Etiology, Diagnosis and Management of Burning Mouth Syndrome: An update

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Abstract:
Burning mouth syndrome (BMS) is multifactorial in origin which is typically characterized by burning and painful sensation in an oral cavity demonstrating clinically normal mucosa. This paper describes various etiologic factors although they often are contradictory, diagnosis and its management. A psychogenic factor which includes anxiety and depression seems to be the most common etiological factor affecting patients with BMS. Lack of success in explaining and treating BMS is because the features of BMS have not been rigidly characterized but can provide symptomatic relief if the cause of BMS is recognized.

Keywords: Burning Mouth Syndrome, diagnosis, anxiety, depression.

Introduction:
Dental practitioners come across patients with history of chief complaint of burning and painful sensation in oral cavity. Often these patients demonstrate clinically normal mucosa resulting in challenging diagnosis. This multifactorial syndrome is referred to as burning mouth syndrome (BMS). The burning mouth syndrome (oral dyesthesia, glossodynia or glossopyrosis) is a well recognized disorder that is characterized by spontaneous burning sensation of tongue, lips and gingiva.\textsuperscript{[1]}

Prevalence:
The prevalence of BMS is determined according to gender, age, race/ethnicity and region of residence.\textsuperscript{[2]}

BMS is a disorder typically observed in middle aged and elderly subjects ranging from 38 to 78 years.\textsuperscript{[3-6]} The predilection is more towards women with female to male ratio of 7:1.\textsuperscript{[3,5-8]} Prevalence rate of BMS among various population ranged from 0.12\% to 4.6\% \textsuperscript{[6,8-10]} and more.\textsuperscript{[11]} Regional prevalence\textsuperscript{[12,13]} of BMS has been shown in Table 1.

Variability in prevalence can be attributed to various criteria used to diagnose BMS. Presently there is no evidence of racial or ethnic background differences for prevalence of BMS.\textsuperscript{[14]} However studies have shown predominance of BMS in post menopausal women.\textsuperscript{[4,7]}

Classification:
Basker has classified BMS into mild, moderate and severe grades.\textsuperscript{[3]} Moderate BMS was most frequently seen followed by severe and mild. Whereas, Lamey has classified BMS into type 1, type 2 and type 3.\textsuperscript{[15]}

Type 1 includes symptom free waking sensations developing in the morning and progressively increasing to severe by evening.
Type 2 includes continuous symptoms throughout the day.
Type 3 includes intermittent symptom free periods throughout the day.
Non psychological causative factors like nutritional deficiencies have been linked to type 1, chronic anxiety to type 2 and allergy to type 3.\textsuperscript{[4]}

Duration:
Duration can range from 3 months to 12 years.\textsuperscript{[1]} Resolution of symptoms is variable and poorly predictable, a spontaneous remission occurs in some patients.\textsuperscript{[9]}

Etiology:
According to Ship AJ\textsuperscript{[16]} etiology for BMS can be grouped into:
1. Oral disorders/local factors
2. Systemic condition.
3. Miscellaneous – menopause, food allergy and drug allergies

1. Oral disorders/local factors include:
   a. Denture acrylic allergies/poorly fitting dentures
   b. Para functional habits
   c. Salivary gland dysfunction
   d. Taste dysfunction
   e. Infectious agents
   f. Periodontal diseases
   g. Peripheral nerve damage

2. Systemic conditions:
   a. Nutritional deficiency/ anemia
   b. Central nervous system disorders
   c. Psychiatric and psychological disorder (depressions, anxiety)
   d. Diabetes mellitus/ Hormonal imbalance
   e. Xerostomia,
   f. Sjogrens syndrome

3. Miscellaneous:
   a. Menopause
   b. Food /allergy
   c. Drugs

1. Local factors/oral disorders:
   a. Denture acrylic allergies and poorly fitting dentures:
      High residual monomer levels have been suggested as a causative factor.[17] However it was found that it was not possible to correlate any signs that implicated dentures as a local etiologic agent.[18] But it is more likely that mechanical irritation due to errors in denture design and parafunctional habits that may cause denture related burning.[16]
   b. Para functional activities:
      Para functional activities resulting in excessive occlusal and denture wear has been shown in 61% of patients with BMS.[19] Also Parafunctional activity of lip sucking, lip licking, lip pressure and mouth breathing were noted with BMS.[20]
   c. Salivary gland dysfunction:
      Many patients with BMS complained of a dry mouth (xerostomia) which is decreased salivary gland secretion in patients with BMS.[20] Irregularities in saliva metabolites like protein, potassium and phosphate concentration have been documented in patients with BMS, where there was significant increase in unstimulated salivary metabolites particularly potassium, phosphate and protein.[21] Complaints of dry mouth may not necessarily be predictive of salivary gland hypo function. It may be due to multiple medical problems and medication rather than BMS.[22, 23]

d. Taste dysfunction:
   Many BMS subjects have reported with persistent dysgeusia (usually bitter or metallic) and altered taste perception. The abnormalities in salt and sweet taste are consistent with anterior tongue involvement which is a common site for BMS. Also altered taste in BMS may be due to effects of salivary hypofunction and alterations in salivary composition.[2] The basis of these is unclear however one possibility is that increased spontaneous firing rate of certain afferent taste fibers (e.g. bitter) or afferent inhibitions of others.[24]

e. Infectious agents:
   Candidiasis has been the most frequently identified infectious agent.[18,25] Prevalence of Candida has been found in patients with BMS than those without symptoms.[26] Fusospirochetal infection and mucosal diseases such as geographic tongue or benign migratory mucositis have been found in patients with BMS.[25, 27]

f. Periodontal diseases:
   Although a periodontal disease as etiological factor has been suggested for BMS.[28,29] There is no scientific evidence of a direct causal relationship of periodontal disease to BMS.[2]

3. Miscellaneous – menopause, food allergy and drug allergies

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   b. Para functional habits
   c. Salivary gland dysfunction
   d. Taste dysfunction
   e. Infectious agents
   f. Periodontal diseases
   g. Peripheral nerve damage

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   b. Central nervous system disorders
   c. Psychiatric and psychological disorder (depressions, anxiety)
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burning, since approximately one third of subjects with burning sensations experienced increased sensation. This could suggest a centrally based neuropathic condition and provide a rationale for the use of centrally acting medication.\[2\]

2. **Systemic conditions:**
   a. **Nutritional deficiency/anemia:**

   Nutritional deficiency including iron, B\(_1\), B\(_3\), B\(_6\), B\(_12\) and zinc have been associated with BMS.\[15,31\] Folic acid deficiency is also a causative factor for BMS.\[32\] However recent studies have little support for nutritional deficiencies as a causative factor.\[33,34\] One explanation for the discrepancy in results of iron deficiency causing BMS is that earlier studies did not always measure serum ferritin levels, as normal level of serum ferritin precludes a diagnosis of iron deficiency even in the presence of decreased serum iron.\[35\] Replacement therapy of vitamin B\(_1\), B\(_2\) and B\(_6\) produced resolution of symptoms in only 30 percent of patients with such deficiency.\[4\]

   b. **Central nervous system disorders:**

   In the trigeminal and spinal somatosensory systems interactions between various sensory inputs occur such that transmission via one pathway (related to pain) can be modulated by other sensory pathways (related to touch) this alteration in one of these pathways might unmask or enhance nociceptive afferent inputs leading to pain such as that of BMS.\[2\]

   c. **Psychiatric and Psychological disorders (depression, anxiety):**

   A complex spectrum of social and psychological disturbance was found in patients with BMS. Patients with BMS tended to be more depressed, angry, doubting, apprehensive, and introverted as a direct result of pain experience. Pain of BMS has been attributed to the manifestation of exogenous or reactive depression caused by the external stress of desolation or anxiety.\[36\] Psychologic factors in BMS have been reported by several authors.\[37,38\] BMS may be regarded as a variant of atypical facial pain in which an association with depression is found.\[39\] When psychiatric disorder is present it usually takes the form of mixed anxiety and depressive symptoms.\[4\] A study confirmed that two aspects of neurosis seen in hospital practice anxiety and depression are involved in BMS\[40\] and there is response to antidepressant medication.\[39,41\]

   d. **Diabetes mellitus/ Hormonal imbalance**

   Laméy has shown an incidence of oral burning in only 2 to 10 percent of diabetics which indicates that diabetes may not be main cause for BMS.\[4\] However it may predispose to candidiasis, responsible for burning. Hormonal changes are still considered to be important factors in BMS.\[3\] The greatest frequency of onset of burning mouth syndrome among post menopausal women was reported from 3 years before to 12 years after menopause.\[7,42\]

   e. **Xerostomia:**

   Xerostomia occurring with age has been suggested as a causative agent in the pathogenesis of BMS. However the evidence of decreased salivary flow with age is still controversial.\[43\]

   f. **Sjogren’s syndrome:**

   BMS had evidence of an immunologic abnormality which may be linked to a more generalized connective tissue disorder like Sjogren’s syndrome.\[44,45\]

   **Miscellaneous:**

   **Menopause:**

   Studies have shown that the oral symptoms compromising BMS are the result of decreased estrogen during menopause.\[46\] However other studies have not demonstrated a dramatic improvement in oral symptoms with estrogen replacement therapy \(\text{ERT}\).\[3,47\] Therefore it appears that the pathogenesis of BMS may be linked in some as yet unclear manner to the physiologic changes that occur at menopause.

   **Food/allergy:**

   Oral allergies to food results in symptoms similar to BMS which includes ingested allergens like sorbic acid \(\text{a preservative found in foods, ointments,creams Cinnamic aldehyde (a flavoring agent in foods and dentifrices) nicotinic acid (used as rubefacient in tooth paste) and propylene glycol (food additive).}\[48,49\]

   **Drugs:**

   Medications are reported to cause BMS. Some of the drugs causing burning mouth syndrome have been enumerated in Table 2.

   **Signs / symptoms:**

   Onset of continuous burning sensation usually begins by midmorning or early afternoon and maximum pain intensity is reached by evening.\[7\] Many BMS subjects reported increased burning with tension, fatigue, speaking and hot foods and decreased burning while sleeping, eating meals or cold foods and working distraction.\[7\] Also symptoms included were altered eating habits, irritability, depression and decreased desire to socialize, altered taste sensation \(\text{(dysgeusia)}\) and dry mouth.\[59,60\]
### Table 1: Prevalence of BMS in various regions

<table>
<thead>
<tr>
<th>REGION</th>
<th>PREVALENCE IN PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finland (Tammiola 1993)</td>
<td>13-15%</td>
</tr>
<tr>
<td>Sweden (Thorstensson 1996)</td>
<td>3.4%</td>
</tr>
<tr>
<td>Florida USA (Riley 1998)</td>
<td>1.7%</td>
</tr>
<tr>
<td>Turkey (Calak H 2011)</td>
<td>0.12%</td>
</tr>
</tbody>
</table>

### Table 2: Various drugs inducing BMS

<table>
<thead>
<tr>
<th>AUTHOR</th>
<th>DRUG</th>
<th>ACTIVITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borras-Blasco et al</td>
<td>Efavirenz</td>
<td>Antiretroviral</td>
</tr>
<tr>
<td>Culhane et al</td>
<td>Clonazepam</td>
<td>Anxiolytic</td>
</tr>
<tr>
<td>Levenson</td>
<td>Sertraline, Venlafaxine</td>
<td>Antidepressant</td>
</tr>
<tr>
<td>Triantos et al</td>
<td>Enalapril</td>
<td>Antihypertensive</td>
</tr>
<tr>
<td>Brown et al</td>
<td>Enalapril</td>
<td>Antihypertensive</td>
</tr>
<tr>
<td>Vlasses et al</td>
<td>Enalapril</td>
<td>Antihypertensive</td>
</tr>
<tr>
<td>Vlasses et al</td>
<td>Captopril</td>
<td>Antihypertensive</td>
</tr>
<tr>
<td>Brown et al</td>
<td>Captopril</td>
<td>Antihypertensive</td>
</tr>
<tr>
<td>Savino et al</td>
<td>Lisinopril</td>
<td>Antihypertensive</td>
</tr>
<tr>
<td>Chen et al</td>
<td>Candesartan</td>
<td>Antihypertensive</td>
</tr>
<tr>
<td>Castells et al</td>
<td>Eprosartan</td>
<td>Antihypertensive</td>
</tr>
</tbody>
</table>
Diagnosis:
Diagnosis includes a detailed history related to oral burning pain (e.g., onset, precipitating factor). Intraoral examinations which include cytology smear from dorsal tongue surface for evidence of candidiasis infection.61

Hematologic examination has to be done for complete blood count(CBC) for iron ([serum iron, total iron –binding capacity(TIBC) percent transferring saturation, serum ferritin levels] vitamin B12 and Folate[serum and red blood cell] rheumatoid factor(RF) antinuclear factor (ANF) and complement c3 and c4 , and erythrocyte sedimentation rate.7 As ESR is elevated in patients with BMS.

Anxiety and depression can be checked using hospital anxiety and depression (HAD) scale.62

Otolaryngology and gastroenterology consultation may assist diagnosis of pharyngeal esophageal or reflux related cause.

Management:
The multiple etiologic factors for treatment of BMS present a challenging scenario for the dental clinician. In the absence of any identifiable cause of BMS pharmacologic therapy has been suggested. Medications used for BMS include antifungal, antibacterial, corticosteroids, analgesics, sialagogues, vitamin mineral replacements. Estrogen replacement therapies [ERT] have reported reduced oral symptoms in post-menopausal women.62 Control of parafnctional activity, prosthesis adjustment in case of patient wearing prosthesis. Suspension of 30ml mycostatin 1000000units/ml, 50ml hydrocortisone (10mg/5ml), 60ml tetracycline (125mg/5ml) and 120ml Benadryl elixir (12.5mg/5ml) 1 teaspoon orally four times per day and expectorate.63 Tricyclic antidepressants (amitriptyline or doxepin 25 to 75mg). Benzodiazepine which includes administration of chlordiazepoxide, chronic use of benzodiazepines is effective for some pains of musculoskeletal origin.64 Lysozyme-Lactoperoxidase may be effective in providing supportive care of BMS patients with xerostomia.65

Conclusion:
BMS remains a poorly understood chronic facial pain that is difficult both to diagnose and treat. Multiple etiologic factors for diagnosis of BMS present a challenging scenario for dental clinician. Lack of success in explaining and treating BMS is because the features of BMS have not been rigidly characterized. Identification of the etiologic group, local, systemic or psychogenic is the first step towards diagnosis and treatment of BMS. Unfortunately no therapy for BMS has been proven to be completely effective but can provide symptomatic relief if etiology for BMS is recognized.

References:
64. Dellemijn PLJ, Field HL. Do benzodiazepines have role in chronic pain management? Pain. 1994;57:137-52.


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