Review

BURNING MOUTH SYNDROME: DIAGNOSIS AND THERAPY

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ABSTRACT

Burning mouth syndrome (BMS) is an oral chronic pain disorder denoted by burning, stinging, or itching the oral cavity without any organic disease. Symptoms can involve the tongue, with or without extension to the lips and oral mucosa. The etiopathogenesis is complex: local, systemic, and psychological factors are involved in causing oral burning and painful symptoms. The major challenge for the clinician is the treatment: identifying the possible causative factors for the BMS is the first step since treating or eliminating these factors could lead to a significant clinical improvement of oral burning and pain symptoms. Considering the growing incidence of BMS in older people, further research is required to determine the efficacy of current management strategies for patients with this disorder. This review aims to report the most recent data concerning BMS to give the clinician a more comprehensive idea of the disease.

KEYWORDS: *pain, oral cavity, neuron, disease, Burning Mouth Syndrome*

INTRODUCTION

Burning mouth syndrome (BMS) is an oral chronic pain disorder denoted by burning, stinging, or itching of the oral cavity without any organic disease. Symptoms can involve the tongue, with or without extension to the lips and oral mucosa (1, 2). Moreover, dysgeusia (distortion in the sense of taste) and subjective xerostomia can be present. Its beginning is spontaneous, and the syndrome has an apparent predisposition in the geriatric patient, primarily women (3, 4).

BMS can be primary or secondary. Primary BMS, also named essential or idiopathic BMS, is a condition where organic local or systemic causes cannot be identified and is likely to have a neuropathological cause.

Secondary BMS is a variant resulting from local or systemic pathological conditions like lichen planus, candidiasis, coeliac disease, hormonal disturbances, psychosocial stressors, vitamin or nutritional deficiencies, diabetes, dry mouth, contact allergies, galvanism, parafunctional habits, cranial nerve injuries (5, 6). Evidence suggests a neuropathic mechanism of disease (7). Oral mucosa biopsies of patients with BMS demonstrated decreased density of epithelial nerve fibers and axonal derangement, indicating a potential role for peripheral small-fiber sensory neuropathy (8).

Blink reflex abnormalities, suggesting brainstem pathology or peripheral trigeminal neuropathy, as well as sensorial modifications such as hypoaesthesia, probably due to peripheral small-fiber neuropathy, have also been described in patients with BMS (9). Lin et al. (10) reported that BMS patients had higher hemoglobin, iron, and vitamin B12 deficiency frequencies, abnormally elevated blood homocysteine levels, and serum gastric parietal cell antibody positivity compared to healthy control individuals. Psychological and psychiatric disorders are present in up to 85 % of

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BMS patients, with anxiety, depression, cancerophobia, hypochondria, and insomnia being the most common diagnoses (11, 12).

Sleep dysfunction may also have a role in BMS (13). A cross-sectional, case-controlled study demonstrated that patients with BMS report more sleep disturbances than age and sex-matched controls with various oral conditions. The authors suggest that sleep dysfunction may be a risk factor and a possible target for treating BMS (14).

Literature reports that patients affected by BMS also presented gastroesophageal reflux disease, hypertension, hypercholesterolemia, autoimmune disorder, thyroid disorder, and anemia (15). Lately, evidence for chorda tympani hypofunction in BMS has been proposed (16), supporting the hypothesis that the tonic inhibition of the sensory pathways of gustatory activity is dysfunctional in BMS patients (17). Grushka et al. (18) suggested that BMS could be linked to hyperactivity of the trigeminal nerve's sensory and motor components due to a loss of central inhibition due to taste damage in the chorda tympani and the glossopharyngeal nerves. The consequence might be higher activity in the mastication and intrinsic tongue muscles. Further studies into the dopaminergic pathway of central pain modulation are essential.

Hagelberg (19) showed decreased endogenous dopamine levels in the putamen in BMS patients. These data are coherent with a theory of presynaptic dysfunction of the nigrostriatal dopaminergic pathway of central pain modulation in BMS. Moreover, thermal stimulation in BMS patients was likened to increased cerebral blood flow, as detected in functional magnetic resonance imaging (20).

In addition, it seems that estrogens work as neuroprotectants of the nigrostriatal dopaminergic system (21, 22), explaining the correlation between menopause and BMS.

This review aims to report the most recent data concerning the diagnosis and treatment of BMS to able to give the clinician a more comprehensive idea of the disease.

Diagnosis

Based on the symptom's framework, clinical classification of BMS has been proposed (23, 24). Three types have been recognized: Type 1 is represented by a pain-free wake-up, with a burning sensation slowly growing in severity during the day and reaching its extreme intensity by the evening. This type affects about 35% of patients and is connected to systemic disorders like nutritional deficiency and diabetes mellitus. In Type 2, symptoms are constant throughout the day. Patients fall asleep with difficulty and usually have psychological disorders. Type 3 BMS is characterized by discontinuous symptoms, with pain-free daytime periods. Commonly, these patients constitute 10% of total patients and show allergic reactions (23, 24).

Current diagnostic criteria consist of constant daily pain in the mouth with normal oral mucosa after excluding local and systemic diseases (25). The International Headache Society first categorized it as a distinct disease in 2004, which described primary BMS as "an oral burning sensation for which no medical or dental cause can be found".

The burning mouth symptoms or pain should be felt deep within the oral mucosa for at least 4-6 months, almost daily. They are never aggravated but almost always are alleviated by eating or drinking. Other symptoms such as xerostomia, oral dysgeusia, a spontaneous metallic taste, abnormal sensory/chemo-sensory, mood changes, and specific personality traits of patients may also help identify the BMS. In addition, patients with BMS show no clinical sign of objective basis of any pathology of the oral mucosa (26). Therefore, the clinical diagnosis is based on thoroughly examining the patient's medical history and carefully analyzing the data obtained from physical and laboratory examinations.

Therapy

The treatment aims mainly to manage the disease as a type of chronic neuropathy (25). As a first step, in a patient affected by BMS, it is essential to exclude different possible causes like local or systemic causes (galvanic current, parafunction, mechanical irritation, allergic reactions, anemia, mineral or nutritional deficiencies, drugs and metabolic, infections, genitourinary, gastrointestinal, neurological, psychiatric disorders).

Following a consultant, it would also be advisable to replace drug therapies that may interfere with the onset of BMS (such as ACE inhibitors). The cure for BMS, however, remains difficult despite the different classes of drugs attempted. The variable response rate to medical therapy is most likely related to the idiopathic BMS.

BMS treatments can be topical and/or systemic. Several topical treatments have been evaluated to treat BMS. Capsaicin acts on the sensory afferent neuron, and topical capsaicin can be used as a desensitizing agent or an analgesic to treat oral mucosal burning (26). However, capsaicin is difficult to accept because of its taste. Furthermore, it generally causes an increase in the burning sensation at the beginning of the therapy (27). In a prospective study with 30 subjects with BMS, a capsaicin rinse (0.02 %) significantly reduced VAS from baseline over placebo (13). Nevertheless, there were seven drop-outs, which may suggest limitations to the treatment due to side effects (28).

Clonazepam is an agonist of butyric acid gamma-amino (GABA). Local application of clonazepam may reduce the sting, despite its systemic adverse effects (26). Lozenges clonazepam is efficacious in patients with predominantly peripheral BMS. Barker et al. (29) noted that a higher percentage of patients reacted to clonazepam (71.4%), but patients also responded to diazepam (55.1%), and there were no statistical differences between the two treatments. Lidocaine and 0.15% benzydamine hydrochlorate have anesthetic effects and are anti-inflammatory. Both are used as a mouthwash to reduce pain or burning symptoms. In any case, they cannot be applied as an effective therapy because of the short duration of the analgesic effect (30).

Aloe vera gel application, combined with a tongue protector, has effectively reduced burning and pain when applied three times daily (31).

It has been observed that systemic capsaicin (0.25%, three times a day, for 30 days) significantly improves pain symptoms compared to a placebo group (26). However, it cannot be used in long-term therapy because, after four weeks of treatment, 32% of patients reported gastric pain (32).

Systemic clonazepam (0.5 mg/day) has effectively reduced BMS symptoms. Amos et al. (33) used combination therapy with clonazepam topical and systemic. Patients were asked to dissolve the tablet clonazepam (0.5 mg/tablet, three times daily) orally before swallowing and were followed for six months. 80% of patients obtained more than a 50% pain reduction during the treatment period. One-third of the patients had complete pain resolution, suggesting the combined treatment's effectiveness.

The alpha-lipoic acid is a powerful antioxidant with a mitochondrial coenzyme neuroprotective effect. It is also an antioxidant that can increase intracellular glutathione levels and eliminate free radicals. Authors (34) have tried alpha-lipoic acid in the 600 mg daily dose for more than two months in treating patients with BMS. Other studies concluded that alfa lipoic acid is inefficient in BMS treatment.

A study by Maina et al. (35) explored the effectiveness and tolerability of Amisulpride (50 mg/day) and selective serotonin reuptake inhibitors (paroxetine 20 mg/day, sertraline 50 mg/day) in BMS treatment for eight weeks. All three treatments were effective in reducing pain and burning, with Amisulpride showing the best results in a shorter time and better compliance. Cognitive-behavioral therapy, when combined with drug therapy in weekly one-hour sessions lasting 12-15 weeks, significantly reduced BMS symptoms in comparison to placebo control (36).

However, it is crucial to note that some studies report high placebo response rates (10). Well-designed prospective multicenter studies are imperative to establishing the efficacy of BMS treatments. These studies should incorporate a substance placebo, a standardized protocol for instructions, and a long-term follow-up analysis to determine the treatment's effectiveness compared to a placebo (7).

CONCLUSIONS

BMS is a reasonably common chronic intraoral pain disorder in peri/post-menopausal women, classically described by intractable burning that may be linked with dysgeusia and xerostomia.

The etiology of BMS is multifactorial, and a secondary form of BMS should be diligently sought for and treated. The etiopathogenesis of BMS is complex: local, systemic, and/or psychological factors are involved in causing oral burning and painful symptoms. BMS has also been found to be associated with either peripheral nerve damage or dopaminergic system disorders.

The major challenge for the clinician is the treatment of BMS: identifying the possible causative factors for the BMS is the first step since treatment or elimination of these factors could lead to a significant clinical improvement of oral burning and pain symptoms. This condition, however, often is idiopathic; in this case, drug therapy should be instituted. In addition, psychotherapy and behavioral feedback may also help eliminate the BMS symptoms. In conclusion, further research is required to determine the true efficacy of current management strategies for patients with this disorder.

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