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Targeting the Endocannabinoid System in Burning Mouth Syndrome: A Case Report on CBD-Dominant Cannabis Oil

Luca Gentili[1*], Paolo Scimia[2], Fabio Nania[1], Chiara Angeletti[2]

[1]Department of Anesthesia and Intensive Care Unit, S. Maria Goretti Hospital, Latina, Italy
[2]Department of Anesthesia and Intensive Care Unit, G. Mazzini Hospital, Teramo, Italy
Email: *luca.gentili89@gmail.com

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Abstract

Burning Mouth Syndrome (BMS) is a chronic orofacial pain disorder characterized by burning sensations of the oral mucosa without evident causative lesions. Current treatment options often provide limited relief, highlighting the need for alternative therapeutic approaches. Recent evidence suggests that dysregulation of the endocannabinoid system plays a role in BMS pathophysiology, with altered expression of cannabinoid receptors in oral mucosa. We present a case of a 62-year-old postmenopausal female with a 3-year history of BMS refractory to conventional treatments including topical clonazepam, gabapentin, and alpha-lipoic acid. The patient was treated with CBD-dominant cannabis oil (20:1 CBD:THC ratio), starting at 5 mg CBD twice daily and titrated to 15mg CBD twice daily over 4 weeks. After 8 weeks of treatment, the patient reported a reduction in burning sensation from NRS 8/10 to 4/10, with concurrent improvement in xerostomia and taste alterations. Pain relief was maintained at 6-month follow-up with stable dosing and no significant adverse effects. This case suggests that CBD-dominant cannabis preparations may offer a promising therapeutic option for BMS through modulation of the endocannabinoid system.

Subject Areas

Pain Managment, Neurological Dysorders

Keywords

Burning Mouth Syndrome, Endocannabinoids, CBD

1. Introduction

Burning mouth syndrome (BMS) is a chronic debilitating oral pain disorder characterized by a burning sensation on oral mucosal surfaces with frequently reported xerostomia, dysgeusia and tingling or paraesthetic sensations [1]. According to the International Classification of Orofacial Pain (ICOP), BMS is classified as an idiopathic orofacial pain with or without somatosensory changes, defined as "an intraoral burning sensation recurring daily for more than 2 hours per day over more than 3 months, without clinically evident causative lesions" [2] [3].

The pathophysiology is complex and likely multifactorial, involving neuropathic, immunological, and hormonal mechanisms [4]. Recent evidence strongly suggests BMS is a neuropathic pain disorder with central and peripheral nervous system involvement [5]. The endocannabinoid system has emerged as a key player in pain modulation and neuroprotection in BMS [6]. Studies have demonstrated dysregulation of this system in BMS patients, with altered expression of cannabinoid receptors in oral mucosa, specifically showing downregulation of CB1 receptors and upregulation of CB2 and TRPV1 receptors [7] [8].

Recent studies have demonstrated that the endocannabinoid system plays a key role in modulating neuropathic pain in BMS. As highlighted by Gambino *et al*. [9], cannabinoids exert their action through selective binding to CB1 and CB2 receptors. CB1 receptors, predominantly expressed in the central nervous system, mediate analgesic effects, while CB2 receptors, primarily located in immune system cells, regulate immunomodulatory responses. This bimodal action offers a unique therapeutic approach compared to conventional treatments, which generally target single mechanisms. Cannabis-based preparations, with a balanced CBD ratio, can simultaneously modulate pain pathways, neuroinflammatory processes, and central sensitization mechanisms involved in BMS pathogenesis, positioning them as particularly promising therapeutic options for cases resistant to conventional monotherapies.

Current management strategies include topical and systemic approaches. Clonazepam remains one of the most studied interventions, showing efficacy in both topical and systemic administration [10]. Other treatments include alpha-lipoic acid, gabapentin, and various antidepressants, though results have been variable [11]. Despite these options, many patients remain refractory to conventional therapies, highlighting the need for alternative treatment approaches [12].

2. Case Presentation

A 62-year-old postmenopausal female presented with a 3-year history of continuous burning sensation primarily affecting the anterior two-thirds of the tongue and hard palate. Her medical history included controlled hypertension and mild anxiety. The patient reported moderate-to-severe pain intensity (NRS 8/10), comparable to toothache in intensity, with a distinctive superficial and burning

character, accompanied by xerostomia and dysgeusia. The pain was less intense in the morning, worsened during the day, and did not disturb sleep. Psychological evaluation using the Hospital Anxiety and Depression Scale (HADS) indicated mild anxiety (score 9/21) but no significant depression (score 6/21). The patient was taking amlodipine 5 mg daily for hypertension, with no recent medication changes. She reported moderate work-related stress but denied clinically significant depression.

Previous treatments had included topical clonazepam (1mg dissolved in mouth three times daily for 3 minutes), gabapentin (up to 300mg three times daily), and alpha-lipoic acid (600 mg daily), all providing minimal relief. The patient had also tried various lifestyle modifications including avoiding spicy foods and alcohol, without significant improvement.

Diagnostic workup included complete blood count, comprehensive metabolic panel, thyroid function tests, vitamin B12, folate, ferritin, zinc, and glycated hemoglobin, all of which were within normal ranges, patch testing ruled out contact allergies to dental materials. Cultures for fungal infection were negative, and salivary flow rate testing confirmed normal salivary production despite subjective xerostomia.

After these comprehensive clinical examination and laboratory testing which excluded local and systemic causes, medical cannabis was initiated. The patient was prescribed CBD-dominant cannabis oil (20:1 CBD:THC ratio) starting at 5mg CBD twice daily, gradually titrated to 15mg CBD twice daily over 4 weeks. After 8 weeks of treatment, the patient reported a reduction in burning sensation from NRS 8/10 to 4/10, with improvement in associated symptoms of xerostomia and taste alterations. No significant adverse effects were reported. At 6-month follow-up, pain relief was maintained with stable dosing.

Comprehensive monitoring at 1, 3, and 6 months included liver function tests, which remained within normal ranges. The patient reported mild drowsiness during the first two weeks of treatment, which resolved spontaneously without dosage adjustment. No significant changes in appetite, weight, or mood were observed. Cognitive function, assessed using the Montreal Cognitive Assessment, showed no decline from baseline. The patient reported improved sleep quality and anxiety reduction (HADS 7) as a beneficial side effect.

3. Discussion

The management of Burning Mouth Syndrome (BMS) presents a significant therapeutic challenge, requiring a thorough understanding of both conventional approaches and emerging treatment modalities [1]. Current treatment strategies encompass both topical and systemic interventions, with varying degrees of success. Among conventional therapies, clonazepam has emerged as one of the most studied interventions, demonstrating efficacy in both topical and systemic forms. Topical clonazepam (0.5 - 3.0 mg daily) has shown significant improvement in pain scores, likely through membrane stabilization in nerve fiber and oral

mucosa cells, with fewer adverse effects compared to systemic administration [1].

The endocannabinoid system has emerged as a crucial player in BMS pathophysiology. Research reveals significant alterations in cannabinoid receptor expression in BMS patients, characterized by downregulation of CB1 receptors and upregulation of CB2 and TRPV1 receptors in oral mucosa [6]. CB1 receptors, predominantly distributed throughout the nervous system, mediate analgesic effects, while CB2 receptors, primarily located in immune system cells, regulate immunomodulatory responses. The upregulation of TRPV1 receptors is particularly relevant as these receptors are activated by noxious heat and capsaicin, with their expression correlating with ongoing pain symptoms [6].

BMS must be approached as a multisystemic disorder with complex interconnections between neuropathic mechanisms, hormonal factors, psychosocial components, and potential systemic comorbidities. Women with BMS demonstrate higher rates of thyroid dysfunction, fibromyalgia, and autoimmune disorders compared to age-matched controls, suggesting shared pathophysiological pathways [4]. The bidirectional relationship between chronic pain and psychological distress warrants consideration of interdisciplinary treatment approaches. Gambino *et al.* observed in their pilot study that anxiety and depression levels decreased significantly after treatment with cannabis oil, suggesting a systemic beneficial effect beyond simple pain modulation [9].

In our case, concurrent improvement in anxiety symptoms alongside pain reduction highlights the potential benefit of integrated care models combining pain specialists, oral medicine practitioners, psychiatrists, and nutritionists. The endocannabinoid system's extensive interactions with hypothalamic-pituitary-adrenal axis function and neuroimmune signaling position cannabinoid therapies as potentially valuable components within comprehensive treatment protocols rather than isolated interventions [13].

Our case demonstrates the potential efficacy of CBD-dominant cannabis oil in BMS management. CBD's mechanism of action involves multiple pathways, including indirect modulation of CB1 and CB2 receptors, and interaction with TRPV1 receptors [1]. The high CBD:THC ratio (20:1) provides therapeutic benefits while minimizing psychoactive effects [14]. The sustained response at 6-month follow-up with stable dosing is particularly significant, as conventional treatments often provide limited or temporary relief [15] [16].

Recent studies have shown alterations in plasma endocannabinoid levels in BMS patients, suggesting a potential role in disease pathogenesis [17]. The neuropathic nature of BMS, involving both small fiber neuropathy and central pain mechanisms, presents multiple potential targets for cannabinoid therapy. The interaction between the endocannabinoid system and other neurotransmitter systems involved inpain processing suggests potential benefits of combining cannabinoid-based treatments with conventional therapies [1] [4].

4. Conclusion

This case demonstrates the potential therapeutic value of medical cannabis in BMS

management, particularly CBD-dominant formulations. The significant pain reduction and improvement in associated symptoms suggest effective modulation of the endocannabinoid system, which is known to be dysregulated in BMS. While this single case cannot establish definitive treatment recommendations, it provides foundation for future controlled trials to determine optimal protocols for cannabis-based BMS therapy. Future research should focus on determining ideal cannabinoid ratios, dosing regimens, and potential synergies with conventional treatments to establish evidence-based guidelines for clinical practice.

Conflicts of Interest

The authors declare no conflicts of interest.

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