

Review Article

Burning Mouth Syndrome

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ABSTRACT

Burning mouth syndrome (BMS), a chronic orofacial pain syndrome is characterized by the presence of burning, stinging, and/or itching of the oral cavity in the absence of specific oral lesion. This condition affects chiefly of middle-aged and elderly woman with hormonal changes or psychological disorders. In addition to burning sensation, patient with BMS can be accompanied by gustatory disturbances such as dysgeusia (distortion in the sense of taste), parageusia, and subjective xerostomia (dry mouth) also complains of oral mucosal pain. This condition is probably of multifactorial origin, involving various local, systemic, and/or psychogenic causes, often idiopathic and its exact etiopathogenesis remains unclear. Female gender, premenopausal, depression and anxiety, Parkinson's disease, and chronic medical conditions including gastrointestinal and urogenital diseases are risk factors for developing BMS. BMS most often involves the tongue with or without extension to the lips and oral mucosa. The present paper discusses several aspects of BMS, updates current knowledge, and provides guidelines for patient management. The aim of this study is to review the current concepts regarding pathogenesis, classification, diagnosis, and treatment for this disorder. A literature review was carried out on Google Scholar and PubMed/Medline about the BMS and the related articles was selected and reviewed. BMS is a painful and often frustrating condition to the patients. There is no universal opinion regarding etiology, diagnosis, and treatment of BMS. BMS is a diagnosis of exclusion which plausibly has multifactorial origin. A thorough understanding of the etiology and psychological impact of this disorder is required for better management. Diverse pharmacological and nonpharmacological therapies are available, but it is unmanageable to achieve curative treatment. Compounding of cognitive behavioral therapy, alpha-lipoic acid, and/or clonazepam had shown promising results.

KEYWORDS: *Burning mouth syndrome, glossopyrosis, neuropathic pain stomatodynia, oral dysesthesia, sore tongue, stomatopyrosis*

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INTRODUCTION

Burning mouth syndrome (BMS) “A pain of at least 4–6 months duration located on the tongue or other oral mucosal membranes associated with normal clinical or laboratory findings” defined by the International Association for the Study of Pain.^[1] In the past, this condition has been referred by variety of names that include scalded mouth syndrome, stomatodynia, sore tongue, burning lips syndrome, glossodynia, glossalgia, stomatopyrosis, oral dysesthesia, burning mouth condition, glossopyrosis, sore mouth, and BMS (the most widely accepted).^[2,3] There are many systemic and local

disorders causing a burning sensation of the oral cavity. However, psychogenic and neurological conditions may be responsible for this symptom. As its name implies, BMS is one of the conditions causing burning sensation of the oral cavity which has various synonyms such as stomatodynia, glossodynia, glossopyrosis, and oral dysesthesia. It is a diagnosis of exclusion having the prevalence ranging from 0.7% to 4.6%.^[3] BMS is more common in premenopausal or postmenopausal women

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which may also be associated with other chronic pain disorders, depression, anxiety or somatization; so the patient usually has poor quality of life.^[4-7] So far, there is no definitive cure for this condition and most of the treatment approaches; medications remain unsatisfactory.

Various attempts to classify BMS based on etiology and symptoms have been made.

- In a classification by etiology or cause
 - “Primary BMS” (or “true BMS”) idiopathic BMS
 - “Secondary BMS” has an identifiable cause.
- Another classification of BMS is based on symptoms, stratifying cases into 3 types, as follows:^[8]
 - Type 1 BMS: Patients have no symptoms on waking, with progression throughout the day. Nighttime symptoms are variable. Nutritional deficiency and diabetes may produce a similar pattern
 - Type 2 BMS: Patients have continuous symptoms throughout the day and are frequently asymptomatic at night. This type is associated with chronic anxiety
 - Type 3 BMS: Patients have intermittent symptoms throughout the day and symptom-free days. Food allergy is suggested as a potential mechanism.

BMS is likely more than one disease process, and the etiology may be multifactorial. The ambiguous definition of BMS makes evaluation of prognosis and treatment difficult.

EPIDEMIOLOGY

It is extremely difficult to establish the true preponderance of BMS due to the lack of appropriate, uniform and reproducible classification system, determinate diagnostic criteria and their awareness among the oral health-care professionals. Many authors fail to differentiate between the syndrome and the symptom as such. The preponderance of BMS reported from different international studies ranges from 0.6% to 15%, respectively.^[9] BMS is basically a disorder of middle-aged and elderly individuals with an age range of 38–78 years.^[3] It seems that their preponderance increases with age in both males and females. BMS exhibits substantial female predilection and the ratio between females and males varies from 3:1 to 16:1 in different literature studies.^[10] Even though it is not yet outlined, these gender differences were explained in the context of biological, psychological, and sociocultural factors. Epidemiological studies reveal that this condition is especially common among pre- and post-menopausal women where their prevalence increases up to

12%–18%.^[11] This condition is exceedingly rare in patients under 30 years and never been reported in children and adolescence.^[12]

ETIOPATHOGENESIS

The pathophysiology of BMS is not yet fully understood, and different hypotheses have been projected to explain its etiopathogenic mechanism. BMS being a diagnosis of exclusion, burning sensation in the mouth caused by various systemic and local disorders has to be ruled out. Burning sensation inside mouth caused by various local conditions includes smoking, dental conditions such as ill-fitting denture, contact hypersensitivity to dental materials, alkaline oral rinses, or acidic foods.

Local causes

Clinical examination followed by biopsy will usually exclude mucocutaneous diseases such as oral candidiasis, lichen planus, lichenoid reactions, pemphigus, and glossitis. Similarly, viral infections such as herpes simplex or zoster may cause burning sensation.

Systemic causes

Endocrine

Menopause is associated with a higher occurrence of BMS, whereas the mechanism is unknown, hormonal (Estrogen) alterations have documented effects on oral mucosa, and deprivation may lead to atrophic changes within the epithelium.^[13] Alternatively, atrophic epithelia may be more prone to inflammation. Peripheral neuropathy occurs in diabetes mellitus is a cause of secondary BMS.^[14]

Immunologic

An immunologic mechanism for BMS has been suggested by the observation of increased serum erythrocyte sedimentation rate and salivary IgA in BMS patients compared with controls.^[10,15,16]

Nutritional

Deficiencies of B vitamins 1, 2, 6, and 12, zinc,^[17] folate, and iron, have been suggested as causes of secondary BMS, either from direct neurologic damage or in relation to anemia.

Infectious

Oral infections have been explored, and a few microbes had been identified to be possibly more prevalent in BMS patients without visible mucosal lesions: *Candida*, *Enterobacter*, *Fusospirochetals*, *Helicobacter pylori*, and *Klebsiella*.^[18,19]

Iatrogenic

Various cases of drug-associated BMS have been reported. Angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs),

antiretrovirals nevirapine, efavirenz, L-thyroxine, and topiramate are the most commonly noted in case reports.^[20-22]

Allergic

Allergies are not frequently identified in patients with BMS but have been proposed as a cause of Type 3 BMS (intermittent symptoms). However, they are typically associated with signs of mucosal irritation. Proposed irritants include dental materials such as mercury (present in amalgam), methyl methacrylate, cobalt chloride, zinc, and benzoyl peroxide.^[16] Components of lotions such as petrolatum cadmium sulfate, octyl gallate, benzoic acid, and propylene glycol have been concerned. Food allergens include peanuts, chestnuts, cinnamon, and sorbic acid.^[8] Nicotinic acid also been suggested as allergen.

The exact etiology of BMS is not clearly understood. Therefore, it is thought to be of multifactorial in origin.^[23] Local and systemic factors have been projected as the possible etiological agents from different studies.^[23-30]

Psychological causes

Anxiety, hypochondriasis, depression, stress, life events, personality disorders, cancerophobia, and neuropathy.^[31-33] It has also been suggested that BMS occurs due to damage to the taste pathways, for example, Chorda tympani nerve; and axonal degeneration of the trigeminal sensory nerve fiber has been demonstrated as well.^[34-37]

CLINICAL FEATURES

The term BMS inculcates to an individual who complains of variety of chronic oral symptoms that admits oral mucosal pain, altered taste sensation, xerostomia, and others that often increases in intensity at the end of each day that seldom interfere with sleep.^[4] The clinical display may vary as some patients can be oligosymptomatic (pain and dysgeusia or xerostomia) or monosymptomatic (pain only).^[3] In general, 63% of patients describe BMS accompanying dry mouth, 60% bitter/metallic taste, and 35% altered taste perception. The pain is represented as burning, scalding, tingling, or numbness. It is of moderate-to-severe intensity and can decrease during eating. It is commonly bilateral and most often involves the tongue succeeded by the palate and lower lip. In contrast, the buccal mucosa and floor of the mouth are rarely involved.^[10] The onset is spontaneous, though some BMS patients report ascendant dental procedures, initiation of medications, or other illnesses.^[3,38] Xerostomia may be immanent; however, some patients have demonstrated alterations in saliva quantity and quality.^[3] Vertical visual analog scale (VAS, 0-10 cm)^[39] is commonly used to describe pain intensity in BMS.

DIAGNOSIS

The diagnosis of BMS remains intriguing as diagnostic criteria are not sufficiently defined or universally accepted, several contradictory diagnoses exist, and the clinical display is often variable. Scala *et al.*^[3] projected the following fundamental criteria:

1. Daily and deep bilateral burning sensation of the oral mucosa
2. Burning sensation for at least 4–6 months
3. Constant intensity or increasing intensity during the day
4. No worsening but possible improvement on eating or drinking; and
5. No interference with sleep.

Additional supportive criteria are^[1] dysgeusia and/or xerostomia;^[2] sensory or chemosensory alterations; and^[3] mood changes or psychopathological alterations.

It is wise for the clinician to obtain a clear and elaborate medical/dental history as well as execute a thorough oral clinical examination including any laboratory studies indicated. A neurological examination can be useful although, unless there is marked inadequacy, the lack of baseline data can present a trouble. If all other causes of oral burning symptom are excluded and/or the patient fails to respond to a normal course of treatment, then a diagnosis of primary BMS is reasonable.^[40]

DIFFERENTIAL DIAGNOSIS

Differentiating primary BMS from secondary BMS is important. The following conditions may produce BMS-like symptoms: ^[19,41-44]

- Anemia
- Anxiety
- Alcohol-based mouthwash
- Aphthous stomatitis
- Areca nut extract exposure
- Bacterial infection
- Candidiasis
- Ciguatera neurotoxin exposure
- Chewing tobacco use
- Contact stomatitis
- Diabetes
- Dehydration
- Erosive lichen planus
- Gastroesophageal reflux disease
- Geographic tongue
- Impacted teeth
- Infections of bone, teeth, or implants
- Leukoplakia
- Multiple sclerosis
- Mouth breathing/nasal obstruction
- Medication reaction (e.g., ACE inhibitors, ARBs,

Table 1: Topical medications

MEDICINE	USES
capsaicin (0.025% cream)	desensitizing agent and is thought to inhibit substance P [23]
0.15% benzydamine hydrochloride	analgesic, anesthetic, and anti-inflammatory effect, but with inconsistent results[45]
Tabasco sauce with water	relieved from pain by using this mouth rinse[46]
hot pepper and water in a dilution between 1:2 and 1:1	relieved from pain by using this mouth rinse[47]
clonazepam (by sucking a tablet of 1 mg)	an agonist of gamma amino butyric acid receptors, found some success in treatment[48]
Lidocaine	anesthetic agent has short duration of analgesic action
0.5 ml Aloe vera gel at 70% combined with tongue protector lactoperoxidase (biotene mouthwash) and 5% doxepin	effective for reducing the burning and pain sensation of tongue[49] attempted and found to be ineffective[50]

Table 2: Systemic medications

MEDICINE	USES
Tricyclic antidepressants such as amitriptyline, desipramine, imipramine, clomipramine and nortriptyline (starting dose of 5-10 mg/day and gradually increases to 50 mg/day)	Useful in treating BMS but some authors contraindicate these drugs in patient with dry mouth as they can worsen the condition[51]
Selective serotonin reuptake inhibitor antidepressants like sertraline (50 mg/day), paroxetine (20 mg/day) for 8 weeks, duloxetine at a dose of 30-60 mg/day	Dual action antidepressants that inhibit both serotonin and noradrenaline result in a significant improvement of oral burning sensation[52]
Antipsychotics such as amisulpride, levosulpride at a dose of 50 mg/day for 24 weeks	Effective and shows a better patient compliance when used in short duration[51]
Alpha-lipoic acid (ALA) at a dose of 600 mg/day, either alone or in combination for 2 months, acts as an antioxidant and a powerful neuroprotective agent	Prevents nerve damage by free radicals, regenerating other antioxidants such as vitamin C and E, able to increase the intracellular levels of glutathione, thereby significantly reduces the symptoms in patients with idiopathic dysgeusia. gastric protection medication needed for ALA therapy[15,52,53]
Systemic capsaicin (0.25% capsules, 3 times a day, for 1 month)	Effective in reducing pain intensity however, it should be used cautiously as it results in gastric pain in some individuals[51]
Benzodiazepines at low doses	Useful in patients with anxiety disorders
Clonazepam (0.5 mg/day) and alprazolam (0.25 mg to 2 mg/day)	Treatment of BMS pain and it acts by probably disrupting the underlying neuropathologic mechanism[54]
Vitamin BC capsules, B12, folic acid and minerals like iron, zinc	Lower the mean serum homocysteine level and boost up the blood hemoglobin level with reported complete remission of oral symptoms[55]
Hormone replacement therapy (conjugated estrogens like premarin, 0.625 mg/day for 21 days and medroxyprogesterone acetate like farlutal, 10 mg/day from day 12 through day 21, for three consecutive cycles)	Relieve oral burning symptoms and improved cytologic features, especially in pre and post-menopausal women[56]
Cognitive behavior therapy	Successful in some individuals[57]

antiretrovirals, psychotropic, anticholinergic, clonazepam, and chemotherapeutic agents)

- Mandibular fracture
- Neoplasia
- Pemphigoid
- Pemphigus
- Radiation-induced stomatitis
- Sjögren Syndrome
- Scleroderma
- Vitamin deficiency (B1, B2, B6, B12, folate, iron)
- Hypothyroidism.

MANAGEMENT

A thorough clinical examination of the oral mucosa is crucial in these patients. The lack of oral mucosal pathology is mandatory for the diagnosis of BMS. Details regarding the quality, onset, persistence, intensity, occurrence, duration, relieving factors, evolution, site(s) involved in pain symptoms are essential. This information will give a vital clue in differentiating the BMS from other chronic orofacial pain disorders. Management of BMS can be broadly discussed under three topics, namely, topical medications [Table 1], systemic medications [Table 2], and behavioral interactions. Medications used for BMS

include antidepressants, analgesics, antiepileptics, antifungals, antibacterials, sialagogues, antihistamines, anxiolytics, antipsychotics and vitamin, mineral, and hormonal replacements.

Successful treatment of BMS patients with combined psychotherapy and psychopharmacotherapy has also been reported in table 2.^[51,52]

CONCLUSION

BMS is a painful and often frustrating condition to the patients. There is no universal opinion regarding etiology, diagnosis, and treatment of BMS. BMS is a diagnosis of exclusion which plausibly has multifactorial origin. A thorough understanding of the etiology and psychological impact of this disorder, combined with novel pharmacological interventions is required for better management. Diverse pharmacological and nonpharmacological therapies are available, but it is unmanageable to achieve curative treatment. Compounding of cognitive behavioral therapy, alpha-lipoic acid, and/or clonazepam had shown promising results.

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Conflicts of interest

There are no conflicts of interest

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