluated 30 patients with BMS and 30 controls who were submitted to a psychiatric evaluation that included a structured interview (MINI-Plus) and five psychometric scales. The results demonstrated that depression was the most frequent disorder, followed by generalized anxiety, hypochondria and cancerophobia. In the patients with BMS, anxiety disorder was significantly associated with depression and social phobia. Cancerophobia was significantly associated with hypochondria.

The causal relationship between anxiety and BMS has not yet been clarified. Some studies have emphasized this relationship, but most investigations have had a cross-sectional design, which does not allow establishing the evolutive sequence of symptoms of BMS associated with the triggering factor of anxiety.[40,44,45]

The patient history is useful to determining whether the burning sensation occurred before or after the change in psychological behavior.[40,44] Most patients with psychological elements, such as stress, anxiety or depression, seek treatment for sensations of severe pain or remain seriously concerned about their health.[44]

e- Etiopathogenesis: The pathophysiology of BMS is unclear, but may involve the interaction of local environmental factors, the peripheral nervous system, central nervous system and psychosocial factors.[19] The symptom of a burning sensation is common to different chronic conditions associated with neural damage. Chronic pain may be associated with changes in the sympathetic nervous system, leading to changes in blood flow. There is evidence of a possible association between neurological changes and etiological factors of BMS,

including neuropathy of small or large diameter fibers and an increase in the excitability of the trigeminal system, suggesting generalized abnormality, possibly on multiple levels, in the processing of somatosensory information in affected patients.[46] This neuropathic mechanism in the pathogenesis of BMS may be central or peripheral.[47]

Oral neuropathy and/or the interruption of neurological transduction caused by a change in the composition of saliva may trigger burning mouth. Hershkovich and Nagler,[48] evaluated patients with BMS and found no significant difference in comparison to the control group regarding salivary flow. However, mean IgG, IgM and albumin were respectively 3.9-fold, 5.7-fold and 7.8-fold higher in the patients with a burning sensation in comparison to the controls.

An immunohistochemical analysis of nerve fibers in a tongue biopsy revealed that patients with persistent BMS have sensory neuropathy of the small trigeminal fibers,[49] characterized by the significant loss of epithelial and subpapillary nerve fibers. Moreover, a reduction in the density of amyelinic nerve fibers in the epithelium and a diffuse disarrangement of axons have been reported. The density of epidermal nerve fibers was negatively associated with the duration of neuropathy, as nerve density was smaller with the increase in the duration of symptoms. Moreover, epithelial nerve fibers were found to be amyelinic, suggesting a function similar to that of polymodal nociceptors. These epithelial nerve fibers have synaptic interactions with the taste buds of fungiform papillae. Thus, the stimulation of these fibers may induce a burning sensation and affect one's sense of taste. This may explain why dysgeusia is a common symptom in BMS. Moreover, axonal degeneration may induce increased sensitivity of nerve fibers, which may account for the persistent hyperalgesia.[50]

Siviero et al.[51] found significant differences in all basic tastes (sweet: $p < 0.001$; salty: $p = 0.004$; sour: $p = 0.001$; and bitter: $p = 0.001$) in patients with BMS, who had higher salty, sweet and bitter thresholds, but lower sour thresholds. The neuropathic mechanisms underlying BMS involve the somatosensory, gustative and olfactory pathways, with abnormal interactions found in such patients.

BMS implies pathologies of the central and peripheral nervous systems induced by an alteration in the taste system on the level of the chorda tympani and/or glossopharyngeal nerve. This causes a loss of central inhibition and consequent hyperactivity of the trigeminal nociceptive pathway, which, in turn, has a more intense response to oral irritants and eventually leads to the appearance of phantom oral pain.[17] Maresky et al.[52] did not consider psychoneurological factors to be involved in the etiology of BMS, which the authors believe is a variant of atypical facial pain with an organic cause.

According to Felice et al.,[53] hypothyroidism may exert a negative influence on the sense of taste and consequent increase in tactile, thermal and pain sensations of the trigeminal nerve. According to Femiano et al.,[54] the treatment of hypothyroidism leads to an improvement in taste disorders and reduces the somatic-sensorial sensitivity of the trigeminal nerve (oral burning). Hypothyroidism may act as a negative factor to the maturation of fungiform papillae, with a reduction in taste, the release of inhibition in the somatic-sensorial sensitivity of the trigeminal nerve in subjects with a large number of taste buds and the subsequent emergence of oral burning.[55]

Minguez-Sanz et al.[33] proposed three hypotheses for the etiology of BMS. The first suggests the occurrence of neural inflammation mediated by a classic axonal reflex that activates a group of nociceptors, inducing these nociceptors to release neuropeptides near the ramus of the trigeminal nerve. The second hypothesis suggests the occurrence of an indirect reflex that develops in afferent nerves of the oral cavity, followed by processing at the central level of the trigeminal nerve and the induction of a response by the autonomous nervous system. The third hypothesis regards capsaicin receptors, which have efferent and sensory activities. These receptors are found in C-polymodal nociceptors, which may be implicated in the regulation of events associated with neurogenic inflammation and may be activated after received afferent signals and the simultaneous release of neuropeptides from the same nerve ending. Another theory is the complete or partial loss of function of the chorda tympani and consequent disinhibition of the trigeminal nerve, resulting in pain along this nerve.[56]

Dopamine receptors play a role in the etiopathogenesis of BMS. A decrease in endogenous dopamine and the dysregulation of dopaminergic receptors have been implicated as one of the physiopathological mechanisms of BMS.[7] The use of carbidopa/levodopa in the treatment of Parkinson's disease can cause burning mouth, with the resolution of this symptom following the replacement of the medication by a dopamine agonist.[57]

The treatment of BMS with amisulpride (antipsychotic), which is a selective dopamine antagonist, resulted in a significant improvement, with a reduction in pain intensity measure using the VAS and a fast response to treatment after two weeks of use as well as good tolerability and an absence of serious side effects other than insomnia, tremors and headache.[58]

Menopause is a physiological process that forms part of the events of climacterium, the basis of which are hormonal changes that can lead to the emergence of oral complications, including BMS.[36,59-61] It was found an improvement in the symptoms of BMS among women submitted to estradiol and estrogen replacement therapy, suggesting that a deficiency in these hormones may be a cause of oral symptoms in some postmenopausal women.

Indeed, estrogen receptors have been found in the epithelium of the oral mucosa in the majority of patients who exhibited positive results stemming from hormone replacement therapy as well as the absence of these receptors in those who did not benefit from this form of treatment.[62]

Problems of a psychological nature may play an important role in the etiopathogenesis of BMS, especially depression, anxiety, obsession, somatization, cancerophobia and hypochondria.[17,30,60,63,64] According to Moura et al.,[65] altered emotional states that affect the subjectivity of individuals with BMS are an important element to the emergence and persistence of the burning sensation. However, contrasting data suggest that BMS may be a symptom of these disorders or vice versa, as psychological problems may stem from the chronic pain found in BMS as well as the difficulty in finding adequate treatment and the uncertainty of the diagnosis.[1,64,66,67]

f- Treatment: A multidisciplinary team should be involved the treatment of such cases, as local and systemic factors may or may not act in synergy with psychiatric disorders stemming from the chronic symptoms,[7,26] as well as neurological changes, neuropathies and vitamin deficiencies induced by medications, which can lead to chronic neuropathy.[2,68,69]

The occurrence of local, systemic, psychogenic and neurogenic factors acting at times separately and at other times in a combined fashion hinders the establishment of an effective therapeutic protocol that can be used universally.[26,27] Thus, treatment continues to be empirical, and should be established based on the individual condition of each patient.[70] In many cases, the symptoms are only attenuated to a certain degree, without the complete remission of the condition.[71]

A reduction in anxiety may also be helpful at reducing the intensity of the pain.[45] Rivera-Campillo and López-López[11] found that improvement in most cases of burning mouth was related to the use of psychotherapy. Alternative treatments have been proposed, such as salivary substitutes, tongue protectors, acupuncture, homeopathic medicine, complementary vitamin diet and electroconvulsive therapy, but none has been proven to offer a satisfactory solution for BMS.[72]

Klasser et al.[41] found that treatment can generally be performed using three approaches (or combinations thereof): topical, such as clonazepam (benzodiazepine), lidocaine (anesthetic), capsaisin (analgesic), lactoperoxidase (antimicrobial) and sucralfate (mucosal protectant); systemic medications, such as clonazepam (benzodiazepine), gabapentin (anticonvulsant) and pilocarpine (salivary stimulant); and behavioral interventions (cognitive behavioral therapy, group psychotherapy and electroconvulsive therapy). One may also include the use of antidepressants, topical and systemic alpha lipoic acid (ALA) and hormone replacement therapy.[8,19,73]

ALA is a potent antioxidant with neuro-regenerative action that has a neuroprotective effect on the brain and nerve tissue and has been used in the treatment of patients with BMS, demonstrating varied effects. A controlled, double-blind, clinical trial proved the efficacy of this substance in comparison to a placebo, as a significant improvement in symptoms was found in the majority of individuals after six months of use and this improvement was maintained in up to 70% of patients after one year of follow up.[74] However, Cavalcanti and Silveira,[75] failed to demonstrate the efficacy of ALA, as similar reductions in symptoms occurred in both the ALA and placebo group. Carbone et al.[76] also found similar results. In contrast, López-D'alessandro and Escovich,[77] found that ALA, used either alone or in combination with gabapentin (anticonvulsant), was an effective form of treatment for BMS, leading to a reduction in symptoms and this reduction was even greater when the two drugs were combined.

Capsaicin is a substance extracted from chili peppers that has therapeutic effects on the central and peripheral nervous systems, with effective analgesic action on type C nerve fibers (primary afferent neurons) and has therefore has been used in topical and systemic form for the treatment of BMS.[73,78] Throughout treatment, this extract reduced and even eliminated circulating levels of substance P and other neurotransmitters, thereby desensitizing type C nociceptors and causing the alleviation of symptoms.[79]

Petruzzi et al.[79] found significant improvements with the systemic administration of capsaicin 0.25% for four weeks. However, substantial secondary gastrointestinal effects (stomach pain) threaten large-scale and long-term use. Such effects were not seen when topical administration was employed, which favors the long-term use of this form of the extract. According to Üçeyler and Sommer,[80] localized pain of a neuropathic origin could be treated with a capsaicin cream or salve at low doses, with good results achieved using concentrations ranging from 0.025 to 0.075%.

Benzodiazepines are also employed in the treatment of pain conditions. The most frequently used are chlordiazepoxide (Librium) and clonazepam,[18] both of which are agonists of the gamma-aminobutyric acid receptor that bind to both peripheral and central receptor sites, thereby inhibiting pain. Low doses of clonazepam led to a reduction in pain symptoms in 70% of patients with BMS. Due to the side effects with the administration of high doses, such as sleepiness and mood alterations, many patients interrupted treatment.[81] Topical clonazepam (Rivotril™) led to improvements in the majority of patients (61.7%), which indicates a peripheral neurological abnormality in patients with BMS.[11]

The treatment approach for BMS induced by psychological factors is controversial and involves both the control of the pain that affects the central nervous system and psychological counseling,[23] as it is very difficult for patients to accept psychological factors as the main triggering component of the burning sensation. Dentists should advise patients to accept the fact that psychogenic factors are associated with symptoms of BMS,[43] and send these patients to a psychiatrist.[22]

Final Remarks

BMS remains a challenge to healthcare professionals due to the complexity and variability of criteria used for the diagnosis as well as the lack of consensus regarding its classification and poor knowledge on the condition. Management should be multidisciplinary, involving a detailed clinical exam and the correct diagnosis of patients with burning mouth, whether or not such patients have the true syndrome. An appropriate, universally accepted definition with consistent criteria is needed to advance progress in the diagnosis and treatment of BMS.

REFERENCES

1. Brailo V, Vuéiaeeviae-Boras V, Alajbeg IZ, Alajbeg I, Lukenda J, Aeurkoviae M. Oral burning symptoms and burning mouth syndrome-significance of different variables in 150 patients. Med Oral Patol Oral Cir Bucal, 2006; 11: E252-255.
2. Nasri C, Teixeira MJ, Okada M, Formigoni G, Heir G, de Siqueira JTT. Burning mouth complaints: clinical characteristics of a brazilian sample. Clinics, 2007; 62: 561-566.
3. Aggarfal A, Panat SR. Burning mouth syndrome: A diagnostic and therapeutic dilemma. J Clin Exp Dent, 2012; 4(3): e180-5.
4. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (Beta version). Cephalalgia, 2013; 33: 629-808.
5. Merskey H, Bogduk N. Classification of chronic pain: descriptions of chronic pain syndromes and definitions of pain terms. In: Merskey H, Bogduk N. eds. Report of the IASP task force on taxonomy 2nd ed. Seatle: IASP Press, 1994: 209-214.
6. Cavalcanti DR, Birman EG, Migliari DA, da Silveira FR. Burning mouth syndrome: clinical profile of Brazilian patients and oral carriage of Candida species. Braz Dent J 2007; 18: 341-345.
7. Scala A, Checchi L, Montevecchi M, Marini I. Update on burning mouth syndrome: overview and patient management. Crit Rev Oral Biol Med, 2003; 14: 275-291.
8. Gurvits GE, Tan A. Burning mouth syndrome. World J Gastroenterol, 2013; 19: 665-672.
9. Brufau-Redondo C, Martín-Brufau R, Corbalán-Velez R, Concepción-Salesa A. Burning Mouth Syndrome. Actas Dermosifiliogr, 2008; 99: 431-440.
10. Silva LA, Siqueira JT, Teixeira MJ, de Siqueira SR. The role of xerostomia in burning mouth syndrome: a case-control study. Arq Neuropsiquiatr, 2014; 72: 91-98.
11. Rivera-Campillo ER, López-López J. evaluation of the response to treatment and clinical evolution in patients with burning mouth syndrome. Med Oral Patol Oral Cir Bucal, 2013; 18: e403-410.
12. Huang W, Rothe MJ, Grant-Kels JM. The burning mouth syndrome. J Am Acad Dermatol, 1996; 34: 91-98.
13. Amenábar JM, Pawlowski J, Hilgert JB, Hugo FN, Bandeira D, Lhüller F, et al. Anxiety and salivary cortisol levels in patients with burning mouth syndrome: a case-control study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod, 2008; 105: 460-465.
14. Jääskeläinen SK. Pathophysiology of primary burning mouth syndrome. Clin Neurophysiol, 2012; 123: 71-77.
15. Spanemberg JC, Dias AP, Barreiro BOB, Cherubini K, Figueiredo MAZ, Salum FG. Impact of burning mouth syndrome on quality of life. Rev Odonto Cienc, 2012; 27: 191-195.
16. Zakrzewska JM. Multi-dimensionality of chronic pain of the oral cavity and face. J Head Pain, 2013; 14: 37.
17. López-Jornet P, Camacho-Alonso F, Andujar-Mateos P, Sánchez-Siles M, Gómez-García F. Burning mouth syndrome: Update. Med Oral Patol Oral Cir Bucal, 2010; 15: 562-568.
18. Silvestre-Rangil J, Silvestre FJ, Tamarit-Santafé C, Bautista D. Burning mouth syndrome: correlation of treatment to clinical variables of the disease. Med Oral Patol Oral Cir Bucal, 2011; 16: e890-894.
19. Patton LL, Siegel MA, Benoliel R, De Laat A. Management of burning mouth syndrome: systematic review and management recommendations. Oral Surg Oral Med Oral Pathol Oral Radiol Endod, 2007; 103 Suppl: S39.e1-13.
20. Palacios-Sánchez MF, Jordana-Comín X, Garcia-Sívoli CE. Burning mouth syndrome: a retrospective study of 140 cases in a sample of catalan population. Med Oral Patol Oral Cir Bucal, 2005; 10: 388-393.
21. Silvestre FJ, Silvestre-Rangil J, Tamarit-Santafé C, Bautista D. Application of a capsaicin rinse in the treatment of burning mouth syndrome. Med Oral Patol Oral Cir Bucal, 2012; 17: e1-4.
22. Cerchiari DP, de Moricz RD, Sanjar FA, Rapoport PB, Moretti G, Guerra MM. Burning mouth syndrome: etiology. Braz J Otorhinolaryngol, 2006; 72: 419-423.
23. Komiyama O, Obara R, Uchida T, Nishimura H, Iida T, Okubo M, Shimosaka M, Narita N, Niwa H, Shinoda M, Kobayashi M, Noma N, Abe O, Makiyama Y, Hirayama T, Kawara M. Pain intensity and psychosocial characteristics of patients with burning mouth syndrome. J Oral Sci., 2012; 54: 321-327.
24. Souza FT, Santos TP, Bernardes VF, Teixeira AL, Kümmer AM, Silva TA, Abreu MH. The impact of

burning mouth syndrome on health-related quality of life. Health Qual Life Out, 2011; 9: 57.
25. Lamey PJ, Lamb AB, Hughes A, Miligan KA, Forsyth A. Type 3 burning mouth syndrome: psychological and allergic aspects. J Oral Pathol Med, 1994; 23: 216-219.
26. Paterson AJ, Lamb AB, Clifford TJ, Lamey PJ. Burning mouth syndrome: the relationship between the HAD scale and parafunctional habits. J Oral Pathol Med, 1995; 24: 289-292.
27. Botha PJ, van der Bijl P,van Eyk AD. A literature review and pilot study to characterise the treatment of burning mouth syndrome. SADJ, 2001; 56: 353-358.
28. Ship JA, Grushka M, Lipton JA, Mott AE, Sessle BJ, Dionne RA. Burning mouth syndrome: an update. J Am Dent Assoc, 1995; 126: 842-853.
29. Cibirka RM, Nelson SK, Lefebvre CA. Burning mouth syndrome: a review of etiologies. J Prosthet Dent, 1997; 78: 93-97.
30. Regezi JA, Sciubba JJ, Jordan RCK. Oral Pathology: Clinical Pathologic Correlations. 6th ed. St Louis: Elsevier Saunders, 2012.
31. Camacho-Alonso F, López-Jornet P, Molino-Pagán D. Fungiform papillae density in patients with burning mouth syndrome and xerostomia. Med Oral Patol Oral Cir Bucal, 2012; 17: e362-e366.
32. Salort-Llorca C, Mínguez-Serra MP, Silvestre FJ. Drug-induced burning mouth syndrome: a new etiological diagnosis. Med Oral Patol Oral Cir Bucal, 2008; 13: 167-170.
33. Minguez-Sanz MP, Salort-Lorca C, Silvestre-Donat FJ. Etiology of burning mouth syndrome: a review and update. Med Oral Patol Oral Cir Bucal, 2011; 16: e144-148.
34. Dahiya P, Kamal R, Kumar M, Niti, Gupta R, Chaudhary K. Burning mouth syndrome and menopause. Int J Prev Med, 2013; 4: 15-20.
35. Moore PA, Guggenheimer J, Orchard T. Burning mouth syndrome and peripheral neuropathy in patients with type 1 diabetes mellitus. J Diabetes Complic, 2007; 21: 397-402.
36. Meurman JH, Tarkkila L, Tiitinen A. The menopause and oral health. Maturitas, 2009; 63: 56-62.
37. Giudice M. Mouths on fire. Drug-induced burning mouth syndrome. Can Pharm J, 2008; 141: 132-134.
38. Soares MSM, Küstner EC, Pifarrè CS, Campillo MERR, López JP. Association of burning mouth syndrome with xerostomia and medicines. Med Oral Patol Oral Cir Bucal, 2005; 10: 301-308.
39. Silva LA, Teixeira MJ, Siqueira JTT, Siqueira SRDT. Xerostomia and salivary flow in patients with orofacial pain compared with controls. Arch Oral Biol, 2011; 56: 1142-1147.
40. Souza FT, Teixeira AL, Amaral TM, dos Santos TP, Abreu MH, Silva TA, Kummer A. Psychiatric disorders in burning mouth syndrome. J Psychosom Res., 2012; 72: 142-146.
41. Klasser GD, Epstein JB, Villines D. Management of burning mouth syndrome. J Can Dent Assoc, 2011; 77: b151.
42. Malik R, Goel S, Misra D, Panjwani S, Misra A. Assessment of anxiety and depression in patients with burning mouth syndrome: a clinical trial. J Mid-life Health, 2012; 3: 36-39.
43. Gupta D, Sheikh S, Pallagatti S, Kasariya K, Buttan A, Gupta M. Burning mouth syndrome due to television moans, an enigma for oral physician: treatment with counseling. J Dent Res Dent Clin Dent Prospects, 2014; 8: 118-122.
44. Bakhtiari S, Khalighi HR, Azimi S, Alavi K, Ayoobi Valoogerdi H, Namazi Z. Correlation between burning mouth syndrome and anxiety in the elderly inmates of Sanitaria in Tehran. J Dent Res Dent Clin Dent Prospects, 2010; 4: 37-41.
45. Komiyama O, Nishimura H, Makiyama Y, Iida T, Obara R, Shinoda M. Group cognitive-behavioral intervention for patients with burning mouth syndrome. J Oral Sci, 2013; 55: 17-22.
46. Forssell H, Jääskeläinen S, Tenovuo O, Hinkka S. Sensory dysfunction in burning mouth syndrome. Pain, 2002; 99: 41-47.
47. Marino R., Torretta S, Capaccio P, Pignataro L, Spadari F. Different therapeutic strategies for burning mouth syndrome: preliminary data. J Oral Pathol Med, 2010; 39: 611–616.
48. Hershkovich O, Nagler RM. Biochemical analysis of saliva and taste acuity evaluation in patients with burning mouth syndrome, xerostomia and/or gustatory disturbances Arch Oral Biol, 2004; 49: 515-522.
49. Dutt P, Chaudhary S, Kumar P. Oral health and menopause: a comprehensive review on current knowledge and associated dental management. Ann Med Health Sci Res., 2013; 3: 320-323.
50. Lauria G, Majorana A, Borgna M. Trigeminal small-fiber sensory neuropathy causes burning mouth syndrome. Pain., 2005; 115: 332-337.
51. Siviero M, Teixeira MJ, Siqueira JT, Siqueira SRDT. Central mechanisms in burning mouth syndrome involving the olfactory nerve: a preliminary study. Clinics, 2011; 66: 509-512.
52. Maresky LS, van der Bijl P, Gird I. Burning mouth síndrome: evaluation of multiple variables among 85 patients. Oral Surg Oral Med Oral Pathol, 1993; 75: 303-337.
53. Felice F, Gombos F, Esposito V, Nunziata M, Scully C. Burning mouth syndrome (BMS): evaluation and thyroid and taste. Med Oral Patol Oral Cir Bucal, 2006; 11: E22-25.
54. Femiano F, Lanza A, Buonaiuto C, Gombos F, Nunziata M, Cuccurullo L, Cirillo N. Burning mouth syndrome and burning mouth in hypothyroidism: proposal for a diagnostic and therapeutic protocol. Oral Surg Oral Med Oral Pathol, 2008; 105: e22-27.
55. Bergdahl M, Bergdahl J. Burning mouth syndrome: prevalence and associated factors. J Oral Pathol Med, 1999; 28: 350-354.

56. Gruska M, Epstein JB, Gorsky M. Burning mouth syndrome and other oral sensory disorders: a unifiying hypothesis. Pain Res Manag, 2003; 8:133-135.
57. Coon EA, Laughlin RS. Burning mouth syndrome in Parkinson's disease: dopamine as cure or cause? J Head Pain, 2012; 13: 255-257.
58. Rodriguez-Cerdeira C, Sanchez-Blanco E. Treatment of burning mouth syndrome with amisulpride. J Clin Med Res, 2012; 4: 167-171.
59. Zakrzewska JM. Differential diagnosis of facial pain and guidelines for management. Br J Anaesth, 2013; 111: 95-104.
60. Lamey PJ, Freeman R, Eddie SA. Pankhurst C, Rees T. Vulnerability and presenting symptoms in burning mouth syndrome. Oral Surg Oral Med Oral Pathol Oral Radiol Endod, 2005; 99: 48-54.
61. Mott AE, Grushka M, Sessle BJ. Diagnosis and management of taste disorders and burning mouth syndrome. Dent Clin North Am, 1993; 37: 33-71.
62. Forabosco A, Criscuolo M, Coukos G, Uccelli E, Weinstein R, Spinato S, Botticelli A, Volpe A. Efficacy of hormone replacement therapy in postmenopausal women with oral discomfort. Oral Surg Oral Med Oral Pathol, 1992; 73: 570-574.
63. Torgerson RR. Burning mouth syndrome. Dermatol Ther, 2010; 23: 291-298.
64. Abetz LM, Savage NW. Burning mouth syndrome and psychological disorders. Aust Dent J, 2009; 54: 84-93.
65. Moura SAB, Medeiros AMC, Leite JF, Dimenstein M, Costa LJ. Aspectos Psicogênicos da Síndrome do Ardor Bucal. Rev Bras Ciê Saúde, 2008; 12: 217-228.
66. Rojo L, Silvestre FJ, Bagan JV, De Vicente T. Prevalence of psychopathology in burning mouth syndrome. Oral Surg Oral Med Oral Pathol, 1994; 78: 312-316.
67. Bergdahl J, Aanneroth G, Perris H. Cognitive therapy in the treatment of patients with resistant burning mouth syndrome: a controlled study. J Oral Pathol Med, 1995; 24: 213-215.
68. Gleber Netto FO, Alves Diniz IM, Grossmann SMC, Vieira do Carmo MA, Ferreira de Aguiar MC. Burning mouth syndrome: clinical characteristics, etiological factors and treatment. (In Portuguese) Rev Cubana Estomatol, 2010; 47: 417-427.
69. Maltsman-Tseikhin A, Moricca P, Niv D. Burning mouth syndrome: will better understanding yield better management? Pain Pract, 2007; 7: 151-162.
70. Sardella A, Gualerzi A, Lodi G, Sforza C, Carrassi A, Donetti E. Morphological evaluation of tongue mucosa in burning mouth syndrome. Arch Oral Biol, 2012; 57: 94-101.
71. Serra MPM, Llorca CS, Donat FJS. Pharmacological treatment of burning mouth syndrome: A review and update. Med Oral Patol Oral Cir Bucal, 2007; 12: E299-304.
72. Azzi L, Costantino D, Tettamanti L, Tagliabue A, Spadari F. management of burning mouth syndrome: a clinical experience. Ann Stomatol, 2013; suppl 2: 6-7.
73. Sun A, Wu KM, Wang YP, Lin HP, Chen HM, Chiang CP. Burning mouth syndrome: a review and update. J Oral Pathol Med, 2013; 42: 649-655.
74. Femiano F, Scully C. Burning mouth syndrome (BMS): double blind controlled study of alpha-lipoic acid (thiocticacid) therapy. J Oral Pathol Med, 2002; 31: 267-269.
75. Cavalcanti DR, da Silveira FR. Alpha lipoic acid in burning mouth syndrome--a randomized double-blind placebo controlled trial. J Oral Pathol Med, 2009; 38: 254-261.
76. Carbone M, Pentenero M, Carrozzo M, Ippolito A, Gandolfo S., Lack of efficacy of alpha-lipoic acid in burning mouth syndrome: A double-blind, randomized, placebo-controlled study. Eur J Pain, 2009; 13: 492-496.
77. López-D'alessandro E, Escovich L. Combination of alpha lipoic acid and gabapentin, its efficacy in the treatment of Burning Mouth Syndrome: A randomized, double-blind, placebo controlled trial. Med Oral Patol Oral Cir Bucal, 2011; 16: e635-640.
78. Morais M, Bezerra BAA, Rocha Neto PC, Soares ACO, Pinto LP, Costa ALL. Randomized trials for the treatment of burning mouth syndrome: an evidence-based review of the literature. J Oral Pathol Med, 2012; 41: 281-287.
79. Petruzzi M, Lauritano D, De Benedittis M, Baldoni M, Serpico R. Systemic capsaicin for burning mouth syndrome: short-term results of a pilot study. J Oral Pathol Med, 2004; 33: 111-114.
80. Üçeyler N, Sommer C. High-Dose capsaicin for the treatment of neuropathic pain: what we know and what we need to know. Pain Ther, 2014 Jul 29. [Epub ahead of print].
81. Grushka M, Epstein J, Mott A. An open-label, dose escalation pilot study of the effect of clonazepam in burning mouth syndrome. Oral Surg Oral Med Oral Pathol Oral Radiol Endod, 1998; 61: 557-561.