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Burning mouth syndrome: Update

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Abstract

Burning mouth syndrome (BMS) refers to chronic orofacial pain, unaccompanied by mucosal lesions or other evident clinical signs. It is observed principally in middle-aged patients and postmenopausal women. BMS is characterized by an intense burning or stinging sensation, preferably on the tongue or in other areas of the oral mucosa. It can be accompanied by other sensory disorders such as dry mouth or taste alterations. Probably of multifactorial origin, and often idiopathic, with a still unknown etiopathogenesis in which local, systemic and psychological factors are implicated. Currently there is no consensus on the diagnosis and classification of BMS. This study reviews the literature on this syndrome, with special reference to the etiological factors that may be involved and the clinical aspects they present. The diagnostic criteria that should be followed and the therapeutic management are discussed with reference to the most recent studies.

Key words: *Glossodynia, stomatodynia, etiopathogenesis, treatment, review.*

Introduction

Burning Mouth Syndrome (BMS), is condition characterized by a sensation described by the patient as stinging, burning that affects the oral mucosa, in the absence of clinical or laboratory data to justify these symptoms. It as a chronic orofacial pain, unaccompanied by mucosal lesions or other evident clinical signs upon examination (1-12). The International Association for the study of Pain defines it as a pain of at least 4-6 months duration located on the tongue or other mucosal membranes in the absence of clinical or laboratory findings. It has been defined principally by the quality or location of the pain. The most affected area is the tongue (tip and

lateral borders), thus denominated 'glossodynia' (painful tongue) and glossopyrosis (burning tongue) and glossalgia; other terms used are stomatodynia, stomatopyrosis, oral dysesthesia and burning mouth syndrome. The frequent association with other symptoms (xerostomia, taste alterations) and the complexity surrounding the condition of the patient means that some authors prefer to use the expression 'burning mouth syndrome' (BMS) to refer to this entity. It is characterized by being continuous and spontaneous with an intense burning sensation reported by the patient as if the mouth or tongue were 'scalded or burnt' (7).

Various groups of investigators have attempted to pro-

vide an answer to the questions regarding this topic, which is the subject of considerable controversy. The multiplicity of factors related with this nosologic entity, which in one form or another are involved in the appearance of the symptoms have made it currently one of the most debated issues (4, 7-17).

Epidemiology

The true prevalence of BMS is difficult to establish due to the lack of rigorous diagnostic criteria in many of the published series that do not distinguish between the symptom of oral burning and the syndrome itself, including BMS as only a symptom of other diseases. Thus, figures vary widely, with prevalence varying between 0.7 and 4.5% (6-11).

Bergdahl and Bergdahl (5) carried out a randomized study in Sweden using a questionnaire on a group of 1427 (669 men and 758 women) aged between 20 and 69 years. All individuals who reported burning mouth were examined, finding that 53 patients (3.7%) presented BMS, 11 men (1.6%) and 42 women (5.5%). In the men, BMS was not found in the groups aged 20-39 years, while the prevalence in the group aged 40-49 years was 0.7%, increasing to 3.6% in the group of 60-69 year-olds. In the women, it did not appear in the group 20-29 years of age, in the group 30-39 years the prevalence was 0.6%, increasing to 12.2% in the strata of 60-69 years. In general, the condition principally affects women, with a relationship of approximately 3:1, these differences between gender may perhaps be explained by biological, psychological and sociocultural factors, however such factors have not yet been defined. This syndrome is rare in patients under 30 years, never having been described in children or adolescents. No studies exist in relation to any occupational, educational or social grouping.

Classification and Subtypes

Different classification types have been proposed based on the daily fluctuations of the symptoms (7, 12-13).

- a) Type 1: characterized by progressive pain, patients wake up without pain, which then increases throughout the day, affects approximately 35% of patients. This type may be associated with systemic diseases, such as nutritional deficiencies.
- b) Type 2: the symptoms are constant throughout the day and patients find it difficult to get to sleep, represents 55%. These patients usually present associated psychological disorders.
- c) Type 3: symptoms are intermittent, with atypical location and pain. Constitutes 10% of patients. It seems that contact with oral allergens could play an important etiologic role in this group.

A more pragmatic approach is proposed by Scala et al. (4), who organize BMS into two clinical forms, 'pri-

mary' or essential/idiopathic BMS, in which the causes cannot be identified, and 'secondary' BMS, resulting from local factors or systemic conditions. Thus, these idiopathic and secondary criteria form two different subgroups of the same pathology.

Danhauer et al. (12) examined 69 patients with BMS (83% women) with a mean age of 62 years, and a mean duration of pain of 2.45 years; the mean pain measured on a visual analogue was 49 mm (on a scale of 0-100 mm). The investigators found no differences between patients with primary or secondary BMS with respect to age, duration or intensity of pain and psychological profile. Differences with respect to treatment were found, secondary BMS improved with treatment, while no positive results were found in the group with primary BMS.

Etiopathogenesis

The various factors related with the etiopathogenesis of this syndrome have been divided into local, systemic and psychological. Frequently several factors coincide, increasing the harmful effect on the mucosa, whether perceptible or not by the observer (4-17).

Local factors

We should consider those factors which have in common a direct irritant effect on the oral mucosa, these maybe either physical, chemical or biological (some bacteria or fungi), and are able to set off the burning symptoms (7) (Fig. 1).

A mechanical factor to consider is the use of poorly-fitting prostheses that produce microtrauma or local erythema. These can also restrict the normal action of the muscles of the tongue. Parafunctional habits such as tongue thrust or certain 'tics', continual rubbing over the teeth or prosthesis; buccal, labial, lingual biting, and compulsive movements of the tongue etc. should be assessed. Local allergic reactions, due principally to high levels of residual monomers; other allergens are nylon, ascorbic acid, nicotinic acid esters, benzoic peroxide, 4-tolyl diethanolamine, N-dimethyl toluidine, nickel sulfate, etc., not to mention certain additives. In fact, some authors have reported allergic reactions, with positive epicutaneous tests in patients with BMS without evident mucosal lesions who have recovered on eliminating contact with the allergen. It may be questionable if these patients with symptoms of burning mouth and clinically relevant positive epicutaneous tests should be classified as BMS or as a subclinical contact dermatitis. In any case, these findings are useful for the diagnosis and treatment of the subgroup of patients with intermittent symptoms.

Oral infections produced by diverse microorganisms have been associated with this syndrome. Infection by *Candida albicans* has been considered one of the most frequent factors in the production of BMS, although

Local factors	Systemic factors	Psychological factors	Idiopathic factors
Poorly fitting prostheses Parafunctional habits Dental anomalies Allergic reactions Infection Chemical factors Galvanism Taste alterations Xerostomia	Endocrine alterations: (hypothyroidism, diabetes, menopause) Deficiencies (Fe, vit B complex, zinc) Anemia Gastrointestinal anomalies Medication Neuropathy Sjögren's syndrome Esophageal reflux	Anxiety Depression Compulsive disorders Psychosocial stress Cancerphobia	

Fig. 1. Most frequent etiopathogenic factors in burning mouth syndrome.

some authors question its importance. Other oral infections caused by bacteria such as Enterobacter, Klebsiella and S. Aureus have been found with high frequency in patients with burning mouth. Helicobacter pylori has also been isolated through oral mucosa biopsies and molecular biology techniques in 86% of patients with burning sensation and lingual hyperplasia and halitosis, while it is detected in only 2.6% of the patients without oral symptoms.

Xerostomia is a concomitant symptom in patients with BMS, prevalence varying between 34 and 39% (7,8), while Grushka et al. (13) find that this is equal to or greater than 60%. In contrast, some authors consider that the composition of the saliva could play a major role in the pathogenesis of BMS, indicating the importance of the identification and characterization of low molecular weight proteins. A significant increase has been found in levels of sodium, total protein, lysozyme, amylase and immunoglobulins in patients with BMS when compared with a control group; however, other studies do not support these findings.

In recent years investigations have been carried out into the alterations in taste perception and tolerance to pain as a possible cause of the burning sensation. Taste is located fundamentally on the fungiform papillae, finding in certain patients with burning mouth, above all women, an elevated number of said papillae, these individuals being denominated 'supertasters'. This theory proposes that certain people, labeled as supertasters due to the high density of fungiform papillae present on the anterior part of the tongue, are more susceptible to developing burning mouth pain. Supertasters are principally women, and are able to perceive the bitter taste of a substance called PROP (6-n-propiltiouracilo) (4-8).

Systemic factors

Systemic factors implicated in BMS; many of these are deficiencies, such as vitamin deficiencies (in particular low levels of vitamin B12, and others such as vitamin B6, folic acid and vitamin C), and anemias. Furthermore, some studies suggest that BMS is associated with low serum levels of zinc. Hormonal changes (reduced plasma estrogens), diabetes mellitus, thyroid dysfunction (hypothyroidism) and immunological diseases have also been described. Many medications are intimately related with burning mouth; among which are found antihistamines, neuroleptics, some antihypertensives, antiarrhythmics and benzodiazepines. Antihypertensives are among the most frequently implicated medicines, principally those that act on the renin-angiotensin system (captopril, enalapril and lisinopril).

Psychological factors

Studies exist that suggest that psychopathologic factors may play an important role in BMS and support the multifactorial etiology, in which physical changes may interact with psychological factors (1,7,14).

Many of these patients have symptoms of anxiety, depression and personality disorders, and it has been demonstrated that patients with burning mouth syndrome have a greater tendency towards somatization and other psychiatric symptoms.

Cancerphobia can be present in up to 20-30% of these patients. A lower level of socialization and higher levels of somatic anxiety have been observed, as well as muscular tension, a higher tendency to worry about health and greater sadness. BMS is considered a chronic pain disorder that adversely affects quality of life (8,15).

Pathogenesis

An increasing number of investigations are being made into a possible underlying neurological disorder. Neurophysiological studies suggest that the central and/or peripheral nervous system are implicated in the pain of BMS (4,8,9,13).

The presence of taste anomalies, and the fact that many with BMS are supertasters, suggests an interaction between the taste and nociceptive mechanisms that would connect the sense of taste and oral pain in the central nervous system, and indicates that BMS implies pathologies of the central and peripheral nervous system induced by an alteration in the taste system at the level of the chorda tympani and/or the glossopharyngeal nerve. This causes a loss of central inhibition and consequently hyperactivity of the trigeminal nociceptive pathway, which in turn carries a more intense response to oral irritants and eventually leads to the appearance of phantom oral pain as a result of this alteration in the taste system.

Findings in patients with BMS (8):

1. Reduction in thermal sensation and low scores for tonic painful stimuli in the oral cavity, similar to that observed in areas with poli or mononeuropathies.
2. Reduction in tolerance to pain caused by heat at the tip of the tongue in 85% of patients with BMS.
3. Anomalies in the blink reflex in patients with BMS, possibly indicating a subclinical trigeminal neuropathy.
4. Alterations in saliva composition with respect to a control group, this directly influences the perception of flavours.

A lower density of epithelial and subpapillary nerve fibres has been found in biopsies of the tongue in patients with BMS with respect to controls, reflecting axonal degeneration, BMS being caused by a sensorial neuropathy of the small trigeminal fibres.

Central neuropathic mechanisms have been demonstrated following thermal stimulation of the trigeminal nerve in patients with BMS. Patients with BMS show patterns of cerebral activity similar to those that appear in other neuropathic pain disorders, suggesting that the cerebral hypoactivity could be an important element in the pathogenesis of BMS.

Clinical Aspects

The symptoms have been described as continuous chronic discomfort, with spontaneous acute periods, with no clearly identifiable precipitating factor, except stress and other psychological factors. The pain is primarily bilateral and symmetrical on the anterior two-thirds of the tongue (71% - 78%), followed by the dorsum and lateral borders of the tongue, the anterior part of the hard palate, the labial mucosa and gingiva, often appearing at several locations. Other, less frequent loca-

tions are the oral mucosa, floor of the mouth, soft and hard palate, and oropharynx. The location of the pain does not seem to affect the course of the disease or the response to treatment. In more than half the patients the symptoms appear spontaneously with no identifiable trigger factors. Approximately 17% to 33% of patients attribute the initiation of the symptoms to a previous condition, such as infection of the upper respiratory airway, dental procedure, or the use of medications. Other patients relate the appearance of symptoms directly with stress (7,9).

The oral burning sensation usually increases progressively during the day, reaching a maximum intensity at the end of the afternoon / early evening, pain being absent during the night in the majority of patients. Patients do not normally awaken during the night, but do find it difficult to get to sleep. These patients often present mood changes, including irritability, anxiety and depression. The majority of studies describe the coexistence of oral burning with other symptoms, such as dry mouth, dysgeusias, metallic taste, bitter taste or combinations thereof, and/or changes in intensity of taste perception. In addition, dysphagia and atypical facial or dental pain may appear. Experience shows that what the patient defines as ‘oral burning’ can be identified by diverse sensations. Although the burning or stinging sensation can exist alone, other disorders of oral perception may appear, either alternatively or simultaneously, such as pruritus, roughness, ‘sticky sensation’, dysphagia, stinging, burning, irritation of the lingual papillae, metallic taste and other dysgeusias, sensation of bad breath, intolerance to prostheses that would include an infinity of subjective perceptions difficult to describe (Table 1).

Table 1. Clinical factors Burning Mouth Syndrome (7,10).

Pain	
Description	Burning
Intensity	Variable, with peaks of intensity
Pattern	Continuous, no paroxysm
Location	Independent of nerve pathway. Frequently bilateral and symmetric
Pain during sleep	Infrequent
Other symptoms	Dysgeusia and xerostomia
Signs /symptoms	Absence of evident clinical signs Sensory / Chemosensory disorders Psychological profile may be implicated

The profile of a patient with burning mouth syndrome is that of a woman in late middle age or advancing years, postmenopausal in the majority of cases, presenting emotional disorders, or at least having a strong psychological component in their symptoms. Apart from their oral sensations, patients can present a series of concomitant symptoms such as frequent headaches, weakness, lower capacity for concentration, insomnia, and almost always manifest non-specific health problems (7,8). Over the natural course of burning mouth syndrome, from among the scant information available, the symptoms occur continuously for months or years with no periods of suspension or remission, in some studies over a mean of around two to three years. Some studies have reported complete or partial remission (with or without intervention) in approximately 50% of patients and complete spontaneous remission in approximately 20% of the patients within six to seven years of the start of the symptoms. The remission of the symptoms, whether partial or complete, is often characterized by a change in the pattern of the pain from a constant to sporadic nature. In contrast, Sardella et al. (17), find complete spontaneous remission in only 3% of the patients after five years of follow-up.

Diagnosis

It is important to emphasize that a diagnosis of BMS should only be established after all other possible causes have been discarded, there are no specific diagnostic tests, thus, the diagnosis is made in the absence of vi-

sible oral lesions, and is therefore a diagnosis of exclusion of other possible diseases. Other systemic diseases that can manifest symptoms similar to BMS should be considered: Sjögren’s syndrome, diabetes, candidiasis, deficiencies of iron, folate, zinc or group B. vitamins. It is essential to obtain the medical, dental and psychological history of the patients; also to quantify the pain on a visual analogue scale and to note the symptoms, duration, location and chronology and temporal relationship (burning/pain), if accompanied by xerostomia and taste alteration, if alleviated or aggravated by foods, and any precipitating factors. Special attention should be paid to the use of medication that can produce xerostomia, the presence of parafunctional habits, and the clinical history should provide information on prior or current psychological and psychosocial stress factors (4,7,16). An oral and extraoral examination should be made to discard lesions such as erythema, erosions, depapillated tongue. The oral cavity should not present any anomalies such as inflammation or atrophy of the mucosa in order to establish a diagnosis of BMS.

Possible dental problems should be ruled out, reviewing any prostheses and their occlusion, any probable oral galvanism and volumetric tests of saliva flow should be made (Table 2).

Complimentary examinations include analytical studies, hemogram, glucoemia, iron, serumal ferritin, folates, vitamin B12, zinc, serumal antibodies in Sjögren’s syndrome and against H. pylori; culture for the detection of candida, taken from the oral mucosa and palate.

Table 2. Diagnosis and treatment of burning mouth syndrome (4,7,18-20).

Oral examination	Salivary Parameters	Hematologic Parameters	Nutritional Parameters	Hormonal Parameters	Medication	Parafunc-tional Habits	Contact Allergies	Psychologi-cal Psycho-social evaluation
Treatment of secondary forms: monitor infection candida albicans, manage medication (antihypertensives renin-angiotensin system), treat xerostomia, allergies, nutritional deficiencies, endocrine disorders								
<p>Topical treatment</p> <ul style="list-style-type: none"> • Clonazepam • Lidocaine • Capsaicin • Benzydamine hydrochlorate at 0.15% <p>Systemic treatment:</p> <ul style="list-style-type: none"> • Nortriptyline • Amitriptyline • Paroxetine • Clonazepam • Gabapentin • Capsaicin • Alfa lipoic acid • Cognitive therapy 								

Epicutaneous tests are made on patients presenting intermittent symptoms (metals and other allergens used in dental prostheses, foods, additives).

The diagnosis is usually late (mean 34 months), often due to a lack of understanding of the nature of this entity, in addition to the patients taking up many health resources, since they frequently consult various specialists. It is important to highlight that the diagnosis of BMS should be established only when all other possible causes have been discounted, being a diagnosis by elimination.

Treatment

Treatment should be adapted to each patient, where a multidisciplinary approach is recommended. Initially the clinician should determine whether the symptom is primary (essential or idiopathic) or secondary BMS, in which the symptoms are attributable to other causes, candidiasis, vitamin deficiencies, galvanic allergies; parafunctional habits should be examined; substitution therapies should be established (in cases of vitamin and mineral deficiencies). Many of these patients take medication (principally antihypertensives which act on the renin-angiotensin system), which should be monitored. It is essential to study and understand the physiopathologic mechanisms of stomatodynia with the aim of selecting treatment. The wide range of treatments used reflects the current situation, the majority of treatments are directed towards suspected causal factors, but these are often unsupported by controlled studies (7,8,10, 18-20).

The most-used medications to treat this syndrome are antidepressants, antipsychotics, antiepileptics, analgesics and oral mucosa protectors. The tricyclic antidepressants such as amitriptyline and nortriptyline at low doses are useful in BMS, although some authors contraindicate their use in patients with dry mouth as they can worsen the condition.

Studies have been made to evaluate the efficacy and tolerance of amisulpiride (50 mg/day) and selective serotonin inhibitors: paroxetine (20 mg/day) and sertraline (50 mg/day) in the treatment of BMS, over eight weeks, with a reasonably high efficacy (around 70%). However, the effect of amisulpiride manifests early, after one week of treatment. No serious adverse effects are referred in any of the three groups. Serotonin reuptake inhibitors are effective, above all with an associated depression, being better tolerated for the absence of anti-cholinergic effects, particularly in dry mouth.

According to the results obtained with gabapentin, it seems to have little or no effect in patients with BMS. The medication was administered at an initial dose of 300 mg/day, increasing by 300 mg/day every two days to a maximum of 2,400 mg/day.

The efficacy of oral clonazepam (0.25 mg/day increa-

sing to a maximum of 3 mg/day) has also been evaluated with variable results, or by topical application (0.5 mg to 1 mg two or three times a day) with better results.

Topical capsaicin has also been applied in BMS, used as a desensitizing agent in patients with BMS, but it is usually unaccepted by patients due to its taste. Systemic capsaicin has been used (0.25%, three times a day, for 30 days) with a significant reduction in pain intensity compared with a placebo group. However, its use is not recommended for extended treatment, since 32% of patients experience gastric pain after four weeks of treatment.

Trials have also been made on rinsing with benzydamine hydrochloride at 0.15%, having an analgesic and anti-inflammatory effect, but finding no significant efficacy, as also found with local anesthetic mouthwash such as lidocaine, which have not been demonstrated as an effective treatment due to the short duration of the analgesic effect.

Hormone replacement therapy (HRT) has also been used, finding that women with symptoms of burning and estrogen receptors in the oral mucosa respond to hormone replacement, while this does not occur in patients without these receptors; however it cannot be guaranteed that HRT could be an effective treatment for the oral symptomatology.

Alpha lipoic acid is a powerful neuroprotector that prevents damage to nerve cells by free radicals, it regenerates other antioxidants such as vitamins C and E, increasing levels of intracellular glutathione. Thanks to its antioxidant properties it significantly reduces the symptoms in the majority of patients with idiopathic dysgeusia and reduces the symptoms of peripheral neuropathy in diabetics. Several studies suggest that alpha lipoic acid can improve the symptoms in BMS, showing that at two months, 97% of the patients treated with alpha lipoic acid (200 mg, three times a day) experienced an improvement in the symptoms. This improvement is maintained during the first year in 70% of the patients. In other studies, the combination of psychotherapy (2 one-hour sessions weekly for two months) and alpha lipoic acid (600 mg/day for two months), was significantly more beneficial than psychoanalysis alone or alpha lipoic acid alone. The results suggest that alpha lipoic acid could complement psychotherapy and be an acceptable alternative to psychoactive medication. However, in studies that compare with a placebo the efficacy is limited (20).

The complex and multifactorial etiology of BMS necessitates collaboration between different specialists for the management of these patients. In addition, it is necessary to carry out trials with a strict agreement on protocols (inclusion/exclusion of patients should be based on clear diagnostic criteria, that exclude those cases with a medical or dental cause, as has been suggested in the literature).

It is important to inform patients about the nature of the disease so they can understand their pathology. Currently, besides the information provided by the clinician, who continues to be the principal source on health matters, Internet has become an important source of information, with accredited webpages containing information directed towards the patient with burning mouth syndrome.

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