This review provides an overview of the recent literature regarding the etiology and management of BMS.

Burning mouth syndrome (BMS):

- Etiology remains poorly understood
  - Complex and multifactorial
  - Emerging data suggests role of circadian rhythm dysfunction

- Pain and discomfort with normal appearance of mucosa

- A diagnosis of exclusion

**Putative causes of BMS**

**Altered Pain Perception**

- Nociceptive pain: noxious insult (inflammation/mechanical) or thermal stimuli.
- Neuropathic pain: generated and maintained by the nervous system. Affects central and peripheral nervous systems
  - Burning, electric shock–like, prickling, and/or numbness.
  - ~30% to 60% of BMS patients suffer from neuropathic pain
- Structural and functional deficits in brain regions associated with pain perception.
- Possible diminished dopamine levels in the putamen
- Possible mechanism linking psychological disorders with brain function
- Elevated artemin (Artn) and TRPV1 expression in BMS patients
  - Artn a ligand for the GDNF (glial cell line–derived neurotrophic factor), regulates expression of TRPV1 (transient receptor potential vanilloid 1)
  - Role of TRP channels in temperature perception and nociception.
  - Increased TRP levels could contribute to heightened pain sensation
- Mouse model studies reveal Artn-neutralizing antibody diminishes heat hyperalgesia
Dysgeusia

- Abnormal taste among patients who have BMS (reason poorly understood)
- Use of electrogustometry (EGMt) to examine taste disturbances
  - Assess the integrity of taste pathways.
  - A case-control study reveals diminished taste sensitivity in fungiform and foliate taste buds
  - Alterations in salivary composition in BMS can affect the salivary pH
    - pH of the saliva critical factor in signal transmission in EGMt

Neuroendocrine and Hormonal Disturbances

- In BMS patients:
  - Plasma adrenaline levels significantly lower
  - Serum cortisol levels are slightly higher
  - Dehydroepiandrosterone (DHEA) significantly lower
- Salivary 17β-estradiol levels correlated with disease severity
- Cortisol levels and the cortisol/DHEA ratio in saliva shows an inverse relationship with the severity of oral burning
- Alterations may be due to abnormal oscillations in the HPA axis
  - Data suggest decreased DHEA is indicative of HPA dysfunction

Psychological Factors

- Higher levels of psychogenic disturbances in BMS patients
- Systematic review of 14 controlled studies found an association between psychological factors and BMS
  - Anxiety and depression are most common observed in BMS patients
  - Higher levels of somatization, obsessive compulsive disorder, and paranoid ideation in females with BMS
  - Depression in BMS correlates with plasma noradrenaline and cortisol levels
  - Further evidence underlying HPA abnormalities may contribute to the psychological disturbances seen in BMS.
Sleep Disorders

- Self-reported poor sleep quality higher for patients who have BMS
- Sleep disorders may increase the risk of BMS development, however:
  o studies relied exclusively on self-reporting,
  o technique to evaluate sleep quality not validated for BMS patients

Circadian Rhythm

- Dysfunction in circadian clock an emergent area of research
- Clock genes are implicated in numerous human pathoses, including mood and sleep disorders
  o Pain perception, depression and anxiety, and sleep disorders intimately linked with circadian disturbances
  o HPA axis regulated by circadian outputs
  o Dopamine is primary modulator of the circadian rhythm in the central nervous system
- Data suggest that continued identification of regulatory mechanisms that control the circadian rhythm can have diagnostic and therapeutic significance

Management

- Rule out systemic conditions or local factors or if the cause is idiopathic.
  o Systemic conditions include esophageal reflux, diabetes, and nutritional deficiencies.
  o Local factors include parafunctional habits, candidiasis, geographic tongue, and xerostomia,
- According to recent Cochrane database systematic, evidence lacking for specific treatment recommendations
  o Need placebo-controlled, double-blind studies with long-term follow-up
- Current treatment divided into 3 categories:
  o Topical therapies
  o Systemic treatments
  o Behavioral strategies
Topical Therapies
Clonazepam

- Effectively reduces symptoms associated with BMS both short-term (<10 wk) and long-term (>10 wk)
- Good for patients unwilling/unable to take systemic medications.

Capsaicin

- Binds to TRPV1, inactivating neuronal responses to heat
  o Prolonged exposure = desensitization of pain receptors
- Increased burning sensation immediately after application and dyspepsia, especially if the capsaicin ingested as a capsule
  o Important for patients with a history of gastric-related disorders.

Low level laser Therapy (LLLT)

- Associated with analgesic, anti-inflammatory, and biostimulatory properties.
- Decrease burning sensation by increasing synthesis and release of serotonin and β-endorphins and decreasing bradykinin secretion.
- Blocks C-fiber depolarization therefore heat, and pain stimuli not transmitted

Systemic Therapies
Clonazepam

- Significant improvement in pain among patients who have BMS
- Most effective for patients with:
  o Normal salivary production
  o Those with greatest severity of symptoms at initial presentation,
  o Those who did not use psychotropics medications
- Mood, taste dysfunction, and xerostomia not improved
- Good short-term option (long term use safety and effectiveness unknown)
Alpha Lipoic Acid (ALA)

- Mitochondrial coenzyme may stimulate production of neural growth factors
- Therapeutic benefits of ALA for BMS are unclear
- ALA as BMS treatment shows promise but more studies are needed

Gabapentin

- Agonist of the inhibitory neurotransmitter GABA.
- Crossover placebo-controlled trial where BMS patients were administered gabapentin, ALA, or a combination
  - 50% in the gabapentin group reported improvements in pain vs 15% in the placebo group
  - 70% reduction in pain with gabapentin +ALA

Amitriptyline

- Amitriptyline is a tricyclic antidepressant with analgesic properties.
- No significant differences between amitriptyline and gabapentin in reducing oral pain

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<tr>
<th>Therapy: Medication</th>
<th>Advantages</th>
<th>Disadvantages</th>
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<td>Topical</td>
<td>Relieves symptoms associated with burning mouth syndrome</td>
<td>May cause drowsiness and dry mouth, Possible dependence, Asthenia</td>
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Emerging Therapeutic Approaches

- Most studies are single reports → Need for larger patient cohorts
- Topical bupivacaine may be effective anesthetic to relieve BMS symptoms
- Paroxetine showed promise in an increase dose study
Although clinically unclear, preliminary work suggests melatonin improves anxiety among patients with BMS,

Catuama:
- Herbal product that combines 4 medicinal plants:
  - *Paullinia cupana* (guarana), *Trichilia catigua* (catuaba), *Zingiber officinale* (ginger), and *Ptychopetalum olacoides* (muira puama).
  - Antinociceptive, antidepressant, and vasorelaxant properties
  - Reduced symptoms in the BMS
- Promising preliminary studies warranting further research

**Behavioral Strategies**

- Cognitive behavioral therapy (CBT) used to manage depression and anxiety as well as physical symptoms
  - Specific techniques include:
    - Biofeedback, relaxation, exposure, and cognitive restructuring.
      - Relaxation techniques: progressive muscle relaxation and focused breathing to alleviate discomfort,
      - Cognitive restructuring: identify and modify destructive thoughts related to emotional and behavioral problems
  - Several CBT sessions required for patient education, distraction, evaluation of harmful automatic thoughts, and replacement with more beneficial thoughts
  - 12 to 15 sessions reduced pain severity and discomfort
  - Improved symptoms maintained for 6 months
  - Cognitive therapy + ALA may be more effective than either approach alone
Reference