Burning mouth syndrome and its management: Review of literature

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Abstract

Burning mouth syndrome (BMS) is a syndrome associated with chronic continuous pain that commonly affects middle- or old-aged women who have hormonal changes or psychological disorders. This syndrome has been stated to have a multifactorial origin. Presently, they are classified into two types, namely, “primary” (idiopathic) and “secondary” (resultant of an identified precipitating factor) BMS. Owing to the various overlapping oral mucosal pathologies, BMS tends to be complicated to diagnose. BMS treatment is still not satisfactory, and there is no definitive cure. There is need of more research to validate the association that exists among BMS and systemic disorders and to consider probable pathogenic mechanisms that involve nerve damage. The present paper deals with several aspects of BMS and provides details regarding a multidisciplinary approach for patient management.

Introduction

Burning mouth syndrome (BMS) is a condition characterized by chronic pain associated with burning, itching and/or stinging in the oral cavity with the absence of any type of organic disease. It is an ill-defined condition that affects mostly middle-aged women. The conditions last for a minimum of 4-6 months and most often is seen involving the tongue with or without involvement to the lips and oral mucosa.[1,2]

BMS can be associated with dysgeusia and xerostomia. BMS was first diagnosed as a condition during the mid-19th century and by the early 20th century the condition was termed as glossodynia by Butlin and Oppenheim.[3] With various researchers presenting various articles on BMS over the period of years, it was termed by different names such as glossopyrosis, oral dysesthesia, sore tongue, stomatodynia, and stomatopyrosis. In 2004, it was first categorized as a distinctive disease, in 2004, by the International Headache Society (IHS).[3] Lamey and Lamb, 1988; Bergdahl et al., 1995b; Jerlang, 1997[4] have all stated that BMS deteriorate the quality of life and patient’s lifestyle due to psychological dysfunction.

Definition

The International Association for the Study of Pain and IHS defines it as a “distinctive nosological entity,” including “all forms of burning sensation in the mouth, including complaints described as stinging sensation or pain, in association with an oral mucosa that appears clinically normal in the absence of local or systemic diseases or alterations.”[3]

Epidemiology

As it is aware that there is a lack of appropriate and ideal classification system, diagnostic criteria, and knowledge among oral health-care professionals regarding BMS, it is hard to validate and authenticate the exact prevalence of the disease.

International estimates of prevalence vary from 0.7% to 0.15%.[3] BMS basically affects middle- and elderly-aged individuals with an average age range of 38-78 years.[4]

This syndrome is stated to primarily affect women in the age group 50-60 years, especially prone toward women in their post-menopausal stage where the prevalence increases to about 13%,...
usually BMS first occurs 3-12 years after the menopause and rarely before the age of 30.\cite{6,8}

**Classification** [Table 1]

**Scala et al.\cite{4} classified BMS into two clinical forms**

- Primary or essential/idiopathic BMS: This type involves the absence to identify any local or systemic causes that give way to neuropathological cause\cite{4}
- Secondary’ BMS: It is a condition that results from local or systemic pathological conditions at risk to etiology directly. A variety of conditions may lead to “secondary” BMS.\cite{4} These include mucosal diseases such as lichen planus, candidiasis, vitamin or nutritional deficiencies, psychosocial stress, diabetes, contact allergies, galvanism, parafunctional habits, cranial nerve injuries, and medication side effects.\cite{4}

**Cerchiari classified BMS according to the associated risk factors**\cite{9}

- Idiopathic
- Psychogenic
- Local and systemic.

**Etiopathogenesis**

1. Local factors\cite{4,6,10-16}
   - Physical/mechanical
     - Denture acrylic allergies
     - Mechanically poor fitting dentures
     - Parafunctional habits
     - Buccal, labial, lingual biting
     - Compulsive movements of the tongue
     - Galvanism
     - Xerostomia
     - Temporomandibular joint (TMJ) disorders
   - Irritant - Brushing of tongue, spicy food, tobacco.
   - Chemical
     - Local allergic reactions, due excess amount of residual monomers
     - Nylon
     - Ascorbic acid
     - Nicotinic acid esters

   - Benzoic peroxide
   - 4-tyol diethanolamine
   - N-dimethyl toluidine.

   C. Biological and oral pathologies
   - *Candida albicans*
   - Bacteria such as *Enterobacter, Klebsiella, Staphylococcus aureus*
   - *Helicobacter pylori*
   - Geographic tongue
   - Periodontal diseases
   - Peripheral nerve damage
   - Vesiculobullous diseases
   - Dysfunction of the salivary glands
   - Taste dysfunction.

   2. Systemic factors\cite{4,6,10-16}
   - Endocrine alterations
   - Hypothyroidism
   - Diabetes
   - Menopause
   - Reduced plasma estrogens.

   3. Nutritional disorders\cite{4,6,10-16}
   - Vitamin B
   - Folate
   - Iron deficiency state
   - Anemia
   - Neurological disorders
   - Sjögren’s syndrome
   - Gastrointestinal tract problems.

   4. Psychiatric and psychological disorders\cite{4,6,10-16}
   - Anxiety
   - Depression
   - Compulsive disorders
   - Stress
   - Cancerophobia.

   5. Medications\cite{17}
   - Antihypertensive
   - Angiotensin converting enzyme inhibitors such as captopril, enalapril, and lisinopril
   - Angiotensin receptor antagonist-like eprosartan and candesartan
   - Antihistamines
   - Antidepressants - Fluoxetine, sertraline, venlafaxine
   - Neuroleptics

**Table 1: Based on the daily fluctuations of the symptoms by Laniev and Lamb\cite{2}**

<table>
<thead>
<tr>
<th>Types</th>
<th>Characterized by</th>
<th>Symptomatology</th>
<th>Associated with</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1 (35% of pt.)</td>
<td>Progressive pain</td>
<td>Symptoms are not present when patient wake up, but they will appear and increase during the day with burning sensation developing late morning then increase throughout the day</td>
<td>Moderate anxiety disorders</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Systemic diseases, such as nutritional deficiencies</td>
</tr>
<tr>
<td>Type 2 (55% of pt.)</td>
<td>Continuous pain</td>
<td>The symptoms are constant throughout the day and patients find it difficult to get to sleep</td>
<td>Severe psychological disorders (anxiety)</td>
</tr>
<tr>
<td>Type 3 (10% of pt.)</td>
<td>Intermittent pain</td>
<td>Symptoms are intermittent, with atypical location and pain</td>
<td>Contact with oral allergens could play an important etiologic role in this group and emotional instability</td>
</tr>
</tbody>
</table>
Burning mouth syndrome

Tarani and Kamakshi

- Antiarrhythmic
- Benzodiazepines
- Hormone replacement therapy
- Antiretroviral agent - Efavirenz.

The probable theories put forward to explain the cause of BMS are:
- One theory states that the individuals termed as supertasters (mainly females) because of the elevated density of fungiform papilla of tongue are at a higher threat of developing burning pain. This could be accredited to abnormal interactions of the sensory branches of facial and trigeminal nerves.[14,15]
- Another theory states that the sensory dysfunction associated with small and/or large fiber neuropathy is present in BMS. This has been further proven by the immunohistochemical and microscopic studies which depicted that axonal degeneration of epithelial and subpapillary nerve fibers are present in the epithelium of the oral mucosa in patients affected by BMS.[20]
- Another theory states that there is a reduction in the nigrostriatal dopaminergic system. This is explained to be associated with alteration in the modulation of nociceptive processing theory which, in turn, reduces central pain suppression in BMS individuals.[21,22]
- It is observed that there is a loss in the balance of autonomic innervation and disturbance in oral blood flow.[23,24]

Clinical Features

BMS has been described to have varied chronic oral symptoms. These symptoms characteristically show increase in their intensity at the end of each day but is never observed to have any interference with sleep.

Two specific clinical features are been given to diagnose a condition as:

BMS
- A "symptomatic triad" including the unrelenting pain of the oral mucosa, dysgeusia, and xerostomia

Table 2: The principal clinical features of BMS are described by Scala et al., Woda and Pionchon and Eli et al. (1994)[29]

<table>
<thead>
<tr>
<th>Pain</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Descriptors</td>
<td>Burning</td>
</tr>
<tr>
<td>Intensity</td>
<td>Variable, weak to intense</td>
</tr>
<tr>
<td>Pattern</td>
<td>Continuous, not paroxysmal</td>
</tr>
<tr>
<td>Localization</td>
<td>Independent of a nervous pathway</td>
</tr>
<tr>
<td></td>
<td>Often bilateral and symmetrical</td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>No</td>
</tr>
<tr>
<td>Pain during sleep</td>
<td>Infrequent</td>
</tr>
<tr>
<td>Other associated signs/symptoms</td>
<td>Dysgeusia, xerostomia, thirst sensory, chemo-sensory anomalies psychological profile may be changed</td>
</tr>
</tbody>
</table>

- "No signs" of lesions or other detectable changes in the oral mucosa, even in the painful areas.[25,26]

The pain in the mucosa lining the oral cavity may be often described by the patient as burning, itching, or an anesthetized feeling associated with dysgeusia. The secondary symptoms, which may or may not be presented by the patient, are dry mouth, thirst, headache, pain in the TMJ, pain in masticatory, suprathyroid muscles extending toward shoulder and neck region.[27]

Dorsal tongue, palate, lips, and gingival tissues either individually or in combination are usually the sites of occurrence that have been observed in the available literature [Table 2].[28]

Diagnosis

An appropriate clinical history along with a careful examination of the oral mucosa is necessary to land at a diagnosis of BMS, without the presence of other overlapping conditions. A complete assessment of quality, intensity, onset, incidence, persistence, overall time period, progression, and the location is mandatory in cases of BMS. BMS should be differentiated systematically and systemically from a variety of chronic pain conditions that could be elicited by the patient.[29] The chief clinical features in various idiopathic orofacial pain conditions have been dealt in Table 3.

Investigations

BMSs are associated with such a wide variety of other referral to a specialist for screening and diagnosis is to be done [Table 4].

Clinical tests that may be helpful

- MRI: To rule out central changes, especially if pain is unilateral, atypical or does not or does not respond to medication.[30,31]
- Salivary flows: For unstimulated and stimulated whole saliva (<1.5 ml/0.5 min, unstimulated <4.5 mg/5 min stimulated)
- Salivary uptake scans: If low salivary flows and Sjögren’s suspected removal of possibly offending medication including angiotensin-convening enzyme inhibitor.[30-32]

Management

Owing to the large range of associated factors, the etiquette for BMS management is an approach for the patients should be based on a strict collaboration among different oral medicine specialists.[31]

Primarily patient management involves a systematic differential diagnosis followed by discrimination between "primary" and "secondary." This is dependent on the identification of probable etiologic factors for the syndrome.

Patients with secondary BMS can fall into specific subcategories according to the identified disorders ("patient stratification"), and subsequently, they undergo appropriate therapy based on identified etiologies. The remaining cases (primary BMS) will undergo proper pain control. This
systematic approach to BMS has been reported to make patient management more predictable and effective.\cite{31}

The available treatment options can be grouped into several major areas, and these are listed in the order of most frequent use:\cite{31}

- **No treatment**
- **Pharmacotherapeutics**, for example, anxiolytics and antidepressants
- **Topical obtundants**, for example, capsaicin
- **Relaxation programs**
- **Exercise programs**
- **Alternative medications**, for example, alpha-lipoic acid
- **Formal psychotherapy**, cognitive behavior therapy
- **Alternative therapies**, acupuncture, massage
- **Physical therapies** such as microwave and laser.

**Caustive therapy in “secondary BMS”**\cite{31,33-41}

- Secondary BMS patients must be treated for the precipitating factors of the disorder initially
- Xerostomia is managed with 7-day periods of saliva substitutes or various saliva-stimulating agents
- Active stimulation of salivation can be induced using chewing gums or sweets (containing sorbitol, not sucrose), passive stimulation can be obtained by specific cholinergic drugs (sialagogues), such as pilocarpine
- Gynecologist referral is a must for peri-/post-menopausal women
- Administration of conjugated estrogens and medroxyprogesterone acetate can be used to relieve from the BMS symptoms
- Vitamin B complex replacement therapy (pyridoxine, riboflavin, thiamine, etc.) must be administered in patients with nutritional deficiency.

**Table 3: Principal clinical features in different idiopathic orofacial pain conditions**

<table>
<thead>
<tr>
<th>Pain</th>
<th>Atypical facial pain</th>
<th>Atypical odontalgia</th>
<th>BMS</th>
<th>Idiopathic facial arthromyalgia (muscle, TMJ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain descriptors</td>
<td>Emotional, mechanical, burning</td>
<td>Varied</td>
<td>Burning</td>
<td>Spontaneous or during function or voluntary movements</td>
</tr>
<tr>
<td>Intensity</td>
<td>Moderate to intense</td>
<td>Moderate to intense</td>
<td>Weak to intense</td>
<td>Weak to intense</td>
</tr>
<tr>
<td>Pattern</td>
<td>Continuous</td>
<td>Continuous with possible remission</td>
<td>Continuous</td>
<td>Continuous with possible remission</td>
</tr>
<tr>
<td>Location</td>
<td>Initially unilateral then bilateral</td>
<td>Initially a single tooth, then may spread</td>
<td>Bilateral symmetrical</td>
<td>Unilateral or bilateral</td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>No</td>
<td>No or little</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Pain during sleep</td>
<td>No</td>
<td>No</td>
<td>Infrequent</td>
<td>Uncommon but disturbed sleep</td>
</tr>
<tr>
<td>Other associated symptoms</td>
<td>Bone cavity osteoporosis</td>
<td>None</td>
<td>Dysgeusia, xerostomia, thirst</td>
<td>TMJ functional limitation, tenderness in masticatory/TMJ palpation, TMJ sounds, bruxism and parafunction</td>
</tr>
<tr>
<td>Neurological signs</td>
<td>Dysesthesia, allodynia, paresthesia</td>
<td>Allodynia</td>
<td>Sensory chemosensory anomalies</td>
<td>Allodynia (trigger point in myofascial pain)</td>
</tr>
<tr>
<td>Psychological profile</td>
<td>Frequently altered</td>
<td>Frequently altered</td>
<td>Frequently altered</td>
<td>Frequently altered</td>
</tr>
</tbody>
</table>

**Behavioral therapy**\cite{31,33-41}

- Cognitive behavioral therapy
- Group psychotherapy
- Electroconvulsive therapy.

**Topical medication**\cite{31,33-41}

- Benzodiazepine: Clonazepam (swish and expectorate)
- Anesthetic: Lidocaine (viscous gel)
- Atypical analgesic: Capsaicin (cream)
- Antidepressant: Doxepin (cream)
- Non-steroidal anti-inflammatory: Benzydamine (oral rinse)
- Antimicrobial: Lactoperoxidase (oral rinse)
- Mucosal protectant: Sucralfate (oral rinse).

**Systemic medication**\cite{31,33-41}

- Benzodiazepine – e.g., Clonazepam, chlordiazepoxide
- Anticonvulsants – e.g., Gabapentin, pregabalin, topiramate
- Atypical analgesic – e.g., Capsaicin
- Antidepressants – e.g., Amitriptyline, imipramine, nortriptyline

**Table 4: Clinical conditions and investigations relevant to BMS**\cite{30}

<table>
<thead>
<tr>
<th>Clinical conditions</th>
<th>Investigation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salivary dysfunction</td>
<td>Sialometry, blood biochemistry</td>
</tr>
<tr>
<td>Candidiasis</td>
<td>Fungal culture before treatment</td>
</tr>
<tr>
<td>Mucosal disease</td>
<td>Biopsy (rarely)</td>
</tr>
<tr>
<td>Mucosal atrophy</td>
<td>Iron studies, folate, vitamin B</td>
</tr>
<tr>
<td>Halitosis</td>
<td>Confirmation (family, clinician)</td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>Patch testing, denture reprocessing</td>
</tr>
</tbody>
</table>

BMS: Burning mouth syndrome
Burning mouth syndrome

Table 5: To summarize efficacy and safety of the drugs used to treat the symptoms of BMS

<table>
<thead>
<tr>
<th>Tammila-Salonen et al.[31]</th>
<th>Trazodone</th>
<th>100 mg od for 4 days followed by 100 mg every 12 h for 8 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maina et al.[32]</td>
<td>Amisulpride</td>
<td>50 mg/day for 8 weeks</td>
</tr>
<tr>
<td>Maina et al.[32]</td>
<td>Paroxetine</td>
<td>20 mg/day for 8 weeks</td>
</tr>
<tr>
<td>Maina et al.[32]</td>
<td>Sertraline</td>
<td>50 mg/day for 8 weeks</td>
</tr>
<tr>
<td>Heckmann et al.[34]</td>
<td>Gabapentin</td>
<td>Initial dose of 300 mg/day, increased at a rate of 300 mg every 48 h to a maximum of 2400 mg/day for 3 weeks</td>
</tr>
<tr>
<td>Petruzi et al.[34]</td>
<td>Capsaicin</td>
<td>Capsaicin 0.25% via the oral route for 4 weeks</td>
</tr>
<tr>
<td>Grushka et al.[35]</td>
<td>Systemic clonazepam</td>
<td>The starting dose of 0.25 mg/day increased at a rate of 0.25 mg/day, to a maximum of 3 mg/day for 8 weeks</td>
</tr>
<tr>
<td>Woda et al.[36]</td>
<td>Topical clonazepam</td>
<td>0.5-1 mg, 2 or 3 times a day instructed to break up the clonazepam tablet retain saliva in the mouth during 3 min</td>
</tr>
<tr>
<td>Sardella et al.[39]</td>
<td>Benzydamine</td>
<td>15 ml of benzydamine hydrochloride 0.15% as a rinse for 1 min, 3 times a day during 4 weeks</td>
</tr>
<tr>
<td>Campisi et al.[40]</td>
<td>Sucralfate</td>
<td>20% suspension of sucralfate 4 times a day during 3 weeks</td>
</tr>
<tr>
<td>Femiano et al.[41]</td>
<td>Alpha-lipoic acid</td>
<td>600 mg/day for 8 weeks</td>
</tr>
<tr>
<td>Gorsky et al.[27]</td>
<td>Chlor Diazepoxide</td>
<td>15-30 mg/day</td>
</tr>
</tbody>
</table>

BMS: Burning mouth syndrome

- Selective serotonin reuptake inhibitors – e.g., Paroxetine, sertraline
- Selective norepinephrine reuptake inhibitors – e.g., Milnacipran
- Antioxidant – e.g., α-lipoic acid
- Antipsychotics - e.g., Amisulpride, levosulpride.
- Atypical antipsychotic – e.g., Olanzapine
- Dopamine agonist – e.g., Pramipexole
- Histamine 2 receptor antagonist – e.g., Lafutidine
- Herbal supplement – e.g., Hypericum perforatum
- Salivary stimulants – e.g., Pilocarpaine, sialor, cevimiline, and bethanecol [Table 5].

Conclusion

BMS is a painful and frequently annoying condition. The precise reason of BMS often is difficult to identify and is possibly multifactorial. The etiopathogenesis of BMS is complex thereby making diagnosis and management of BMS is complicated. Further research is required for better understanding of the etiology and psychological effect. This understanding must be combined with ideal pharmacological interventions is required for appropriate management.

References