Burning mouth syndrome: a literary review and an uptade

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Abstract

Burning mouth syndrome is a debilitating condition of chronic oral pain and/or burning, which mainly affects pre and postmenopausal women. It can be characterized by the presence of other symptoms, such as a sensation of dry mouth (xerostomia), a bitter or metallic taste (dysgeusia) and tingling. BMS can be classified into two clinical forms: primary and secondary BMS. The primary BMS is essential or idiopathic, in which the organic local/systemic causes cannot be identified.
The secondary BMS is caused by local, systemic, and/or psychological factors; thus, its diagnosis depends on identification of the exact causative factor.
Its etiology is complex and not well defined, suggesting neuropathic mechanisms. Its diagnosis continues to be a challenge for the clinician since there are no sufficiently objective and universally accepted criteria. This disease is usually characterized by presenting many symptoms, but without clinical signs, which makes its diagnosis difficult as it excludes lesions in the oral mucosa by its own definition.
Therapy has been found to be effective for reducing the oral burning or pain symptom in some BMS patients previous clinical trials found that drug therapy with capsaicin, alpha-lipoic acid, clonazepam, and antidepressants may provide relief of oral burning or pain symptom but given the complexity of this syndrome, there are currently no widely accepted guidelines for its treatment.
Aim :Update knowledge on burning mouth syndrome treatment, pathophysiology, analyzing current and innovative therapeutic procedures and assessing their effective efficacy.

Keywords: Burning mouth syndrome, xerostomia, dysgeusia, glossodynia; oral pain; burning tongue.

Introduction

Definition Burning mouth syndrome (BMS) is an enigmatic, idiopathic, chronic and often painful clinical form for which no validated and standardized definitions, diagnostic criteria or classifications have yet been established. It was first described by Fox in 1935 (1). The American Academy of Orofacial Pain defines BMS as a burning sensation in the oral mucosa despite the absence of clinical findings and abnormalities in laboratory tests or imaging (2,3).
The International Association for the Study of Pain (IASP) defines BMS as a burning pain of the tongue or other oral mucosal membrane associated with normal signs and laboratory findings lasting at least 4 to 6 months. The current version of the World Health Organization International Classification of Diseases uses the term glossodynia, which includes additional terms such as glossopyrosis and painful tongue, and describes the condition as painful sensations in the tongue, including burning sensations (2,4).
The epidemiology of BMS is difficult and imprecise since there are no universally accepted definitions, the different epidemiological studies often refer to different clinical entities in which there are no lesions of the oral mucosa. Therefore, the prevalence varies greatly from one study to another, probably in relation to the diagnostic criteria. The prevalence of glossodynia in the general population is estimated at 2.5 to 5.1% (5). In a study by Bergdahl and Bergdahl (6), the prevalence was estimated at 3.7% of 1,427 subjects aged between 20 and 69 years ,especially postmenopausal women (7).

Etiology

Primary BMS is essential or idiopathic, in which the causes cannot be identified, and it is probable that there is a neuropathological cause that manifests itself with sensory alterations (hypoesthesia), is due to the reduction of the nociceptive trigger threshold, or due to neurophysiological where there are no defined findings.
Secondary BMS is caused by systemic,local and psychological nature factors like, anemia, vitamin B deficiency, folic acid and zinc, diabetes, thyroid disease, drugs such as angiotensin-converting enzyme inhibitors and hypoglycemic agents, irritations, parafunctional habits and oral infections. At the immunological level, there could be those of allergic origin, such as the hypersensitivity reaction to dental materials. In fact, it is possible that allergies may play a role in the development of burning mouth syndrome (2,8).

Among the psychological factors that predispose to suffering from BMS are psychiatric disorders of anxiety and severe depression. In fact, in one study Suresh et al. Identified anxiety and depression as the most common disorders presented by patients with BMS (9).

Pathophysiology

Patients with BMS usually show a series of typical symptoms of alteration of the trigeminal nerve: altered perception of pain, alteration of neural transmission, increased excitability and finally, a negative affectation of the trigeminal-vascular system, which shows the presence of a multifactorial component (10).
Recent studies such as those by Feller et al. 2017 (11), Silvestre et al. 2015 (12), and Coculescu et al. 2015 (13), where neurophysiological, psychophysical and neuropathological factors are included, have clarified that several neuropathic mechanisms, mostly subclinical, act at different levels and contribute to the pathophysiology of primary BMS. Demonstration of loss of small-diameter nerve fibers in the epithelium of the tongue with an upregulation of the TRPV1 and P2X3 receptor accounts for the thermal hypoesthesia and increased taste detection thresholds seen on quantitative sensory testing. As in neuropathic pain, decreased brain activation to heat stimuli has been shown in patients with primary BMS.

Diagnosis

The clinical diagnosis is fundamentally based on the discomfort reported by the patient, also taking into account that the typical profile will be that of an older woman, between the 5th and 7th decades of life, accompanied by a significant anxious component (14,15). In the oral examination, it is necessary to rule out the presence of lesions that demonstrate the existence of some local or systemic process that can explain the appearance of symptoms. Parafunctional habits and alterations secondary to them can only be seen occasionally.
According to the studies by Zakrzewska et al. (2016) and Sun et al. (2013) the criteria to be taken into account when diagnosing a patient with BMS are based on (15,16) presence of symptoms including daily deep burning sensation of the oral mucosa (bilateral),pain for at least 4-6 months, with variable intensity during the day that do not interfere with sleep.

Treatment

There are several therapeutic methods that are used in BMS. From a clinical perspective, clinicians should initially determine signs and symptoms consistent with primary (essential/idiopathic) BMS or with secondary BMS in which symptoms are caused by underlying local or systemic conditions. Secondary BMS requires proper diagnosis and treatment of such conditions.
In primary BMS, the cause is unclear, so management options are based on the patient's symptoms, often leading to unsatisfactory results (16). The complex and multifactorial etiology of BMS requires a systematic and interdisciplinary approach for the proper management of these patients. Although many drugs have been proposed, none of them prove to be a number one standard. Treatment planning must be personalized for each patient. If local, systemic, or psychological factors are evident, treatment or elimination should be attempted (17). A complete clinical examination of the oral mucosa is crucial in these patients to define a treatment. The lack of pathology of the oral mucosa is mandatory for the diagnosis of BMS. Details related to quality, onset, persistence, intensity, onset, duration, relieving factors, course, sites involved in pain symptoms are essential.

Non-pharmacological treatment

The initial treatment will be non-pharmacological, trying to treat those medical processes that can give rise to discomfort or burning in the mouth, managing all those irritative situations that can give rise to small traumas on the tongue or lips, such as fractures or very prominent dental cusps, as well as as areas of hyperpressure of the prosthesis on the mucous membranes. The patient should be informed about her situation, avoiding all doubts that could increase her level of anxiety. Mucous protectors can be used, which protect against friction, rubbing and thermal changes (2,14,15).

Pharmacological treatment

The use of Capsaicin is an alternative that has been used to control neuropathic pain. It is based on the desensitization of thermal, chemical and mechanical stimuli by acting on C fiber receptors. It is used as a gel or mouthwash with which a certain degree of improvement can be obtained, but with a limited effect over time (2) .
The use of topical Clonazepam has had very good short-term results, being effective in 2/3 of patients. This drug acts by inhibiting pain transmission and suppressing central neuronal hyperactivity in cases of deafferentation. In patients resistant to clonazepam, Gabapentin can be used, but its results are contradictory (2). Other types of treatments used have been Amilsupride, Paroxetin and Sertraline. At low concentrations it has an analgesic action, but the studies carried out do not provide a sufficient level of efficacy and evidence.
In traditional medicine, the first-line treatment of choice for BMS generally consists of selective serotonin reuptake inhibitors (SSRIs) or serotonin and norepinephrine reuptake inhibitors (SNRIs). As an alternative treatment, the traditional Japanese medicine (kampo) Rikkosan was also used. Rikkosan consists of five raw herbs (Asiasarum root (saishin), Cimicifuga rhizome (shoma), Saposhnikovia root (boufu), Glycyrrhiza (kanzou), and Japanese Gentian (ryutan)) and are indicated as natural pain relievers (18).They observed Rikkosan mouthrinse produces pain relief lasting approximately 1 hour.
The treatment of BMS requires an interdisciplinary approach for the proper management of these patients. In this regard, low-level laser therapy (LLLT) has been considered as an alternative for the treatment of SBA due to its analgesic and regenerative action on peripheral nerve fibers. The results of the studies are highly satisfactory and show a significant improvement in symptoms

after treatment. According to Ana Liz Pereira de Matothe best energy dosage should be between 0.5 and 8 J / cm 2 because it can reduce inflammation and accelerate wound healing. LLLT has an analgesic effect; however, the application it must be successive, continuous and in several sessions

The therapy that the low-level laser has is described minimal side effect and has a reduction in symptoms in BMS (19).

Alpha-lipoic acid (ALA), which is an antioxidant that can scavenge free radicals and exert nerve repair activity, has also been studied. Clinical trials have investigated the efficacy of this substance in the treatment of BMS, but the results are conflicting (19).

According to Wenqing Zhang photobiomodulation (PBM) can help relieve pain, speed up the resolution of inflammation process and promote healing of damaged tissues. By stimulating mitochondrial cytochromes and then initiating secondary cell signaling pathways. Studies have shown that PBM was effective in many parts of the body, such as for the treatment of musculoskeletal injuries, degenerative diseases and dysfunctions.A single treatment is generally sufficient for acute and postoperative therapy. However, up to 10 treatments may be needed for chronic pain and degenerative diseases presenting minimal side effects with improvements over clonazepam in reducing pain sensation over the 12-week follow-up period (21).

According to daniela adamo et all. Vortioxetina is well tolerated and effective in the treatment of BMS, suggesting a new frontier in the management of this disease and other chronic pain conditions by offering good safety and tolerability, with lower latency of action, especially in middle-aged or elderly patients. with medical comorbidities, also offering improved cognitive function. Treatment should be performed for at least 12 months to achieve satisfactory response or remission rate and stabilize efficacy (22).

According to Daniel L. Neuman the use of variable dosage naltrexone up to 4.4 mg has been shown to relieve symptoms after 8 weeks, the patient reported a reduction of at least 50% in the severity of subjective pain associated with the symptoms of burning mouth syndrome and the improvements remained consistent during the follow-up visits at 11 months, with no need for modification. the dosage (23).

Psychological treatment

Likewise, Komiyama et al. (24) have investigated the effectiveness of group cognitive behavioral treatment to improve pain and anxiety in patients with BMS. They designed a brief group CBT intervention to provide disease self-management skills and introduce behavioral strategies to manage chronic and persistent BMS pain. Pain intensity and disturbance in daily life decreased significantly from the first to the second CBT session. The state anxiety score also decreased after the CBT session and approached the control value. They report that individual and group cognitive therapy has been shown to be equally effective in managing chronic pain, since there were no significant differences between the two. But according to the patients' narrative impressions, the CBT group intervention may be more useful to control persistent pain in patients with BMS, since it provides mutual psychological support. Therefore, they conclude that a brief cognitive-behavioral intervention group is effective in reducing pain and anxiety in patients with BMS. Likewise, the reduction of anxiety can also be useful to reduce the intensity of pain in these patients. Although studies of the effect of duration of CBT therapies on burning sensation complaints are needed.

AUTORES	ÁCIDO ÁLFA LIPÓICO (ALA)	TERAPIA LASER	GABAPENTINA	BENZODIACEPINAS	OTROS
Barbosa y cols. (2018) (19)	X	X			
Liu, y cols. (2018) (50)	X		X	X	X
Nakazawa, y cols. (2017) (18)					X
Restivo, y cols., (2017) (43)					X
Al-Maweri, y cols. (2017) (51)		X			
Arduino y cols. (2016) (44)		X			
Palacios-Sanchez y cols. (2015) (45)	X				
Sardella y cols. (2013) (9)					X
Sun, y cols. (2013) (17)			X	X	X
Komiyama y cols. (2013) (46)					X
López-D'alessandro y cols (2011) (47)	X		X		
Rivera-Campillo, y cols, (2011) (48)				X	
Matsuoka y cols. 2010 (49)					X
Steele y cols. (2008) (52)	X				
Guarneri, y cols. (2008) (53)				X	

Conclusion and perspective

The treatment of SBA 1 it"s difficult, therapies are varied, none show overwhelming results, and almost all require more larger randomized clinical trials, and longer duration.

Therefore, since there is not a single drug capable of solving this pathology alone, today the recommendation is to use a combination of drugs gradually adapting them to the patient's symptomatic response taking into account that Gabapentin and ALA, administered together, were more useful. in reducing burning in the mouth.

The topical and systemic use of clonazepam has been found to be advantageous, with the precaution of taking individual measures with the chronic diseases they present. It can be associated with laser therapy (LLLT) which reduces the symptoms of patients by offering slightly more consistent therapeutic results compared to those obtained solely with clonazepam, without negative effects.

Cognitive behavioral therapy is effective in reducing pain and anxiety, reducing pain intensity and should always accompany drug treatment.

Other alternative therapies such as: gargling with Rikkosan, Acupuncture may be effective but alone may not be sufficient to obtain satisfactory results.

In the future, with the proper use of diagnostic tests, patients with BMS may benefit from interventions specifically targeting the underlying pathophysiological components and thus apply better procedures. It is necessary to encourage the scientific community to continue with this line of research, which will benefit both the experts and the patients who suffer from this syndrome.

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