



Treatment for Burning Mouth Syndrome: A Clinical Review

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Burning mouth syndrome (BMS) is a chronic idiopathic orofacial pain. BMS is currently classified as a neuropathic pain condition, but it is difficult to pinpoint the precise neuropathic mechanisms involved in each patient. It is challenging to complete the cure for BMS. Clinicians should treat BMS patients based on evidence. There is pharmacological and non-pharmacological therapy in the treatment modalities of BMS. The provision of objective information and reassurance as part of cognitive behavioral therapy is critical in the treatment of BMS. This paper will review the evidence-based treatment of BMS and discuss what we need to do.

Keywords: Burning mouth syndrome; Clonazepam; Cognitive behavioral therapy

INTRODUCTION

The International Classification of Orofacial Pain (ICOP) categorizes burning mouth syndrome (BMS) as idiopathic orofacial pain and defines it as an intraoral burning or dysaesthetic sensation, recurring daily for more than 2 hours per day for more than 3 months, without evident causative lesions on clinical examination and investigation [1]. In ICOP, previously called primary BMS was defined as BMS. Burning sensation, xerostomia, and taste disturbance make up the triad of symptoms for BMS. BMS commonly affects the tongue, lip, palate, gums, and other oral mucosa. Anxiety, depression, and insomnia are frequent comorbid conditions [2]. BMS, formerly thought to be psychogenic pain, is now considered neuropathic pain. In clinical settings, determining the precise neuropathic mechanism in individuals is difficult. Furthermore, there are no global guidelines on BMS treatment and BMS has low spontaneous remission prevalence [3]. As a result, treating BMS is difficult.

Burning pain is caused by a variety of factors, and it is

critical to identify these factors in each patient. Clinicians should try to find factors through diagnostic tools, and appropriate treatment should be provided according to the factors. BMS treatment should be evidence-based, with evidence-based on BMS pathogenesis, treatment meta-analysis, and predictors of treatment outcome reported in previous studies. This paper will review the evidence-based treatment of BMS and discuss what we need to do. It is clarified that all referred to BMS in this review are primary BMS according to the definition of ICOP.

PATHOGENESIS OF BMS

From the great advances in the understanding of the etiology and pathogenesis of BMS, it is accepted that BMS is neuropathic pain [4-7]. Chronic anxiety, menopause, neurotoxic agents, and genetic susceptibility such as dopamine D2 receptor polymorphism have all been implicated as causes of BMS [2]. Many studies have indicated that peripheral and central neuropathic mechanisms are involved in the genesis of BMS. Large myelinated A β afferent damage

in the trigeminal nerve or its brainstem circuits, as well as decreased A δ fiber signaling with relatively normal C fiber function, are linked to taste changes and ongoing burning pain in BMS [4]. Tongue biopsy revealed that peripheral sensitization was caused by increased expression of nerve growth factor, transient receptor potential vanilloid 1, and P2X3 receptor [2,8-10]. Central neuropathic mechanisms in BMS are associated with hypofunction of the central dopaminergic system in the basal ganglia and decreased endogenous inhibitory control [2,4,11]. Patients of BMS with central neuropathic mechanisms often seem to have associated psychiatric disorders such as depression and anxiety [12,13].

DIAGNOSIS OF BMS

Because BMS is an exclusion diagnosis, a thorough diagnostic procedure is required. Local and systemic factors that can cause a “burning sensation” should be excluded. Local factors include decreased salivary secretion quality and quantity, microtrauma from parafunctional habits, fungal infection, and allergic reactions. Systemic factors are nutritional deficiencies of serum iron, ferritin, zinc, vitamin B12, or folic acid, hormonal changes, diabetes mellitus, thyroid disease, and drugs [2]. Oral examinations, radiography, salivary secretion tests, laboratory tests, psychological, and sleep evaluations will be performed on patients who have intraoral burning symptoms. Electrogustometry, taste threshold testing with a taste strip, and quantitative sensory testing can all be performed if possible.

It is difficult to differentiate between the peripheral and central neuropathic mechanisms of BMS in individuals in clinical settings. If patients experience immediate pain

relief with lingual nerve block anesthesia or a specific topical treatment, it indicates that the patients are most likely affected by the peripheral neuropathic mechanism of BMS [14]. Most patients complain of bilateral symptoms, but, some patients complain of unilateral symptoms. Unilateral symptoms are frequently associated with trauma, such as dental treatment, and are more likely to be caused by a peripheral neuropathic mechanism [15]. If the patients show high scores of anxiety or depression, it means that the patients are more likely to be related to the central neuropathic mechanism of BMS [2].

TREATMENT OF BMS

A complete cure is difficult because BMS is a chronic idiopathic orofacial pain and neuropathic pain. Patients tend to focus on each symptom and cause. Clinicians should concentrate on improving function and daily life rather than on individual symptoms. The ultimate goal of treatment is to reduce the patient’s pain so that it does not interfere with daily life, and to eventually improve the patient’s quality of life. Pharmacological treatment, cognitive behavioral therapy (CBT), tongue protector, low-level laser therapy (LLLT), and repetitive transcranial magnetic stimulation (rTMS) are the treatment modalities [16]. The treatment for BMS is summarized in Table 1.

1. The importance of Informative Intervention and Reassurance

The first step in the BMS treatment is informative intervention and reassurance. Patients with BMS are likely to believe they have a major problem, so they visit numerous

Table 1. The Protocol of BMS treatment

Diagnosis of BMS through	BMS treatment	
	Non-pharmacological intervention	Pharmacological intervention
Oral examination	Informative intervention/reassurance	Topical clonazepam ^a
Radiography	Cognitive behavioral therapy ^a	Systemic clonazepam ^a
Salivary secretion test	Low-level laser therapy ^a	Gabapentin 300 mg+ALA 600 mg/day
Laboratory test	Lubricant	Nortriptyline 10-30 mg/day
Taste threshold test	Psychiatric intervention	Duloxetine 30-60 mg/day
Evaluation of psychological factors and sleep		

BMS, burning mouth syndrome; ALA, alpha lipoic acid.

^aThe efficacy was demonstrated in a meta-analysis [16,23].

doctors. Pain catastrophizing is defined as a set of exaggerated and negative perceptions and emotions about pain and pain experience [17]. Catastrophizing has three dimensions: rumination (I cannot seem to get it out of my mind), magnification (I wonder if something serious is going to happen), and helplessness (It is awful and feels like it is going to overwhelm me) [17]. Catastrophizing contributes to the aggravation of symptoms and emotional stress, affecting the intensity of pain and how patients cope with pain [18]. BMS patients show high pain catastrophizing scores [19]. A doctor's reassurance is very important. Reassurance is the removal of fears and concerns about illness [20]. As a result, the oral medicine specialist must provide consistent objective information about BMS, reassure the patient, transform negative thoughts into positive attitudes, and eliminate catastrophizing. Oral medicine specialists should set the goal of treatment and explain this. This procedure could be incorporated into CBT. CBT is a type of psychological treatment that has been shown to be effective for depression, anxiety disorders, chronic pain, and a variety of mental illnesses.

The following information and reassurances are provided to BMS patients: a chronic pain condition that is relatively common among the elderly; the unknown etiology; explanation about possible mechanisms of BMS development; the reassurance of patients' anxiety and concerns about the malignant disease; Treatment options, including medications, as well as their reported outcomes and side effects; focusing on maintaining normal functioning, not on symptoms and cause of BMS. After 6 months, the informative

intervention and reassurance in BMS treatment reduced pain intensity, pain catastrophizing, and improved quality of life [18]. A case-control study of CBT on BMS showed a significant reduction of pain scores for both short and long-term [21]. Another study found that an "initial approach" of detailed explanation, patient education, instruction on avoiding local irritants, and the use of lubricant reduced the intensity of symptoms in 34% of patients [22]. The information and instructions for BMS patients are shown in Table 2.

2. Pharmacological Treatment

Neuropathic pain medications such as clonazepam, anti-convulsant, tricyclic antidepressant (TCA), serotonin-norepinephrine reuptake inhibitors, and topical capsaicin have been used and studied for the treatment of BMS. Only topical capsaicin and clonazepam were found to be effective in both short- and long-term studies in systematic reviews and meta-analysis [16,23].

The most widely used and studied medication is clonazepam. According to systematic reviews and meta-analyses, clonazepam is effective for symptom remission in patients with BMS in both short-term and long-term applications with topical and systemic administration [16,23,24]. Clonazepam binds to γ -Aminobutyric acid type A (GABA_A) receptors and inhibits neuron hyperexcitability in the peripheral and central nervous systems. Peripheral GABA_A receptors are abundant in the oral cavity (oral mucosa, mandible, palate, salivary gland, and taste pathway) [25]. The use of topical clonazepam reduced pain more quickly but

Table 2. Information and instructions for burning mouth syndrome patients

Burning mouth syndrome (BMS) is a chronic pain condition that has no abnormalities in the oral cavity but has pain and discomfort. It is a kind of neuropathic pain. If you're diagnosed with BMS, here are the information and instructions to follow.

1. BMS is a chronic painful condition relatively common.
2. The etiology is unknown, but stress, menopause, neurotoxic agent, and genetic susceptibility are reported. The central and peripheral nervous systems are involved in the genesis of BMS.
3. BMS is not an infectious and not a malignant disease.
4. Spontaneous remission is rare. You had better be treated with medications and other modalities.
5. The complete treatment is difficult.
6. Because BMS symptoms do not reduce with only one visit of treatment or medication, it is important not to go visit a doctor here and there and to receive treatment steadily.
7. The medication is a neuropathic pain medication. It acts on the pain mechanisms and calms down the nerve.
8. Do not focus on each symptom and cause.
9. Please focus on maintaining normal function. The ultimate purpose of treatment is to reduce your pain and eventually enhance your quality of life.

for a shorter period than systemic clonazepam [26]. When the majority of BMS patients were prescribed clonazepam, 66% of patients showed complete remission or improvement of oral symptoms [22]. Greater initial pain intensity and an irregular pain pattern are predictors of better clonazepam therapeutic efficacy. The presence of depression is a negative predictor of clonazepam therapeutic efficacy [22,27].

Topical capsaicin activates the transient receptor potential vanilloid 1 and desensitizes the peripheral nociceptive C and A δ fibers. Because topical capsaicin causes initial burning pain, it is recommended that it be used in combination with lidocaine to reduce this pain. One randomized controlled trial reported that capsaicin rinse significantly decreased burning pain [28].

Although the efficacy of alpha lipoic acid, gabapentin, TCA, and SSRIs in BMS treatment has not been demonstrated in a meta-analysis, several studies have reported efficacy [16,29,30].

3. Non-pharmacological Treatment

Non-pharmacological treatments for BMS have included LLLT, rTMS, and tongue protectors. LLLT has an analgesic effect via anti-inflammatory effects and can penetrate tissue deeper, reaching the nerve fibers. In a meta-analysis, LLLT demonstrated a favorable outcome in both short- and long-term assessments [16,31]. rTMS is stimulation of the focal brain cortex via a localized pulsed magnetic field. Dorsal lateral prefrontal cortex (DLPFC) stimulation is used to treat medication-resistant depression as well as acute and chronic pain conditions [32]. A randomized controlled study found that rTMS of the left DLPFC, used in the treatment of depression, reduced pain significantly in BMS patients compared to controls. LLLT and rTMS are non-invasive methods and could be a complement to medication. A randomized controlled study [33] found that using a tongue protector as a shield against trauma or irritation on the tongue reduced pain scores [33]. Tongue protector is a unique device that is beneficial in that it blocks irritation on the tongue, however, it appears difficult to use in general because a tongue protector can be swallowed while being used and cannot be used for an extended period.

Patients with BMS often have anxiety, depression, and

sleep disorders as comorbidities. It has been reported that psychological factors such as depression and anxiety play an important role in BMS [34]. If the patients scored high on anxiety or depression, it is strongly advised that they be referred to a psychiatrist for psychiatric intervention.

CONCLUSION

BMS is difficult to manage and completely cure. As BMS is a chronic pain without obvious causative lesions, it is necessary to focus on the patient's functions and quality of life rather than the patient's symptoms. Because the prevalence of spontaneous remission in BMS is low, treatment such as pharmacological or non-pharmacological therapy is required to alleviate discomfort. Objective information and reassurance are very important in treating BMS and should be delivered to the patient. It is critical to comprehend the patient's symptoms and distress and to never disregard or dismiss symptoms. And the clear goal of treatment should be explained. This process requires a lot of time and doctor's efforts. We cannot currently request a fee such as a "chronic pain management fee" for CBT in dental clinics. I hope that oral medicine specialists' efforts and management are reflected in the oral health policies.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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