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Burning mouth syndrome: An overview and current update

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Abstract
Introduction: Burning mouth syndrome is one of the most common in dentistry. It is chronic and presents a burning sensation in the oral mucosa with appearance in the tongue, mucous tissue, lips and / or palate that lasts from days, weeks or even months.
Objective: To analyze the literature on the characteristics of burning mouth syndrome of etiology, epidemiology, classification, differential diagnosis and treatment.
Methodology: For the bibliographic review with electronic search by the PUBMED and Google Scholar search engine with the keywords "burning mouth syndrome, etiology, epidemiology, classification, differential diagnosis and treatment" with 2015-2020 dates.
Results: The etiology is classified as primary and secondary although it has multifactorial effects with local, systemic and psychological factors. The prevalence ranges from 0.7% to 5.1%, with a gender ratio of 7:1, with menopausal women having the greatest number of conditions. The classification is type I (35%), II (55%) and III (10%). The differential diagnosis is very extensive because of the confusion of symptoms, therefore a specific laboratory study is needed to rule out and obtain a single result. The treatment must be handled individually and include multidisciplinary approaches to achieve its long-term success.
Conclusion: Burning mouth syndrome is a relatively common chronic intraoral pain disorder that can last from weeks to months. The etiology is multifactorial with a multidisciplinary approach and it is important to include medical and psychosocial therapy to ensure better management in the relief of symptoms.

Keywords: burning mouth syndrome, SBA, stomatodinia, glosodinia, mouth pain and mouth burning

1. Introduction
Burning mouth syndrome (BMS), also called "stomatodynia" or "glossodynia", is one of the most common medically unexplained oral syndromes [1] and a chronic pain disorder of the oral mucosa, without any systemic dysfunction [2]. The International Association for the Study of Pain describes the condition as a burning and itching sensation in various regions of the oral mucosa for which no cause can be found [3, 4]. This extremely painful burning condition occurs most frequently in the anterior two-thirds of the tongue, palate, mucosa and lips with a duration ranging from days, weeks or even months [5, 6]. The incidence is 3:7 times more likely in women going through menopause, its prevalence is estimated between 0.7 to 15% while in other studies it varies from 18% to 33% [7, 8]. BMS is rarely seen in patients younger than 30 years and the prevalence may increase 3 to 12 times with age in both sexes [9, 10]. Symptoms and diagnosis always vary from person to person, so a patient-specific investigation is performed to rule out other etiologies of oral pain, possible tongue discolorations and changes in taste sensation. For the moment, no standard management has been established for BMS in the office; studies have not revealed a single treatment to be prescribed for all patients [6, 11]. In the literature there is no complete and specific review for the field of dentistry and it is of utmost importance to raise awareness of this disease, to know how to diagnose and provide

adequate treatment depending on the degree and type of involvement of the patient. So far it has not been possible to establish a unique and global treatment, but this study can guide dentists so that they have all the tools and are constantly updated on ways to deal with the syndrome when it presents itself. The objective of the study is to analyze the information in the literature on the characteristics that burning mouth syndrome may have, particularly regarding its etiology, epidemiology, classification, differential diagnosis and treatment.

2. Methodology

Articles on the subject published through the PubMed, SCOPUS and Google Scholar databases were analyzed, with emphasis on the last 5 years. The quality of the articles was evaluated using PRISMA guidelines, i.e., identification, review, choice and inclusion. The quality of the reviews was assessed using the measurement tool for evaluating systematic reviews (AMSTAR-2).

The search was performed using Boolean logical operators AND, OR and NOT.

It was constructed with the words “burning mouth syndrome”, “etiology”, “epidemiology”, “diagnosis”, “treatment”. The keywords were used individually, as well as each of them related to each other. Initially, the titles of all the articles were selected, the abstract of each one was evaluated, and the articles were chosen for a complete reading review.

3. Results

3.1 Etiology

Although different classifications have been developed to describe the etiology of burning mouth syndrome, the true cause of BMS is unknown, it is identified as a complex set of biological and psychological factors, suggesting a multifactorial etiology [12, 13]. BMS can be classified into two forms: primary (essential/idiopathic), peripheral, neuropathic or central cause, and secondary determined by local, systemic or psychiatric factors [14]. The condition appears to be multifactorial and numerous local factors have been associated with it, such as prostheses, drugs, food, infections and/or allergies, systemic factors such as vitamin deficiency, systemic diseases, autoimmunity and radiotherapy or pharmacotherapy, and finally psychological factors such as anxiety, depression and personality [15, 16]. The syndrome may arise without a history of oral cavity pathology or follow an infection or other condition within the oral cavity [6]. It is a finding that has been attributed to mucosal dryness as a result of age-related reductions in estrogen and progesterone levels and an increase in the frequency of psychological disorders in middle-aged and older women [17]. Seventy percent of patients with BMS report "phantom taste," which is a disorder of the gustatory system. It is notable that the most commonly affected site is the anterior two-thirds of the tongue, which is also where the largest number of taste buds are located [18].

3.2 Epidemiology

It is extremely difficult to establish the true prevalence due to the lack of a classification system, diagnostic criteria and awareness among oral health professionals. BMS exhibits a significant predilection for postmenopausal women who are more affected by the disease than men, the gender ratio is 7:1 [19]. It has a strong association with advancing age in both sexes.The condition is essentially nonexistent in children and is rarely seen in those under 30 years of age [6]. The mean age of the patients was 62 years, with a range between 40 and 85 year [20, 21]. When establishing the epidemiology, BMS is difficult and imprecise because there are no universally accepted definitions, different epidemiological studies often refer to different clinical entities where oral mucosal lesions are lacking. The prevalence of glossodynia in the general population is estimated to range from 0.7 to 5.1% [1, 22]. Due to the paucity of universally accepted diagnostic criteria, it is difficult to collect accurate epidemiological data so additional studies evaluating the impact of medication intake, nutritional status and the presence of both local and systemic diseases should be performed [18, 23].

3.3 Classification

The main symptoms present are formed by a triad: The first ones present pain in the oral mucosa, generalized burning, tingling sensation, numbness, swelling. The second in the form of dysgeusia that may present with persistence or alteration of certain specific taste. The third with xerostomia which may be a secondary symptom associated with drug therapy or a disease in the mouth [24]. The condition has recently been recognized in the current International Classification of Headache Disorders (ICHD-III beta) as a burning sensation or intraoral dysesthesia, recurring daily for more than 2 h per day for more than 3 months, without clinically evident causal lesions [25].Recently, Scala *et al*. have proposed classification terms: "Primary" and "Secondary" [18]. Primary (essential / idiopathic): Local organic / systemic causes cannot be identified, but peripheral and central neuropathic pathways are involved. The secondary: It is the result of local pathological, systemic or psychological conditions and, therefore, this form responds well to etiology-directed therapy [21, 26]. One of the classifications proposed by Lamey and Lewis, 1989 is based on the intensity of pain divided into 3 types. Type I (35%) with the presence of daily burning. It is progressive since it is absent upon awakening, but is present as the day progresses, being maximal at night and presenting problems in falling asleep. It may be related to systemic disorders, such as nutritional deficiencies and endocrine disorders. Type II (55%) occurs at all times of the day. It is present upon awakening and is sometimes present at night. The most important symptom is the altered sleep pattern that brings with it mood changes, alterations in eating habits and decreased desire to socialize, and consequently may present psychological disorders. Type III (10%) is characterized by intermittent burning, with atypical localization in the floor of the mouth, buccal mucosa and throat, pain and presence on some days. These patients frequently present anxiety and allergic reactions, especially to food additives, these being an important etiological point in this group [27, 28]. In contrast to the previous classification, other authors describe it as follows: Type I with absence of symptoms in the morning, but their presence is varied in the evenings. Type II is associated with chronic anxiety and presents symptoms throughout the day. Type III shows intermittent diurnal symptoms or may have periods without any symptoms [6, 29].

3.4 Differential Diagnosis

It is essential to be able to differentiate between primary and secondary burning mouth syndrome. When the case is secondary, it should be treated and the symptoms should successfully disappear. It may be primarily idiopathic with no known underlying pathology or it may be secondary to the underlying condition, these may include: fungal infections, mechanical trauma, thermal injury, chemical injury,

hyposalivation/xerostomia, parafunctional habits, oral mucosal injury and allergic contact stomatitis [18]. Other important causes of mouth pain to consider are allergic reactions to food antigens and dental metals, diseases such as Sjögren's syndrome, systemic lupus erythematosus, diabetes, HIV, herpes simplex virus, nutritional deficiencies including vitamin B1, B2, B6, B12, folic acid and zinc, among others [6, 30]. As already noted it is of utmost importance not to rule out the numerous list of local conditions that must be considered and ruled out. The first and most common cause is local irritation followed by a rough denture or dental restoration will irritate the tongue and cheeks [31]. Sometimes patch testing for contact allergy to dental materials such as cobalt, mercury, gold, palladium or food allergens such as ascorbic acid, cinnamon, nicotinic acid, propylene glycol and benzoic acid will reveal a diagnosis of BMS [24]. Patients may also present with oral burning not accompanied by visible oral mucosal lesions in cases of burning mouth syndrome [32]. If patients are unaware of the presence of lesions, oral burning sensation may present as the main symptom. Caustic oral rinses or acidic foods may cause generalized oral mucosal irritation and hypersensitivity [33]. Last and not least oral candidiasis can be a primary infection, but most often is secondary to local irritation or systemic predisposition. A direct smear is the ideal way to make this diagnosis rather than sampling for microbiological culture as the organism, candida albicans is commensal in most mouths. If suspected a course of antifungal therapy, such as mycostatin [34], should be tried first. El diagnóstico diferencial del SBA es muy extenso ya que en ocasiones se puede confundir con otras causas de dolor o ardor bucal. La cavidad oral presenta un gran número de condiciones locales con sintomatología en común por eso es importante realizar estudios de laboratorio y muestras del área afectada en boca para descartar que pueda ser de origen idiopático sin patología subyacente conocida o secundario a la afección subyacente.

4. Treatment

4.1 Laser Therapy

In recent years, the use of biostimulatory lasers has been proposed in various medical fields for the treatment of chronic and acute pain conditions; favoring re-epithelialization, fibroblast proliferation, collagen synthesis, increasing vascularization and decreasing nerve impulse conduction disturbances. Therefore, it is evident that the laser has been shown to have an anti-inflammatory and analgesic effect [35]. The first study revealed that LLLT was performed with the GaAlAs laser (830 nm) used in non-contact mode at the site of the mouth where burning symptoms were present. There was a significant decrease in pain symptoms [36]. The second study the mean initial VAS score was 8.9 for the LG and 8.3. After the eighth session and after two months, the improvement was marginally significant in the multivariate analysis of: dry mouth, dysgeusia and pain [37]. The third study evaluated the efficacy of low level laser (LLL) in improving the symptoms of burning mouth syndrome. They underwent LLL irradiation at a wavelength of 630 nm and a power of 30 mW for 10 seconds twice a week for 4 weeks. It can be concluded that low level laser could decrease the intensity of burning mouth syndrome [38]. The last study according to their protocol low level laser therapy is as beneficial for BMS patients as placebo treatment, indicating a large emotional component of involvement in the symptomatology. However, there were positive results in some statistical analyses, which encouraged further research on BMS laser therapy with other irradiation parameters [39].

4.2 Gabapentin

Doses between 100-300 mg, 2 or 3 times a day are recommended. This drug was created to act as an agonist of GABA, an inhibitory neurotransmitter of essential activity, since it is easily transferred to the central nervous system (CNS) due to its high lipid solubility. The mechanism of action of gabapentin is unknown, since it acts by increasing the promoted discharge of GABA, however, it does not constantly reduce the action potentials or the effect of the calcium channel current [17].

4.3 Clonazepam

Clonazepam is a benzodiazepine that has an inhibitory effect on the central nervous system and is widely used as an anxiolytic agent [40]. Clonazepam has been the most widely accepted therapy in terms of efficacy for improvement of discomfort in patients with BMS. It is used orally in doses of 0.75 mg at bedtime and 0.25 mg after eating, but is mostly administered as a topical medication in the form of a 0.5 mg/5 mL solution for 5 min mouthwashes 2 to 4 times daily, with a satisfactory response of 61%, and is well tolerated and relatively safe. Another form of administration is tablets, sucked until they melt in the mouth, but without swallowing the saliva, it is recommended to suck the 1 mg tablet 3 times a day for 14 days [17, 22]. Studies have shown a decrease in pain levels with clonazepam and a 70% reduction was reported. We evaluated outcome predictors affecting the efficacy of clonazepam and found that those with greater severity of taste disturbance symptoms and xerostomia at baseline showed better therapeutic outcomes after clonazepam treatment than those without those complaints; and patients with tongue symptoms had a significant decrease in pain compared to those with intraoral symptoms excluding the tongue [18].

4.4 Cognitive Therapy

Cognitive-behavioral therapy can improve the intensity of symptoms compared to placebo in people with burning mouth syndrome and psychological treatment is vital in management [7, 42]. Cognitive therapy, or psychotherapy, is increasingly emerging in the literature and has been shown to be more effective in the management of patients, lowering the level of anxiety and improving their discomfort. Bergdahl *et al*. conducted a study where they demonstrated an improvement in the symptoms of BMS patients who received only cognitive therapy treatment, showing a significant difference with the placebo group. "Femiano *et al*. studied a group with cognitive therapy only (2 h/week, for 2 months), another group was given only ALA (600 mg/day for 2 months), another group was given a combination of the two (cognitive therapy and ALA), and the control group was the placebo. The most significant result was observed in the group that used cognitive therapy with ALA, with complete resolution in 53% and some improvement in 90%" [17, 40]. Cognitive-behavioral intervention can increase awareness of the causes and help provide skills to self-manage the condition and introduce strategies to manage constant and persistent pain. This was confirmed by Komiyama *et al*. where they demonstrated that pain intensity and disruption of daily life decreased significantly from the first to the second session [18]. "A small randomized controlled trial investigated the role of cognitive behavioral therapy (CBT) weekly for 12 weeks in 30 patients with 3 follow-up sessions for 12 weeks). The study reported that the CBT group had significantly reduced

pain intensity at 6 months after treatment compared with the placebo group. In the CBT group, 27% of patients were symptom-free at 6 months compared to 0% in the placebo group" [42].

4.5 Capsaicin

Capsaicin has been successfully used both topically and systemically in the treatment of BMS, presumably to achieve symptomatic relief. Topical capsaicin has the ability to bind to TRPV1 ion channels of small diameter peripheral sensory nerve fibers, mediating desensitization of afferent nociceptors and causing reversible degeneration of peripheral sensory nerve endings, with consequent reduction of the syndromic burning sensation. It can be used as a substitute, although the initial burning elicited when applied is undesirable for the BMS patient and, therefore, it is difficult to obtain patient compliance. Silvestre *et al*. in a prospective, double-blind, crossover study concluded that rinsing with capsaicin (0.02%) for one week was effective, however, its use has some limitations [18]. A case series reported that systemic oral capsaicin 0.25% improved short-term symptoms in patients with BMS during 30 days of treatment. This was most marked in patients with severe symptoms at baseline, and more than 90% reported a reduction in symptoms after treatment. However, about one third of patients experienced significant gastric pain during treatment [42].

5. Conclusions

The etiology of BMS is classified as primary and secondary or type I, II and III, although it is not really fully understood due to its multiple theories, multifactorial affectations and its numerous forms of manifestation, such as local, systemic and psychological factors. BMS has a very marked prevalence in women being the ratio of 3:1 to 16:1 compared to men, the average age being 62 years old. The differential diagnosis is very extensive as it can sometimes be confused by other causes of mouth pain or burning, therefore a number of local conditions must be considered and ruled out first. Various treatments and management have been developed according to the patient's signs and symptoms. The most common treatments include clonazepam, gabapentin and capsaicin.

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