BURNING MOUTH SYNDROME; DIAGNOSIS AND MANAGEMENT

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KINGS COLLEGE LONDON
Orofacial Pain
Demystifying chronic pain in the head, face and mouth

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LEARNING OBJECTIVES

- To outline diagnostic criteria for BMS
- To provide a summary of aetiological factors and possible mechanisms
- To provide some key diagnostic tips and provide some novel strategies in management for patients with BMS
- To highlight the possible future management of patients with BMS
TYPES OF PAIN

Review series introduction

What is this thing called pain?

Clifford J. Woolf

Program in Neurobiology and Department of Neurology, Children's Hospital Boston, and Department of Neurobiology, Harvard Medical School, Boston, Massachusetts, USA.

To paraphrase Cole Porter’s famous 1926 song, “What is this thing called pain? This funny thing called pain, just who can solve its mystery?” Pain, like love, is all consuming: when you have it, not much else matters, and there is nothing you can do about it. Unlike love, however, we are actually beginning to tease apart the mystery of pain. The substantial progress made over the last decade in revealing the genes, molecules, cells, and circuits that determine the sensation of pain offers new opportunities to manage it, as revealed in this Review series by some of the foremost experts in the field.

Classifying pain

What exactly, from a neurobiological perspective, is pain? Pain is actually three quite different things, although we and many of our physicians commonly fail to make the distinction. First, there is the pain that is an early-warning physiological protective system, essential to detect and minimize contact with damaging or noxious stimuli. This is the pain we feel when touching something too hot, cold, or sharp. Because this pain is concerned with the sensing of noxious stimuli, it is called nociceptive pain (Figure 1A), a high-threshold pain only activated in the presence of intense stimuli (1). The neurobiological apparatus that generates nociceptive pain evolved from the capacity of even the most primitive nervous systems to signal impending or actual tissue damage from envi-
TYPES OF PAIN

Healthy

- **NOCICEPTIVE HEALTHY FEELING PAIN ‘PAIN’**
- **INFLAMMATORY PAIN**
  HEALTH SHORT LIVED AFTER INSULT

Unhealthy

- **NEUROPATHIC PAINS**
- **DYSFUNCTIONAL PAIN**

Unhealthy Pain

BUT?

Is Burning Mouth Syndrome Neuropathic pain???

Burning Mouth Disorder or secondary BMS IS Neuropathic

Neuropathic pain

Nociplastic pain

Posttraumatic neuropathy PDAP/PHN BMS???
UNHEALTHY PAIN

Neuropathic pain

Dysfunctional pain, Corresponds to a dysfunction of the central inhibitory processes of pain control (Crofford et al., 2005).
Including:
• fibromyalgia
• irritable bowel syndrome
• Tension headaches
• idiopathic orofacial pain
• complex regional pain syndrome
• Burning mouth syndrome?
With a marked co-morbidity between some of these pain syndromes (Kato et al., 2006).

Dysfunctional Pain
BMS????
ICOP STATES BMS IS IDIOPATHIC

International Classification of Orofacial Pain, 1st edition (ICOP)

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The Orofacial Pain Classification Committee
The committee is a collaborative group consisting of members of the Orofacial and Head Pain Special Interest Group (OFHP SIG) of the International Association for the Study of Pain (IASP), the International Network for Orofacial Pain and Related Disorders Methodology (INFORM), the American Academy of Orofacial Pain (AAOP) and the International Headache Society (IHS).

Co-chairmen
Rafael Benoliel, USA; Arne May, Germany; Peter Svensson, Denmark
Features of Neuropathic pain

- **Patient over 50 years**
  - Migraines
  - FM other chronic pain conditions
  - Genetics COMT

- **Multiple insults**
  - Non respondent to anti inflammatory pain killers (NSAIDs Paracetamol)

- Better in mornings
- Does not disturb sleep
- Worsens during day
- Worsens with stress, tiredness and illness
- Either
  - Constant burning
  - Elicited neuralgic (electric shock)
  - Or combination

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**Table 2**
Definitions of common features suggestive of neuropathic pain

<table>
<thead>
<tr>
<th>Feature</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paresthesia</td>
<td>An abnormal sensation, whether spontaneous or evoked</td>
</tr>
<tr>
<td>Dyesthesiasa</td>
<td>An unpleasant sensation, whether spontaneous or evoked</td>
</tr>
<tr>
<td>Hypoesthesia</td>
<td>Decreased sensitivity to stimulation (tactile or thermal; both are frequent)</td>
</tr>
<tr>
<td>Hyperesthesia</td>
<td>Increased sensitivity to stimulation (tactile or thermal; both are rare)</td>
</tr>
<tr>
<td>Hypalgesia</td>
<td>Diminished pain response to a normally painful stimulus</td>
</tr>
<tr>
<td>Hyperalgesia</td>
<td>An increased response to a stimulus that is normally painful</td>
</tr>
<tr>
<td>Allodynia</td>
<td>Pain due to a stimulus that does not normally activate the nociceptive system</td>
</tr>
</tbody>
</table>
The Trigeminal nerve

Complex region
Consequences
  Social function
  Eating
  Drinking
  Speaking
  Kissing
  Make up / shaving
  Sleeping

IDENTITY?
BURNING MOUTH SYNDROME

- **First described in mid-nineteenth century, this condition was further characterized in the early twentieth century by Butlin and Oppenheim as glossodynia.**

- **Over the ensuing years, BMS has been referred to as glossopyrosis, oral dysesthesia, sore tongue, stomatodynia, and stomatopyrosis.**

- **It was first categorized as a distinct disease in 2004 by the International Headache Society, which defined primary BMS as “an intraoral burning sensation for which no medical or dental cause can be found.”**
IS BMS A SYNDROME?

EDITORIAL

Is burning mouth a syndrome or a disorder? A commentary

Why is it that burning mouth continues to be referred to as a “syndrome”? This etymologic and long-described pain disorder has been defined by several international organizations.1 In 1994, the International Association for the Study of Pain (IASP) defined burning mouth syndrome (BMS) (also known as glossodynia, glossoparosis, oral dysesthesia, or stomatodynia) as a chronic oral mucosal pain or discomfort that has no identifiable causative lesion and is not caused by any other condition or disease.2 The IASP recognized the clinical features to include burning, tingling, picking, or discomfort. In 2004, the International Headache Society (IHS) defined BMS as “an introral burning sensation for which no medical or dental cause can be found.”3 In the latest IHS revision (2018), BMS is defined as “an introral burning or dysesthetic sensation, recurring daily for more than two hours over more than three months, without clinically evident causative lesions.” The World Health Organization (WHO), which publishes the International Classification of Diseases (ICD), codifies a similar definition in their 2016 classification system (ICD-10 code). Here, glossodynia (K14.6), which includes additional terms, such as glossoparosis and painful tongue, is described as “painful sensation in the tongue including a sensation of burning.” The definitions published by these organizations have been updated several times over the years, and many other entities and authors also have provided input into our understanding of this disorder.3,4,5,6

These definitions provide a clinical perspective, yet differences between the descriptions are clearly evident. Despite the many attempts to define this pain disorder more specifically, the name of the condition — “burning mouth syndrome” — has not been critically assessed and scrutinized for years.

Appropriately naming a medical condition is an important undertaking. The ICD, which is managed by the WHO, is responsible for disease nomenclature. The WHO recently called upon scientists and national organizations to follow best practices in naming new “human infectious” diseases to minimize unnecessary negative effects.7 And it is logical to extend this to all human disorders, with the goal of improving the understanding of diseases, disorders, and conditions to achieve optimal treatment outcomes. Best practices state that a “disease name should consist of generic descriptive terms, based on the disease symptoms and more specific descriptive terms when robust information is available on how the disease manifests, what it affects, its severity or seasonality.”8

These guidelines promote consideration of why the word syndrome is being used for burning mouth. Merriam-Webster defines syndrome as “a group of signs and symptoms that occur together and characterize a particular abnormality or condition.”9 Implied in this definition is a common cause or biologic abnormality that leads to physiologic changes, contributing to a collection of clinical and physical features. Key to the definition of syndrome is a predictable group of clinical and physical features that are present in a wide range of persons affected by the syndrome.

Naturally, patients who have burning mouth syndrome do not always display a consistent set of clinical features. Thus, the features are not present across the full gamut of affected persons, and the consistent with the word syndrome, features (i.e., anxiety, depression), somatic (subjective feeling of dryness, abnormalities and paraesthesia have been in this population), the frequency of these clinical features is variable addressed fully in the diagnostic diagnostic and treatment outcome. For example, when a topical or administered to affected individual visits the burning sensation, and anesthetic has no effect or worse.10,11 Inasmuch as the etiology of burning mouth remains an enigma and is a problem of a predictable set of clinical features that may or may not be present, it is time to consider this condition as an abnormal physical condition.

As such, we recommend that the IHS begin discussing a new “burning mouth disorder.” The dissection of the etiology from the inclusion of practice of patients and appropriate knowledge among others addressed this topic 15 years been done to make a meaningful recently rekindled this discussion which oral mouth (WWOM) November 26–27, 2018, meeting in this meeting served as an impetus to promote future discussion. Our expectation is that this name...
Burning Mouth Syndrome

Diagnosis by exclusion

Burning Mouth Syndrome = The International Association for the Study of Pain (IASP) defines BMS as:

‘A distinctive nosological entity’ characterised by ‘unremitting oral burning or similar pain in the absence of detectable oral mucosal changes’ that can last at least 4-6 months. No known cause

If cause found .............. Burning Mouth Disorder or Secondary BMS or Type 2 BM

altered taste  dry mouth
BMS DIAGNOSTIC CRITERIA

Diagnostic criteria ICHD
Burning mouth syndrome (BMS)

- PREVIOUSLY USED TERMS:
  Stomatodynia, or glossodynia when confined to the tongue.

- DESCRIPTION:
  An intraoral burning or dysesthetic sensation, recurring daily for more than two hours per day over more than three months, without clinically evident causative lesions.

- DIAGNOSTIC CRITERIA:
  A. Oral pain fulfilling criteria B and C
  B. Recurring daily for >2 hr per day for >3 months
  C. Pain has both of the following characteristics:
    1. Burning quality
    2. Felt superficially in the oral mucosa
  D. Oral mucosa is of normal appearance and clinical examination including sensory testing is normal
  E. Not better accounted for by another ICHD-3 diagnosis.

- COMMENTS:
  The pain of 13.10 Burning mouth syndrome (BMS) is usually bilateral and its intensity fluctuates. The most common site is the tip of the tongue.
  Subjective dryness of the mouth, dysesthesia and altered taste may be present.
  There is a high menopausal female prevalence, and some studies show comorbid psychosocial and psychiatric disorders. Recent laboratory and brain imaging investigations have indicated changes...
• 102 BMS patients 25.5% misdiagnosed as candidiasis

Results. One hundred and two patients (86.3% females) were included (median age 60 years). Median time from onset of symptoms to referral to the Oral Medicine clinic was 12 months (range 4-370 months). Patients saw a median of 3 providers (range 1-7); 30.4% had undergone a diagnostic test; 63.7% had been given a provisional diagnosis; and 78.4% had received treatment. Candidiasis was the most common misdiagnosis (25.5%), and antifungal medication was the most frequently prescribed therapy (27.5%).

Conclusions. Patients with BMS experience delay in diagnosis and management despite seeking and receiving professional care. Many undergo unnecessary tests and tend to be misdiagnosed or receive no diagnosis at all. Even those correctly diagnosed with BMS often receive inappropriate or ineffective treatment. (Oral Surg Oral Med Oral Pathol Oral Radiol 2020;129:120–124)

Table III. Provisional diagnoses received by patients for oral burning before the Oral Medicine consultation

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMS</td>
<td>30 (29.4)</td>
</tr>
<tr>
<td>Candidiasis</td>
<td>26 (25.5)</td>
</tr>
<tr>
<td>Viral Infection</td>
<td>8 (7.8%)</td>
</tr>
<tr>
<td>GERD</td>
<td>8 (7.8%)</td>
</tr>
<tr>
<td>Allergic reaction</td>
<td>6 (5.9%)</td>
</tr>
<tr>
<td>OLP</td>
<td>4 (3.9%)</td>
</tr>
<tr>
<td>Hyposalivation/Xerostomia</td>
<td>4 (3.9%)</td>
</tr>
<tr>
<td>Other†</td>
<td>13 (12.7%)</td>
</tr>
<tr>
<td>Total</td>
<td>99</td>
</tr>
</tbody>
</table>

*More than one provisional diagnosis per patient possible.
†Other past diagnoses included Sjogren syndrome, benign migratory glossitis, referred tooth pain, urtica, laryngopharyngeal reflex, temporomandibular disorder, fibromyalgia, tongue ulceration, effects of cholesterol medication, denture irritation, BMS, burning mouth syndrome; GERD, gastroesophageal reflex disease; OLP, oral lichen planus.

Burning mouth syndrome: a diagnostic challenge

Jacob E. Freilich, BA,‡ Michal Kuten-Shorrer, DMD, DMSc,§ Nathaniel S. Treister, DMD, DMSc,∥ and Alessandro Villa, DDS, PhD, MPH∥

Objectives. The aim of this study was to characterize the diagnostic process that patients with burning mouth syndrome (BMS) undergo and to identify the potential pitfalls encountered in the workup and management of BMS.

Study Design. A retrospective chart review of patients with BMS seen at the Oral Medicine clinic at Brigham and Women’s Hospital (Boston, MA) was conducted from January 2014 to April 2017. Abstracted data focused on the variety of symptoms and signs, referrals to the Oral Medicine clinic for diagnostic tests performed, and provisional diagnostic hypotheses.

Conclusions. One hundred and two patients (86.3% females) were included (median age 60 years). Median time from onset of symptoms to referral to the Oral Medicine clinic was 12 months (range 4-370 months). Patients saw a median of 3 providers (range 1-7); 30.4% had undergone a diagnostic test; 63.7% had been given a provisional diagnosis; and 78.4% had received treatment. Candidiasis was the most common misdiagnosis (25.5%), and antifungal medication was the most frequently prescribed therapy (27.5%).

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Conclusions. Patients with BMS experience delay in diagnosis and management despite seeking and receiving professional care. Many undergo unnecessary tests and tend to be misdiagnosed or receive no diagnosis at all. Even those correctly diagnosed with BMS often receive inappropriate or ineffective treatment. (Oral Surg Oral Med Oral Pathol Oral Radiol 2020;129:120–124)

Classification of Headache Disorders

Intraoral burning or dysesthetic sensations daily for greater than 2 hours per day for 3 months, without clinically evident cause. The reported prevalence of BMS in the literature ranges from 0.1% to 3.9%, but a recent study conducted at a tertiary care hospital found a prevalence of 7.9%. Despite its prevalence, BMS is not well understood.

Conclusion: The level of TSH, Anti-TPO, and Anti-TG, Free T3, and TSH indicate abnormalities in Hashimoto’s patients were associated with the presence and severity of BSM. However, Free T4 level was only associated with the presence of BMS and not the intensity.
Burning mouth syndrome: a diagnostic challenge

Jacob E. Freilich, BA;* Michael Kuten-Shorrer, DMD, DMSSc;* Nathaniel S. Treister, DMD, DMSSc;* Sook-Bin Woo, DMD, MMS Sc;* and Alessandro Villa, DDS, PhD, MPH*†

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Study Design. A retrospective chart review of patients with BMS seen at the Oral Medicine clinic at Brigham and Women’s Hospital (Boston, MA) was conducted from January 2014 to April 2017. Abstracted data focused on the period from onset of symptoms to referral to the Oral Medicine clinic for definitive diagnosis and included providers consulted, symptom characteristics, diagnostic tests performed, and provisional diagnoses and treatments offered.

Results. One hundred and two patients (86.3% females) were included (median age of 60 years). Median time from onset of symptoms to referral to the Oral Medicine clinic was 12 months (range 4-370 months). Patients saw a median of 3 providers (range 1-7); 30.4% had undergone a diagnostic test; 61.7% had been given a provisional diagnosis; and 78.4% had received treatment. Candidiasis was the most common misdiagnosis (25.5%); and antifungal medication was the most frequently prescribed therapy (27.5%).

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Table II. Reported comorbidities in patients with burning mouth syndrome

<table>
<thead>
<tr>
<th>N = 102</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Psychiatric</strong></td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>61 (59.8%)</td>
</tr>
<tr>
<td>Depression</td>
<td>51 (50.0%)</td>
</tr>
<tr>
<td>Panic Attacks</td>
<td>24 (23.5%)</td>
</tr>
<tr>
<td>PTSD</td>
<td>12 (11.9%)</td>
</tr>
<tr>
<td>OCD</td>
<td>7 (6.9%)</td>
</tr>
<tr>
<td><strong>Pain</strong></td>
<td></td>
</tr>
<tr>
<td>Low back pain</td>
<td>43 (42.2%)</td>
</tr>
<tr>
<td>Neck and shoulder pain</td>
<td>41 (40.2%)</td>
</tr>
<tr>
<td>Headaches/Migraines</td>
<td>35 (34.3%)</td>
</tr>
<tr>
<td>TMD/Myofascial pain</td>
<td>22 (21.6%)</td>
</tr>
<tr>
<td><strong>Extraoral dyesthesias</strong></td>
<td></td>
</tr>
<tr>
<td>Dry Eyes</td>
<td>35 (34.3%)</td>
</tr>
<tr>
<td>Skin</td>
<td>10 (9.8%)</td>
</tr>
<tr>
<td>Eyes (other than dryness)</td>
<td>9 (8.8%)</td>
</tr>
<tr>
<td>Genital</td>
<td>4 (3.9%)</td>
</tr>
<tr>
<td><strong>Functional somatic syndromes</strong></td>
<td></td>
</tr>
<tr>
<td>IBS</td>
<td>15 (14.7%)</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>13 (12.7%)</td>
</tr>
<tr>
<td>Chronic fatigue syndrome</td>
<td>10 (9.8%)</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
</tr>
<tr>
<td>Current stressors</td>
<td>64 (62.7%)</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>19 (18.6%)</td>
</tr>
<tr>
<td>Palpitations</td>
<td>26 (25.5%)</td>
</tr>
</tbody>
</table>

BMS, burning mouth syndrome; IBS, irritable bowel syndrome; OCD, obsessive-compulsive disorder; PTSD, post-traumatic stress disorder; TMD, temporomandibular disorder.
### Medical comorbidities of patients with burning mouth syndrome

#### TABLE 1: Chronological changes of patient demographics and physical comorbidities

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Patients</th>
<th>Male Sex, %</th>
<th>Hypertension, %</th>
<th>Hyperlipidemia, %</th>
<th>Cancer, %</th>
<th>Heart Disease, %</th>
<th>Uraline Fibrold, %</th>
<th>Thyroid Disease, %</th>
<th>Cerebrovascular Diseases, %</th>
<th>Diabetes Mellitus, %</th>
<th>Glaucoma, %</th>
<th>Autoimmune Disease, %</th>
<th>Prostatomegaly, %</th>
<th>Epilepsy, %</th>
<th>Parkinson's Disease, %</th>
<th>No Diseases, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>309</td>
<td>43 (14.0%)</td>
<td>55 (17.8%)</td>
<td>59 (19.1%)</td>
<td>29 (9.4%)</td>
<td>21 (6.8%)</td>
<td>24 (7.8%)</td>
<td>19 (6.1%)</td>
<td>16 (5.2%)</td>
<td>12 (3.9%)</td>
<td>8 (2.6%)</td>
<td>8 (2.6%)</td>
<td>4 (1.3%)</td>
<td>1 (0.3%)</td>
<td>1 (0.3%)</td>
<td>36 (11.7%)</td>
</tr>
<tr>
<td>2015</td>
<td>421</td>
<td>42 (10.0%)</td>
<td>72 (17.1%)</td>
<td>90 (21.4%)</td>
<td>43 (10.2%)</td>
<td>28 (11.0%)</td>
<td>43 (10.2%)</td>
<td>27 (9.2%)</td>
<td>20 (4.8%)</td>
<td>25 (5.9%)</td>
<td>36 (3.0%)</td>
<td>16 (3.0%)</td>
<td>3 (1.2%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>34 (8.1%)</td>
</tr>
<tr>
<td>2016</td>
<td>255</td>
<td>41 (16.1%)</td>
<td>61 (23.9%)</td>
<td>38 (14.9%)</td>
<td>41 (13.9%)</td>
<td>29 (11.0%)</td>
<td>44 (17.2%)</td>
<td>27 (10.7%)</td>
<td>11 (4.3%)</td>
<td>20 (7.8%)</td>
<td>9 (3.5%)</td>
<td>9 (3.5%)</td>
<td>2 (1.0%)</td>
<td>0 (0.0%)</td>
<td>1 (0.4%)</td>
<td>25 (9.8%)</td>
</tr>
<tr>
<td>2017</td>
<td>295</td>
<td>39 (13.2%)</td>
<td>53 (18.0%)</td>
<td>46 (15.6%)</td>
<td>35 (13.3%)</td>
<td>27 (9.2%)</td>
<td>41 (13.9%)</td>
<td>16 (5.4%)</td>
<td>20 (6.8%)</td>
<td>10 (3.4%)</td>
<td>12 (4.1%)</td>
<td>10 (3.4%)</td>
<td>2 (0.8%)</td>
<td>0 (0.0%)</td>
<td>1 (0.0%)</td>
<td>36 (12.2%)</td>
</tr>
<tr>
<td>2018</td>
<td>263</td>
<td>37 (14.1%)</td>
<td>52 (19.8%)</td>
<td>33 (12.5%)</td>
<td>35 (13.3%)</td>
<td>30 (11.4%)</td>
<td>24 (8.1%)</td>
<td>17 (6.5%)</td>
<td>12 (4.6%)</td>
<td>12 (4.6%)</td>
<td>19 (7.2%)</td>
<td>12 (4.6%)</td>
<td>2 (0.7%)</td>
<td>0 (0.0%)</td>
<td>1 (0.4%)</td>
<td>20 (7.6%)</td>
</tr>
<tr>
<td>total</td>
<td>1,543</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**Abbreviation:** BMS, burning mouth syndrome.

**TABLE 2:** Prevalence of diabetes mellitus and thyroid disease in patients with BMS.

<table>
<thead>
<tr>
<th>Year</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMS</td>
<td>309</td>
<td>421</td>
<td>255</td>
<td>295</td>
<td>263</td>
<td>1,543</td>
</tr>
<tr>
<td>DM</td>
<td>62 (20.2%)</td>
<td>74 (17.6%)</td>
<td>58 (22.8%)</td>
<td>58 (19.6%)</td>
<td>60 (22.8%)</td>
<td>294 (19.0%)</td>
</tr>
<tr>
<td>TDM</td>
<td>59 (19.1%)</td>
<td>90 (21.4%)</td>
<td>53 (20.8%)</td>
<td>33 (11.2%)</td>
<td>35 (13.3%)</td>
<td>297 (19.1%)</td>
</tr>
</tbody>
</table>

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The psychiatric aspect of BMS is very important. A relationship has been found between BMS and depression, increased anxiety, hypochondria, cancerophobia and emotional instability [4, 5].

The most common diagnosis associated with BMS is depression, anxiety disorders being on the second place [6]. Sleep disorders are also frequent [7].

These conditions may be possible triggering factors of the BMS symptoms, but, on the other hand, chronic symptoms of BMS can possibly lead to the appearance of depression and anxiety.

Furthermore, BMS symptoms can be somatic forms of anxiety or depression [8]. In a Polish study published in 2004, it has been demonstrated that frequency of co-morbid depressive and anxiety disorders was more than a half of patients with BMS [9].

FUNCTIONAL IMPACT

- **Burning mouth syndrome patients showed poorer scores on all scales compared to the healthy subjects with a lower OHRQoL.**

- **OHIP-14 gives a greater weight to psychological and behavioural outcomes in evaluating oral health than GOHAI, and therefore, it is a more effective questionnaire in terms of the evaluation of the treatment response.**

- **The management of BMS can improve pain, anxiety and depression and the OHRQoL.**
BURNING MOUTH SYNDROME

• **Burning mouth syndrome by definition has no known cause** = PRIMARY (IDIOPATHIC) BURNING MOUTH SYNDROME

• **Thus exclusion of secondary burning mouth syndrome (BMS) or burning mouth disorder is important in diagnosis**

• **The following conditions may produce BMS-like symptoms:**
BMD DISORDER: SECONDARY NEUROPATHY

- **Endocrine**
  - Menopausal
  - Hyperthyroid
  - Diabetes
- **Immunological Autoimmune**
  - Sjögren Syndrome
  - Scleroderma
- **Vitamin Deficiency** (B1, B2, B6, B12, Folate, Iron)
- **Medication Reaction** (e.g., ACE inhibitors, ARBs, antiretrovirals, psychotropic, anticholinergic, clonazepam, [37] chemotherapeutic agents)
- Ciguatera neurotoxin exposure [38]
- **Psychometric**
- **Allergy**
- **Supertasters**
- **Gastro reflux GERD**
- **Neuropathy??**

- **Anemia**
- Multiple sclerosis
- Anxiety
- Dehydration
- Mouth breathing/nasal obstruction
- Alcohol-based mouthwash
- Radiation-induced stomatitis
- Vesiculous bullou conditions
  - Aphthous stomatitis
  - Contact stomatitis
  - Erosive lichen planus
  - Pemphigoid
  - Pemphigus
  - Geographic tongue
- Leukoplakia
- Neoplasia
- Chewing tobacco use
- Areca nut extract exposure [39]

- **Infection**
  - Bacterial infection [40]
  - Candidiasis [28]
  - Viral

Do you have any of the following illnesses or medical symptoms?

- Antibiotics
- ACE inhibitors
- ARB
- Antiretrovirals
- Anticholinergic
- Clonazepam
- Xerostomia-inducing drugs
- Thiadize-diuretics
- Antihistamines
- Other drugs which can induce taste disturbance
- Corsodyl and alcohol mouthwash
- Cinnamon-aldehyde toothpaste

Are you taking, or have you taken, any of the following medications with symptoms?

- Antibiotics
- ACE inhibitors
- ARB
- Antiretrovirals
- Anticholinergic
- Clonazepam
- Xerostomia-inducing drugs
- Thiadize-diuretics
- Antihistamines
- Other drugs which can induce taste disturbance
- Corsodyl and alcohol mouthwash
- Cinnamon-aldehyde toothpaste

• Morr Verenzuela CS, Davis MDP, Bruce AJ, Torgerson RR. Burning mouth syndrome: results of screening tests for vitamin and mineral deficiencies, thyroid hormone, and glucose levels—experience at Mayo Clinic over a decade.

• **BACKGROUND:** Burning mouth syndrome (BMS) is a disorder characterized by chronic mouth pain in the absence of objective clinical abnormalities. Vitamin or mineral deficiencies may have a role in BMS, but data regarding the prevalence and relevance of hematologic deficiencies are conflicting. We aimed to determine the frequency of specific laboratory abnormalities in patients with BMS.

• **METHODS:** We retrospectively reviewed the results of screening blood tests in patients with BMS at our institution between January 2003 and December 2013.

• **RESULTS:** Among 659 patients with BMS, the most common decreased values or deficiencies were vitamin D₃ (15%), vitamin B₂ (15%), vitamin B₆ (5.7%), zinc (5.7%), vitamin B₁ (5.3%), thyrotropin (TSH) (3.2%), vitamin B₁₂ (0.8%), and folic acid (0.7%). Laboratory values for fasting blood glucose and TSH were increased in 23.7% and 5.2%, respectively.

• **CONCLUSIONS:** In patients with symptoms of BMS, our results suggest it is reasonable to screen for fasting blood glucose, vitamin D (D₂ and D₃), vitamin B₆, zinc, vitamin B₁, and TSH. Deficiencies of vitamin B₁₂ and folic acid were rare (<1% abnormal).
## MEDICATIONS CONTRIBUTING TO BMD

### Table 2: Medications that possibly cause hyposalivation/xerostomia as a side-effect

<table>
<thead>
<tr>
<th>Medications</th>
<th>Examples (generic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tricyclic antidepressant</td>
<td>Amitriptyline, nortriptyline</td>
</tr>
<tr>
<td>Antipsychotic</td>
<td>Carbidopa/levodopa, chlorpromazine</td>
</tr>
<tr>
<td>Antihistaminic</td>
<td>Phenergan</td>
</tr>
<tr>
<td>Bronchodilator (anticholinergic and β-2 agonist)</td>
<td>Tiotropium, formoterol</td>
</tr>
<tr>
<td>Decongestant</td>
<td>Oxymetazoline</td>
</tr>
<tr>
<td>Antidepressant</td>
<td>Venlafaxine</td>
</tr>
<tr>
<td>Skeletal muscle relaxant</td>
<td>Tizanidine</td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>Furosemide, clonidine, lisinopril, verapamil</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>Cyclophosphamide</td>
</tr>
<tr>
<td>Protease inhibitor (for HIV)</td>
<td>Reyataz, Norvir, Kaletra</td>
</tr>
<tr>
<td>Opioid</td>
<td>Hydrocodone, oxycodone</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>Diazepam</td>
</tr>
<tr>
<td>Triptan</td>
<td>Rizatriptan</td>
</tr>
</tbody>
</table>

Atkinson *et al.*, 1989; Fox 1998; Bergdahl and Bergdahl 2000; Saleh *et al.*, 2015
2

TABLE 1: Some systemic and local causes of a burning sensation in the mouth, which, therefore, by definition is not BMS [4, 8, 12, 13, 18, 26].

| Oral mucosal conditions | (i) Erythema/erosion of whatever cause | (ii) Atrophic tongue | (iii) Candidiasis | (iv) Geographic tongue | (v) Lichen planus | (vi) Pemphigoid, pemphigus | (vii) Parafunlctional habits | (i) Cheek sucking | (ii) Tongue thrusting | (iii) Trauma: mechanical, chemical, thermal | (iv) Xerostomia and altered salivary quality | (v) Radiotherapy | (vi) Chemotherapy | (vii) Other drugs | (viii) Sjögren's syndrome | (ix) Systemic factors | (i) Diabetes | (ii) Decreased levels of vitamins B1, B2, B12, folate, iron, zinc | (iii) Abnormal thyroid function | (iv) Allergic reaction to food or dental materials | (v) Lichenoid tissue reactions | (vi) Autoimmune conditions | (vii) Hormonal disturbances | (viii) Parkinson disease | (ix) Drugs | (i) Paroxetine | (ii) Angiotensin-converting enzyme inhibitors | (vii) Local nerve damage | (i) Chemotherapy-associated neuropathy | (ii) Local physical irritation | (viii) Various peripheral or central neuropathies |

FIGURE 1: The interrelation between chronic pain, anxiety, depression, and other emotions. The greater the intensity of the pain the greater the suffering, and anxiety, depression, and the stressful emotions may aggravate the experience of pain.

TABLE 2: Available agents or strategies for the management of BMS based on expert opinion and common clinical practice. Adapted from [2].

Pharmacological agents

<table>
<thead>
<tr>
<th>(i) Topical</th>
<th>(ii) Oral</th>
<th>(iii) Systemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i) Clonazepam</td>
<td>(ii) Capsaicin</td>
<td>(iii) Donepezil</td>
</tr>
<tr>
<td>(ii) Antidepressants</td>
<td>(ii) Selective serotonin reuptake inhibitors</td>
<td>(iii) Serotonin-adenalin reuptake inhibitors</td>
</tr>
<tr>
<td>(iii) Anticonvulsants (e.g., gabapentin)</td>
<td>(iv) Antidepressants</td>
<td>(v) Opioids</td>
</tr>
<tr>
<td>(v) Benzodiazepines</td>
<td>(vi) Alpha-lipoic acid</td>
<td></td>
</tr>
</tbody>
</table>

Nonpharmacological therapy

| (i) Cognitive-behavioural therapy | (ii) Mindfulness meditation | (iii) Other relaxation techniques |

Systemic and topical medications (Table 2) have been used in the treatment of BMS with varying degrees of success [8]. Psychological/psychiatric intervention should be considered only when BMS does not respond favourably.
PREVALENCE: BMS

In a cross-sectional analysis of over 1000 randomly selected Swedish patients from Public Dental Health Service registers, 3.7% of subjects were diagnosed with BMS after reporting burning mouth symptoms and undergoing a subsequent physical examination.

In contrast, Lipton et al reported a prevalence of 0.7% based solely on self-reported symptoms from over 45,000 American households.

Haberland et al noted that 10% of new patients observed in his practice were diagnosed with BMS.

Most recently, a large retrospective study of over 3000 Brazilian patients referred to an oral pathology service reported a prevalence of about 1%.
WHAT CAUSES BMS?

• BMD IS SECONDARY AND CAUSES CAN BE FOUND
• BMS (PRIMARY) NO CONSENSUS EXISTS REGARDING A DEFINITIVE CAUSE. RATHER, BURNING MOUTH SYNDROME (BMS) APPEARS TO BE MULTIFACTORIAL IN ORIGIN.
  • + SOMATOSENSORY CHANGES
  • - SOMATOSENSORY CHANGES
• MANY OF THE CURRENTLY PROPOSED ETIOLOGIES DESCRIBE SECONDARY, RATHER THAN PRIMARY BURNING MOUTH SYNDROME (BMS).
• THERE MAY BE 3 TYPES OF BMS
TYPES OF BMS

PERIPHERAL

- Approximately 20% of clinically diagnosed primary BMS patients belong to a subgroup that actually has a subclinical, neurophysiologically evident trigeminal system lesion that may be located within the peripheral nerves (lingual nerve, mandibular nerve, or entire trigeminal nerve) or within the brainstem (Jääskeläinen et al., 1997; Forsell et al., 2002).

CENTRAL

- Another 25–36% of primary BMS patients show signs of decreased inhibition of the blink reflex in the form of absent or deficient habituation of the reflex when stimulating the supraorbital nerve distribution outside the symptomatic intraoral trigeminal area (Jääskeläinen et al., 1997; Forsell et al., 2002). This may indicate a defect within the descending dopaminergic inhibitory system as similar loss of habituation occurs in Parkinson’s disease (Kimura, 2001) due to deficient dopamine-mediated striatal inhibition of the brainstem (Evinger et al., 1993).

MIXED LESIONS BOTH PERIPHERAL AND CENTRAL

CLINICAL CLASSIFICATION OF BMS

- Type 1 pain free waking and worsening during the day 35% linked to systemic disorders (BMD or secondary)
- Type 2 continuous symptoms throughout the day difficulty getting to sleep 55% associated with psychological disorders
- Type 3 intermittent symptoms with pain free periods during the day 10% of total and associated with allergic reaction

Laney and Lewis classification of BMS

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Prevalence %</th>
<th>Clinical characteristics</th>
<th>Associated etiologies</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>35</td>
<td>Symptom-free waking, progressive burning sensation developing in the late morning, gradually increasing in intensity, reaching its peak by evening</td>
<td>Nutritional deficiencies and endocrine disorders (like diabetes mellitus, etc.)</td>
</tr>
<tr>
<td>2</td>
<td>55</td>
<td>Continuous burning symptom throughout the day, present on awakening, difficulty in getting in to sleep</td>
<td>Associated psychological disorders, mood changes</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>Intermittent burning, present only on some days, affecting unusual sites</td>
<td>Display anxiety and allergic reactions</td>
</tr>
</tbody>
</table>

BMS: Burning mouth syndrome

- Subgroup 1 (50-65%) is characterized by peripheral small diameter fibre neuropathy of intraoral mucosa.
- Subgroup 2 (20-25%) consists of patients with subclinical lingual, mandibular, or trigeminal system pathology that can be dissected with careful neurophysiologic examination but is clinically indistinguishable from the other two subgroups.
- Subgroup 3 (20-40%) fits the concept of central pain that may be related to hypofunction of dopaminergic neurons in the basal ganglia.

The peripheral subgroup demonstrates good analgesic response to local anesthesia, whereas the central subgroup shows no response or even hyperalgesia after peripheral nerve block.16

This easy procedure also seems to be able to predict the response to topical clonazepam treatment that was beneficial only in the peripheral subgroup of patients with BMS.

Nasri-Heir et al., 2011 demonstrated that BMS patients with complaints of longer durations presented with a significantly elevated tingling/taste electrical detection threshold ratio, indicating a possible neurodegenerative process, pointing to the hypofunction of the chorda tympani.

The central subgroup showed higher scores in hospital anxiety and depression scores.

The Dopamine hypothesis of BMS pain comes from noninvasive brain stimulation studies showing that repetitive transcranial magnetic stimulation, by initially releasing dopamine in the striatum thereby activating the endogenous opioid system,32 also effectively relieves BMS pain.
primary BMS were included. Among them, 324 patients who complained of oral symptoms on both sides of the oral cavity were assigned to the bilateral group and 97 patients who complained of symptoms only on one side of the oral cavity were assigned to the unilateral group. Clinical characteristics, psychological status, and salivary secretion were compared between the two groups. There were no significant differences in the mean age, sex ratio, unstimulated and stimulated salivary flow rates, or duration of symptoms between the two groups. The bilateral group had higher levels of psychological distresses compared with the unilateral group. The bilateral group had higher prevalence rates in burning, taste alteration, and xerostomia than the unilateral group. The proportion of patients who considered dental procedures as an initiating factor of BMS symptoms was higher in the unilateral group than in the bilateral group. Conclusively, BMS patients with
CURRENT HYPOTHESES FOR (PRIMARY) BMS

- **Neuropathic pain mechanism**
  - Measured abnormalities of physiologic responses of the trigeminal nerve in burning mouth syndrome (BMS) patients.\(^2,3\)
  - There is also evidence to suggest histopathologic changes in nociceptive fibres in BMS patients.\(^4\)
  - The differentiation between a peripheral versus a central aetiology has not been determined

- **Noci-plastic pain**
- **Psychogenic illness**
- **Supertasters**
- **Brain connectivity/ Dopaminergic**
- **Genetic**
Sleep disorders increase the risk of burning mouth syndrome: A retrospective population-based cohort study

Burning Mouth Syndrome and Menopause

Relevance of sleep, pain cognition, and psychological distress with regard to pain in patients with burning mouth syndrome

Cytokine levels and their role in the etiopathogenesis of Burning Mouth Syndrome: A systematic review
BMS AND NEUROPATHOGENIC AETIOLOGY

- Persistent peripheral neuropathy, the central afferent nociceptor terminals in the dorsal horn of the spinal cord release excitatory biological mediators which can activate postsynaptic NMDA receptors which under physiological conditions are silent, thus resulting in central sensitization with increased excitability [1].

- There may also be a decrease in the functional activity of the GABA-mediated pain-inhibitory interneuron circuits in the dorsal horn of the spinal cord which under physiological circumstances inhibit the glutamate / NMDA-mediated central sensitization [1], possibly contributing to the neuropathic pain of BMS [2].

- Thus, central sensitization characterised by structural and functional neural plasticity results in increased excitability and increased tonic activity of central nociceptive neurons, playing an important role in the pathogenesis of BMS [3,4].

- However, surprisingly, despite the possible roles of central sensitization and of psychogenic factors such as anxiety or depression in BMS neuropathic pain, it appears that, in persons with BMS, the co-occurrence of other chronic neuropathic pain disorders (central sensitivity syndromes) including fibromyalgia, atypical facial pain, trigeminal neuralgia, temporomandibular joint pain, back pain, and vulvodynia is rare [4, 5].

- This suggests that the neural pathogenic mechanisms of BMS are distinct, probably localised some where in the trigeminal nerve pathway [5].


NEUROPATHY CAUSING NEUROPATHIC PAIN

• **At the tip of the tongue compared to healthy controls (Grushka et al., 1987)**

• **With laser Doppler flowmetry, vasoreactivity of the intraoral mucosa to dry ice stimulation has been shown to be higher in BMS patients than controls (Heckmann et al., 2001), which, as a positive sign, is in line with the sensory phenomenon of decreased pain tolerance.**

• **More convincing evidence for focal involvement of the intraoral small fibre system came from a QST study utilizing argon laser stimulator (Svensson et al., 1993) and showing increased detection thresholds to warming and heat pain (hypoesthesia and hypalgesia, i.e. negative signs) together with low pain to sensory threshold ratios on the tongue mucosa of BMS patients compared to control subjects.**

• **Large and small fiber neuropathy.**

• **Neuroanatomical studies applying methods developed for the investigation of intraepidermal nerve fibre density from skin biopsies to the study of epithelial density of small fibre endings (ENFD) in tongue mucosal biopsies (Lauria et al., 2005; Yılmaz et al., 2007; Beneng et al., 2010; Puhakka et al., 2010). These structural studies have now repeatedly shown significant loss of epithelial small diameter fibres in the tongue mucosa of BMS patients**

• **Lauria et al., 2005; Albuquerque et al., 2006; Eliav et al., 2007; Yılmaz et al., 2007; Puhakka et al., 2010.**

• **Lower threshold to blink reflex**

• **Another 25–36% of primary BMS patients show signs of decreased inhibition of the blink reflex in the form of absent or deficient habituation of the reflex when stimulating the supraorbital nerve distribution outside the symptomatic intraoral trigeminal area (Jääskeläinen et al., 1997; Forsell et al., 2002).**
Sodium channel Na v 1.7 immunoreactivity in painful human dental pulp and burning mouth syndrome.

Sensory purinergic receptor P2X3 is elevated in burning mouth syndrome.

TRPV1 -IR

TRPV1 fibres staining in control and in BMS x20.

Bar chart shows the mean ± SEM of % area of TRPV1 fibres in control (n=10) and BM (n=10) tongue. * P =0.0011
'SUPERTASTERS'

Studies report

- **Increased fungiform papillae** (taste buds that are related to chorda tympani viability)

- **Increased taste sensitivity**

INTERACTION TASTE NERVE FIBRES AND TOUCH FIBRES IN TONGUE MIMICKING ‘PHANTOM LIMB PAIN’

• One small study proposed that unilateral chorda tympani (taste) hypofunction results in lingual nerve (somatosensory) hyperfunction by disruption of a centrally mediated equilibrium between the two.[6]

• Observation in other conditions has shown that when a sensory circuit loses afferent signals that hyperactivity may result in hallucinatory sensations.

• Examples of this include phantom limb sensation following amputation and tinnitus in hearing loss. It would tend to account both for pain and for gustatory disturbances in burning mouth syndrome (BMS).

• Metallic or sour tastes are considered symptomatic manifestations of an understimulated gustatory circuit while understimulated sensory circuitry manifests burning sensations. The cause of this proposed neuropathy is unknown.

CENTRAL MECHANISMS

• FMRI studies has shown less volumetric activation in the entire brain to painful hot stimuli in primary BMS patients compared to control subjects and, more specifically, in the bilateral thalamus (Albuquerque et al., 2006); findings similar to those previously reported in neuropathic pain patients (Apkarian et al., 2005).

• The neurophysiologic phenomenon of deficient habituation of the R2 components of the blink reflex with supraorbital nerve stimulation in primary BMS patients initiated a series of studies on the role of brain dopamine system in pain (Jääskeläinen et al., 2001; Hagelberg et al., 2003, 2004).

• Neurotransmitter positron emission tomography (PET) studies have demonstrated a significant decrease in fluoro-DOPA-tracer uptake in the presynaptic nerve terminals of the putamen on both sides indicating low level of dopamine in the nigrostriatal neurons of BMS patients compared to age matched controls (Jääskeläinen et al., 2001).

• However, on individual patient level, not all primary BMS patients show PET findings compatible with decrease in striatal dopamine. Deficient dopaminergic top-down inhibition may thus be a contributing factor to the clinical symptomatology in a subgroup of BMS patients, simultaneously with or independent of focal peripheral neuropathy.
CENTRAL FUNCTIONAL IMAGING STUDIES

- The results showed that BMS patients had higher depression and anxiety levels than controls.
- BMS patients showed lower gray matter volume (GMV) in the bilateral ventromedial prefrontal cortex (VMPFC) and increased functional connectivity between this region and the bilateral amygdala.
- Region of interest (ROI) analysis suggested that the functional connectivity between the bilateral VMPFC and amygdala correlated with the years of BMS illness in patients.
- The brain measures could predict the years of symptoms in the BMS group. These results suggest a potential neuromarker for the diagnosis and treatment of BMS.
PERIPHERAL NERVE BLOCK (LINGUAL NERVE)

- **Unilateral peripheral lingual nerve block with lidocain has been shown to result, on the group level, in significant, ipsilateral or bilateral symptom resolution in primary BMS (Gremeau-Richard et al., 2010).**

- **However, on individual patient level, primary BMS patients were shown to respond in two very distinct ways, one subgroup, called “peripheral BMS”, showing clinically meaningful pain reduction on visual analogue scale and another “central” subgroup showing no pain reduction or even an increase in burning pain after technically successful lingual nerve block.**

- **In addition, hospital anxiety and depression (HAD) scores were significantly higher in the “central” than the “peripheral” BMS subgroup.**
BRAIN CONNECTIVITY

- **Burning mouth syndrome (BMS) is a chronic intragral pain syndrome featuring idiopathic oral pain and burning discomfort despite clinically normal oral mucosa. The etiology of chronic pain syndrome is unclear, but preliminary neuroimaging research has suggested the alteration of volume, metabolism, blood flow, and diffusion at multiple brain regions. According to the neuromatrix theory of Melzack, pain sense is generated in the brain by the network of multiple pain-related brain regions. Therefore, the alteration of pain-related network is also assumed as an etiology of chronic pain. In this study, we investigated the brain network of BMS brain by using probabilistic tractography and graph analysis.**

- **METHODS:** Fourteen BMS patients and 14 age-matched healthy controls underwent 1.5T MRI. Structural connectivity was calculated in 83 anatomically defined regions with probabilistic tractography of 60-axis diffusion tensor imaging and 3D T1-weighted imaging. Graph theory network analysis was used to evaluate the brain network at local and global connectivity.

- **RESULTS:** In BMS brain, a significant difference of local brain connectivity was recognized at the bilateral rostral anterior cingulate cortex, right medial orbitofrontal cortex, and left pars orbitalis which belong to the medial pain system; however, no significant difference was recognized at the lateral system including the somatic sensory cortex. A strengthened connection of the anterior cingulate cortex and medial prefrontal cortex with the basal ganglia, thalamus, and brain stem was revealed.

- **CONCLUSION:** Structural brain network analysis revealed the alteration of the medial system of the pain-related brain network in chronic pain syndrome.

Burning mouth syndrome (BMS) is a chronic pain disorder characterized by severe burning sensation in normal looking oral mucosa. Diagnosis of BMS remains to be a challenge to oral healthcare professionals because the method for definite diagnosis is still uncertain. In this study, a quantitative saliva proteomic analysis was performed in order to identify target proteins in BMS patients' saliva that may be used as biomarkers for simple, non-invasive detection of the disease. By using isobaric tags for relative and absolute quantitation labeling and liquid chromatography-tandem mass spectrometry to quantify 1130 saliva proteins between BMS patients and healthy control subjects, we found that 50 proteins were significantly changed in the BMS patients when compared to the healthy control subjects (p ≤ 0.05, 39 up-regulated and 11 down-regulated).

Four candidates,

- alpha-enolase
- interleukin-18 (IL-18)
- kallikrein-13 (KLK13)
- cathepsin G, were selected for further validation.

Based on enzyme-linked immunosorbent assay measurements, three potential biomarkers

- Alpha-enolase
- IL-18
- KLK13, were successfully validated. The fold changes for alpha-enolase, IL-18, and KLK13 were determined as 3.6, 2.9, and 2.2 (burning mouth syndrome vs. control), and corresponding receiver operating characteristic values were determined as 0.78, 0.83, and 0.68, respectively.


Potential protein biomarkers for burning mouth syndrome discovered by quantitative proteomics. Ji EH¹, Diep C¹, Liu T², Li H², Merrill R¹, Messadi D¹, Hu S¹.
ASSESSMENT OF PATIENT WITH BMS
INVESTIGATIONS
DURHAM & CURRIE

Haematological:
- CBC/FBC (Hb, MCV, MCH, WCC)
- B12, Fe, Folate (81, 2, 6, 12)
- Zinc
- HbA1c
- T3, T4, TSH
- LFT (ALT, GGT, ALK Phos, Albumin)
- ESR or CRP
- Menopausal index
- H pylori
- Autoantibodies:
  - Anti-Ro and Anti-La
  - ANA
  - ENA

Saliva

Patch test: adjunctive for clinical suspicion

Candida

OST: see copy and pasted table taken from Devine-M et al-Prospero-review of diagnostic criteria for PPTTN
**SENSORY TESTING ALL BMS PATIENTS**

**RECOMMENDED REGIME FOR RESEARCH**

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Step-wise diagnostic work-up of burning mouth patients. Step 1 examinations aid in the differential diagnostics of BMS symptoms, Steps 2 and 3 examinations define the level and extent of neuropathic abnormalities in primary BMS, Step 4 reveals deficiencies in top-down inhibition. Different alternative tests for intraoral small fibre function can be used at Step 1, according to availability. Step 5 describes additional tests for further investigation of aetiology, exact location, and extent of nervous system pathology related to BMS.

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1 alternative A</td>
<td>Electrogustometry: Ratio of taste-to-tingling detection thresholds to electrical stimuli</td>
<td>High ratio</td>
</tr>
<tr>
<td>Step 1 alternative B</td>
<td>Thermal quantitative sensory testing (QST) on the tongue mucosa (small thermode, both sides: warm, cool, heat pain and cold pain detection thresholds; pain tolerance)</td>
<td>Normal ratio</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Thermal hypoesthesia/anaesthesia or thermal hypoalgesia/analgesia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Thermal allodynia/hyperesthesia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Normal</td>
</tr>
<tr>
<td>Step 2</td>
<td>Blink reflex with stimulation of supraorbital, mental, and lingual nerve distributions Masseter reflex</td>
<td>Abnormal (afferent pattern)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abnormal partial/mixed patterns</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Normal brainstem reflexes</td>
</tr>
<tr>
<td>Step 3</td>
<td>Tongue mucosal punch biopsy: epithelial (ENFD) and subepithelial (SENFD) nerve fibre density</td>
<td>Decreased ENFD only</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Decreased ENFD and SENFD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Normal</td>
</tr>
<tr>
<td>Step 4</td>
<td>Habituation of the blink reflex: 1 Hz repetitive electrical stimulation of the supraorbital nerve</td>
<td>Abnormal excitability and normal findings at steps 1, 2 and 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Abnormal excitability and abnormal findings at steps 1A, 1B, 2 or 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Normal findings steps 1, 2, 3 and 4</td>
</tr>
<tr>
<td>Step 5 Optional</td>
<td>a. ENMG: bulbar region, extremities</td>
<td>Abnormal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>b. Thermal QST or skin biopsy for ENFD in the extremities</td>
</tr>
<tr>
<td></td>
<td></td>
<td>c. MRI targeted according to abnormal findings at Step 2</td>
</tr>
</tbody>
</table>

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Satu K. Jääskeläinen Pathophysiology of primary burning mouth syndrome Clinical Neurophysiology Volume 123, Issue 1, January 2012, Pages 71-77
Burning mouth syndrome

Sari K. Jääskeläinen1 and Alain Woda2

Abstract

Objectives: To review the clinical entity of primary burning mouth syndrome (BMS), its pathophysiological mechanisms, and the current diagnostic methods and evidence-based treatment options, and to describe novel lines for future research regarding etiology, pathophysiology, and new therapeutic strategies.

Background: Chronic BMS is a common neurosensory oral pain condition characterized by persistent burning, discomfort, and pain in the mouth region. The definition of BMS has evolved over time, and various diagnostic criteria have been proposed.

Methods: A systematic review of clinical and experimental studies on BMS was conducted. The search included PubMed, Embase, and other relevant databases.

Results: The prevalence of BMS varies widely, ranging from 0.5% to 10% of the general population. BMS is typically diagnosed based on clinical symptoms and exclusion of other causes. Therapeutic strategies include lifestyle modifications, medication, and non-pharmacological interventions.

Conclusion: BMS is a complex disorder involving multiple factors. Further research is needed to identify the underlying mechanisms and develop effective treatment options.

Keywords

Burning mouth syndrome, epidemiology, pathophysiology, diagnosis, treatment

Data received: 5 November 2016; revised: 30 December 2016; 30 January 2017; accepted: 31 January 2017

References

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Burning mouth syndrome

Jääskeläinen and Woda

Table 1. Tests currently available for the diagnostic work-up of burning mouth syndrome (BMS) patients. With appropriate combinations, diagnostic and grading of subclinical trigeminal neuropeptides and neurotransmitter pathology can be done. In addition, multiple tests profile the pathophysiological processes on individual patient level, enabling a rational search for more specific antinociceptives and mechanism-based treatment approaches.

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(continued)
Burning mouth syndrome

Sattu K Jääskeläinen and Alain Woda

Abstract

Objectives: To review the clinical entity of primary burning mouth syndrome (BMS), to path characterize the clinical presentation, disease, and evidence-based treatment options, and to describe the new regimens of therapy and pathophysiologic processes in the future.

Methods: A literature search was performed using PubMed, Medline, and other databases. A total of 50 articles were included.

Results: Primary BMS is a chronic neuropathic pain disorder that is due to clinical signs of neuropathic involvement. A review of the literature reveals that the condition is primarily a diagnostic problem, as no specific diagnostic criteria have been established. Treatment options include medications, nerve block, and physical therapy. The prognosis is variable, and the condition may recur.

Conclusion: BMS is a significant clinical problem, and further research is needed to better understand the pathophysiology and develop effective treatment strategies.

Keywords: Burning mouth syndrome, epidemiology, pathophysiology, diagnosis, treatment

Date received: 5 November 2016; revised: 31 December 2016; accepted: 31 January 2017

Table 1. Tests currently available for the diagnosis work-up of burning mouth (BMS) patients. With appropriate combinations, diagnosis and grading of subclinical trigeminal neuropathies and brainstem pathology can be done. In addition, multiple tests profile the pathophysiologic processes on individual patient level, enabling a rational search for more specific aetiologies and mechanism-based treatment approaches.

Test and measured variables | Result | Interpretation in patients with intraoral burning pain
--- | --- | ---
Electrogustometry | Ratio of taste-to-tingling detection thresholds to electrical stimuli | High ratio | Primary BMS
 | Normal ratio | Secondary BMS or healthy

Thermal quantitative sensory testing (QST) on the tongue mucosa:

- Warm, cool, heat pain and cold pain detection thresholds Pain tolerance
- Thermal hypoesthesis/anaesthesia
- Thermal hyperesthesia
- Normal

Brainstem reflexes:

- Blink reflex with stimulation of supraorbital, mental, and lingual nerve distributions

- Abnormal (afferent pattern)
- Abnormal partial / mixed patterns

- Masseter reflex
- Normal brainstem reflexes

- Lingual/mandibular/trigeminal neuropathic pain
- Central pain due to brainstem pathology
- Not neuropathic pain, or pure small fibre neuropathy
Burning mouth syndrome

Satu K Jääskeläinen1 and Alain Woda1

Abstract

Objectives: To review the clinical entity of primary burning mouth syndrome and evaluate evidence-based treatment options regarding pathophysiology, pathophysiology and new therapeutic approaches.

Description: Primary BMS is a chronic neuropathic condition affecting the oral mucosa, characterized by burning or dysesthesia sensations. A diagnosis of BMS should be made after excluding other potential causes.

Conclusion: BMS is a challenging condition that requires a comprehensive approach to diagnosis and treatment.

Keywords

Burning mouth syndrome, epidemiology, pathophysiology, diagnosis

Data received: 5 November 2014; revised: 31 December 2014; 30 January 2015

Blink reflex with stimulation of supraorbital, mental, and lingual nerve distributions

- Abnormal (afferent pattern)
- Normal brainstem reflexes
- Lingual/mandibular/trigeminal neuropathic pain

Masseter reflex

- Abnormal partial / mixed patterns
- Central pain due to brainstem pathology
- Not neuropathic pain, or pure small fibre neuropathy

Tongue mucosal biopsy:

- Epithelial (ENFD) and subepithelial (SENFD) nerve fibre density
- Decreased ENFD, normal SENFD
- Decreased ENFD and SENFD
- Normal
- Pure peripheral small fibre neuropathy
- Peripheral lingual/mandibular/trigeminal neuropathy
- Central or not neuropathic pain

Habituation of the blink reflex:

- Decrease in R2 component area with 1 Hz repetitive electrical stimulation of the supraorbital nerve
- Abnormal excitability and normal findings in tests for peripheral nerves
- Central pain due to top-down disinhibition (maybe related to striatal dopamine depletion)

Definition

The International Headache Society (IHS) defines burning mouth syndrome (BMS) as an “intermittent burning or dysesthetic sensation, occurring daily for more than 2 hours per day for more than 3 months, without clinically evident causative lesions.” This definition does not regard BMS as a psychiatric pain disorder, as was generally held to be until a decade ago (2,3), but on the contrary lists it under the heading “painful oral neuropathies” in the IHS classification (1) and further describes it as “burning or dysesthetic sensation,” clearly referring to neuropathic mechanisms. This newer view has been substantiated by recent histopathological, neurophysiological, brain imaging, and quantitative sensory testing (QST) data, as will be described in detail further on.

Classification

The International Association for the Study of Pain (IASP) first recognized BMS in 1994 as an identified pain syndrome.

Tests to further localize nervous system pathology

- ENMG: Face, bulb area, extremities
- Thermal QST or skin biopsy for ENFD in the extremities
- MRI targeted according to abnormal findings in neurophysiologic tests
- Abnormal
- Normal
- Neuropathic pain combined with deficient top-down inhibition
- More exact localization of peripheral neuropathy: Focal or generalized
- Generalized peripheral small fibre neuropathy
- Exact location of structural central nervous system pathology

(continued)
52% of primary BMS patients have abnormal sensory responses. Another theory is taste disturbance.
RAPID COMMUNICATION

Central mechanisms in burning mouth syndrome involving the olfactory nerve: a preliminary study

Mariana Siviero,1 Manoel Jacobsen Teixeira,2 José Tadeu Tesseroli de Siqueira,3 Silvia Regina Dowgan Tesseroli de Siqueira4

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INTRODUCTION

Burning mouth syndrome (BMS) is characterized by a continuous sensation of burning or heat in the oral cavity, mainly on the tongue, palate and/or gingiva 1-3, in the absence of a primary cause. 4-5. Systemic diseases, such as diabetes mellitus or anemia, must be ruled out. 6. It is most common among postmenopausal women and causes intense discomfort and suffering.

There is no defined etiology for BMS other than precipitating causative factors, and it is still considered idiopathic. One of the most widely accepted theories is that the partial or total loss of chorda tympani (facial) nerve function diminishes the trigeminal nerve, resulting in pain along trigeminal pathways, as both taste and pain systems are regulated by interconnections of the central nervous system

other lesions and no diseases included in the exclusion criteria.

Inclusion criteria: The study included 20 patients newly diagnosed with BMS who had not begun pharmacological treatment and 30 healthy controls with no complaint of facial or intraoral pain within the last 6 months who were consecutively selected from patients receiving dental treatment at the Dentistry Division of the hospital.

Exclusion criteria: (for patients and controls) Exclusion criteria included Sjögren syndrome, rheumatological diseases (i.e., fibromyalgia and rheumatoid arthritis), diabetes, anemia, hyper- or hypothyroidism, generalized pain, and history of surgery in the facial/oral region. The patients and controls underwent a systematic evaluation by the hospital’s general physicians to investigate the presence of

Sweet (glucose): 0.01; 0.032; 0.1; 0.32; 1.0.
Sour (citric acid): 0.01; 0.032; 0.1; 0.32; 1.0.
Bitter (urea): 0.01; 0.032; 0.1; 0.32; 1.0.

A single drop of each concentration was applied and swallowed by the patient; the results were compared to results from a single drop of distilled water. When the stimulus was not perceived, the next concentration was applied. The patient’s mouth was washed with distilled water between different tastes.

(5) Olfactory threshold with isopropanol solutions (9.9; 15; 23.3; 32; 48; 53; 79%) 5-7. Each concentration was offered to the patient along with a bottle of water, and the patient was asked to choose the bottle containing the substance three times. The threshold was established when the patient correctly chose all three times. If the patient chose incorrectly, the next concentration was offered along with a bottle of water.

All subjects were evaluated in the sitting position, with the head resting on a flat surface and the Frankfurt line parallel to the ground. All evaluations took place at the same time of day (between 1 and 4 pm) in a silent room with acoustic protection on the walls and with the door closed.

Only the patient and the researcher were in the room during evaluations. All patients were evaluated by the same researcher. The subjects received the same instructions after being positioned, which were to keep their eyes closed during the exam and to identify and report whether they felt the stimuli being applied to the face (by saying “yes” or “no”) and what they felt (by naming the stimulus). Only the researcher knew the order in which the stimuli would be presented. Finally, all findings were tabulated and statistically analyzed.

analyze facial and oral sensitivity. Finally, gustative and olfactory thresholds were evaluated with the Knorr-Kall- Wallis test followed by Dunns test. The level of significance was p = 0.05.

RESULTS

Demographic characteristics

The mean age of subjects was 60.95, and there were 16 women and 4 men in the BMS group. There was a significant age difference between groups (Table 1).

Somatosensory findings

There were no between-group differences in the somatosensory results for the ophthalmic branch, and similar cold thresholds were noted between the groups. The BMS patients had higher tactile thresholds at the maxillary branch (p = 0.001) and higher warm thresholds at the maxillary (p = 0.002) and mandibular (p = 0.001) branches (Table 2). The BMS patients had higher pain thresholds at the ophthalmic and maxillary branches (p = 0.05) (Table 3).

There were no intrasensory sensitivity differences between the studied groups (p = 0.07).

Gustative evaluation

The gustative evaluation showed significant differences in all basic tastes (sweet p = 0.001; salty p = 0.004; sour p = 0.001; bitter p = 0.003). The BMS patients had higher salty, sweet and bitter thresholds but lower sour thresholds (Figure 1).

Neither group exhibited difficulties with taste identification.

Olfactory evaluation

The BMS patients had higher olfactory thresholds (Figure 2).

DISCUSSION
WILL IT GET BETTER?

• FOR PATIENTS WITH PRIMARY BURNING MOUTH SYNDROME (BMS), AN ESTIMATED 50-66% MAY HAVE IMPROVEMENT IN SYMPTOMS AFTER 6-7 YEARS.\textsuperscript{[11]}

• A SMALL STUDY OF 32 PATIENTS REPORTED NEAR UNIVERSAL IMPROVEMENT IN SYMPTOMS WITHIN 16 WEEKS FOR PATIENTS RECEIVING ONGOING MULTIDISCIPLINARY TREATMENT.\textsuperscript{[42]}

• SPONTANEOUS REMISSION IS RARE BUT DOES OCCUR IN ROUGHLY 3% OF PATIENTS.\textsuperscript{[43]}

• THESE FINDINGS ARE SIMILAR TO OTHER IDIOPATHIC CHRONIC PAIN SYNDROMES AND SUPPORT THE IDEA THAT TREATMENT SHOULD BE INDIVIDUALIZED BASED ON SYMPTOMS
Burning mouth syndrome: a review and update

Introduction

Burning mouth syndrome (BMS) is typically described by the patients as a burning sensation of the oral mucosa in the absence of clinically apparent mucosal alterations. It occurs more commonly in middle-aged and elderly women and often affects the tongue tip and lateral borders, lips, and hard and soft palate. In addition to a burning sensation, the patients with BMS may also complain unrelenting oral mucosal pain, dysgeusia, and xerostomia. BMS can be classified into two clinical forms: primary and secondary BMS. The primary BMS is essential or idiopathic, in which the organic local/systemic cause cannot be identified and a neuropathological cause is likely. The diagnosis of primary BMS depends mainly on exclusion of etiological factors. The secondary BMS is caused by local, systemic, and/or psychological factors; thus, its diagnosis depends on identification of the exact causative factor. When local, systemic or psychological factors are present, treatment or elimination of these factors usually results in a significant clinical improvement of BMS symptoms. Vitamins, zinc, or hormone replacement therapy has been found to be effective for

Diagnostic criteria

The diagnosis of BMS needs a careful analysis of the symptom pattern experienced by each patient. The main symptoms of oral burning or pain should be experienced deep within the oral mucosa, unrelenting for at least 4-6 months, and continuous throughout almost all the day.
TREAT THE PATIENT - HOLISTIC CARE WITH INFORMED EDUCATION

- MANAGE PATIENTS' EXPECTATIONS
- EXPLAIN DIAGNOSIS
- EXCLUDE CAUSES FOR BMD CONFIRM DIAGNOSIS BMS
- RECTIFY NUTRITIONAL DEFICIENCIES (B COMPLEX, ZINC, ANXIOLYSIS)
- PSYCHOLOGICAL SUPPORT
- MEDICAL INTERVENTIONS
  - TOPICAL
  - SYSTEMIC
- ALTERNATIVE
  - ACUPUNCTURE
  - HYPNOTHERAPY
- OTHER
  - LASER
  - DBS

Tricyclic antidepressants
Alpha-lipoic acid [45]
Hormone replacement therapy
SSRIs
Gabapentin or pregabalin
Topiramate [50]
Olanzapine [51]
Burning mouth syndrome: pathogenic and therapeutic concepts

Ewa Ferensztajn, Dorota Lojko, Janusz Rybakowski

Summary

Burning mouth syndrome (BMS) is a chronic pain condition characterized by pain, burning sensations and dryness within an oral mucosa, without any clinical changes of the latter. It occurs approximately seven times more frequently in women, mostly in perimenopausal age. The psychiatric aspect of BMS is significant: the most frequent co-morbidities are depression and anxiety disorders, and a number of psychotropic drugs play an essential role in its treatment. In the present review, the most important pathogenic and treatment concepts of BMS have been discussed. BMS may be similar to neuropathic pain and has some related pathogenic elements with fibromyalgia and the restless leg syndrome. In primary BMS, the features of presynaptic dysfunction of dopaminergic neurons and deficiency of endogenous dopamine levels have been demonstrated. Other neurotransmitters such as serotonin, noradrenaline, histamine as well as hormonal and inflammatory factors may also play a role in the pathogenesis of BMS. In the pharmacological treatment of BMS, a variety of drugs have been used including benzodiazepines, antidepressants, antipsychotic drugs. In the final part of the paper, the possibility of using atypical antipsychotic drugs, olanzapine, in the treatment of BMS has been discussed. In the context of the recent studies on this topic, a case of female patient with the BMS lasting more than ten years has been mentioned, in whom the treatment with olanzapine brought about a rapid and significant reduction of symptoms. The probable mechanism of the therapeutic effect of olanzapine in BMS can include its effect on dopaminergic receptors and probably also on histaminergic, noradrenergic and serotonergic ones.

Key words: burning mouth syndrome, dopaminergic system, olanzapine

Table 1. Selected therapeutic interventions in BMS according to [42], modified

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<tr>
<th>Topical treatment</th>
<th>Oral administration</th>
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<td>Clonazepam – anxiolytic drug</td>
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<td>Lidocaine – anaesthetic drug</td>
<td>Capsaicin – atypical analgesic drug</td>
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<tr>
<td>Capsaicin – atypical analgesic drug</td>
<td>Doxepin (cream) – tricyclic antidepressant</td>
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<td>Dextromethorphan – non-steroidal antiinflammatory drug</td>
<td>Benzdipine – non-steroidal antiinflammatory drug</td>
</tr>
<tr>
<td>Lactoperoxidase – antibacterial drug</td>
<td>Sulphuric acid – protective agent for mucous membrane</td>
</tr>
</tbody>
</table>

Other methods

- Cognitive-behavioral therapy
- Group therapy
- Electroconvulsive therapy
- Acupuncture
- Laser therapy
- Tongue protector (shield)
- Biofeedback
OPTIMAL TREATMENT FOR BMS BEST EVIDENCE?

- **The interventions were grouped into:**
  - **Medical**
    - Antidepressants and antipsychotics
    - The anticonvulsant Gabapentin (one study, 100 participants) RR 4.00, 95% CI 2.09 to 7.67
    - Topical benzodiazepine (two studies, 111 participants) MD -1.89 95% CI -2.19 to -1.59. Long term symptom relief was achieved with topical benzodiazepine (one study, 66 participants) MD -1.39 95% CI -1.96 to 0.83
  - **Dietary supplements**
  - **Electromagnetic radiation**
  - **Psychological therapies**
    - Topical treatments. Short-term symptom relief was demonstrated by:
      - Laser energy waves (one study, 58 participants) MD -30.36, 95% CI -44.22 to -16.50,
      - Physical barriers (one study, 50 participants) MD -1.1 95% CI -2.14 to 0.06,
  - **Conclusions** From studies mostly classified as high risk of bias, there is insufficient evidence to support or refute the use of any particular intervention for the management of BMS.

OPTIMAL TREATMENT FOR BMS
BEST EVIDENCE?

ABSTRACT

BACKGROUND: Burning mouth syndrome (BMS) is a term used for oral mucosal pain (burning, pain or discomfort in the tongue, lips or entire oral cavity) without identifiable cause. General population prevalence varies from 0.1% to 3.2%. Many BMS patients indicate anxiety, depression, personality disorders and impaired quality of life (QoL). This review updates the previous versions published in 2000 and 2005.

OBJECTIVES: To determine the effectiveness and safety of any intervention versus placebo for symptom relief and changes in QoL, taste, and feeling of dryness in people with BMS.

SEARCH METHODS: Cochrane Oral Health's Information Specialist searched the following databases: Cochrane Oral Health's Trials Register (to 31 December 2016), the Cochrane Central Register of Controlled Trials (CENTRAL; issue 11) in the Cochrane Library (searched 31 December 2015), MEDLINE Ovid (1946 to 31 December 2015), and EMBASE Ovid (1980 to 31 December 2015). We searched ClinicalTrials.gov and the World Health Organization International Clinical Trials Registry Platform for ongoing trials. We placed no restrictions on the language or date of publication when searching the electronic databases. Selection criteria: A randomised controlled trial (RCT) comparing any treatment against placebo in people with BMS. The primary outcomes were symptom relief (pain/burning) and change in the electronic QoL. Secondary outcomes included change in taste, feeling of dryness, and adverse effects.

DATA COLLECTION AND ANALYSIS: We used standard methodological procedures expected by Cochrane. Outcome data were analysed as short-term (up to three months) or long-term (three to six months).

MAIN RESULTS: We included 23 RCTs (1121 analysed participants: 83% female). Interventions were categorised as: antidepressants and antipsychotics, anticonvulsants, benzodiazepines, cholinergics, dietary supplements, electromagnetic radiation, physical barriers, psychological therapies, and topical treatments. Only one RCT was assessed at low risk of bias overall, four RCTs' risk of bias was unclear, and 18 studies were at high risk of bias. Overall, the quality of the evidence for effectiveness was very low for all interventions and all outcomes. Twenty-one RCT's assessed short-term symptom relief. There is very low-quality evidence of benefit from electromagnetic radiation (one RCT, 58 participants), topical benzodiazepines (two RCTs, 111 participants), physical barriers (one RCT, 50 participants), and anticonvulsants (one RCT, 100 participants). We found insufficient/contradictory evidence regarding the effectiveness of antidepressants, cholinergics, systemic benzodiazepines, dietary supplements or topical treatments. No RCT assessing psychological therapies evaluated short-term symptom relief. Four studies assessed long-term symptom relief. There is very low-quality evidence of a benefit from psychological therapies (one RCT, 30 participants), capsaicin oral rinse (topical treatment) (one RCT, 18 participants), and topical benzodiazepines (one RCT, 66 participants). We found no evidence of a difference for dietary supplements or lactoferrin or capsaicin oral rinse. No studies assessed anticonvulsants, anticonvulsants, cholinergics, electromagnetic radiation or physical barriers evaluated long-term symptom relief. Short-term change in QoL was assessed by seven studies (none long-term). The quality of evidence was very low. A benefit was found for electromagnetic radiation (one RCT, 58 participants); however, findings were inconclusive for antidepressants, benzodiazepines, dietary supplements and physical barriers. Secondary outcomes (change in taste and feeling of dryness) were only assessed short-term, and the findings for both were also inconclusive. With regard to adverse effects, there is very low-quality evidence that antidepressants increase dizziness and drowsiness (one RCT, 57 participants), and that aminotriazole acid increased headaches (two RCTs, 118 participants) and gastrointestinal complaints (3 RCTs, 138 participants). We found insufficient/contradictory evidence regarding adverse events for anticonvulsants or benzodiazepines. Adverse events were poorly reported or unreported for cholinergics, electromagnetic radiation, and psychological therapies. No adverse events occurred from physical barriers or topical therapy use.

AUTHORS' CONCLUSIONS: Given BMS' potentially disabling nature, the need to identify effective modes of treatment for sufferers is vital. Due to the limited number of clinical trials at low risk of bias, there is insufficient evidence to support or refute the use of any interventions in managing BMS. Further clinical trials, with improved methodology and standardised outcome sets are required in order to establish which treatments are effective. Future studies are encouraged to assess the role of treatments used in other neuropathic pain conditions and psychological therapies in the treatment of BMS.
Pharmacological treatment of oro-facial pain - health technology assessment including a systematic review with network meta-analysis.

Häggman-Henrikson B¹,²,³, Alstergren P¹,⁴,⁵, Davidson T³,⁶, Högestätt ED⁷, Östlund P²,⁸, Tranaeus S²,⁸, Vitols S⁸,⁹, List T¹,⁴,⁵.

This health technology assessment evaluated the efficacy of pharmacological treatment in patients with oro-facial pain. Randomised controlled trials were included if they reported pharmacological treatment in patients ≥18 years with chronic (≥3 months) oro-facial pain. Patients were divided into subgroups: TMD-muscle [temporomandibular disorders (TMD) mainly associated with myalgia]; TMD-joint (TMD mainly associated with temporomandibular joint pain); and burning mouth syndrome (BMS). The primary outcome was pain intensity reduction after pharmacological treatment. The scientific quality of the evidence was rated according to GRADE. An electronic search in PubMed, Cochrane Library, and EMBASE from database inception to 1 March 2017 combined with a handsearch identified 1552 articles. After screening of abstracts, 178 articles were reviewed in full text and 57 studies met the inclusion criteria. After risk of bias assessment, 41 articles remained: 15 studies on 790 patients classified as TMD-joint, nine on 375 patients classified as TMD-muscle and 17 on 868 patients with BMS. Of these, eight studies on TMD-muscle, and five on BMS were included in separate network meta-analysis. The narrative synthesis suggests that NSAIDs as well as corticosteroid and hyaluronate injections are effective treatments for TMD-joint pain. The network meta-analysis showed that clonazepam and capsaicin reduced pain intensity in BMS, and the muscle relaxant cyclobenzaprine, for the TMD-muscle group. In conclusion, based on a limited number of studies, evidence provided with network meta-analysis showed that clonazepam and capsaicin are effective in treatment of BMS and that the muscle relaxant cyclobenzaprine has a positive treatment effect for TMD-muscle pain.
WE SEARCHED FOR EVIDENCE FROM RCTs AND SYSTEMATIC REVIEWS OF RCTs ON SELECTED INTERVENTIONS IN PEOPLE WITH BURNING MOUTH SYNDROME.

COGNITIVE BEHAVIOURAL THERAPY MAY IMPROVE SYMPTOM INTENSITY COMPARED WITH PLACEBO IN PEOPLE WITH BURNING MOUTH SYNDROME, ALTHOUGH WE FOUND NO GOOD-QUALITY STUDIES.

CLONAZEPAM MAY REDUCE PAIN COMPARED WITH PLACEBO IN PEOPLE WITH BURNING MOUTH SYNDROME, BUT EVEN WHEN IT IS ADMINISTERED TOPICALLY IT MAY BE ABSORBED SYSTEMICALLY, WITH INCREASED RISK OF DEPENDENCE OVER TIME.

WE DON'T KNOW WHETHER TRICYCLIC ANTIDEPRESSANTS, SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIs), OR BENZYMADINE HYDROCHLORIDE CAN IMPROVE SYMPTOMS OF BURNING MOUTH, AS WE FOUND FEW STUDIES.

GIVEN THE LACK OF KNOWLEDGE ABOUT MECHANISMS INVOLVED, BOTH LOCAL AND CENTRALLY ACTING TREATMENTS MAY BE EFFECTIVE. GIVEN ITS SIGNIFICANT IMPACT ON QUALITY OF LIFE AND MOOD, ANTIDEPRESSANTS MAY HAVE A ROLE TO PLAY.

THERE IS INSUFFICIENT EVIDENCE TO SHOW THAT THE DIETARY SUPPLEMENT ALPHALIPHOIC ACID, USED IN A VARIETY OF FORMS, HAS AN IMPACT ON SYMPTOM RELIEF.

CONCERNING THE EVIDENCE OVERALL, IT WAS IMPORTANT TO ASCERTAIN THAT THE DIAGNOSTIC CRITERIA WERE FULFILLED. OUTCOME MEASURES ARE VARIED AND, EVEN IF THE SAME ONES ARE USED, THEY ARE APPLIED DIFFERENTLY, THUS MAKING COMPARISONS OF TRIALS DIFFICULT. THERE IS A HIGH RISK OF BIAS IN THE MAJORITY OF STUDIES.

• BACKGROUND: Burning mouth syndrome (BMS) is a major diagnostic and therapeutic problem. Systemic and topical treatments (capsaicin, lidocaine, anti-histamines, sucralfate and benzylamine) have been tried, but they appear to be inadequate. Topical capsaicin is bitter, may cause burning and has low therapeutic efficacy. We hypothesized that systemic administration of capsaicin could reduce the limitations of topical administration and have better therapeutic efficacy; this hypothesis was tested in a controlled trial.

• METHODS: Systemic oral capsaicin 0.25% was used for patients with BMS, recruited in our single centre. After the diagnosis of BMS, patients were dentally and medically examined. They were alternatively assigned to treatment with capsaicin or to a shape/smell/taste/color matched placebo. The severity of symptoms was scored at trial entry and 30 days thereafter by investigators who were unaware of the assigned intervention. The visual analogical scale (VAS) measure was used to score the severity of pain, and results for the treated and untreated groups were compared by Fisher’s exact test. Analysis was performed by intention-to-treat. Statistical significance was considered for values of P < 0.05. Data are expressed as mean +/- SD.

• RESULTS: Fifty patients were enrolled (25 assigned to systemic capsaicin and 25 to placebo). The VAS score was significantly lower in treated patients (5.84 +/- 1.17) as compared to the placebo-control group (6.24 +/- 0.96). The use of systemic capsaicin implied significant gastric toxicity (referred gastric pain) with eight cases (32%) documented in the treatment group as compared to zero cases (0%) in the placebo control group.

• CONCLUSION: Systemic capsaicin is therapeutically effective for the short-term treatment of BMS but. This preliminary study suggests that more, adequately powered, randomized controlled trials are necessary and worthy to come to a definitive assessment of this matter.
MANAGEMENT OF COMORBID PSYCHOLOGICAL ISSUES ANXIETY, DEPRESSION ETC

- **Non Pharmacological**
  - Psychotherapy (Cognitive Behavioral Modification, Relaxation) \[45\]
  - Education
  - Counselling
  - Interpersonal Skills - Reassurance
  - Hypnosis
  - Acupuncture
  - TENS

- **Pharmacological Anti-Anxiety Treatments**
  - Single Drug Sedation (Conscious)
  - Multiple Drug Sedation (Deep)

- **Medical Treatment for Underlying Anxiety Disorders**

Thirty-five patients with primary BMS were included in the study: 31% of them had a DN4i score in favour of neuropathic pain and 34.3% had a HADS overall score in favour of anxiety and depressive disorder.

Bilateral BMS had higher levels of psychological distresses compared with the unilateral group.

Vitamins recommended for Migraine
- Riboflavin 400ug BD
- Q10 co enzyme A 100ug TDS
- Magnesium 550ug/day Or Melatonin 4ug90mins before bed


Comparison of clinical characteristics between burning mouth syndrome patients with bilateral and unilateral symptoms. Kim MJ\(^1\), Kim J\(^1\), Kho HS\(^2\).
Psychological interventions show great promise in treating patients with BMS. Weekly one-hour sessions of cognitive behavioral therapy lasting for 12-15 weeks significantly reduced BMS symptoms in all study patients compared to placebo control group, with an estimated 27% of patients remaining symptom-free at 6-month follow up (none in placebo group)[2].

Weekly group psychotherapy administered for three consecutive months achieved symptom improvement in 70% of the patients[3].

Femiano et al[4] noted a statistically significant symptom improvement with cognitive psychotherapy (40%).

MANAGEMENT TOPICAL MEDICATIONS

**Topical Medical interventions**

- **Clonazepam** (low-dose) dissolvable wafers (may be better than tablets) \(^{[45]}\). A literature review by Miziara et al of treatment studies indicated that topical clonazepam, although not a cure, offers short-term improvement of burning mouth syndrome, with studies on alpha-lipoic acid and cognitive therapy showing their effectiveness as well. However, the investigators found few randomized, controlled studies demonstrating the long-term effectiveness of alpha-lipoic acid, although they reported that research did indicate that cognitive therapy produces lasting results.\(^{[53]}\)

  - **Capsaicin**
    - Topical capsaicin \(^{[1]}\)
    - Intermittent oral capsaicin \(^{[46]}\)
  - **CBD oil**
  - **Local anaesthetic agents**
  - **Pregabalin** No evidence
CLONAZEPAM

Studies have shown a decrease of pain levels with clonazepam, a gamma amino butyric acid (GABA) agonist. GABA is a neurotransmitter possibly involved with taste,[46] reinforcing the evidence that BMS is probably a neuropathic pain condition involved with the gustatory system.

Grushka et al. reported a 70% reduction in pain levels with the oral administration of clonazepam, 0.5–1.5 mg/day in divided doses to a maximum of 3 mg/day.

Heckmann et al., demonstrated in a double-blind randomized controlled study that treatment with clonazepam 0.5 mg/day significantly reduced pain levels in BMS patients compared to controls after 9 weeks of treatment. However, there was no follow-up.

Interestingly, Ko et al. (2012) evaluated the outcome predictors affecting the efficacy of clonazepam and they found that those with greater symptom severity of taste disturbance and xerostomia at baseline, showed better therapeutic results after clonazepam therapy than those without those complaints; and patients with tongue symptoms had a significantly decrease in pain compared to those with intraoral symptoms excluding the tongue.

Topical

Woda et al., in a study with 25 patients, dissolved clonazepam 1.0 mg, 3 times/day for 3 min in the mouth with 66% of patients reporting a reduction in symptoms, and 29% reporting partial reduction in symptoms after 6 months.[70] Gremeau-Richard et al. (2004), in a randomized placebo-controlled study instructed the patients to suck a tablet of 1 mg of clonazepam (or placebo) and hold their saliva near the pain location without swallowing for 3 min and then tospit. This protocol was repeated 3 times a day for 14 days. The authors then concluded that topical administration of clonazepam improves intraoral burning sensation in some but not in all BMS patients.

Rodríguez de Rivera Campillo et al. also reported benefits of using clonazepan topically.

TOPICAL CLONAZEPAM

OBJECTIVES: CLONAZEPAM HAS BEEN USED IN THE TREATMENT OF BURNING MOUTH SYNDROME (BMS) FOR SEVERAL DECADES. WE CONDUCTED A META-ANALYSIS TO INVESTIGATE THE EFFICACY OF CLONAZEPAM IN THE TREATMENT OF BMS.

METHODS: WE CONDUCTED A SEARCH OF THE PUBMED, MEDLINE, EMBASE, WEB OF SCIENCE (TS), AND THE COCHRANE LIBRARY DATABASES FOR RELEVANT STUDIES THAT MET OUR ELIGIBILITY CRITERIA (UP TO SEPTEMBER 22, 2015). STATISTICAL ANALYSES WERE CONDUCTED USING REVMAN 5.2 AND STATA 11.0 SOFTWARE.

RESULTS: THREE RANDOMIZED CONTROLLED TRIALS (RCTS) AND TWO HIGH-QUALITY CASE-CONTROL STUDIES INVOLVING 195 BMS PATIENTS WERE SELECTED FOR THIS STUDY. OUR RESULTS SHOW THAT CLONAZEPAM CAN REDUCE THE ORAL PAIN SENSATION IN PATIENTS WITH BMS (WMD: -3.72, 95% CI: -4.57, -2.86; P < 0.05; FOR ALL FIVE STUDIES). A POSITIVE THERAPEUTIC EFFECT WAS DEMONSTRATED FOR BOTH SHORT-TERM (≤10 WEEKS) APPLICATION (WMD: -1.44, 95% CI: -2.06, -0.82; P < 0.05) AND LONG-TERM (>10 WEEKS) APPLICATION (WMD: -4.50, 95% CI: -4.98, -4.03; P < 0.05). BOTH TOPICAL (WMD: -1.50, 95% CI: -2.14, -0.85; P < 0.05) AND SYSTEMIC (WMD: -3.81, 95% CI: -4.63, -2.98; P < 0.05) ADMINISTRATION OF CLONAZEPAM WERE CONFIRMED TO BE EFFECTIVE.

CONCLUSION: CLONAZEPAM IS EFFECTIVE IN INDUCING SYMPTOM REMISSION IN PATIENTS WITH BMS.

Topical Clonazepam for Burning-Mouth Syndrome (BMS)¶

This prescription is symptomatic treatment of burning mouth syndrome. Clonazepam is a benzodiazepine and is often used as an anxiolytic, hypnotic, and anticonvulsant agent.¶

Clonazepam expresses the analgesic effect in BMS by potentiating the inhibitory gamma-aminobutyric acid (GABA) signaling pathways and antagonizing the hyperexcitability of neurotransmission. Clonazepam-binding-to-the-GABA receptor acts as a positive allosteric modulator to facilitate the opening of GABA-activated chloride channels and reduce the firing of action potentials. The GABA receptor is widely found in central nervous systems and peripheral tissues. Clonazepam is rapidly absorbed after oral administration, reaching maximum plasma concentrations within 2-4 hours. This change may require regular use of clonazepam over two weeks and above. You are advised to review regularly with your doctor to find the right dose for you for optimal analgesic effect and minimal adverse drug reactions.¶

<table>
<thead>
<tr>
<th>Clonazepam dosage (mg)</th>
<th>Frequency</th>
<th>Instruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25 mg/d</td>
<td>Twice-daily</td>
<td>To suck the tablet ¶</td>
</tr>
<tr>
<td>0.50 mg/d</td>
<td>Three-times-daily</td>
<td>Retain saliva in mouth near the pain site for 3 to 5 minutes ¶</td>
</tr>
<tr>
<td>1.00 mg/d</td>
<td>After meal</td>
<td>Followed by expectoration of saliva ¶</td>
</tr>
</tbody>
</table>

There is no need to increase the dose further if the pain has settled and may be reduced to twice daily topically usage.¶

Despite the promising results of clonazepam for pain relief symptoms, there are possible side effects that may occur at low doses. If any of the following side effects continue or become troublesome, you are advised to seek immediate review with your doctor. Below are the reported adverse drug reactions of topical clonazepam (French, Richard et al., 2004; Simeon, 2008) ¶

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drowsiness</td>
<td>Decreased alertness; feeling sleepy during the day ¶</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Feelings of unsteadiness; instability; feeling of spinning ¶</td>
</tr>
<tr>
<td>Altered mental status</td>
<td>Confusion; altered mood; anxiety ¶</td>
</tr>
<tr>
<td>Burning sensation</td>
<td>Increased in burning feeling ¶</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>Feeling of dryness in the mouth but no clinical salivary flow changes ¶</td>
</tr>
<tr>
<td>Gastrointestinal disturbance</td>
<td>Nausea; gastrointestinal reflux ¶</td>
</tr>
<tr>
<td>Others</td>
<td>Skin reaction; tinnitus ¶</td>
</tr>
</tbody>
</table>

Other possible side effects (NICE: BNF 2019) are: alopecia; concentration impaired; coordination abnormal; increased risk of fall; increased risk of fracture; muscle tone decreased; myalgias; seizures; tremor; sexual dysfunction; speech impairment; vertigo; vision disorders; withdrawal

Efficacy evaluation of clonazepam for symptom remission in burning mouth syndrome: a meta-analysis. Cui Y1, Xu H1, Chen FM1, Liu JL1, Jiang L1, Zhou Y1, Chen QM1.
TOPICAL CAPSAICIN (TOBASCO SAUCE!)

Burning mouth syndrome is defined as an intraoral burning sensation for which no medical or dental cause can be found. Recently, researchers have demonstrated an altered trophism of the small nerve fibres and alterations in the numbers of TRPV-1 vanilloid receptors. Capsaicin is a molecule that is contained in hot peppers and is specifically detected by TRPV-1 vanilloid receptors that are distributed in the oral mucosae. We aimed at verifying if TOPICAL CAPSAICIN could prove to be an effective treatment of Burning Mouth Syndrome. A group of 99 BMS patients were recruited. We subdivided the BMS patients into two groups: the collaborative patients, who expressed a predominantly neuropathic pattern of symptoms, and the non-collaborative patients, who were characterised by stronger psychogenic patterns of the syndrome. Both groups underwent topical therapy with capsaicin in the form of a mouthrinse 3 times a day for a long period. After 1 year of treatment, the final overall success rate was approximately 78%, but with a significant difference in the success rates of the two groups of patients (87% and 20% among the collaborative and non-collaborative patients, respectively; p=0.000).

The use of TOPICAL CAPSAICIN can improve the oral discomfort of BMS patients, especially during the first month of therapy, but it is more effective for those patients in which the neuropathic component of the syndrome is predominant. Our hypothesis is that chronic stimulation with capsaicin leads to decreases in burningsymptoms. This phenomenon is called desensitisation and is accompanied by substantial improvements in oral symptoms.

Capsaicinoids first recorded use, in the form of chilies, for the treatment of pain dates back to 4000 BC.
A literature review, observed trials dosing up to 1500mg/day of oral CBD in human patients, with no consequential adverse reactions, however future clinical studies may be needed to further investigate potential drug interactions with CBD. 9,10 CBD exhibits anticonvulsant, anxiolytic, antipsychotic, anti-inflammatory, antibacterial, and neuroprotective effect.
TOPICAL CANNIBIDIOIL (CBD)

- **But I have experimented on myself with CBD oil (swish for 30/30 sec) and expectorate, and I do get immediate relief which lasts long enough for me to get to sleep.**

- **Start with .025%. As an alternative you can instruct the patient to use Tabasco sauce in a 1 to 4 dilution with water. They can increase the dilution as tolerable. As with most therapies for burning mouth, the efficacy is low to moderate.**
Topical application in burning mouth syndrome

Junad Khan, Moin Anwer, Noma Noboru, Davis Thomas, Mythili Kalladka

*Orofacial Pain and Temporomandibular Joint Disorders, Eastman Institute for Oral Health, University of Rochester, NY, USA
*Department of Diagnostic Sciences, Rutgers School of Dental Medicine, NJ, USA
*Department of Diagnostic Sciences, Nihon University, Tokyo, Japan
*Sechenov Medical University, Moscow, Russia

Keywords: Burning mouth syndrome; Burning mouth symptoms; Topical anesthetic; Pain; Orofacial

Abstract: Background/purpose: Intracutaneous and perioral burning sensations may be sequelae of burning mouth syndrome (BMS) or burning mouth symptoms (BMSp), which present a diagnostic challenge. The aims of the study were to evaluate the efficacy of a topical anesthetic as a diagnostic tool to differentiate BMD from BMSp and to assess the comorbidities and responses to various pharmacologic treatments in BMS and BMSp patients.

Materials and methods: A total of forty-four charts of patients with burning mouth that visited the Rutgers School of Dental Medicine Orofacial Pain Clinic between January 1st, 2000 and November 1st, 2014 were retrospectively reviewed. Twenty patients were diagnosed with BMS, and 24 patients were diagnosed with BMDP attributed to local and systemic causes. The diagnosis was determined per the guidelines of the International Association for the Study of Pain and American Academy of Orofacial Pain. The main goal of this study was to evaluate the effect of topical anesthetic medication applied to the burning site.

Results: The percentage change in pain reduction following topical anesthetic application in the BMDP group was significantly higher than that of the BMS group (p < 0.05). In the BMS group, 77% of females and 78% of males responded to clonazepam. One third of the females in the BMDP group also suffered from hyperesthesia.

Conclusion: Topical anesthetics can be used as a simple, swift and efficient chair-side diagnostic tool to differentiate BMD and BMSp. Females have a better response to clonazepam in BMS.
INTERVENTIONAL PAIN MANAGEMENT FOR BMS

• **BOTOXIN INJECTIONS**  
  THESE HAVE TO BE PLACED AT NERVE ENDINGS WITH OBVIOUS RISK OF  
  CAUSING TEMPORARY 3 MONTH MOTOR PALSY TO LOCAL NERVES

• **NEUROSTIMULATION**
  • **SPINAL CORD STIMULATION (NOT FOR OFP)**
  • **DEEP BRAIN STIMULATION**
  • **SUPERFICIAL SESSIONAL NEUROSTIMULATION**
  • **GANGLIA IMPLANTED NEUROSTIMULATION**
  • **TRANSMAGNETIC STIMULATION**

• **ABLATIVE TECHNIQUES**
  • **GASSERIAN GANGLION INTERVENTIONS**
    • **PULSED RADIOFREQUENCY ABLATION**
    • **THERMOCOAGULATION**
    • **BALLOON COMPRESSION**
    • **GLYCEROLYSIS**
  • **Sphenopalatine Ganglion injections**
  • **STEREOTACTIC RADIOSURGERY**
  • **Gamma Knife may be indicated if there is medical contraindications to MVD**

*Not indicated for BMS*
Botulinum Toxin for Burning Mouth Syndrome

Domenico A. Restivo, MD, PhD; Giuseppe Lauria, MD; Rosario Marchese-Ragona, MD; Riccardo Vigneri, MD

Background: Burning mouth syndrome is characterized by burning pain in the oral mucosa (mainly the tongue and lips) in the absence of medical causes (1). It is also known as oral dysesthesia. It is common; mostly affects women of advanced age; and is often associated with systemic diseases, such as diabetes, nutritional deficiencies, depression, and anxiety (1). The etiopathogenesis of burning mouth syndrome is unclear, although some studies of biopsy specimens suggest an underlying trigeminal small-fiber neuropathy (2). No effective treatment is available for this condition; antidepressants, analgesics, clonazepam, topical capsaicin, and psychotherapy have...
PHOTOBIOMODULATION

• Near infrared irradiation of the stellate ganglion, to inhibit sympathetic discharge and improve blood flow to the tongue in glossodynia (still experimental) [47]


Abstract. The aim of the present study was to assess the effect of low-level laser therapy (LLLT) in the treatment of burning mouth syndrome (BMS). A diode laser was used in 78 BMS patients who were randomly assigned into four groups: IR1W, n=20 (830 nm, 100 mW, 5 J, 176 J/cm², 50 s, LLLT weekly sessions, 10 sessions); IR3W, n=20 (830 nm, 100 mW, 5 J, 176 J/cm², 50 s, three LLLT weekly sessions, 9 sessions); red laser, n=19 (685 nm, 35 mW, 2 J, 72 J/cm², 58 s, three LLLT weekly sessions, 9 sessions); and control group (CG), n=19. Symptoms were assessed at the end of the treatment and eight weeks later; quality of life related to oral health was assessed using the Oral Health Impact Profile (OHIP-14). Statistical analysis was carried out using repeated measures analysis of variance followed by the posthoc Tukey test. There was significant reduction of the symptoms in all groups at the end of the treatment, which was maintained in the follow-up. The scores of the IR1W and IR3W laser groups differed significantly from those of the CG.

• There was also a decrease in the OHIP-14 scores in the four groups. The IR3W laser group scores differed significantly from those of the CG. LLLT reduces the symptoms of BMS and may be an alternative therapeutic strategy for the relief of symptoms in patients with BMS.
• Group A (Laser treatment) was composed of 43 patients while Group B (sham therapy) of 42 patients.

• Patients treated with PBMT showed a significant decrease in symptoms \((p=0.0008)\) and improved quality of life related to oral health \((p=0.0002)\).

• Conclusions: PBMT has demonstrated to have a positive effect in relieving BMS symptoms and in improving a patient’s overall quality of life.

• No significant difference in pain but improved OHIP 14?

Efficacy of the photobiomodulation therapy in the treatment of the burning mouth syndrome

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Received: 07/04/2018
Revised: 07/09/2018

Abstract: Background: This study aimed to evaluate the efficacy of the photobiomodulation therapy (PBMT) - in terms of pain and of quality of life- in patients affected by burning mouth syndrome (BMS). Material and Methods: This study was designed as a randomised double-blinded prospective study. Patients diagnosed with BMS in the period from June 2015 to June 2016 were recruited. The patients were randomised into two groups and each received treatment once a week for ten weeks: group A received laser therapy (K Laser Cube 3B) while group B was given sham therapy (placebo). Pain was evaluated through the Visual Analog Scale (VAS) and quality of life was assessed with the short form of the Oral Health Impact Profile (OHIP-14). Assessment was done at baseline and after every therapy session. The researchers were blinded to the randomised allocations. Results: A total of 85 patients were analysed. Group A (laser treatment) was composed of 43 patients while group B (sham therapy) of 42 patients. Patients treated with PBMT showed a significant decrease in symptoms \((p=0.0008)\) and improved quality of life related to oral health \((p=0.0002)\). Conclusions: PBMT has demonstrated to have a positive effect in relieving BMS symptoms and in improving a patient’s overall quality of life.

Keywords: Burning mouth syndrome, oral cavity, lasers, life quality.
WHERE NEXT?

• CHRONIC PAIN IS BEST MANAGED BY MAXIMISING THE PATIENTS OWN RESOURCES FOR ENDOGENOUS PAIN SUPPRESSION AND REDUCE FACILITATION

• WEBSITES ONLINE INFORMATION

• FACEBOOK GROUPS

• FUTURE RESEARCH

• IDENTIFY SOMATOSENSORY CHANGES

• IDENTIFY PERIPHERAL OR CENTRAL BMS USING LA INFILTRATIONS

• PRECISION MEDICINE

Abstract

Objective: To determine the frequency of use of the core outcome domains published by the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) in burning mouth syndrome (BMS) randomized controlled trials (RCTs). Methods: This systematic review, conducted as part of the World Workshop on Oral Medicine VII (WWOM VII), was performed by searching the literature for studies published in PubMed, Web of Science, PsychINFO, Cochrane Database, Cochrane Central, and Google Scholar from January 1994 (when the first BMS definition came out) through October 2017. Results: A total of 36 RCTs (n = 2,175 study participants) were included and analyzed. The overall reporting of the IMMPACT core and supplemental outcome domains was low even after the publication of the IMMPACT consensus papers in 2003 and 2005 (mean before IMMPACT consensus publication = 2.6 out of 6; mean after IMMPACT consensus publication = 2.4).
Burning Mouth Syndrome

What is Burning Mouth Syndrome?

Burning mouth syndrome (BMS) is a chronic intra-oral burning sensation that has no identifiable medical or dental cause—either local or systemic condition or disease. BMS usually lasts for more than six months with no visible signs of oral mucosa pathology. It is also known as glossodynia, glossasthesia, stomatodynia, or oral dysesthesia.

Who does it affect?

The lack of universally consistent BMS diagnostic criteria, the epidemiology data collected are of poor quality. Prevalence of BMS in general populations varies from 1% to 15%. BMS affects more women than men and usually at menopause or post-menopause age (4th to 6th decade of age).

What causes BMS?

The etiology of BMS remains not fully understood. However, studies have shown increasing evidence of BMS as neuropsychiatric illness with central and peripheral nervous system involvement. BMS may be associated with systemic factors such as diabetes, hormonal changes, nutritional deficiencies and psychological disorders, or local causes including oral infections, allergies, salivary gland dysfunction, dental treatments and ill-fitting dentures, are known as secondary BMS and is not true BMS.

What kind of problems might I have?

<table>
<thead>
<tr>
<th>Location</th>
<th>Usually bilateral burning oral mucosa-pain</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Affects commonly on the tongue, followed by palate, lips and oropharynx</td>
</tr>
<tr>
<td>Onset</td>
<td>Spontaneous with continuous gradual-continuous increasing of burning pain</td>
</tr>
<tr>
<td>Character</td>
<td>Burning pain</td>
</tr>
<tr>
<td>Severity</td>
<td>Moderate to severe intensity that may vary during the day. It is usually at the lowest heat on awake, worsening after the first meal and reach maximum intensity in late evening</td>
</tr>
<tr>
<td>Associated features</td>
<td>Altered taste (bitter, metallic taste), &quot;superstition,&quot; and dry mouth</td>
</tr>
<tr>
<td></td>
<td>Psychology disorders such as anxiety, irritability and depression</td>
</tr>
</tbody>
</table>

How is it diagnosed?

The diagnosis of BMS is by exclusion of local or systemic conditions or diseases. Based on history and detailed clinical examination, the burning sensation secondary to a primary cause is differentiated from a true BMS.

BMS Profile

Name
Email
Age
Gender
Ethnicity
Country
Date BMS Began
Was there an initiating event for the BMS (yes/no)
If yes, describe the event
Have you been given a BMS diagnosis (yes/no)
Current State of BMS (Pain level 0 = no pain; 10 = pain as bad as it can be)
What words do you use to describe your symptoms?
What areas of your mouth does it affect (list in order of worst to least)
**GOOD PAPERS**

**Burning mouth syndrome.**
Jääskeläinen SK¹, Woda A².

**Botulinum Toxin for Burning Mouth Syndrome.**
Restivo DA¹, Lauria G¹, Marchese-Ragona R¹, Vigneri R¹.
IMPAIRED TASTE SENSITIVITY IN BMS PATIENTS

- **Taste function assessed by electrogustometry in burning mouth syndrome: a case-control study.**
- **Beaud A, Deschênes Y, 2, Ungheier MD, Bougeot CP, Boucher Y.**
- **Author Information**
- **Abstract**
- **Objective:**
  - Idoopathic burning mouth syndrome (IBMS) is characterized by oral persistent pain without any clinical or biological abnormality. The aim of this study was to evaluate taste function in IBMS subjects and healthy controls.
- **Material and Methods:**
  - Electrogustometric thresholds (EGM) were recorded in 21 IBMS patients and 21 paired-matched controls at nine loci of the tongue assessing fungiform and foliate gustatory papillae function. Comparison of EGM was performed using the nonparametric Wilcoxon signed-rank test. A correlation between EGM and self-perceived pain intensity assessed using a visual analogic scale (VAS) was analyzed with the Spearman coefficient. The level of significance was fixed at \( P < 0.05.\)
- **Results:**
  - Mean EGM were significantly increased with IBMS for right side of the dorsum of the tongue and right lateral side of the tongue \( P < 0.05.\) In the IBMS group, VAS scores were significantly correlated to EGM at the tip of the tongue \( r = -0.39; P < 0.05.\) and at the right and left lateral sides of the tongue \( r = -0.49; r = -0.47; P < 0.05.\)
- **Conclusion:**
  - These data depict impaired taste sensitivity in IBMS patients within fungiform and foliate taste bud fields and support potent gustatory/nociceptive interaction in IBMS.
FUNGIFORM PAPILLAE COUNT?

- **LARYNGOSCOPE.** 2017 Aug 22. doi: 10.1002/lary.26828. [Epub ahead of print]
- **A case-control evaluation of fungiform papillae density in burning mouth syndrome.**
- **NAUD JM̃, BENCÁ L̃, DRANGSHOLT MT̃, LERESCHE L̃, COLDWELL SẼ.**
- **AUTHOR INFORMATION**
- **ABSTRACT**
- **HYPOTHESIS:**
  It has been hypothesized that high fungiform papillae density may be a risk factor for developing the taste and pain alterations characteristic of burning mouth syndrome.
- **OBJECTIVE:**
  Evaluate whether fungiform papillae density, taste sensitivity, and mechanical pain sensitivity differ between burning mouth syndrome cases and controls.
- **STUDY DESIGN:**
  This case-control study compared cases diagnosed with primary burning mouth syndrome with pain-free controls.
- **METHODS:**
  Participants (17 female cases and 23 female controls) rated the intensity of sucrose, sodium chloride, citric acid, and quinine applied separately to each side of the anterior tongue and sampled whole mouth. Mechanical pain sensitivity was assessed separately for each side of the tongue using weighted pins. Digital photographs of participants’ tongues were used to count fungiform papillae.
- **RESULTS:**
  Burning mouth syndrome cases had increased whole mouth taste intensity. Cases also had increased sensitivity to quinine on the anterior tongue, as well as increased mechanical pain sensitivity on the anterior tongue. Fungiform papillae density did not differ significantly between cases and controls. Fungiform papillae density on the left and right sides of the tongue were correlated in controls; however, there was no left/right side correlation in cases.
- **CONCLUSION:**
  Cases had increased pain and taste perception on the anterior tongue. The lack of correlation between left and right fungiform papillae density in cases may be an indication of asymmetrical lingual innervation in these patients.
INTRAORAL CAMERA FOR FFP COUNT

• Fungiform papillae density in patients with burning mouth syndrome and xerostomia.
• CAMACHO-AURES P. LÓPEZ-YÑEZ P. MONER-PARGA D.

AUTHOR INFORMATION

ABSTRACT

OBJECTIVE:

The aim of this study was to analyze fungiform papillae density in patients with burning mouth syndrome (BMS) and xerostomia.

STUDY DESIGN:

In this cross-sectional clinical study, sixty patients were included (20 with BMS, 20 with xerostomia, and 20 healthy controls). The fungiform papillae density was analyzed over a small region on the anterior 1/3 of the tongue with the aid of a digital camera. The number of papillae was measured in an area of 19 mm².

RESULTS:

The patients with BMS showed significantly higher fungiform papillae density than the patients with xerostomia. Though no statistically significant differences were recorded versus the control group. In the BMS group, 65% of all cases presented a density of 71-90 papillae (within an area of 19 mm²); while 10% had more than 90 papillae. On the contrary, 70% of the patients with xerostomia had fewer than 70 papillae in the studied area.

CONCLUSIONS:

The digital camera offers a rapid, non-invasive, and relatively simple way to study fungiform papillae density. The patients with BMS have higher fungiform papillae density than the patients with xerostomia.

• CONTINUOUS NEUROPATHIC OROFACIAL PAIN: A RETROSPECTIVE STUDY OF 23 CASES.

• SOTORRA-FIJUELOLA D1, SÁNCHEZ TORRES A1, VALMASEDA-CASTELLÓN E2, GAY-ESCODA C3.

• AUTHOR INFORMATION

• ABSTRACT

• BACKGROUND:

• TO DETERMINE THE CLINICAL CHARACTERISTICS OF CONTINUOUS NEUROPATHIC OROFACIAL PAIN IN PATIENTS THAT SUFFER PERSISTENT IDIOPATHIC FACIAL PAIN (PIFP), PAINFUL POST-TRAUMATIC TRIGEMINAL NEUROPATHY (PPTIN) OR BURNING MOUTH SYNDROME (BMS) AND TO DESCRIBE THEIR TREATMENT.

• MATERIAL AND METHODS:


• RESULTS:

• THE AVERAGE AGE OF THE PATIENTS WITH CONTINUOUS NEUROPATHIC OROFACIAL PAIN WAS 54.5, WITH A CLEAR FEMALE PREDOMINANCE (86.9%, n=20). OF ALL PATIENTS, 60.9% (n=14) WERE SUFFERING A PIFP, 21.7% (n=5) HAD A BMS AND 17.4% (n=4) WERE PRESENTING A PPTIN. THE PAIN QUALITY DESCRIBED BY THE PATIENTS WITH CONTINUOUS NEUROPATHIC OROFACIAL PAIN WAS OPPRESSIVE (43.47%, n=10), WIDELY REPRESENTED BY PATIENTS WITH PIFP, AND BURNING (39.13%, n=9) BEING THE ONLY QUALITY THAT DESCRIBED PATIENTS WITH BMS. THE TREATMENT CARRIED OUT WITH THE PATIENTS WAS ONLY PHARMACOLOGIC. THE MOST USED DRUGS FOR THE TREATMENT OF PIFP AND PPTIN WERE CLONAZEPAM (50%, n=9) AND AMITRIPTYLINE (44.44%, n=8). HOWEVER, A 55.5% (n=10) OF THE PATIENTS WITH PIFP OR PPTIN REQUIRED THE ASSOCIATION OF TWO OR MORE DRUGS FOR A CORRECT PAIN CONTROL. ALL THE PATIENTS WITH BMS RESPONDED SATISFACTORY TO CLONAZEPAM.

• CONCLUSIONS:

• CONTINUOUS NEUROPATHIC OROFACIAL PAIN IS A LITTLE KNOWN CONDITION AMONG THE GENERAL POPULATION, PHYSICIANS AND DENTISTS. THIS FAVORS A LATE DIAGNOSIS AND INACCURATE TREATMENTS WHICH ENTAIL UNNECESSARY SUFFERING. IT IS IMPORTANT TO INFORM BOTH THE GENERAL POPULATION AND HEALTH PROFESSIONALS CONCERNING THIS PAINFUL CONDITION.

• KEY WORDS:

• CONTINUOUS NEUROPATHIC OROFACIAL PAIN, PERSISTENT IDIOPATHIC FACIAL PAIN, PAINFUL POST-TRAUMATIC TRIGEMINAL NEUROPATHY, BURNING MOUTH SYNDROME, ATYICAL ODNTALGIA.