Burning Mouth Syndrome: A Critical Clinicotherapeutic Appraisal with a Spotlight on Alternative Medical Acupuncture Therapy

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ABSTRACT

Background: Burning mouth syndrome (BMS) is an idiopathic chronic condition characterized by bilateral symmetrical intraoral pain involving 2/3rd of anterior part of the tongue, burning, scalding sensation, distaste, and xerostomia with no obvious oral lesion and normal results of laboratory investigations. Objective: This critical review aimed to describe clinical and therapeutic options directed towards burning mouth syndrome with a special focus on medical acupuncture. Methods: E-searches of relevant data prior to 2018 published in PubMed, MEDLINE, Google Scholar, ScienceDirect and OvidSP databases were made using the Boolean operators and keywords. Finally, 58 articles were retained for this narrative review. Results: Burning mouth syndrome, primary idiopathic and secondary, is a clinicotherapeutic dilemma that preferentially afflicts postmenopausal females around the world. Given its multiple intricacies including ill-understood etiopathogenesis, pathophysiology, absence of standard care and universal treatment guidelines, BMS posits several clinicotherapeutic challenges to professionals who need to use individualized patient-centered approach and opt for most effective therapies from a variety of local, systemic and behavioral approaches targeting burning mouth syndrome. Evidently, medical acupuncture, a traditional Chinese holistic modality with safe clinical profile has been effectively used as an alternative therapy in patients with BMS worldwide, and for that purpose specific acupuncture needles, acupoints sites and number of treatment sessions and duration of treatment are important components of acupuncture therapy. Outcome results from partial to complete recovery or remission to spontaneous remission of patient with BMS vary with integrative approaches, modern therapies, behavioral interventions and medical acupuncture. Conclusion: Burning mouth syndrome is a clinicotherapeutic dilemma and needs further research about etiologies, pathophysiology, and therapeutic modalities. Medical acupuncture is emerging as an alternative safe holistic treatment for patients with primary burning mouth syndrome but certainly needs evidence-based data to further support its efficacy in burning mouth syndrome around the world.

Keywords: Burning mouth syndrome, burning sensations, dysgeusia, xerostomia, menopause, medical acupuncture

INTRODUCTION

Burning mouth syndrome (BMS), first described in 1880s and further explained in early 20th period by Butlin and Oppenheim as glossodynia, is an idiopathic chronic intraoral pain condition that preferentially affects middle-aged and elderly peri or post-menopausal women. BMS is characterized by bilateral, symmetrical non-specific persistent symptoms of burning or itching or scalding and pain (dysthesias) of oral cavity especially two-thirds of anterior part of tongue with clinically healthy appearance of the oral mucosa [1-4]. Various synonyms of BMS, a benign condition, described in literature are glossodynia (painful tongue), glosopyrosis (burning tongue), glossalgia, stomotodynia, and stomatopyrosis but sore tongue and oral pain is the core symptom of this neuropathic condition [2-4]. In addition, this pain condition has other important symptoms such as dysgeusia and xerostomia and, hence, BMS or burning mouth disorder is the most appropriate term for this disease [5]. Overall, BMS is most frequently used and accepted term across the world.

METHODS

Search Strategy

The relevant literature published in English prior to 2018 was searched in PubMed, MEDLINE, Google Scholar, ScienceDirect and OvidSP databases. The Boolean operators and keywords used in multiple electronic searches were “burning mouth syndrome AND definition OR classification OR types OR etiological factors OR etiopathogenesis OR working mechanisms OR diagnosis
OR evaluation AND laboratory investigations AND imaging procedures AND treatment interventions AND medical OR clinical OR laser acupuncture AND action mechanism AND “adverse effects” OR “complications”. The search strategy and the keywords were modified as appropriate according to the searched database. In addition, references included in full text articles focused mainly on medical and laser acupuncture were reviewed for inclusion in this critical review.

Search Results

Hundreds of thousands articles concerning medical acupuncture and burning mouth syndrome (n=37,893) were retrieved and reviewed by two independent researchers (NAQ & HAS). Our focus was on full articles describing BMS, socioclinical, diagnostic and treatments along with medical acupuncture. In addition, we also reviewed articles that gave adverse effects and complications of various therapies used in BMS. These articles were reviewed critically and the brief sketches of important contents were incorporated in this review. The additional inclusion criteria were free access to full articles, papers containing salient socioclinical features and treatment intervention of BMS and oral burning sensations. All types of related studies such as systematic reviews and meta-analyses, randomized clinical trials, observational studies, case series and single case reports were included for reviewing. Screening of retrieved records excluded 34,592 papers. More than three thousands records were reviewed for eligibility purpose (n=3377). After removing duplications (n=1127), unrelated articles (n=1132), no abstract (n=273), duplications (n=1127), and irrelevant information (n=470), 68 articles were left for further review. Finally, both reviewers agreed to include 58 published studies. (Fig. 1).

RESULTS

Definition

BMS evades a universal definition due to its variegated complex nature. The International Association for the study of Pain defines “BMS as a pain condition of at least 4-6 months duration, pain localized mostly on the tip and lateral sides of tongue or other mucosal membranes in the absence of clinical or laboratory findings, and the quality or location of the pain are the primary defining criteria” [6]. The International Headache Society defined BMS as “an intra-oral burning or dysesthetic sensation, recurring daily for more than 2 h/day for more than 3 months, without clinically evident causative lesions especially in the oral cavity or elsewhere in the body.” [7], and an analysis of these two definitions obviously depicts some differences particularly timeline, specific location and quality of core symptom of pain without naming specifically secondary BMS. In sum, these two definitions of BMS are a little short of comprehensiveness; therefore, this chronic pain condition needs more inclusive description to reflect a universal acceptable definition.
Classification

There is converging evidence that a well-defined classification of BMS will guide researchers to explore its multiple debatable controversial issues. Oral pain (dysesthesia), distaste (dysgeusia) and xerostomia with variable severity and diurnal presentation are the core triad symptoms of patients with BMS who often lead a poor quality life [2,5,8,9]. Based on main symptom of pain intensity and variations during the day/night, BMS is classified into the following types: 1) Type 1 typically has no symptoms on waking and progressively worsens throughout the day with nearly no nighttime symptom and affects about 35% of patients with BMS. This BMS type 1 is related to nutritional deficiencies or diabetes or shared common symptoms, such as, dryness of mouth and distaste in other systemic diseases; 2) Type 2 is associated with psychological factors such as chronic anxiety or depression or stress and displays symptoms at waking and throughout the day with disturbed sleep and affects about 55% of BMS patients; and 3) Type 3 displays intermittent daytime symptoms with periods without any symptoms and affects about 10% of patients with BMS, and food and many other chemicals causing allergic reactions are its underlying potential etiological factors [3,10-12]. Scala and associates proposed a more pragmatic classification of BMS; primary or, idiopathic or essential in which etiology is not known and secondary form (SBMS) is attributed to known pathologies, either local or systemic or behavioral or psychological causes [13]. Notably, PBMS responds not or poorly to treatment compared to secondary BMS [14] is debatable and this perspective needs further comparative research.

Epidemiological Trend

The epidemiology of BMS varies considerably due to different classifications, forms (primary or secondary), definitions and diagnostic criteria, gender, settings, age, comorbidities, differences in methodology, clinical signs and laboratory findings around the world. Burning mouth syndrome is much more common in females than males: 3 to 7 times higher in postmenopausal females. The prevalence of BMS is reported to increase by 3-to 12 fold with advancing age [15]. Overall, the highest prevalence of BMS tends to occur in the perimenopausal and postmenopausal periods of women life trajectories. Conversely, BMS is non-existent in male and female children and rarely seen in pediatric population and those under age 30. Occurrence of BMS in males is rare before the age of 50 years. The overall prevalence of burning mouth syndrome is reported to be around 4% [16]. In another study, about 0.7% to 4.6% of general population was reported to suffer from BMS [2,3,5]. Notably, the prevalence of BMS has increased exponentially from 5.6% to 57.4% in Japanese population of age 65 to ≥75 years over the past 10 years [15], and this trend may be true in the older population of other countries. Although sociodemographic determinants of BMS are not fully studied, however, biological, psychological and sociocultural factors may also explain the divergent epidemiological trends of this pain condition. Overall, the prevalence of BMS is unpredictable and contingent on a variety of biopsychosocial factors which need delineation in order to estimate precise prevalence and also proactively plan preventive strategies directed towards this disease.

Clinical Features

Clinical salient features of a disease supported by diagnostic criteria and laboratory tests findings is important guide to make a correct diagnosis (Table 1). BMS may present as a sudden bilateral, symmetrical orofacial pain characterized as burning, scalding, tingling, pins, electric shock or numbness, possibly precipitated by psychosocial stresses including irritability, anxiety, depression or medical factors, such as, infections or medications in less than 50% of patients and pain intensity tends to fluctuate with 24-time [2,5,10,17]. Intraoral mucosal areas most commonly affected in BMS are anterior two-thirds of the tongue and its lateral borders (71%-78%) followed by palate and other areas including lips [5,18,19]. Other symptoms characterizing BMS are dysgeusia in terms of metallic taste and bitter taste, halitosis, sticky sensations, stinging, insomnia (due to pain) and xerostomia (dryness of mouth), the later symptom is reported in up to 60% of patients with BMS [1-5]. Dysphagia, dental and atypical facial pain and a combination of other symptoms emerge during long trajectory of BMS [3,5,9,20]. In sum, oral dyssthesias, dysgeusia and xerostomia without any evidence of local and systemic organic and psychological factors complemented by normal laboratory results will suggest a possible diagnosis of primary BMS.

Etiopathogenesis

There is no disease without etiological factors which may or may not be apparent in all diseases including idiopathic conditions. The several etiologies underlying BMS are scientifically examined yet are not well understood. As an idiopathic pain condition, it develops without any abnormality within the oral cavity or in other body systems [5,18,22]. Multiple theories exist regarding the etiopathogenesis of BSM, and most researchers believe the condition to be multifactorial and neuropathic. The BMS is mostly reported in postmenopausal women that supports the theory about the deficiency of estrogen in BMS. Decreased levels of estrogen lead to the atrophy of oral mucosa leaving the area more vulnerable to inflammatory changes and, hence, the development of burning mouth symptoms [19]. In some cases, infections by microorganisms precede the onset of burning mouth symptoms, and certain pathogens including candida, enterobacter, fusospirochetal, helicobacter pylori (HP), and klebsiella are commonly found in the oral cavity of patients with BMS [5,9,18]. Interestingly, HP has been isolated using oral mucosa biopsy material and biology procedures in 86% of patients with burning sensation, lingual hyperplasia and halitosis and only 2.6% of the
Clinical features and diagnostic criteria of BMS [3,5,13,21]

<table>
<thead>
<tr>
<th>Pain</th>
<th>Features</th>
<th>Diagnostic criteria</th>
</tr>
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<tbody>
<tr>
<td>Onset</td>
<td>Sudden or slow insidious</td>
<td><strong>Fundamental Criteria</strong></td>
</tr>
<tr>
<td>Description</td>
<td>Burning mouth-symmetrical and bilateral &amp; intraoral</td>
<td>Daily deep burning sensation of the bilateral oral mucosa</td>
</tr>
<tr>
<td>Intensity</td>
<td>Variable, with peaks of intensity, mild, moderate and severe</td>
<td>Burning sensation for at least 4–6 months</td>
</tr>
<tr>
<td>Pattern</td>
<td>Continuous, no paroxysm</td>
<td>Constant intensity or increasing intensity during the day</td>
</tr>
<tr>
<td>Location</td>
<td>Independent of nerve pathway, intraoral and 2/3 of anterior of tongue</td>
<td>No worsening on eating or drinking. Instead, the burning sensation may reduce</td>
</tr>
<tr>
<td>Pain during sleep</td>
<td>Infrequent in type II compared to Type I &amp; III</td>
<td>No interference with sleep</td>
</tr>
<tr>
<td>Other symptoms</td>
<td>Dysgeusia, xerostomia (&amp; oral pain-triad of BMS)</td>
<td></td>
</tr>
<tr>
<td>Signs/symptoms</td>
<td>Absence of evident clinical signs, sensory chemosensory disorders, psychological stress and anxiety/depression precipitate</td>
<td>1. Dysgeusia and/or xerostomia</td>
</tr>
<tr>
<td>Concomitant extraoral symptoms</td>
<td>Frequent headaches, weakness, laziness, poor attention, lower concentration, insomnia, fatigue, and multiple non-specific health concerns about psychological and physical disorders</td>
<td>2. Sensory or chemosensory alterations</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. Mood changes or psychopathological alterations such as depression, anxiety state or OCD or personality disorders</td>
</tr>
</tbody>
</table>

patients without intraoral manifestations had this bacterium. Diabetes mellitus and associated peripheral neuropathy may also cause symptoms related to BMS, although the underlying mechanism is primarily neuropathic [4,5,16,18]. Immunologic factors tied to BMS include a correlation with elevated sedimentation rate and over salivation; elevated salivary IgA has been found in patients with BMS. There is an association with certain irritants, including dental materials such as mercury, amalgam, methyl methacrylate, cobalt chloride, zinc, and benzoyl peroxide [23]. In addition, certain food allergies including peanuts, sorbic acid, chestnuts, and cinnamon have an etiological association with BMS, which is mimicked by oral allergy syndrome [24]. Evidently, BMS is precipitated by overwhelming stress and also associated with neuropsychiatric conditions, such as major depression, chronic anxiety, OCD, and personality disorder. The most common association of BMS is with a major depression, and it may follow acute symptoms or share an association as a comorbid condition at some point in BMS patients’ life [2,25]. Other causes include the presence of orthodontic equipment, possible prescription drug adverse effects, and increase in bradykinin as well as comorbid dermatologic conditions [25]. Newer investigations into perceptual alterations concerning dysgeusia and pain tolerance opened another etiological window for mouth burning sensation [3-5,9]. Accordingly taste located on the anterior part of the tongue with fungiform papillae, which are found in high density especially in women called “superstasters” are theoretically highly vulnerable to develop burning mouth as they tend to perceive the bitter taste of 6-n-propiltiouracilo (PROP) [3-5,11-13]. Overall, BMS comprises a spectrum of acute or chronic symptoms both in severity and temporal occurrence and may have multiple sharing etiological associations with aforesaid local, systemic and psychiatric conditions (Table 2).

Pathophysiology

Like etiopathogenesis, the pathophysiology of BMS is also poorly understood. However, pathophysiology of burning mouth sensation concerns various processes between peripheral and CNS pathways [2,8,16,22]. Of note, disruptions in circadian rhythm and the HPA axis are considered the main contributing factors in BMS [2,5,18,22]. Psychological factors including anxiety, depression, parafunctional habits and saliva flow reduction that impact HPA axis and steroid hormone, taste, and small nerves in oral cavity contribute to the pathophysiology of mouth burning sensations [2,5,18,22]. The underlying mode of the pain conduction is likely along the trigeminal nerve distribution (peripheral pathway) to higher pathways in CNS, and some studies have evidenced histopathologic changes in nociceptive nerves in patients with burning mouth symptoms [2,5,18]. One study showed a link between hypofunction of the chorda tympani and or/glossopharyngeal nerve resulting in reduced taste while hyperstimulating the lingual nerve (trigeminal nociceptive pathway) that cause BMS symptoms [5,18]. Other mechanisms similar to phantom limb as well as small fiber neuropathy concern xerostomia, one of the core symptoms of BMS. In fact, xerostomia in BMS reflects neuropathy and consequently abnormal function of glandular issue, i.e., hyposalivation [5,9]. Mechanical damage from multiple sources such as bruxism, teeth clenching and tongue thrusting and biting.
### Table 2: Diagnosis, evaluation and interventions of BMS [1-4,5,8,11-13,16-8,20,33-38]

<table>
<thead>
<tr>
<th>Etiologies and diagnoses</th>
<th>Therapies of SBMS&amp; PBMS</th>
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<tbody>
<tr>
<td><strong>Local</strong></td>
<td><strong>Therapies of SBMS</strong></td>
</tr>
<tr>
<td>1. Local irritation from poor-fitting denture</td>
<td>1. Monitor infection by Candida albicans, use oral nystatin, avoid allergens</td>
</tr>
<tr>
<td>2. Dental abnormalities and surgery</td>
<td>2. Manage medications - antihypertensive renin-angiotensin drugs**8, antipsychotics antidepressants, benzodiazepines and anticholinergic</td>
</tr>
<tr>
<td>3. Oral mechanical and chemical trauma, amalgam disease (galvanism) &amp; sharp edges of teeth, abrasive toothpaste</td>
<td>3. Manage xerostomia, avoid tobacco use</td>
</tr>
<tr>
<td>4. Parafunctional habits: bruxism (teeth grinding), tongue posturing, tongue thrust, tics, continual rubbing over the teeth or prosthesis, intraoral biting &amp; compulsive acts of the tongue</td>
<td>4. Treatment of galvanic allergies</td>
</tr>
<tr>
<td>5. Allergic contact stomatitis from dental prosthetic material, foods, oral care products and chemicals</td>
<td>5. Manage nutritional deficiencies</td>
</tr>
<tr>
<td>6. Xerostomia due to aging, radiotherapy, salivary gland dis., and different drugs such as ACEs, psychotropics</td>
<td>6. Treatment of endocrine disorders such as thyroid diseases, and metabolic diseases such as diabetes,</td>
</tr>
<tr>
<td>7. Infectious: Herpes simplex infection, HIV, oral candidiasis, infections of teeth and gums,</td>
<td>7. Treatment of psychological disorders such as depression and anxiety</td>
</tr>
<tr>
<td>8. Ciguatera*</td>
<td>8. Manage autoimmune diseases</td>
</tr>
<tr>
<td>9. Leukoplasia</td>
<td>9. Treat neuropathies-mono and poly forms</td>
</tr>
<tr>
<td>10. Oral lesions: lichen planus, migratory glossitis, geographic tongue (benign migratory glossitis), bullous pemphigoid, pemphigus vulgaris, herpetic lingual neuroalgia</td>
<td>10. Mouthwashes- lactoperoxidase (oral rinse)</td>
</tr>
<tr>
<td>11. Areca nut and chronic tobacco exposure</td>
<td>11. Mucosal protectant: sucralfate (oral rinse)</td>
</tr>
<tr>
<td>12. Thermal injury (from hot food and liquids)</td>
<td>12. Tongue protector</td>
</tr>
<tr>
<td><strong>Systemic</strong></td>
<td><strong>Common Therapies: PBMS</strong></td>
</tr>
<tr>
<td>1. Endocrine disorders: diabetes mellitus, thyroid disorders, menopause &amp; hormone deficiency</td>
<td>A. <strong>Topical treatment</strong></td>
</tr>
<tr>
<td>3. Hyposalivation: Sicca syndrome, Sjogren syndrome, connective tissue diseases such as scleroderma and other autoimmune diseases</td>
<td>2. Clonazepam</td>
</tr>
<tr>
<td>4. Medications use: ACE inhibitors, antihyperglycemics, antihistamines, antiretroviral drugs, antipsychotics, chemotherapeutic agents, benzodiazepines, anti-arrhythmia drugs</td>
<td>3. Lidocaine</td>
</tr>
<tr>
<td>5. Anemia</td>
<td>4. Benzydamine hydrochlorate at 0.15%</td>
</tr>
<tr>
<td>6. GERD</td>
<td>5. Aloe Vera,</td>
</tr>
<tr>
<td>7. Fibromyalgia</td>
<td>6. Doxepin cream</td>
</tr>
<tr>
<td>8. Urogenital diseases</td>
<td><strong>B. Systemic treatment</strong></td>
</tr>
<tr>
<td>9. Hypertension</td>
<td>1. Nortriptyline</td>
</tr>
<tr>
<td>10. CNS disorders</td>
<td>2. Amitriptyline</td>
</tr>
<tr>
<td><strong>2.1 Psychological</strong></td>
<td>3. Paroxetine (selective serotonin reuptake inhibitors, SSRI)</td>
</tr>
<tr>
<td>1. Depression,</td>
<td>4. Clonazepam</td>
</tr>
<tr>
<td>2. Anxiety including OCD</td>
<td>5. Gabapentin, pregabalin, topiramate</td>
</tr>
<tr>
<td>3. Somatoform disorder</td>
<td>6. Capsaicin</td>
</tr>
<tr>
<td>4. Cancer phobia (20% to 30% BMS pts)</td>
<td>7. Alfa lipoic acid</td>
</tr>
<tr>
<td>5. Psychosocial stressors</td>
<td>8. HRT</td>
</tr>
<tr>
<td>6. Psychotropics medications**</td>
<td>9. St John’s Wort (Hypericum perforatum)</td>
</tr>
<tr>
<td>7. Personality disorders</td>
<td>10. Cognitive behavior therapy, relaxation therapy, group therapy, meditation</td>
</tr>
<tr>
<td><strong>2.2 Neurological</strong></td>
<td>11. Acupuncture alone or combined with other CAM therapies and modern drugs</td>
</tr>
</tbody>
</table>
| 1. Neuropathy, | ***ACE-angiotensin converting enzymes (antihypertensive medications, such as, captopril, enalapril and lisinopril that act renin-angiotensin system); Like many other drugs, topiramate also causes BMS-like symptoms

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*Eating reef fish contaminated with ciguatoxin and others; **Psychotropics especially antipsychotics, benzodiazepines, and antidepressants, and anticholinergics; all may cause dryness of mouth but their minimal doses alleviate xerostomia in BMS; ***ACE-angiotensin converting enzymes (antihypertensive medications, such as, captopril, enalapril and lisinopril that act renin-angiotensin system); Like many other drugs, topiramate also causes BMS-like symptoms*
Burning mouth syndrome (parafuncional habits) and psychological disorders may also contribute to the pathophysiology of orofacial pain that certainly mimics MBS [2,5,26]. The pathophysiology of BMS may also be explained by other means including medications that impact peripheral and CNS. It has been postulated that BMS symptoms may have an association with certain medications, specifically angiotensin-converting enzyme inhibitors and angiotensin blockers (and psychotropic drugs) that increased bradykinin linked with the development of secondary angioedema. Although the mechanism is not well understood, kallikrein, an active molecule in the kinin pathway and linked with inflammation, pain, blood pressure control and coagulation is elevated in the saliva of BMS patients [18]. Anti-retroviral medications, such as, efavirenz and nevirapine (Non-nucleoside reverse transcriptase inhibitors) [27] and other drugs including levotheroxine, topiramate, and dental materials are also associated with BMS but the relevant studies are needed to fully understand the underlying pathophysiological mechanisms concerning BMS [5,9,18]. However, irritation to the oral mucosa and underlying nerves via either contact dermatitis or direct nerve irritation by aforesaid medications and dental materials may partially explain the pathophysiology of burning mouth syndrome [28]. Concerning histopathology of BMS, certain changes such as dysplasia to nociceptive nerve fibers in the oral cavity are reported, although symptoms can occur without evidence of histologic alterations especially in primary BMS. There are no well-defined known histopathologic findings exclusive to essential BMS [2,5,18]. Based on an old research, Lopez and colleagues summarized the important pathophysiological findings; intraoral reduction in heat and pain perceptions as also found in polyneuropathy; heat mediated reduction in tolerance to pain at the tip of the tongue in 85% of patients with BMS; irregularities in blink reflex in patients with BMS possibly reflecting a subclinical trigeminal neuropathy; and the alteration in saliva composition compared to controls impacting the perception of flavors [2,5,9,21]. Overall, peripheral nerves density especially of trigeminal micro nerve fibers in the oral cavity of patients with BMS is reduced that indicates axonal degeneration and sensorial neuropathy. In addition, revealed central neuropathic mechanism underpinning BMS is cerebral hypoactivity through heat stimulation of trigeminal nerve in BMS patients. Thus, a variety of factors and multiple processes mediate degeneration of peripheral micro-nerves located on the tongue in tandem with cerebral hypoactivity might be the important bidirectional components in the pathophysiology of BMS. This avenue needs further basic translational research in order to understand fully the pathophysiology of BMS.

Diagnosis

Burning mouth syndrome is a diagnosis of exclusion and, hence, it is highly desirable to first rule out local and systemic organic causes including malignancy of intraoral pain sensations [29]. Professionals need to explore the details of onset (acute or slow), duration (6-month or more) and severity (mild, moderate or severe) of burning mouth sensations along with several medical conditions including infections, metabolic disorders, autoimmune disorders, diverse prescribed and OTC medications, use of oral prosthesis, oral abnormalities, teeth malocclusion, nutritional deficiencies, and multiple physical and psychiatric comorbidities in order to precisely diagnose BMS [1,2,5,8,18,19]. Exclusion of these conditions (Table 2) may or may not confirm the diagnosis of idiopathic PBMS and, hence, focus should not only be on excluding systemic and neuropsychiatric diseases by specific laboratory tests but also specifically intraoral mucosa and tongue lesions. In specific terms, clinical findings in terms of bilateral symmetrical intraoral burning, xerostomia, dysgeusia, chronic anxiety, stress, depression, and female gender will help in diagnosing PBMS. Overall, the diagnosis of BMS is based on specified diagnostic criteria including exclusion of all diseases mimicking PBMS.

Laboratory Investigations

Laboratory evaluation needs to focus on ruling out other causes of oral pain sensations together with comorbid conditions which may cause secondary BMS. These tests include CBC with differential, serum folate, serum B12, ferritin, metabolic panel for diabetes, urinalysis, thyroid-stimulating hormone and free T4, thyroid binding globulin, antithyroglobulin abs, antithyroidperoxidase abs, erythrocyte sedimentation rate, anti-SSA autoantibodies (anti-Sjogren syndrome antigen)abs, SSB abs, Ro abs, SS-La abs, antinuclear antibody, rheumatoid factor, anti-citrullinated abs, sialochemistry, luteinizing hormone, follicle stimulating hormone, and hemoglobin A1c. Imaging of head and cervical spine is not useful for idiopathic BMS but may identify underlying etiologies, such as, mass lesions, abscess, and multiple sclerosis for SBMS. Similarly, CT of head and maxillofacial region may also reveal findings suggestive of SMBS. Furthermore, ultrasound evaluation of the thyroid may reveal the underlying mass, multinodular goiter, or other thyroid pathology that might suggest SBMS. Positive results concerning blood and fungal cultures, biopsy of oral mucosa, lumbar puncture with gel electrophoresis, tests for allergy, sialometry/sialochemistry (to measure flow of saliva and analysis of saliva), Schirmer test (for diagnosing conditions associated with dry eyes), and laryngoscopy or endoscopy will help in excluding the diagnosis of PBMS [1,2,4,8,18,30-32]. Overall, despite a list of laboratory tests and imaging techniques, the diagnosis of PBMS remains a dilemma and challenges acumen of expert professionals.

Differential Diagnosis

Exclusion of differential diagnoses may help in the diagnosis of PMBS. Burning mouth sensations happen to occur in a variety of diseases including primary and secondary BMS. Differential diagnosis of BMS (Table 2) includes atypical facial pain, atypical odontalgia, idiopathic facial
arthromyalgia, herpes simplex and zoster infection, oral candidiasis, HIV, several psychotropic medications, GERD, scleroderma, Sjogren’s syndrome, neuropathy, diabetes, hypothyroidism, nutritional deficiencies, multiple sclerosis, fibromyalgia, anemia, dehydration, anxiety, anticholinergic medications effects, stomatitis, pemphigus, malignancy, hyperplasia, areca nut exposure, infections of teeth and gums, acoustic neuroma, trauma to lingual or mandibular nerves after dental surgery, denture design or tooth restoration failures, ciguatera, leukoplakia, psychiatric disorders and parafunctional habits and chronic tobacco use [1,2,8,11,13,18,16,33].

**Prognosis**

Evidently, the prognosis of BMS is variable and based on multiple factors including co-morbidities, sociodemographic and clinical specificities, and treatment interventions. Symptoms of BMS may be transient and resolve with time or symptomatic treatment; however, chronic symptoms usually persist for months to years. Complete resolution of BMS with treatment is a robust possibility. The spontaneous complete remission is found in 3% of population with BMS after 5 years followup; however, partial or complete remission with or without treatment is reported in 20% to 50% of BMS patients after 6 to 7 years followup [17,22] and this divergent finding might be due to loose versus stringent diagnostic criteria of BMS and different interventions or no intervention. Of note, patients treated in accordance to algorithm (n=10/21, 48%) improved compared to non-algorithm (n=1/26, 4%) concerning pain and burning sensation and a significant number of patients tend to discontinue followup in non-algorithm group (p=0.001) [1]. The BMS is not progressive rather a benign condition and not known to cause death [5,18]; however, adversely affects the quality of life of sufferers and linked with healthcare burden.

**Management**

The management of BMS is multifaceted and often challenging [5,17]. Prior to initiation of intervention, professionals should make sure that the condition under treatment is primary or secondary BMS. A patient with PBMS often of long duration necessitates customized-treatment approach as one size fist never fits to all patients with BMS. Main effective interventions associated with 50% to 80% improvement and in some cases complete remission in PBMS could be categorized into local, systemic and behavioral treatments (Table 2); oral topical medications include clonazepam (1 mg tab with saliva at the oral pain sites for 3 min and then to spit, repeat this regimen tid for 14 days) and capsaicin (0.025% cream to the site of discomfort qid for 4 weeks), lidocaine or benzylamine hydrochlorate (0.15% use as mouthwash) and aloe vera (0.5 ml gel at 70% to the sore areas of the tongue tid combined with a tongue protector), and mostly all are effective in less than 80% of patients in reducing oral pain and burning sensations with better quality of life. Systemic medications used effectively in BMS patients with substantial reduction in pain and burning sensations are clonazepam (initially 0.25 mg daily, then 0.5 mg second week or 0.5 mg/day for 4 weeks, may cause addiction if doses increased further and used long period of time) and SSRIs (variable low doses of each SSRI such as paroxetine, 20 mg/day, sertraline 50 mg/day), alphalipoic acid (600 mg/day alone or psychotherapy alone or both combined, each for two months), HRT(conjugated Premarin), 0.625 mg/day for 21 days plus medroxyprogesterone acetate (Farlutal), 10 mg/day from day 12 through day 21 of the treatment cycle, for 3 consecutive 21-day cycles), tricyclic antidepressants (variable low doses of each antidepressant), olanzapine (2.5 mg to 5 mg/day), and amisulpride (50mg/ day for 8 to 24-week) and anticonvulsants such as gabapentin (900 mg/day), pregabalin (150 mg/day), and topiramate (weekly titration of doses to reach 100 mg BD with clinical evaluation). Local and systemic use of clonazepam (0.5 mg tid, first dissolve in mouth, then swallow and follow for six months or so) is also used in BMS with effectiveness, 50% reduction in pain [35,39,40]. Systemic use of clonazepam (5mg/day) combined with antidepressant venlafaxine (a serotonin norepinephrine-reuptake inhibitor, 300mg/day) was reported to be effective in eight resistant BMS patients (>50% reduction visual analogue score [VAS]) after 3-month who failed to respond to a variety of drug interventions [35,41]. Other systemic medications such as dopamine agonist (pramipexole, 0.25mg OD to 0.5mg BD), histamine, receptor antagonist (laftudine, 5mg BD), and herbal supplement (St. John’s wort, 300mg BD) and salivary stimulants (cholinergic agonists -pilocarpaine, 5mg per oral, anetholtrithion-sialor, 25mg/daily, cevimeline, 30mg/day and bethanechol 25 BD) are also used in BMS with good results, about 50% improvement in patients with BMS. Behavioral therapies either alone or combined with other CAM approaches used effectively in patients with BMS are cognitive behaviour therapy (once a week for 12–15 weeks) and group therapy [3,18,35,40] and currently, electroconvulsive therapy is no more used in BMS. Estrogen replacement therapy acts on estrogen receptors on the tongue and improves BMS symptoms; however, has potentially dangerous adverse effects including risk of breast cancer, thromboembolism, cardiovascular diseases, stroke and dementia, and, hence, not advisable its use in BMS. Patients are instructed not to take high doses of these medications (such as anticholinergics, antidepressants, antipsychotics, ACE inhibitors etc) directed towards underlying disorders as they tend to provoke symptoms especially burning mouth and dryness of BMS [1-4,28,35]. Other efficacious therapies in BMS include clinical acupuncture, cognitive behavioral therapy, and near-infrared irradiation of the stellate ganglion to inhibit sympathetic discharge as well as improving blood flow to the tongue [3,18,22,40]. Overall, many of these therapies are complementary to modern therapies (integrative approach) in the management of patients with BMS.

**BMS and Laser Therapy**

HRT, capsaicin, herbal supplements, topical analgesics, and antidepressants as efficacious modalities for BMS but less effective in recalcitrant PBMS [1]. However, low doses of antipsychotics, lidocaine, relaxation therapy, repeated transcranial magnetic stimulation (rTMS, non-invasive), laser therapy and topiramate (100-300 mg/day) were effective therapies in patients with resistant BMS [8,42-46]. Yang and Huang reported only initial reduction in pain score and burning sensations in 17 BMS patients but overall improvement was not maintained after 2-year followup [44], and accordingly low-level energy diode laser may be an effective treatment for non-resistant BMS. In another small study of 10 diagnosed patients with BMS, all patients treated with low-level laser therapy (LLLT) showed about 60% reduction in VAS. Santos et al (2011) suggested that LLLT may be an alternative modality for improving intraoral burning in patients with BMS [47]. Conversely, a study involving 20 patients with BMS treated with laser therapy and another 20 BMS patients treated with placebo (laser therapy machine was on switch off mode) found no significant differences between two groups regarding symptoms intensity. However in both group BMS symptom intensity was decreased attributed to placebo effect rather than laser therapy [48]. To some extent, the complicated BMS may benefit from concurrent use of oral hygiene and non-alcoholic mouthwash, intake of adequate fluid, patient education, vitamin and alpha-lipoic acid supplementation, hypnosis and psychiatric interventions [1-3,18,32,49]. The poor response to local, systemic and behavioral interventions may be attributed to poor compliance, inadequate doses, irregular and short duration of treatment, variegated socioclinical factors, comorbidities and nature of BMS. From this perspective, the patients with multifactorial PBMS will require collaborative referrals to and consultations from several departments including internal medicine, rheumatology, neurology, neuropsychiatry, dentistry, pain, CAM, and obstetrics and gynecology. Overall, although management of BMS is highly challenging, integrative holistic treatment approach will provide the best quality-based services to patients with primary and secondary BMS.

Rationale to use Chinese Acupuncture in PBMS

Given many clinico-therapeutic intricacies including the absence of global treatment guidelines and gold standard care, ill-understood etiology and pathophysiology, and in light of several short- and long-term interventions without complete recovery, the prevention and management of PBMS becomes very difficult and challenging to healthcare providers [1-3,8,32,37,49] and, consequently, pertinent question arises; is medical acupuncture alone without other complementary and modern therapies effective in PBMS? Medical acupuncture alone is reported to be effective in PBMS, and we will examine this point by reviewing focused literature.

Concepts of traditional Acupuncture

Traditional acupuncture has its origin in Traditional Chinese Medical system and has been practiced in a variety of medicosurgical conditions since ancient times. Medical acupuncture follows TCM concepts which are; the human body made up of polarity and the union of two opposites strikes a balance in the entire body by a mutual relationship, connectivity, interaction, control and relevant changes through flow of fluids (blood in microvascular system) and energy (through meridian channels) [1,2,11,17,18]. Acupuncture holistically targets the patient with variegated BMS for achieving a balance of Yin and Yang energy between the organs. Consequently, analgesia, muscle relaxation, sedation, mitigation of depression, reduction in inflammation and spasm, quick repair and promotion of immunity follow, and all this will give a sense of improvement to patients with BMS. In addition, clinical acupuncture also works by means of bidirectional neurophysiological pathways including effecting peripheral nerve fibers (A-delta and C), spinal cord, connected synapses and established reflex arcs, preganglionic neurons, and CNS spinoreticular and spinohalamic tracts [50]. The detailed discussion of traditional and conventional action mechanisms and effects of medical acupuncture in BMS is beyond this paper.

Acupuncture Points and Needles

Acupuncture points, size and depth of needles, number of treatment sessions and frequency, timeline and followup are important components of acupuncture therapy. The careful selection of acupuncture points and needles size and depth in each patient with BMS are highly desirable and mandatory which are based on the principles of western conventional medicine (especially anatomy, physiology, neurophysiology, & neuroanatomy) and TCM that defined the ancient Yin and Yang theory, five elements (water, wood, fire, earth and metal), Zang-Fu (set of organs that produce qi energy) and meridian and sub-meridian points. However, the most common acupuncture used in BMS include E (stomach meridian), Ig (large intestine), R (kidney), F (liver), P (lung), and VG (governing vessels). The needles usually applied to both sides of the body, systemic and local acupuncture used in BMS are: R-3, R-7, F-3, E-36, LI-4, IG-11, VG-20,P-7, R-6 (distal/systemic) and E-3 to E-7, Ig-20 and VG-26. In addition, ear acupuncture used in BMS include: Shen-Men, CNS, nutritionally variant streptococci, kidney, spleen/pancreas, and mouth [50,51]. Overall, besides disseminating energy through meridian acupoints, medical acupuncture modulates vascular pattern by means of decreasing arborescent ties and increasing vascular density compatible with the physiology of microcirculation and, consequently, improves various symptoms of patients with BMS.

Evidence-based literature

English literature on medical acupuncture used in the treatment of BMS is limited [52]. Susano and colleagues (2017) reported a 53-year old female patient with BMS who neither responded to rescue therapy nor gabapentin (antiepileptic and pain reliever) nor tramadol (opioid analgesic). Then, the patient was given eight acupuncture
treatment sessions with a weekly frequency. Standard needles were applied to several acupoints ST 5, ST 6, ST 7, SI 18, GB 2 & TE 21 (local) and GV 24, L14, ST 44 & ST 36 (systemic). Most of the symptoms improved and the patient showed very much improvement at six months follow-up. Acupuncture was considered safe, tolerable, and effective in BMS with few minor side effects including sleepiness, the tiredness, and bleeding at the sites of insertion of needles. Acupuncture in the hands of incompetent, inexperienced and unqualified professional may cause some complications such as pneumothorax and local infection with its dissemination to other parts of the body [17]. In a single arm clinical trial with eight patients (out of 60) of BMS, combined use of acupuncture and auriculotherapy was found to be effective and all patients showed good improvement on VAS with better quality of life (measured by Short-Form [SF] Oral Health Impact Profile-14) at 2-year follow-up [52]. In a systematic review of nine comparative Chinese studies involving randomized patients (n=547) treated with acupuncture/ acupoint injection (medical herbs, analgesics or vitamins injected into acupuncture points) participants in seven studies showed a significant improvement in BMS compared with other treatments, especially in reducing pain and burning sensations of BMS [53]. However, the limitations of all nine studies were; questionable methodologies and published in local magazines rather than in scientific journals [37]. Using videocapillaroscopy for observing microcirculation, Scardina and colleagues (2010) used traditional acupuncture in PMS patients (n=30) who showed significant improvement after 3-week treatment and remained stable at 18 months of follow up [54]. Furthermore, acupuncture caused significant increase in the capillary tortuosity and density and a reduction of the arborescence in mouth and, thus, improved the burning sensation in all the patients. In a pilot study, Sardella et al (2013) found significant improvement in intraoral pain of 10 BMS patients treated with acupuncture which lasted 8 weeks with 20 sessions but quality of life measured by SF-36 remained unaffected, though all patients were better able to express themselves [22]. In a short correspondence, Braiolo et al (2013) reported the use of laser acupuncture (laser light as an alternative to needles to stimulate acupoints; eight sessions, each lasting 15 min, every other day) in 16 patients with chronic BMS using selected acupoints (ST1 to ST3, ST4, ST5, L14, LU7, GV14, CV17, SP10, SP9, and SP6) and the laser wavelength was 660 nm, output power 50, the dose 1.5 2.0 J/cm. According to VAS, all patients showed a reduction in the symptoms of oral burning [55]. Another comparative study involving 20 patients with BMS treated with acupuncture; half-an-hour session 3 times per week for four weeks. Needles of 0.25 mm in diameter and 30 mm length were inserted at the depth of the 0.5-1 cm. The elicited response considered was “de qi” in terms of redness and a feeling of numbness around the needles. The selected acupoints on both sides of the body were ST 8 (stomach- tou wei), GB 2, TE 21, SI 19 (small intestine- ting gong), SI 18 (small intestine- quan liao), LI 4 (large intestine-Yuan) and GV 20 (Governing vessel-bai hui). Comparator clonazepam was given to 20 BMS patients (0.5mg daily for first two weeks and the next two weeks four tablets/daily). This study found that both interventions were equally effective in patients with BMS [56]. Acupuncturists may use the acupuncture technique protocol of this study [56] with different comparators in order to effectively treat the growing number of patients with primary or secondary BMS. In a nutshell, medical acupuncture alone using selected acupoints is relatively safe, cost-effective and fairly improves patients with PBMS. Medical acupuncture needs to be combined with other suitable complementary modality or conventional medications in order to treat resistant cases of BMS. Further rigorous comparative studies on medical acupuncture are globally needed in BMS patients in future.

**DISCUSSION**

This critical review describes sociodemographic, prevalence trends and clinicotherapeutic aspects of burning mouth syndrome (BMS) with a special focus on medical acupuncture. This syndrome is characterized by intraoral burning pain-dysthesias-localizing on tip of the tongue, distaste and dry mouth of long duration, and based on level of burning pain categorized into three types, each one with its own distinctive features [3,10-12]. The primary BMS is idiopathic in nature whereas its counterpart is caused by a variety of local, systemic and neuropsychiatric diseases and, hence, classified as secondary BMS [13]. BMS with clear diagnostic criteria specially affects elderly postmenopausal women, never reported in children, and rarely occurs in people below the age of 30 years. The prevalence of BMS varies, seven times more common in females, and certainly increases with advancing age especially in menopausal women [3,5,13,21]. In the background of lack of universal definition, poorly defined etiopathogenesis and pathophysiology, the diagnosis of BMS is by exclusion of many diseases and, therefore, is very much challenging [1,5,17], and possibly missed or misdiagnosed in many patients with BMS. Evidently, thorough history workup, physical and systemic examination, extensive laboratory investigations, and imaging procedures tend to exclude a wide variety of etiological factors which are identified to be genetic predisposition (polymorphism), numerous prescribed medications, oral local mucosa lesions caused by trauma, physical and chemical irritants, and many physical and psychiatric diseases [4,18,30-32,57]. According to Kim et al (2017), the T allele of IL-1β−511 tends to increase the risk of BMS mediated by functional asthenia [57]. Asthenia, a broader term, may arise from a variety of diseases including chronic anxiety and depression.

Similarly, the treatment of BMS is also equally complicated and challenging. Given the diverse non-specific interventions of idiopathic BMS with variable efficacy, a personalized holistic approach would be the most ideal for managing patients with BMS. Evidently, medical acupuncture alone is effective in patients with BMS, up to 80% improvement with better quality; however, may be used as an adjunct with other suitable CAM therapy or modern therapies in
difficult patients with BMS [1-5,17,18, 22, 50,52-56]. Overall, medical acupuncture, an ancient healing practice is used increasingly in the prevention and treatment of many diseases associated with pain in the western world [58], and acupuncture technique is also found to be reasonably effective in the management of burning mouth syndrome.

This narrative review has some limitations. This paper is not a systematic review and not very comprehensive. Selection and publishing biases are quite obvious. These caveats are because of related literature especially on BMS, acupuncture use in other diseases, and mimicking health conditions is too huge to incorporate into this critical review. The strengths of this review are; 1) this is the first review from Saudi Arabia; 2) it is directed towards complementary and alternative (CAM) practitioners across the globe; 3) this review highlights the global concepts of medical acupuncture and polycomplexities of primary and secondary BMS, the latter would guide researchers to focus on their solutions in future; and 4) this paper may draw the attention of health policy makers to integrate CAM practitioners into mainstream integrative medical system and for achieving this goal they will certainly require targeted practical training in related multiple health disciplines.

CONCLUSION

Burning mouth syndrome is a common idiopathic complex oral condition mostly reported in postmenopausal women who primarily manifest intraoral burning pain on the tip of tongue without any oral lesions. Evidently, patients with BMS posit various clinicotherapeutic challenges and complete recovery and spontaneous remission rates are variable attributed to a variety of factors especially socioclinical specificities, not well understood etiopathogenesis and pathophysiology and nonspecific therapies. Though the use of medical acupuncture as an alternative therapy in patients with BMS is evidently encouraging because a substantial number of BMS patients improve considerably, comparative studies are needed to further support its efficacy, safety, and low cost in patients with burning mouth syndrome.

CONFLICTS OF INTEREST

None

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