

# Journal of Advanced Medical and Dental Sciences Research

@Society of Scientific Research and Studies

NLM ID: 101716117

Journal home page: www.jamdsr.com    doi: 10.21276/jamdsr    Indian Citation Index (ICI)    Index Copernicus value = 100

(e) ISSN Online: 2321-9599;

(p) ISSN Print: 2348-6805

## Review Article

### Burning mouth syndrome: A Review

Jasjot Sahni

Clinical Assistant Professor, Department of Oral Medicine and Diagnostic Sciences, College of Dentistry, University of Illinois Chicago, IL, USA

Received: 23 March, 2023

Accepted: 26 April, 2023

**Corresponding author:** Jasjot Sahni, Clinical Assistant Professor, Department of Oral Medicine and Diagnostic Sciences, College of Dentistry, University of Illinois Chicago, IL, USA

**This article may be cited as:** Sahni J. Burning mouth syndrome: A Review. J Adv Med Dent Scie Res 2023;11(5):123-128.

#### INTRODUCTION

Burning mouth syndrome (BMS) is a chronic intraoral burning sensation without any specific medical or dental cause. It is known to affect the quality of the life of the patients and also poses a diagnostic challenge for both the patients and practitioners.

Burning mouth syndrome has been defined by International Classification of Orofacial Pain as: "An intraoral burning or dysaesthetic sensation, recurring daily for more than 2 hours per day for more than 3 months, without evident causative lesions on clinical examination and investigation (table 1)." (1).

The International Association for the Study of Pain has identified it as a distinctive nosological entity characterized by pain episodes lasting at least 4–6 months (2)

Burning mouth syndrome (BMS) is a chronic pain disorder, affecting oral mucosa, affecting around 1-15 % population within the United States (2). BMS affects females more than males in the ratio of 7:1 and was reported in 10–40% of women who were undergoing treatments for managing their menopausal symptoms (3). It is also known by other names as glossodynia, glossopyrosis, stomatodynia, stomatopyrosis, oral dysaesthesia. (1)

It is mainly characterized by symptoms, mostly present bilaterally, such as burning, pain, dysesthesia, hyperesthesia, tingling, or discomfort in absence of oral pathology. (3)

The symptoms involve mainly the tongue, esp. the tip and anterior two-thirds, accompanied with mild to moderate discomfort in the hard palate, lips, and alveolar ridges. In rare cases, there could be sometimes pain or discomfort affecting the buccal mucosa and floor of the mouth. Some patients also complain of some other symptoms such as dysgeusia in 35 % cases, xerostomia in 63 % cases, and decreased taste sensation or altered taste sensation in 60 % cases (3, 4, Scala et al., 2003). The patients report the symptoms increase by the late afternoon or evening hour and generally does not affect the patient during sleep, but it might find it difficult to get to sleep.

Since, BMS is by far an exclusion diagnosis and has a multifactorial etiology. It is thus diagnosed, after possibly ruling out local and systemic factors. It is important that if the provider can differentiate primary BMS from secondary BMS, as if we are able to eliminate the secondary cause for secondary BMS, it might help in managing the BMS symptoms successfully.

#### Diagnostic Criteria: Table 1

- |  |
|--|
| <p>A. Oral pain fulfilling criteria B and C</p> <p>B. Recurring daily for &gt;2 hours per day for &gt;3 months<sup>1</sup></p> <p>C. Pain has both of the following characteristics:</p> <p>1. burning quality</p> |
|--|

- 2. felt superficially in the oral mucosa
- D. Oral mucosa is of normal appearance, and local or systemic causes have been excluded
- E. Not better accounted for by another ICOP or ICHD-3 diagnosis.

**CLASSIFICATION**

There are many kinds of classification types proposed. Scala et al. has proposed to organize BMS into two clinical forms as follows (5): ‘primary’ or essential/idiopathic BMS, in which the causes cannot be identified, and ‘secondary’ BMS, resulting from local factors or systemic conditions. Another classification that has been proposed based on the intensity of pain and variance of pain during the day(6-9): Type 1: characterized by progressive pain, patients wake up without pain, which then increases throughout the day, affects approximately 35% of patients. This type may be associated with systemic diseases, such as nutritional deficiencies. Type 2: the symptoms are constant throughout the day and patients find it difficult to get to sleep, represents 55%. These patients usually present associated psychological disorders. Type 3: symptoms are intermittent, with atypical location and pain. Constitutes 10% of patients. It seems that contact with oral allergens could play an important etiologic role in this group.

**ETIOPATHOGENESIS**

Its etiology is mostly idiopathic, unknown or multifactorial. It has a complex and multifactorial etiology involving both neurophysiological and psychological factors. (10,11,12).As per this study, certain individuals, who have high density of fungiform papilla on anterior aspect of tongue, mostly females, have being labeled as supertasters, are at risk of developing burning pain symptoms(13).Sensory dysfunction has been associated with small and/or

large fiber neuropathy.[14] Immuno-histochemical and microscopic observation studies have revealed axonal degeneration of epithelial and subpapillary nerve fibers in the affected epithelium of the oral mucosa[15].It also has been shown that centrally mediated alteration is present during the modulation of nociceptive processing.[16]. In addition, disturbances in the autonomic innervation and oral blood flow have been observed [17]. Furthermore, chronic anxiety could result in the alteration of gonadal, adrenal, and neuroactive steroid levels in skin and oral mucosa. [18] Central neuropathic mechanisms and patterns of cerebral hypoactivity have been observed in patients with BMS. (19).

**CLINICAL CRITERIA**

It is an exclusion diagnosis and is made after ruling out local and systemic causes. Diagnostic criteria are developed by Scala et al(see table 2) for the diagnosis of BMS.

The patients generally have complaint of burning sensation, which could be intermittent or continuous and affecting mainly the anterior one third of the tongue, lips, palate. Pain worsens by evening or late afternoon and eating or drinking might help reduce the symptoms. Patients have altered taste or presence of bitter or metallic taste. It does not affect patient during sleep, but most patients can have difficulty falling asleep, because of the discomfort. The patient could have additional symptoms such as sensory or chemosensory alterations or associated psychopathological changes (5).

<b>Table 2- Criteria for BMS:</b>
<b>Fundamental Criteria for BMS:</b>
1. Daily deep burning sensation of oral mucosa (bilateral) 2. Pain of at least 4-6 months 3. Constant intensity or increasing intensity during the day 4. Characteristic symptoms are not getting worse/ sometimes there may be an improvement over the ingestion of food and liquid 5. No interference with sleep
<b>Additional Criteria for BMS:</b>
6. The occurrence of other oral symptoms (dysgeusia +/- xerostomia) 7. Sensory changes/ chemosensory alterations 8. Psychopathological alterations/ mood changes that translate the patient’ personality disorder

**DIFFERENTIAL DIAGNOSIS**

It is a complex diagnosis to establish and essentially an exclusion diagnosis. An extensive medical and dental history should be taken and tests could be ordered to rule out systemic causes contributing to pain. A comprehensive oral exam should be conducted to rule out any oral pathologies. The Primary form of BMS is defined as BMS without any proven etiology.

Secondary BMS is on the other hand, is linked with some other local or systemic cause.

Systemic diseases that could cause symptoms similar to BMS have to be ruled out as: autoimmune diseases such as Sjogrens syndrome, lichen planus, other vesiculobullous diseases, aphthous ulcers, Lupus, candidiasis, deficiencies of iron, folic acid, zinc, Vitamin B. It is also important to obtain a thorough

dental, medical and psychosocial history. There are many medications that can cause xerostomia and can contribute to dryness observed in these patients. Because xerostomia can be an important contributing factor to symptoms of burning in the mouth, another

diagnostic test includes evaluation of salivary gland function.

Sialometric studies, including minor salivary gland biopsy can be performed, that help in determining the presence of salivary gland diseases linked to xerostomia.

**Table 3:**

<b>Etiological Factors</b>		<b>Investigations</b>	<b>Treatments</b>
Local	Poorly fitting dentures Denture material allergies Fungal infections Parafunctional habits Xerostomia	Check dentures Oral cultures to confirm suspected bacterial, viral, and fungal infections Patch test for allergic individuals Sialometric tests	Removal or correction of dentures Allergies medication Anti- fungal medications Splint therapy sialagogues
Systemic	Endocrine disorders(Diabetes/Hypothyroidism, Menopause) Salivary gland disorders Autoimmune disorders	Autoimmune panel Endocrinology opinion CBC blood work including TSH levels, glycemic controls, iron, ferritin levels, Hb A 1c,folic acid, vitamin B12, B1, B2, B6, zinc.	Medications
Psychological	Anxiety, depression Cancer phobia	Psychometric tests	Psychotherapy or psychiatrist referral and management.
Miscellaneous	Medication (ACE inhibitors, anti-hyperglycemic) Neurological disorders GERD, acid reflux Radiotherapy Disturbance of serum hormone (estradiol) levels in women Allergies	Neurological imaging and examination to rule out any pathology and degenerative disorders Gastric reflux studies Determination of serum estradiol levels Patch tests to identify allergies	Discontinuing or changing the medication helps improve the patients symptoms Hormonal replacement therapy

### **TREATMENT**

Since there are many mimickers of BMS, the differentiation of primary and secondary BMS is very important to establish, based on the identification and ruling out of etiological factors. In case of secondary BMS, it is essential to manage or treat the secondary cause.

Unfortunately, even though many treatments have been proposed over the years, none of the modalities have been proven as a satisfactory.(10).It is important to set realistic expectations along with providing reassurance at the initial appointment (20).

Management of BMS can be divided under three topics namely topical medications, systemic medications and behavioral interactions (see table 4). Topical medications can be used successfully in many cases, before the use of systemic medications.

### **TOPICAL MEDICATIONS**

Capsaicin is “hot” component of chili pepper, used for symptomatic management of the symptoms. It can bind to the TRPV1 ion channels of small- diameter peripheral sensory nerve fibers causing desensitization of afferent receptors, with subsequent reduction on pain symptoms It has some role in inhibiting central sensitization via downregulating the biosynthesis and axonal transport of neurotransmitters. [21, 22].Topical application of capsaicin (0.025% cream) has been used

in BMS as a desensitizing agent and is thought to inhibit substance P. There is generally less patient compliance due to its taste (23). Some patients have found some relief by using a mouth rinse mixing tabasco sauce with water in a dilution of 1:1 or 1:2 (24).

Topical application of clonazepam (benzodiazepine)as an orally dissolving tablet(ODT) for 3 times a day for 2 weeks, has been used with some success in many cases. (25). Clonazepam has been also used in the form of a rinse (0.5 mg/5 ml) or mixing 0.5 mg tablet with a I teaspoon of water to make a slurry for swish and spit.

Some studies have tried using 0.15% Benzydamine hydrochloride-3 times daily with inconsistent results. (26). Topical lidocaine has not proven to be an effective treatment due to shorter duration of action.

Topical 0.5 ml *Aloe vera* gel at 70% concentration along with a tongue protector for 3 times a day, is found to be effective for reducing the pain symptoms involving the tongue.[27]

### **SYSTEMIC MEDICATIONS**

Systemic capsaicin capsules were used in one study, where dosing of 0.25% for three times a day for 1 month, has been associated with a significant reduction in pain intensity compared with a placebo group. Nevertheless, long-term use has not been

recommended, as 32% of patients experienced gastric pain after 1 month of use (28).

Benzodiazepines at low doses are useful in patients with anxiety disorders. One of the best evidence is for use of Clonazepam which has been effective as it is known to activate pain- inhibitory pathways in the spinal cord and in peripheral nociceptors. It is a GABAergic agonist and tongue has a high expression of GABA-A receptors (29).

Clonazepam and other benzodiazepines such as Alprazolam can act centrally on serotonergic modulation and thereby reducing central neuronal hyperactivity(30).Peripherally, it acts by reducing the disinhibition of chorda tympani nerve, thus moderating the effect on the trigeminal nerve system (30). It also has been shown to have central sedative, anxiolytic and analgesic effects, which further helps to manage the chronic pain symptoms. (29, 31, 32, 33,23).

Anti- depressants such as Tricyclic antidepressants have been used to treat BMS, esp. with the patients having anxiety and depressive disorders, as it has significant effects in treating neuropathic pain. Furthermore, there is a close association between BMS and generalized anxiety and depressive disorders [34].Medications such as amitriptyline, nortriptyline (starting dose of 5-10 mg/day and gradually increases to 50 mg/day) are useful in treating BMS. Sometimes these drugs in patient with dry mouth, can worsen the condition of the patient.

Selective serotonin reuptake inhibitor (SSRI) like antidepressants such as sertraline (50 mg/day),

paroxetine (20 mg/day) for 2 months and Selective serotonin nor-epinephrine inhibitor (SNRI) such as Cymbalta (at a dose of upto60 mg/day), have shown to have a significant improvement of burning sensation.[35]

Alpha- lipoic acid(ALA) is a mitochondrial coenzyme, potent antioxidant and has neuroprotective properties. It has been shown to increase the production of neural growth factors. (36) It potentiates the intracellular levels of glutathione and helps in regenerating other antioxidants such as Vitamin C and E. (37) ALA can be prescribed in the dosing range of anywhere from 200 to 800 mg/day (38). Side effects include headaches and gastric irritation and so a gastro protective agent must be concomitantly advised for the patient. (36, 39).ALA can be also used in combination with anticonvulsants such as Gabapentin along withwith the use of cognitive behavioral therapy and psychotherapy modalities. (28, 40,41).In patients with vitamin or mineral deficiencies, the patients could be given substitutes of respective vitamins such as vitamin B12, folic acid and minerals like iron, zinc. This can greatly improve the symptoms of these patients. (42)Hormone replacement therapy, such as premarin (0.625 mg/day for 3 weeks) can be used especially in peri and post menopausal females can relieve oral burning symptoms. (43)Acupuncture has been shown to be being beneficial as an adjunctive modality, for the relief of symptoms in some patients. (44)

**Table 4:**

Classification of drug	Medications	Dosing	Important points
<b>Topical</b>			
Red chilly peppers, activates the TRPV1 receptors, depletes the Substance P neurotransmitter.	Capsaicin	0.25 % - 3 times a day Or 1:2 dilution (or higher) of hot pepper and water; increase strength of capsaicin as tolerated to a maximum of 1:1 dilution	Initiation or initial burning at the site of application might be the side effect leading to poor compliance amongst the patients.
Benzodiazepine ( BZD)	Clonazepam	0.5 mg/5ml – TID rinse	Caution advised for the addictive potential
Tricyclic Antidepressant	Amitriptyline	10 mg at bedtime; increase dosage by 10 mg every 4 to 7 days until oral burning is relieved or side effects occur	Dry mouth is a consideration for these patients.
Anticonvulsants	Gabapentin (binds to the $\alpha 2\delta$ subunit of voltage-gated calcium channels)	300 mg TID, titrating upwards to 2400 mg/ day.	Dizziness, Xerostomia, sedation is a side effect.
Serotonin Norepinephrine Re-uptake Inhibitors	Cymbalta	Start with 20 mg and increase per week by 20 mg up to 60 mg/ day.	Suicidal ideation, dizziness, Xerostomia is a potential side effect
Serotonin Selective Reuptake Inhibitors	Sertaline / Zoloft	50 mg/ day for 8 weeks	Sedation, Xerostomia is a potential side effect
<b>SYSTEMIC</b>			
Herbal ( made from red chilly hot	Capsaicin	0.25% capsules, 3 times a	Gastric pain is the main side

peppers)		day, for 1 month;	effect and so gastroprotective agent might be advised. Nausea, dyspepsia
Serotonin Norepinephrine Re-uptake Inhibitors	Cymbalta	20 mg, increase dose by 1 tab in 1 week, to up to 60 mg.	
Benzodiazepines	Clonazepam	0.5 mg/ day up to TID	
Hormone replacement therapy	Estrogen replacement therapy		Given in post- menopausal agent.
Antioxidant/ neuroprotective agent	Alpha-Lipoic Acid	600 mg per day- up to BID.	Gastroprotective agent might be advised.

## CONCLUSION

Burning mouth syndrome is often frustrating condition to the patients and for the providers who manage these patients. This is especially, because its etiopathogenesis is complex and although the short-term follow-up studies may show potential symptomatic improvement with treatment in patients with BMS, the long-term outcomes for BMS remain unclear. Thus interdisciplinary treatment modalities should be used for proper evaluation and comprehensive management of these complex set of patients.

## REFERENCES

- International Classification of Orofacial Pain, 1st edition (ICOP). Cephalgia. 2020;40(2):129-221. doi:10.1177/0333102419893823
- Merksey H, Bugduk N. Classification of chronic pain. Description of chronic pain syndromes and definition of pain terms. In: Merksey H, Bugduk N, editors. Task on taxonomy. Seattle: IASP press; 1994. p.742.
- (Bergdahl and Bergdahl, 1999; Ferguson et al., 1981; Lamey and Lewis, 1989; Mareski et al., 1993; Riley et al., 1998; Tammiala-Salonen et al., 1993).
- Grushka M. Clinical features of burning mouth syndrome. Oral Surg Oral Med Oral Pathol, 1987;63(1):30-36.
- Scala A, Checchi L, Montevecchi M, Marini I, Giamberardino MA. Update on burning mouth syndrome: overview and patient management. Crit Rev Oral Biol Med. 2003;14(4):275-91. doi: 10.1177/154411130301400405. PMID: 12907696.
- Klasser GD, Fischer DJ, Epstein JB. Burning mouth syndrome: recognition, understanding, and management. Oral Maxillofac Surg Clin North Am. 2008;20:255-71.
- Danhauer SC, Miller CS, Rhodus NL, Carlson CR. Impact of criteria-based diagnosis of burning mouth syndrome on treatment outcome. J Orofac Pain. 2002;16:305-11.
- Grushka M, Epstein JB, Gorsky M. Burning mouth syndrome and other oral sensory disorders: a unifying hypothesis. Pain Res Manag. 2003;8:133-5.
- Med Oral Patol Oral Cir Bucal. 2010 Jul 1;15 (4):e562-8. Stomatodynia
- Aravindhan R, Vidyalakshmi S, Kumar MS, Satheesh C, Balasubramaniam AM, Prasad VS. Burning mouth syndrome: A review on its diagnostic and therapeutic approach. J Pharm Bioallied Sci. 2014;6(Suppl 1):S21-5.
- Aggarwal A, Panat SR. Burning mouth syndrome: A diagnostic and therapeutic dilemma. J ClinExp Dent. 2012;4:e180-5. [PMCID: PMC3917644] [PubMed: 24558551]
- Sameera A, Suman SV, Raviraj J, Muruges J, Suresh D. Burning mouth syndrome – A review. J Adv Oral Res. 2014;3:90-5.
- Bartoshuk LM, Snyder DJ, Grushka M, Berger AM, Duffy VB, Kveton JF. Taste damage: Previously unsuspected consequences. Chem Senses. 2005;30(Suppl 1):i218-9.
- Forssell H, Jääskeläinen S, Tenovuo O, Hinkka S. Sensory dysfunction in burning mouth syndrome. Pain. 2002;99:41-7.
- Lauria G, Majorana A, Borgna M, Lombardi R, Penza P, Padovani A, et al. Trigeminal small-fiber sensory neuropathy causes burning mouth syndrome. Pain. 2005;115:332-7.
- Jääskeläinen SK, Rinne JO, Forssell H, Tenovuo O, Kaasinen V, Sonninen P, et al. Role of the dopaminergic system in chronic pain – A fluorodopa-PET study. Pain. 2001;90:257-60.
- Heckmann SM, Heckmann JG, Hilz MJ, Popp M, Marthol H, Neundörfer B, et al. Oral mucosal blood flow in patients with burning mouth syndrome. Pain. 2001;90:281-6.
- Woda A, Dao T, Gremeau-Richard C. Steroid dysregulation and stomatodynia (burning mouth syndrome) J Orofac Pain. 2009;23:202-10. [PubMed: 19639097]
- Brufau-Redondo C, Martín-Brufau R, Corbalán-Velez R, de Concepción-Salesa Actas Dermosifiliogr. 2008 Jul-Aug; 99(6):431-40.
- Bergdahl J, Anneroth G, Perris H. Cognitive therapy in the treatment of patients with resistant burning mouth syndrome: A controlled study. J Oral Pathol Med. 1995;24:213-5.
- De Moraes M., Do Amaral Bezerra B. A., Da Rocha Neto P. C., De Oliveira Soares A. C. A., Pinto L. P., De Lisboa Lopes Costa A. Randomized trials for the treatment of burning mouth syndrome: An evidence-based review of the literature. *Journal of Oral Pathology & Medicine*. 2012;41(4):281-287. doi: 10.1111/j.1600-0714.2011.01100.x.
- Lakloul M., Baranidharan G. Profile of the capsaicin 8% patch for the management of neuropathic pain associated with postherpetic neuralgia: Safety, efficacy, and patient acceptability. *Patient Preference and Adherence*. 2016;10:1913-1918. doi: 10.2147/PPA.S76506.

23. Grushka M, Epstein JB, Gorsky M. Burning mouth syndrome. *Am Fam Physician*. 2002;65:615–20. [PubMed: 11871678]
24. Moreno Gimenez J. Glosodynia before and after diagnosis. *Piel*. 2005;20:524–9.
25. Gremeau-Richard C, Woda A, Navez ML, Attal N, Bouhassira D, Gagnieu MC, et al. Topical clonazepam in stomatodynia: A randomised placebo-controlled study. *Pain*. 2004;108:51–7.
26. Buchanan J, Zakrzewska J. Burning mouth syndrome. *ClinEvid*. 2004;12:1899–905.
27. López-Jornet P, Camacho-Alonso F, Molino-Pagan D. Prospective, randomized, double-blind, clinical evaluation of Aloe vera *Barbadensis*, applied in combination with a tongue protector to treat burning mouth syndrome. *J Oral Pathol Med*. 2013;42:295–301.
28. López-Jornet P, Camacho-Alonso F, Andujar-Mateos P, Sánchez-Siles M, Gómez-García F. Burning mouth syndrome: an update. *Med Oral Patol Oral Cir Bucal*. 2010 Jul 1;15(4):e562–8. doi: 10.4317/medoral.15.e562. PMID: 20038880.
29. Tan SN, Song E, Dong XD, Somvanshi RK, Cairns BE. Peripheral GABAA receptor activation modulates rat tongue afferent mechanical sensitivity. *Arch Oral Biol*. 2014;59(3):251–257.
30. Bartoshuk LM, Snyder DJ, Grushka M, Berger AM, Duffy VB, Kveton JF. Taste damage: previously unsuspected consequences. *Chem Senses*. 2005;30(suppl 1):i218–i219.
31. Gurvits G. E., Tan A. Burning mouth syndrome. *World Journal of Gastroenterology*. 2013;19(5):665–672. doi: 10.3748/wjg.v19.i5.665.
32. Grushka M., Epstein J., Mott A. An open-label, dose escalation pilot study of the effect of clonazepam in burning mouth syndrome. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*. 1998;86(5):557–561. doi: 10.1016/S1079-2104(98)90345-6.
33. Speciali J. G., Stuginski-Barbosa J. Burning mouth syndrome. *Current Pain and Headache Reports*. 2008;12(4):279–284. doi: 10.1007/s11916-008-0047-9.
34. Buchanan J. A. G., Zakrzewska J. M. Burning mouth syndrome. *BMJ Clinical Evidence*. 2010.
35. Shinoda M., Kawashima K., Ozaki N., Asai H., Nagamine K., Sugiura Y. P2X3 receptor mediates heat hyperalgesia in a rat model of trigeminal neuropathic pain. *The Journal of Pain*. 2007;8(7):588–597. doi: 10.1016/j.jpain.2007.03.001.
36. Kisely S, Forbes M, Sawyer E, Black E, Lalloo R. A systematic review of randomized trials for the treatment of burning mouth syndrome. *J Psychosom Res*. 2016;86:39–46.
37. Bacceti M. L., Fitzgerald M. Development of pain pathways and mechanisms. In: McMahon M. B., Tracey I., Koltzenburg M., Turk D. C., editors. *Wall and Melzack's Textbook of Pain*. Philadelphia, PA, USA: Elsevier; 2013. pp. 143–154.
38. Liu YF, Kim Y, Yoo T, Han P, Inman JC. Burning mouth syndrome: a systematic review of treatments. *Oral Dis*. 2018;24(3):325–334.
39. Moisset X., Calbacho V., Torres P., Gremeau-Richard C., Dallel R. Co-occurrence of pain symptoms and somatosensory sensitivity in burning mouth syndrome: A systematic review. *PLoS ONE*. 2016;11(9, article e0163449) doi: 10.1371/journal.pone.0163449.
40. Gremeau-Richard C, Woda A, Navez ML, Attal N, Bouhassira D, Gagnieu MC, et al. Topical clonazepam in stomatodynia: A randomised placebo-controlled study. *Pain*. 2004;108:51–7.
41. Van Houdenhove B, Joostens P. Burning mouth syndrome. Successful treatment with combined psychotherapy and psychopharmacotherapy. *Gen Hosp Psychiatry*. 1995;17:385–8.
42. Sun A, Lin HP, Wang YP, Chen HM, Cheng SJ, Chiang CP. Significant reduction of serum homocysteine level and oral symptoms after different vitamin-supplement treatments in patients with burning mouth syndrome. *J Oral Pathol Med*. 2013;42:474–9.
43. Forabosco A, Criscuolo M, Coukos G, Uccelli E, Weinstein R, Spinato S, et al. Efficacy of hormone replacement therapy in postmenopausal women with oral discomfort. *Oral Surg Oral Med Oral Pathol*. 1992;73:570–4.
44. Sardella A, Lodi G, Tarozzi M, Varoni E, Franchini R, Carrassi A. Acupuncture and burning mouth syndrome: a pilot study. *Pain Pract*. 2013; 13(8):627–32.