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Review on Effective Treatments of Burning Mouth Syndrome

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1. Abstract

1.1. Background and Objectives: Burning mouth syndrome (BMS) is defined as intraoral burning without evident etiology, which may be annoying for patient and may require treatment. This study aimed to review the treatments of BMS with special focus on novel treatments.

1.2. Materials and Methods: In this review article, key words related to BMS were searched in databases such as Pubmed, Scopus, Web of Science, Science Direct, Google Scholar and Persian databases such as SID and Magiran. Also the treatment methods which their effectiveness were confirmed by systematic reviews and meta-analysis were included.

1.3. Results: Based on results of this study, pharmacologic treatments such as Clonazepam, Alpha Lipoic Acid (ALA), Capsaicin and non-pharmacologic treatments such as Aloe vera, low level laser therapy, non-invasive brain stimulation, self-treatment, hormone therapy and education have shown significant improvement in BMS patients.

Conclusions: Despite all of the presented treatments, there is still no definite treatment for BMS and all of the recommended treatments are supportive.

2. Background and Objectives

Burning Mouth Syndrome (BMS) is a type of mouth burning with unknown etiology with chronic pain or itching [1]. Other names with a broader meaning such as "Stomatodynia", "Stomatopyrosis", "Glossopyrosis", "Glossodynia", "Sore mouth", "Sore tongue" and "Oral Dysesthesia" are also used to express this syndrome [2]. Symptoms of this disease include dry mouth, loss or change of taste, mostly bitter taste in the mouth [3]. Severity of burning sensation varies and is more prevalent in middle-aged people and women about 3 to 12 years after menopause [4]. Diseases such as candidiasis, lichen planus, geographic tongue, atrophic tongue, and inappropriate denture can be associated with BMS, which is called Secondary BMS. These conditions do not cause BMS, but patients may avoid brushing due to mouth irritation caused by BMS, resulting in localized diseases in the mouth [4]. Various systemic conditions have been observed with BMS, including diabetes, hormonal changes, mineral and nutritional deficiencies, but the relation of these systemic conditions with BMS has not been proved yet. Psychological factors such as anxiety, stress, depression, personality disorders, fear of cancer have been observed in BMS patients, but these psychological factors are not the exact cause of BMS and may be due to chronic pain in these patients [5]. Burning mouth syndrome is divided into two main categories: The peripheral type that results from the accumulation and increase of neurotransmitters, which is improved with clonazepam, and the central type, which is improved by a variety of antidepressants.

The pattern of the disease can be migratory, with different areas of the mucosa being affected one after the other or simultaneously. The tongue, and especially the anterior 2/3, is the most common site affected by BMS. Other areas, including the lips, buccal mucosa, floor of the mouth, gums, and hard palate, can also be affected by BMS [3, 6].

The diagnosis is made through various causes of burning mouth being ruled out. Many diagnostic tests are prescribed in such a

condition such as:

- CBC and blood chemistry tests (blood lipid test, fasting blood sugar and monitoring the status of vitamins and minerals)
- Allergy test
- Monitoring iron, folate and cobalamine of serum
- Cell culture and biopsy

The diagnosis of BMS is confirmed when the test results were negative and the duration of these symptoms was between 4-6 months and more. Various studies have been performed on salivary biomarkers such as IL1, IL2 and IL6 in which some of them confirm the relation of these biomarkers with BMS and some of them express them independently [4].

A study by Bell et al. revealed that 69% of patients with chronic oral pain, including Burning Mouth Syndrome refer to general practitioners and 31% to general dentists and since general practitioners and dentists have not adequate knowledge, these Patients will be referred to specialists eventually [7]. Spontaneous recovery after 5 years of the disease onset has been reported in only 3% of cases [8]. The first step in treating patients with BMS is to determine if their symptoms are related to systemic conditions with local factors or not. Local factors include parafunctional habits, candidiasis, geographical tongue, and dry mouth. Systemic conditions include esophageal reflux, diabetes, and malnutrition [9]. Due to the diagnostic and etiological complexities of the disease, no definite treatment has been explored, and specialists use a variety of pharmacological, non-pharmacological, traditional medicine and modern treatments to improve the symptoms. Therefore, this review study was conducted to evaluate the effective treatments for Burning Mouth Syndrome.

3. Materials and Methods

In this review study, studies related to the treatment of Burning Mouth Syndrome were reviewed. Keywords were "Burning Mouth Syndrome", "Oral facial pain", "Orofacial pain", "Glossalgia", "Stomatodynia","Stomatopyros", "Glossodynia", "Glossopyros", "Sore mouth", "Sore tongue". Keywords were searched in databases including PubMed, Scopus, Web of Science, Science Direct and Google Scholar. In addition, Persian keywords ("Burning Syndrome", "Burning Mouth") were searched in Persian databases including SID and Magiran. The search process was conducted up to May 29, 2020. The term "Burning Mouth Syndrome" was also searched on the PROSPERO website. In addition, the search was performed manually by reviewing the bibliography of articles used. Researchers independently reviewed the articles and studies related to epidemiology and pathology were excluded. After abstract and full text review of the articles, the studies in which the effectiveness of BMS treatment was mentioned emphasizing systematic review and meta-analysis studies of the last 5 years, were selected; however, other articles related to BMS treatment were also mentioned.

4. Results

4.1. Pharmacological treatments:

Different pharmacological therapies for symptom relief have been reported including Duloxetine [10], Zinc supplementation [11], Milnacipran [12], Amisulpiride [13], Aripiprazole [14], Gabapentin [15], Pregabalin [16], Venlafaxine [17] and Lafutidine [18], but recent review studies have shown the effects of Alpha-lipoic Acid (ALA), Clonazepam, and Capsaicin, which will be discussed below.

4.2. Systemic drug treatments

Alpha-Lipoic Acid: Acts as a biological antioxidant and reduces the oxidized form of other antioxidants such as vitamin E and C and Glutathione (GSH) [19]. In a systematic review study by Souza In 2018, evaluating 7 studies on the efficacy of this drug on BMS, 6 studies reported significant improvement [20].

Clonazepam: It is a benzodiazepine (GABA receptor agonist) that affects central and peripheral receptors and the brain serotonergic system. Its main usage is to treat seizure and panic disorders. Studies have shown that Clonazepam is more effective in controlling BMS symptoms than other benzodiazepines due to its tendency to bind to the central benzodiazepine receptors and its long half-life, which reduces withdrawal complications [21]. A study by Henrikson et al. in 2017 showed that topical Clonazepam was more effective than other orofacial pain medications in treating BMS [22]. A meta-analysis study by Cui In 2016, reviewing 5 articles and examining the effect of Clonazepam on 195 patients, showed the positive effect of this drug in short-term (less than ten weeks) and long-term (more than ten weeks) treatment. It also revealed the drug administration effectiveness either systemically or topically. Dose of Clonazepam showed a complex relation with the symptoms of BMS so that with increasing the dose from 0.25 to 2 mg, the symptoms disappeared in some patients but also intensified in some, and some patients withdraw the drug in doses higher than 1 mg due to the side effect intolerance [23].

4.3. Topical drug treatments:

a. Clonazepam: According to Häggman - Henrikson et al. [22], the effectiveness of this topical drug has been reviewed and confirmed in several systematic review and meta-analysis studies. Clonazepam mouthwash for 3 minutes is recommended although it can have side effects such as dry mouth.

b. Capsaicin: Due to its anti-allergic properties on pain receptors, Capsaicin is administered to treat musculoskeletal pain, diabetic neuropathy and rare diseases in the form of gels, liquids and topical creams. Capsaicin mouthwash is a combination of this substance and water which is used in different studies with different concentrations. At the beginning of its use, irritation may occur in patients with gastrointestinal problems, so prescribing this drug should be done with caution. A meta-analysis study in 2017 showed the effectiveness of topical Capsaicin in the treatment of

BMS [22].

4.4. Non-pharmacological treatments:

a. Aloe vera: Due to the side effects of systemic drug treatments, many researches on aloe vera is administered today as an alternative treatment in form of gel, mouthwash and etc. A systematic review by Nair et al. in 2016 showed that topical application of aloe vera has a significant effect in treatment of oral mucosal disease. Controlling parafunctional habits using topical aloe vera, reduces the risk of mucosal trauma and BMS-related discomfort [24].

b. Kampo: A combination of herbs used in traditional Japanese and Chinese medicine. These plants have various names such as "Fuxi", "Shennong" and "Yellow Emperor" and are the basis of traditional treatments in Japan and China. In traditional Japanese medicine, the body and mind are believed to interact with each other, and both are considered treatment of such disorders. A study by Okamoto et al. on the effect of herbal medicine, Kampo showed a positive effect of this drug in 69.2% of resistant specimens [25].

c. Hormone replacement therapy: Hormone Replacement Therapy (HRT) has been proposed due to the relation of this syndrome to the endocrinological factors and sex hormones and can be used for patients during or after menopause [26, 27]. This treatment is not recommended as a first treatment choice for elderly individuals with a history of diabetes, coronary artery disease, and myocardial infarction due to side effects such as increased mucosal epithelial thickness and increased risk of thrombogenesis, as well as dose-independence [28].

d. Low level laser therapy (LLLT): It is used as a minimally invasive, non-pharmacological method with minimal side effects [29]. Items such as type of laser device, wavelength, radiation area, beam intensity, duration of application at each area, number of placement points, distance between points and number of sessions are among the factors affecting treatment. A meta-analytic study in 2020 examined the effect of LLLT on the treatment of orofacial pain and in all 10 studies, it was shown to have a significant impact on pain relief and the best effects of pain reduction caused by LLLT was with three sessions a week with a wavelength of 830 nm and a power of 100 MW. Applying LLLT with 815 nm wavelength and power of 300 MW and radiation area of 0.228 cm in continuous frequency for 10 seconds at any point for 10 sessions, leads to a satisfactory result in reducing pain. Also studies have shown a better effect of LLLT compared to Clonazepam and ALA [30].

In a single-blind randomized clinical trial in 2020, 10 patients with BMS underwent LLLT at a dose of 212 J/cm^2 in ten sessions, and all patients reported pain relief. Among 90% of them, pain relief lasted up to 4 months [31].

Non-invasive brain stimulation: Transcranial Magnetic Stimulation (TMS) and Transcranial Direct Current Stimulation (TDCS) are non-invasive techniques and can be used as an alternative treatment for a wide range of local pains. TMS with electromagnetic force increases or decreases the activity of neurons. It is important to pay attention to the location and frequency in this method, so that low frequencies (less than 1 Hz) accelerate the inhibitory function of neurons and higher frequencies (more than 5 Hz) typically increase cortical activity.

TDCS is applied with weak electric currents at specific times [32-34]. A systematic review study in 2019 reported the positive effect of these two methods in reducing chronic orofacial pain [35]. In the systematic review study conducted in 2018 [36], 14 studies (3 TMS studies and 11 TDCS studies) were performed on 228 patients and the results showed that both TMS and TDCS methods are safe and effective treatments for reducing chronic orofacial pain. In Lindholm et al. study [37], use of this treatment method (secondary motor cortex stimulation and secondary somatosensory cortex stimulation) showed a significant reduction in pain. Also, results of a study by Umezaki et al. [38] on effect of TMS on the left prefrontal cortex in the treatment of BMS showed a significant reduction in pain immediately after treatment and had the greatest persistence in pain relief 60 days after the start of treatment.

4.5. Self-medication

Self-medication is a psychotherapeutic approach in which the patient plays an active role in improving the condition of the patient instead of being passive in the treatment process, which improves the patient's performance and emotions. The goal of this treatment is to change dysfunctional behavior, change lifestyle and maladaptive cognitive themes, and increase cognition and adaptive behavior [39]. Skills training and strengthening are the two main components of this approach. In the 2019 meta-analysis-meta regression study [40], researchers examined the effect of self-medication interventions in adults with orofacial pain compared to other treatments and achieved positive and effective results of this therapeutic approach. Komiyama et al. investigated the effect of cognitive therapy among groups of BMS patients in two sessions and results showed a significant reduction in pain intensity and anxiety in these patients [41].

Patient education and anxiety management: Medication is not the only way for BMS treatment, and physicians should not only seek for it and quality of life should be considered in treatment procedures. Patient education and anxiety control without any treatment might be helpful in situations where there is not enough access to a psychologist [42]. This therapeutic approach needs further investigations.

5. Conclusion

According to different studies, different treatments for this syndrome are listed in (Figure 1). The purpose of this study was to compile the latest systematic review and meta-analysis studies on the effectiveness of various treatments for Burning Mouth Syndrome. Despite all available treatments, still no definite treatment

for BMS has been found and all treatments are supportive. Other treatments such as acupuncture [43], tongue protectors with or without aloe vera [44], local anesthesia [45] and Cannabinoids [46] have reported improvement in symptoms; However, due to the limited number of studies, more studies are needed on the effectiveness of these treatments.

6. Conflict of interest

None

7. Funding source

None

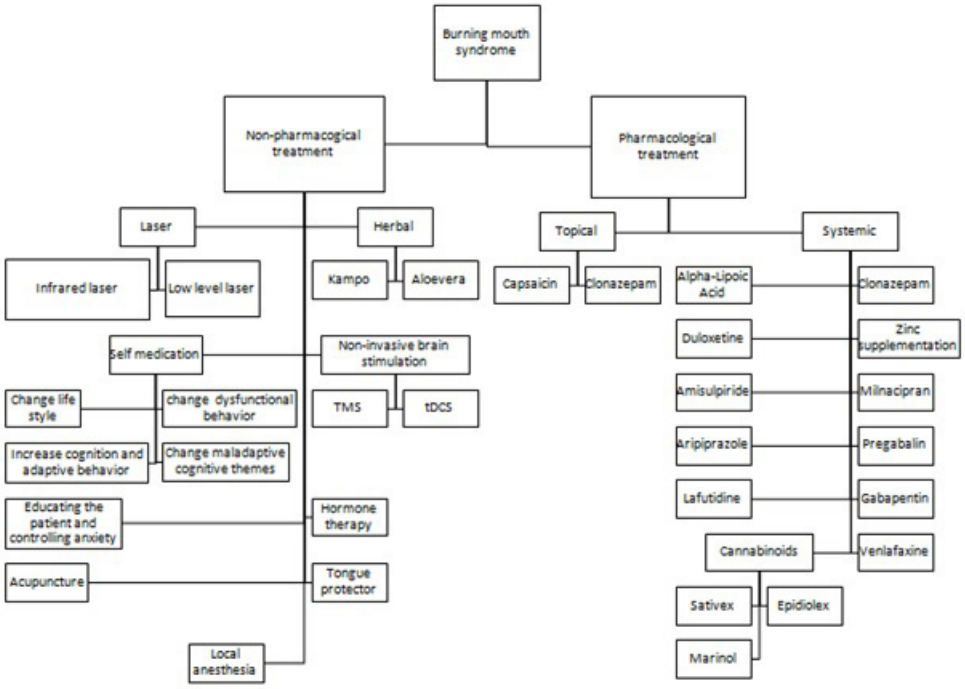

Figure: A review of burning mouth syndrome treatments from the past to the present

References

1. Glick M. Burket's oral medicine: PMPH USA; 2015.
2. Scully C, Carrozzo M. Oral mucosal disease: Lichen planus. Br J Oral Maxillofac Surg. 2008; 46(1): 15-21.
3. Arbabi-Kalati F, Bakhshani N-M, Rasti M. Evaluation of the efficacy of low-level laser in improving the symptoms of burning mouth syndrome. J clin Exp Dent. 2015; 7(4): e524.
4. Momota Y, Kani K, Takano H, Matsumoto F, Aota K. High-wattage pulsed irradiation of linearly polarized near-infrared light to stellate ganglion area for burning mouth syndrome. Case Rep Dent. 2014: 171657.
5. Buchanan JA, Zakrzewska JM. Burning mouth syndrome. BMJ Clin Evid. 2016; 7: 1301.
6. Mock D, Chugh D. Burning mouth syndrome. Int J Oral Sci. 2010; 2(1): 1-4.
7. Bell G, Smith G, Rodgers J, Flynn R, Malone C. Patient choice of primary care practitioner for orofacial symptoms. Br Dent J. 2008; 204(12): 669-673.
8. McMillan R, Forssell H, Buchanan JA, Glenny AM, Weldon JC. Interventions for treating burning mouth syndrome. Cochrane Database Syst Rev. 2016; 11(11): CD002779.
9. Spanemberg JC, Cherubini K, De Figueiredo MAZ, Yurgel LS, Salum FG. Aetiology and therapeutics of burning mouth syndrome: an update. Gerodontology. 2012; 29(2): 84-89.
10. Mignogna MD, Adamo D, Schiavone V, Ravel MG, Fortuna G. Burning mouth syndrome responsive to duloxetine: a case report. Pain Med. 2011; 12(3): 466-469.
11. Cho GS, Han MW, Lee B, Roh JL, Choi SH. Zinc deficiency may be a cause of burning mouth syndrome as zinc replacement therapy has therapeutic effects. J oral Pathol Med. 2010; 39(9): 722-727.
12. Ukai K, Kimura H, Arao M, Aleksic B, Yamauchi A, Ishihara R. Effectiveness of low - dose milnacipran for a patient suffering from pain disorder with delusional disorder (somatic type) in the orofacial region. Psychogeriatrics. 2013; 13(2):99-102.
13. Rodriguez-Cerdeira C, Sanchez-Blanco E. Treatment of burning mouth syndrome with amisulpride. J Clin Med Res. 2012; 4(3): 167-171.
14. Umezaki Y, Takenoshita M, Toyofuku A. Low-dose aripiprazole for refractory burning mouth syndrome. Neuropsychiatr Dis Treat. 2016; 12: 1229-1231.
15. López-D'alessandro E, Escovich L. Combination of alpha lipoic acid and gabapentin, its efficacy in the treatment of Burning Mouth Syndrome: a randomized, double-blind, placebo controlled trial. Med Oral Patol Oral Cir Bucal. 2011; 16(5): e635-40.
16. Ito M, Tokura T, Yoshida K, Nagashima W, Kimura H. Five patients with burning mouth syndrome in whom an antidepressant (serotonin-noradrenaline reuptake inhibitor) was not effective, but pregabalin markedly relieved pain. Clin Neuropharmacol. 2015; 38(4): 158-161.

17. Mitsikostas DD, Ljubisavljevic S, Deligianni CI. Refractory burning mouth syndrome: clinical and paraclinical evaluation, comorbidities, treatment and outcome. J Headache Pain. 2017; 18(1): 40.

18. Toida M, Kato K, Makita H, Long N, Takeda T. Palliative effect of lafutidine on oral burning sensation. J oral Pathol Med. 2009; 38(3): 262-268.

19. Palacios-Sanchez B, Moreno-Lopez LA, Cerero-Lapiedra R, Llamas-Martinez S, Esparza-Gomez G. Alpha lipoic acid efficacy in burning mouth syndrome. A controlled clinical trial. Med Oral Patol Oral Cir Bucal. 2015; 20(4): e435-40.

20. De Souza IF, Marmora BC, Rados PV, Visioli F. Treatment modalities for burning mouth syndrome: a systematic review. Clin Oral Investig. 2019; 23(9): 3657.

21. Grushka M, Epstein J, Mott A. An open-label, dose escalation pilot study of the effect of clonazepam in burning mouth syndrome. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1998; 86(5): 557-561.

22. Haggman-Henrikson B, Alstergren P, Davidson T, Hogestatt ED, Ostlund P. Pharmacological treatment of oro-facial pain - health technology assessment including a systematic review with network meta-analysis. J Oral Rehabil. 2017; 44(10): 800-826.

23. Cui Y, Xu H, Chen F, Liu J, Jiang L. Efficacy evaluation of clonazepam for symptom remission in burning mouth syndrome: a meta - analysis. Oral Dis. 2016; 22(6): 503-511.

24. Nair GR, Naidu GS, Jain S, Nagi R, Makkad RS. Clinical effectiveness of aloe vera in the management of oral mucosal diseases-a systematic review. J clin Diagn Res. 2016; 10(8): ZE01-7.

25. Okamoto H, Chino A, Hirasaki Y, Ueda K, Raimura M. A valid approach in refractory glossodynia: a single-institution 5-year experience treating with Japanese traditional herbal (Kampo) medicine. Evid Based Complement Alternat Med. 2013.

26. Wardrop R, Hailes J, Burger H, Reade P. Oral discomfort at menopause. Oral Surg Oral Med Oral Pathol. 1989; 67(5): 535-540.

27. Imamura Y, Shinozaki T, Okada-Ogawa A, Noma N, Shinoda M. An updated review on pathophysiology and management of burning mouth syndrome with endocrinological, psychological and neuropathic perspectives. J oral rehabil. 2019; 46(6): 574-587.

28. Forabosco A, Criscuolo M, Coukos G, Uccelli E, Weinstein R. Efficacy of hormone replacement therapy in postmenopausal women with oral discomfort. Oral Surg Oral Med Oral Pathol. 1992; 73(5): 570-574.

29. Pandeshwar P, Roa MD, Das R, Shastry SP, Kaul R. Photobiomodulation in oral medicine: a review. J investig Clin Dent. 2016; 7(2): 114-126.

30. De Pedro M, Lopez-Pintor RM, De la Hoz-Aizpurua JL, Casanas E, Hernandez DG. Efficacy of Low-Level Laser Therapy for the Therapeutic Management of Neuropathic Orofacial Pain: A Systematic Review. J Oral Facial Pain Headache. 2020; 34(1): 13-30.

31. De Pedro M, Lopez-Pintor R, Casanas E, Hernandez G. Effects of Photobiomodulation with Low-Level Laser Therapy in Burning Mouth Syndrome: A randomized clinical trial. Oral Dis. 2020; 26(8): 1764-1776.

32. Rossi S, Hallett M, Rossini PM, Pascual-Leone A, Group SoTC. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. Clin Neurophysiol. 2009; 120(12): 2008-2039.

33. Barker AT, Jalinous R, Freeston IL. Non-invasive magnetic stimulation of human motor cortex. Lancet. 1985; 1(8437): 1106-1107.

34. Nitsche MA, Paulus W. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. J Physiol. 2000; 527: 3(pt 3): 633-639.

35. Ferreira NR, Junqueira YN, Corrêa NB, Fonseca EO, Brito NB. The efficacy of transcranial direct current stimulation and transcranial magnetic stimulation for chronic orofacial pain: A systematic review. PLoS One. 2019; 14(8): e0221110.

36. Babiloni AH, Guay S, Nixdorf DR, De Beaumont L, Lavigne G. Non-invasive brain stimulation in chronic orofacial pain: a systematic review. J Pain Res. 2018; 11: 1445-1457.

37. Lindholm P, Lamusuo S, Taiminen T, Pesonen U, Lahti A. Right secondary somatosensory cortex-a promising novel target for the treatment of drug-resistant neuropathic orofacial pain with repetitive transcranial magnetic stimulation. Pain. 2015; 156(7): 1276-1283.

38. Umezaki Y, Badran BW, DeVries WH, Moss J, Gonzales T. The efficacy of daily prefrontal repetitive transcranial magnetic stimulation (rTMS) for burning mouth syndrome (BMS): a randomized controlled single-blind study. Brain Stimul. 2016; 9(2): 234-242.

39. Nicholas MK, Blyth FM. Are self-management strategies effective in chronic pain treatment? Pain Manag. 2016; 6(1): 75-88.

40. Aggarwal VR, Fu Y, Main CJ, Wu J. The effectiveness of self-management interventions in adults with chronic orofacial pain: A systematic review, meta-analysis and meta-regression. Eur J Pain. 2019; 23(5): 849-865.

41. Komiyama O, Nishimura H, Makiyama Y, Iida T, Obara R. Group cognitive-behavioral intervention for patients with burning mouth syndrome. J oral Sci. 2013; 55(1): 17-22.

42. Tu TT, Takenoshita M, Matsuoka H, Watanabe T, Suga T. Current management strategies for the pain of elderly patients with burning mouth syndrome: a critical review. Biopsychosoc Med. 2019; 13(1): 1.

43. Jurisic Kvesic A, Zavoreo I, Basic Kes V, Vucicevic Boras V, Ciliga D. The effectiveness of acupuncture versus clonazepam in patients with burning mouth syndrome. Acupunct Med. 2015; 33(4): 289-292.

44. López-Jornet P, Camacho-Alonso F, Molino-Pagan D. Prospective, randomized, double-blind, clinical evaluation of A loe vera B arbadensis, applied in combination with a tongue protector to treat burning mouth syndrome. J Oral Pathol Med. 2013; 42(4): 295-301.

45. Treldal C, Jacobsen CB, Mogensen S, Rasmussen M, Jacobsen J. Effect of a local anesthetic lozenge in relief of symptoms in burning mouth syndrome. Oral Dis. 2016; 22(2): 123-131.

46. Pereira SR, Tello Velasquez J, Duggan S, Ivanisevic B, McKenna JP. Recent advances in the understanding of the aetiology and therapeutic strategies in burning mouth syndrome: Focus on the actions of cannabinoids. Eur J Neurosci. 2020.