**Review Article**

**Burning Mouth Syndrome: Will Better Understanding Yield Better Management?**

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**Abstract:** “Burning mouth syndrome” (BMS) refers to a chronic orofacial pain disorder usually unaccompanied by mucosal lesions or other clinical signs of organic disease. BMS is typically characterized by a continuous, spontaneous, and often intense burning sensation as if the mouth or tongue were scalded or on fire.

Burning mouth syndrome is a relatively common condition. The estimated prevalence of BMS reported in recent studies ranges between 0.7 and 4.6% of the general population. About 1.3 million American adults, mostly women in the postmenopausal period, are afflicted with BMS. The etiology of this disorder is poorly understood even though new evidence for a possible neuropathic pathogenesis of idiopathic BMS is emerging.

Burning mouth syndrome may present as an idiopathic condition (primary BMS type) distinct from the symptom of oral burning that can potentially arise from various local or systemic abnormalities (secondary BMS type), including nutritional deficiencies, hormonal changes associated with menopause, local oral infections, denture-related lesions, xerostomia, hypersensitivity reactions, medications, and systemic diseases including diabetes mellitus. In more than a third of patients, multiple, concurrent causes of BMS may be identified. It is important to note that the diagnosis of BMS should be established only after all other possible causes have been ruled out. Professional delay in diagnosing, referring, and appropriately managing of BMS patients occurs frequently. Treatment should be tailored to each patient and it is recommended to practice the treatment in a multidisciplinary facility.

This article discusses our current understanding of the etiology and pathogenesis of BMS. The authors have tried to emphasize new pharmacological approaches to manage this challenging disorder.

**Key Words:** burning mouth syndrome, stomatodynia, oral dysesthesia

According to classification system initiated by the International Association for the Study of Pain, with additional data supported by the International Headache Society and the American Academy of Orofacial Pain, the term “burning mouth syndrome” (BMS) is a category of non-neuropathic orofacial pain with an intraoral localization.1-4 “Burning mouth syndrome” refers to a chronic orofacial pain disorder usually unaccompanied by mucosal lesions or other clinical signs of organic disease.5-8 BMS is a relatively common condition. About 1.3 million American adults, mostly postmenopausal women, are affected by BMS.5-9 It seems to be a condition that affects people of all races and all socioeconomic backgrounds.

The etiology of this disorder remains poorly understood despite emerging evidence for a possible neuro-
pathic pathogenesis of idiopathic BMS. The syndrome has been termed by various names, including stomatodynia, stomatopyrosis, and oral dysesthesia. Symptoms include: oral burning pain, thirst, dry mouth, dysgeusia (persistent altered taste perception), irritability, changes in eating habits, depression, and a decreased desire to socialize. The pain is described as constant and not “triggered” in nature. Various oral sites may be affected, including the lips, palate, and tongue. The tongue is found to be the most common site for the burning sensations in the oral cavity. It is accepted at present to characterize BMS by both positive (burning pain, dysgeusia, and dysesthesia) and negative (loss of taste and paraesthesia) sensory symptoms.

Burning mouth syndrome has no specific histological features, and diagnosis should be limited to patients with an apparently normal oral mucosa. BMS, therefore, presents as an idiopathic condition distinct from the symptom of oral burning that can potentially arise from various local or systemic abnormalities, including nutritional deficiencies, hormonal changes associated with menopause, local oral infections, denture-related lesions, xerostomia, hypersensitivity reactions, medications, and systemic diseases including diabetes mellitus. It is important to note that the diagnosis of BMS should be established only after all other possible causes have been ruled out.

**EPIDEMIOLOGY**

Burning mouth syndrome is typically characterized by a continuous, spontaneous, and often intense burning sensation as if the mouth or tongue were scalded or on fire. BMS affects women seven times more frequently than men. It most commonly affects a population of postmenopausal women, in which it may be very disabling. The mean age of BMS patients is between 55 and 60 years, with rare occurrence under age of 30s, and has not been reported in children. The average duration of BMS is 2 to 3 years. Long-lived symptoms, lasting from months to up to 18 years, were noted only in rare cases. Various studies have investigated the incidence and prevalence of BMS; however, few studies have compared random samples of healthy patients that represent the entire population.

Locker and Grushka conducted a mail survey of more than 1000 Canadians. Among the 594 respondents, 4.5% reported a burning mouth sensation in the last month. Follow-up by telephone revealed that only 35% of these had symptoms, which were diagnosed as BMS. According to that calculation, the prevalence rate is of 1.5%, of which 75% are women with a median age of 50 years. In 1989, the National Institute of Dental Research and National Center for Health Statistics performed a survey of adults to determine the magnitude and distribution of orofacial pain symptoms, including burning mouth. The survey was conducted by trained interviewers and included 45,711 households, with a 92% response rate. Of these respondents, 0.8% reported having experienced prolonged oral, burning sensations at least once during the previous 6 months. Sixty-nine percent of these people reported that the symptoms were intermittent rather than continuous. The study concluded that 0.71% of the study population reported some pattern of oral, burning pain. This included 0.8% of the female population and 0.6% of the male population, with a female/male ratio of 1.33. No conclusions concerning a diagnosis of BMS prevalence can be made because the survey did not include any physical assessment. However, the prevalence appears to be lower than that reported by Locker and Grushka.

Other investigators have reported different prevalence rates for BMS in selected populations. In Finland, the prevalence was about 7%. Women were more commonly affected than men. When patients were asked about burning sensation at other body sites, they also frequently report burning in the anogenital region. The estimated prevalence of BMS reported in the recent studies ranges between 0.7% and 4.6% of the general population. Such variability of data of these various studies reflects the lack of accurate diagnostic criteria for BMS, with studies often including all patients with oral burning symptoms. At present the importance of this information is not clear, but BMS may be a systemic disorder.

**CLASSIFICATION OF THE BMS TYPES AND SUBTYPES**

According to associated etiologies, BMS may be divided into primary and secondary types. Primary type includes idiopathic, non-neuropathic BMS. Burning mouth sensations (formerly, secondary BMS) are associated with established organic/therapeutic-related etiologies (e.g., oral cavity disorders, including oral local neuropathy, systemic disorders, nutritional deficiencies, drug-induced, neurological and psychiatric abnormalities). Burning mouth sensations are symptoms of these alterations and nowadays, according to available literature, do not represent a distinct type of BMS. The latter starts with a differential diagnosis based on the exclusion of...
Burning Mouth Syndrome

Both other orofacial chronic pain conditions and painful oral diseases exhibiting mucosal lesions. However, the occurrence of overlapping/overwhelming oral mucosal pathologies, such as infections, may cause difficulties in the diagnosis (“complicated BMS”).

Burning mouth syndrome has been divided into three subtypes based on the daily variation of the symptoms. Type 1 BMS (relative frequency: 35%) refers to complaints of burning pain every day, that is not present on awakening but develops as the day progresses, being maximal in the evenings. Type 2 BMS (relative frequency: 55%) constant burning pain is present all day, every day. The patients with Type 2 BMS tend to be most resistant to therapy. Type 3 BMS (relative frequency: 10%) pain is present intermittently on some days with pain-free intervals and affects unusual sites, such as buccal mucosa, the floor of the mouth, and the throat.

Nonpsychiatric factors have been linked with Type 1 BMS, psychiatric factors, especially chronic anxiety with Type 2, and food additives or flavoring allergies with Type 3 BMS. Patients with Type 3 BMS are considered psychologically normal.

ETIOLOGY AND PATHOGENESIS

It is not surprisingly that, like many types of chronic pain, BMS can have multiple causes. The etiology of BMS can be divided into the four main categories: (1) local oral, (2) systemic, (3) psychogenic, and (4) idiopathic disorders. In more than a third of the patients, multiple, concurrent causes of BMS may be identified.

Local Oral Category

Denture design faults may account for complaints of oral burning. Denture-bearing areas of the oral mucosa are subjected to extreme stress and assume the role of periodontal membrane on transferring forces to the underlying bone. A study of 33 patients with BMS found an error in denture design to be the cause of the burning symptoms in 50% of the patients. However, replacing the dentures did not always provide a solution. Another study found that replacing the dentures cured the burning symptoms in only 25% of the patients.

High residual monomer levels in acrylic denture bases have been suggested as a cause of oral burning; however, most studies have not found an allergic reaction to acrylic denture to be an important cause of BMS. Similarly, galvanic currents were thought to cause oral burning, but controlled studies did not agree with this theory.

Parafunctional activity leads to excessive occlusal loading and is probably quite common. Patients who grind and clench their teeth frequently thrust their tongue against their teeth and this can lead to BMS. This habit may be unconscious. It may also be related to anxiety or increased muscle activity.

Salivary gland dysfunction has been suggested as a cause of BMS. Many patients with BMS complain of xerostomia (dry mouth). It is a frequent complaint among BMS patients and can be found in up to 25% of patients with these complaints. In addition, many of the medications used to treat psychiatric disease can cause xerostomia and exacerbate BMS.

It is not clear if salivary gland function is decreased with age. BMS is most common in postmenopausal women, but data demonstrating a reduction in salivary flow are controversial.

One study demonstrated a reduction in postmenopausal parotid flow rate (resting and stimulated); another study found no differences in resting saliva in postmenopausal patients with burning tongues and those without. Yet, another study investigated resting and stimulated whole saliva and parotid saliva in pre- and postmenopausal women and in men with BMS and matched controls. Women with BMS had slightly, but not significantly, higher flow rates than their controls. The total protein concentration in stimulated saliva of women with BMS was significantly lower than that of controls. This difference was not associated with the flow rate. The proportional amount of sialic acid, used as an indicator of mucin concentration, was higher in subjects with BMS than in their controls.

There are also studies on the oral microflora of patients with BMS. Approximately 40% of the healthy population has Candida species intraorally. A higher prevalence of Candida species and coliforms are noted in BMS patients than controls; most frequently found
are Candida albicans, Enterobacter, and Klebsiella.\textsuperscript{59} One study demonstrated that 5\% of patients had prolonged improvement following antifungal therapy and eradication of Candida.\textsuperscript{16} Unfortunately, treating the BMS patient with antifungal therapy is usually not beneficial in alleviating the symptoms.

Even though allergy to dental resin is rare, contact allergy has been suggested as an etiological factor in BMS. Helton and Storrs investigated eight patients with BMS to determine whether contact urticaria, allergic contact dermatitis, or pressure urticaria played a role in the symptoms.\textsuperscript{60} Contact urticaria and patch testing with control substances was performed with a panel of 25 potential denture allergens. No patient had a positive urticarial reaction to the potential dental allergens. Two patients with nonimmunologic urticaria to cinnamic aldehyde improved with avoidance. All patch tests were negative. In the six patients tested for pressure urticaria, the results were negative. The authors concluded that contact dermatitis, contact urticaria, and pressure urticaria were not a cause of the BMS in the denture-wearing patient who has a normal-appearing mucosa. Similarly, Virgili et al. studied the role of contact hypersensitivity.\textsuperscript{61} Patch tests were performed on 15 patients with BMS. The same tests were carried out on 12 healthy age- and sex-matched controls. No association could be found between positive reaction during patch testing, exposure to allergens, and BMS.

In contrast, Dutree Meulenberg et al. studied 22 patients with BMS and found folate, iron and pyridoxine deficiency, and Candida infections.\textsuperscript{62} However, correction of the deficiency or treatment of the infection was of no benefit. Contact allergy to allergens used in the production of acrylate-based dentures was observed in six (27\%) of the cases (all wore a denture); positive reactions were seen to N,N\textsubscript{2}-dimethyl-4-toluidine (three cases), to 4-tolyldiethanolamine (two cases), to benzoylperoxide (two cases), and to oligotriacrylate (one case). In six cases (27\%), a possible relevant sensitization was seen to dental metals and in particular to gold chloride (four cases). The authors concluded that a possible role of local hypersensitivity reactions to denture or dental components as etiologic factors in BMS must be considered.

Patients with Type 3 BMS constitute a subgroup in which either emotional instability (approximately 50\%) or food allergies (approximately 50\%) appear to be of major etiological significance.\textsuperscript{63} Other materials have been associated with BMS by being allergenic in particular individuals. These include: sorbic acid, nicotinic acid esters, epoxy resin, gold, pyrethroid (an insecticide), palladium, octyl gallate (an antioxidant), benzoyl peroxide, peanut extract, cinnamon aldehyde, and nickel sulfate.\textsuperscript{64}

The oral mucosa is extensively innervated by nociceptive, polymodal, mechanoreceptive, thermosensitive, and chemosensitive sensory fibers to provide a wealth of sensory information about material entering the mouth, and for sensory components of oral functions and reflexes. When local oral neuropathy related to oral sensorial complaints is considered, recent studies have hypothesized that the pain of BMS may be neuropathic in origin and originates both centrally and peripherally (eg, a trigeminal small fiber neuropathy).\textsuperscript{10,11,65,66} Possibly, a comprehensive mechanism for BMS is based on a regional small fiber idiopathic neuropathy, which affects oral sensation and salivary secretion and expresses itself by specific complaints of BMS. Alternatively, a primary idiopathic salivary dysfunction might cause sensory neural dysfunction at the receptor level by changing the oral cavity milieu.\textsuperscript{10,11} These findings are very significant, both to the biological background of BMS complaints and to the possible therapeutic modalities that might be offered to suffering patients.\textsuperscript{11}

Various systemic medical problems are associated with BMS. Most investigators have not found any consistent specific medical conditions that are linked to BMS. Because of rapid cell turnover and trauma, the oral cavity is especially sensitive to nutritional deficiencies and may be the first indicator of such a problem. Deficiency in various trace elements and vitamins can lead to complaints of oral mucosal burning. These include sideropenia, iron-deficiency anemia, folic acid deficiency, zinc deficiency, and pernicious anemia.\textsuperscript{54,67-69} Nutritional deficiencies have been claimed to cause BMS in as few as 2\%\textsuperscript{70} and as many as 33\%\textsuperscript{69} of patients. In addition, BMS has been linked to nutritional deficiencies of vitamins B1, B2, B6, B12, zinc, and folic acid.\textsuperscript{16,71} However, this does not mean that most patients with BMS suffer from deficiency states. In fact, many other studies have not found a high prevalence of nutritional deficiency in patients with BMS.\textsuperscript{70,72,73}

The reported response to replacement therapy is variable. One study demonstrated that replacement therapy of vitamins B1, B2, and B6 produced resolution of symptoms in 30\% of patients with deficiencies.\textsuperscript{16} A different study reported replacement therapy was no more effective than placebo.\textsuperscript{74} In contrast, other authors have reported better response to replacement therapy. Basker et al. reported that 33\% of those responding to replace-
ment therapy suffered from B12 or folic acid deficiency.\textsuperscript{65} The authors thought, based on the response to replacement therapy, that this is the sole cause for BMS. In a later study, 40\% of 37 patients were found to have deficiencies of iron, B12 or folic acid.\textsuperscript{66} Similarly, the authors of that study thought that the cause for BMS was related to those deficiencies.

As to drug-related effects, the ACE inhibitors (e.g., enalapril, captopril, and lisinopril) can cause scalded mouth or BMS. There is improvement with reduction or discontinuation of these medications.\textsuperscript{75}

The link of diabetes mellitus to oral complaints was reported as early as 1942.\textsuperscript{76} In one study that investigated 43 previously undiagnosed noninsulin-dependent diabetics, 16 had BMS, and all resolved following therapy.\textsuperscript{77} Similar results have been noted in other studies.\textsuperscript{16} When studying the relationship between BMS and diabetes mellitus, BMS was found in 2\% to 10\% of patients.\textsuperscript{16,40,68,70,72} All the BMS patients need to have fasting blood glucose levels tested in order to exclude diabetes mellitus. Patients with abnormal findings should be referred for management and education.

Proposed mechanisms behind BMS in patients with diabetes mellitus have been related to metabolic alterations in oral mucosa, diabetic neuropathy, and angiopathy. Xerostomia and oral candidiasis may also contribute to the problem. Control of diabetes mellitus may lead to improvement or cure of BMS.

The majority of patients with BMS are postmenopausal women. Most of the available literature on BMS finds that this condition is more common in women than men with a ratio of 7 to 1.\textsuperscript{40} The onset in women usually occurs within 3 to 12 years after menopause, and is higher in women who have more systemic diseases.\textsuperscript{18} It has been claimed that the lack of estrogen produces atrophic changes in the oral and vaginal epithelium that cause the symptoms of BMS.\textsuperscript{78} Some studies have not demonstrated a substantial reduction of oral symptoms after the initiation of estrogen replacement therapy.\textsuperscript{75} In contrast, several have reported reduced oral symptoms, including mouth burning.\textsuperscript{73,79,80}

Forabosco et al. evaluated the efficacy of hormone replacement therapy (HRT) in 27 postmenopausal patients age 48 to 58 years with BMS, and in 47 postmenopausal women with no oral discomfort.\textsuperscript{79} Patients were treated with conjugated estrogens for 21 days and medroxyprogesterone acetate from day 12 through day 21. HRT had no effect on oral cytology in the 40 symptom-free, postmenopausal women compared with a group of 47 postmenopausal women who had no oral symptoms and were not under treatment. HRT relieved symptoms and improved oral cytohormonal features in 15 of 27 patients with symptoms. Nuclear estrogen receptors were found by immunohistochemical assay in eight of 10 randomly selected patients with symptoms who responded to HRT, but not in two patients who did not benefit from HRT. Estrogen receptors were also found in six of 10 fertile women with no oral disease. The authors concluded that oral discomfort may be related to steroid hormone withdrawal only in some postmenopausal women, and that replacement therapy may improve the clinical picture and cytohormonal features in this group of patients. In addition, immunohistochemical identification of estrogen receptors was thought to be useful in identifying patients for whom HRT might be advantageous.

Santoro et al. evaluated the effectiveness of the estrogen-progestin replacement therapy in postmenopausal women suffering from idiopathic BMS. A total of 28 patients suffering from persistent burning and painful oral sensation underwent careful clinical and laboratory examinations in order to distinguish primary form of BMS from a secondary one. Patients suffering from primary BMS underwent to incisional biopsy for the research of estrogens receptors. It was concluded that in postmenopausal patients suffering from idiopathic BMS, good results may be obtained by an estrogen-progestin replacement therapy with a considerable reduction if not a disappearance of the burning symptomatology in most of them.\textsuperscript{80}

Different psychiatric or psychological disorders are of importance in BMS, including fear of cancer,\textsuperscript{81} depression,\textsuperscript{78} personality disorders,\textsuperscript{15} and chronic anxiety.\textsuperscript{15} A psychiatric disease association has been reported in many series ranging from 19\% to 85\%.\textsuperscript{13,16,28,36,38,40,43,44,63,82,83} At least one-third of the patients may have an underlying psychiatric diagnosis, most commonly depression or anxiety disorders,\textsuperscript{26} especially Type 2 BMS. Emotional instability is present in approximately 50\% of Type 3 BMS patients.\textsuperscript{63} Such patients might react quickly to a stressful situation by developing symptoms of BMS that resolve when the situation normalizes.

Various investigators have studied the personality characteristics of patients with BMS. The personality characteristics of 32 patients with BMS who have undergone treatment of underlying medical and odontologic diseases were compared with a sex- and age-matched control group.\textsuperscript{84} After evaluation of burning mouth symptoms, the personality, psychological func-
tioning, and the quality of life were determined by using four scales, the Karolinska Scales of Personality, another personality scale, psychological functioning scale, and quality of life scale. The results showed that, when compared to a control group, the patients with BMS had a significantly lower score in the socialization scale and significantly higher scores in the somatic anxiety, muscular tension, and psychasthenia scales. Furthermore, the patients with BMS were significantly more easily fatigued and more sensitive and showed a tendency to be more concerned about their health. With regard to the psychological functioning, the BMS patients had significantly more difficulty taking initiative, became dizzy more easily, and had more sad thoughts. These differences in personality and psychological functioning suggest that the burning sensations are psychosomatic symptoms. The investigators recommended that patients with BMS undergo psychological investigation and treatment when warranted.

Trombelli et al. studied 33 patients with BMS. Psychological factors were present in 67% of the patients. Anxiety was the most common disorder and the most difficult to treat. A remission or resolution of oral symptoms following reassurance as to the benign nature of BMS was found in 24% of the patients. These results suggest an association between oral complaints and personality disturbances. However, whether the psychogenic disorder was causative or whether it was a result of the burning sensation was not clear.

Although BMS may be a somatic symptom of depression in some cases, the association does not always correlate with a causal relationship. Depression and psychological disorders are common in chronic pain population and may be secondary to chronic pain rather than the cause of BMS. Paterson et al. investigated 84 patients with BMS, who were asked to complete a hospital anxiety-and-depression-scale questionnaire. A control group of 69 patients was also included. All patients were interviewed with regard to parafunctional habits and were subjectively examined for signs of occlusal wear of the natural teeth or dentures. The results demonstrated that parafunctional habits were present in 61% of patients with BMS. In addition, a relationship was demonstrated between parafunctional habits and anxiety but not depression.

Psychological intervention can be of benefit in patients with BMS. Bergdahl et al. used cognitive therapy to treat patients with BMS. Thirty patients with resistant BMS after odontological and medical treatment were randomly divided into two equal groups; one was treated with cognitive therapy and a placebo group served as a control. The intensity of BMS, as estimated by the use of a visual analog scale, was significantly reduced in the cognitive-therapy group directly after therapy was completed and was further reduced at 6-month follow-up. The control group did not show any decrease in intensity of BMS.

Although psychiatric disorders are clearly significant for some patients with BMS, it is important not to leap to the conclusion that all BMS is caused by psychiatric problems. Unfortunately, psychiatric causes are frequently postulated when no “easy answer” is apparent. Each patient with BMS should receive a careful evaluation for both psychiatric and organic causes of pain. This thorough examination may unveil a local or systemic cause for their complaints and may often have therapeutic solution.

According to comprehensive research data and the authors’ personal experience, a multidisciplinary approach is very important, including neurological and psychological assessments. BMS is commonly considered to be idiopathic if no underlying cause for the condition is found.

EVALUATION AND MANAGEMENT

When approaching a patient with BMS, a thorough diagnostic approach is suggested. Treatment of secondary BMS is aimed at correcting the underlying condition. The history should include a review of major illnesses, systemic diseases, and medication usage. Special interest should be given to conditions related to BMS. A review of the patient’s complaint should focus on onset, duration, anatomic location, association with certain food or activities, and interference with daily activities such as work, sleep, and eating. It is important to inquire about parafunctional habits such as tongue thrusting or tooth clenching. However, it can be difficult to break these habits.

Physical examination should screen for soft-tissue lesions, damaged mucosa, or signs of irritation. Deficient salivary gland function and signs of tooth wear are also important. Assessment of denture status is likewise important. Qualified personnel should treat any problems such as restricted tongue space, underextended denture bases, or lack of free-way space.

Advice on denture hygiene may be warranted. In some patients, it is worthwhile to measure the stimulated parotid flow rate with a Carlsson-Crittenden cup and stimulated citric acid. Flow of less than 0.7 mL/min is low and may warrant saliva substitutes. Citric acid
mouthwash or pilocarpine can be used to stimulate salivary flow. Xerostomia can cause oral burning. It is a common side effect of many medications. Screenby and Schwartz have published a reference guide of xerostomia-inducing drugs. It is often possible to replace a drug with a similar medication that has less xerostomic side effects.

In patients with Type 3 BMS who are psychologically normal, patch testing is warranted. If an allergen is identified, avoidance will resolve the complaint. It is important to clarify to the patient that patch testing and resolution, following avoidance of the allergen, take several months.

It is justified to rule out oral Candida infection that may relate to BMS. Laboratory studies may include an assay of hemoglobin, ferritin, vitamin B12, and folic acid. Detected nutritional deficiencies need to be evaluated as to the cause prior to supplementation. An assay of vitamin B1, and vitamin B6 may also be performed; however, this may not be as readily available. Alternatively, empiric treatment with vitamin B1 and vitamin B6 for several weeks is acceptable. Lamey recommends empiric replacement of vitamins B1 (300 mg, once a day) and vitamin B6 (50 mg, three times a day) for 4 weeks.

Diabetes mellitus should be ruled out. This may be performed with a fasting glucose level or a glucose tolerance test. Diabetes mellitus may be present in 5% of BMS cases. The patients should be appropriately treated. Control of diabetes mellitus may lead to decrease in BMS. Change of the diabetic medications can sometimes be helpful. Some patients may need oral agents or some may need insulin therapy.

Although clearly a significant link between BMS and postmenopausal age group of women exists and may be tied with menopause, the benefit of HRT in BMS is still controversial. In previously controlled clinical trials with systemic or local estrogen treatment, however, neither was more effective than placebo in the treatment of BMS. Treatment outcomes with HRT have been difficult to interpret because of the failure to distinguish between patients with primary BMS and patients presenting with oral burning sensation resulting from other organic clinical abnormalities (secondary BMS). Further research will be required to determine the efficacy of estrogen replacement therapy in primary (idiopathic) and secondary (organic) BMS, and to attitude the cohort of patients most likely to benefit from HRT treatment.

The patient’s psychological status should be assessed. Particular attention should be paid to anxiety, depression, fear of cancer, and other psychological stressors.

Obviously, it is vital to stress to the patient that he or she does not have cancer and that the condition is benign. Often this has to be mentioned repeatedly.

Certainly, medications are appropriate for the management of BMS, both primary (idiopathic) type and secondary (organic; burning mouth sensations). But it must be said that the management of BMS is still not satisfactory.

Professional delay in diagnosing, referring, and appropriately managing BMS patients occurs frequently. Most BMS patients have consulted multiple dentists, physicians, and other healthcare providers for their complaint and may have tried a host of over-the-counter medications before their presentation without any visible benefit.

In open trials, only antidepressants (tricyclic drugs, and SSRIs (selective serotonin reuptake inhibitors)/SNRIs (serotonin noradrenaline reuptake inhibitors) drugs), benzodiazepines, and anticonvulsants have shown beneficial effects in patients with BMS. Antidepressants are useful for chronic pain disorders, including BMS. Their analgesic effects are largely independent of antidepressant activity. Typical doses include amitriptyline and doxepin, 10 to 75 mg. Low doses of tricyclic antidepressants may have an analgesic affect that is separate from their action as antidepressants. Sedative antidepressants are useful when patients have difficulty sleeping and may help reduce their use of hypnotic medications. Dose may be limited by anticholinergic side effects (dry mouth, constipation, blurred vision, and urinary retention). Unlike the tricyclic antidepressants, trazodone is a useful drug in that it has fewer of these side effects while retaining the sedative properties of the tricyclic antidepressants.

The SSRI antidepressants (eg, Paroxetine) are less sedating and function through the inhibition of reuptake of serotonin. The newer SNRI antidepressant (eg, Duloxetine) functions through the combined inhibition of reuptake of serotonin and norepinephrine. It was found to be effective against chronic pain of neuropathic origin. SSRIs/SNRIs antidepressants also have fewer side effects than the older tricyclic antidepressants. Further research will be required to determine if these drugs are efficacious in patients with BMS; however, they can certainly benefit the depressed patient with BMS.

Use of benzodiazepines, including systemic and local clonazepam, has been reported to be effective in BMS. Grushka has used systemic clon-
Burning mouth syndrome is a treatable syndrome. Our knowledge of BMS has increased over the last few years. Careful patient analysis and care should enable us to better help patients with BMS based on sound scientific principals. Efforts should be directed toward different pathogenetic mechanisms, including the possible neuropathic origin of BMS.

Burning mouth syndrome is a treatable syndrome. Considering BMS as a form of local oral neuropathy, the authors propose some new pharmacological approaches, which include the use of local anesthetic through a systemic route of administration (mexiletine in doses of up to 10 mg/kg) and use of newer SNRI antidepressant, Duloxetine (Cymbalta; Eli Lilly), 30–60 mg/day with slow titration. These results also support the hypothesis of BMS as “neuropathic-related” in origin. Controlled studies are required to determine the efficacy of these treatments.

Gabapentinoids or $\alpha^2\gamma$ subunit VGCC (voltage-gated calcium channels)-ligands, including Gabapentin (Neurontin; Pfizer) and Pegabalin (Lyrica; Pfizer), the new anticonvulsants, have been found to be effective for the treatment of some chronic neuropathic pain conditions. In addition, gabapentinoids have few adverse effects and a low level of addiction. They represent an additional therapeutic option for patients in whom other treatments have failed or are contraindicated.

Apart from that, Gabapentin has been indicated to be effective in low dosages when used in combination with other medications in the treatment of BMS. With increasing evidence that the pain of BMS may be neuropathic in origin and originate both centrally and peripherally, these drugs may be a cure option for patients with stomatodynia, but their effect is still controversial and controlled studies of high methodological quality are needed in order to establish effective forms of treatment for patients suffering from BMS. Finally, a few studies have reported relief of BMS without intervention, but spontaneous remission of pain in BMS suffers has not been definitely demonstrated.

CONCLUSIONS

Our knowledge of BMS has increased over the last few years. Careful patient analysis and care should enable us to better help patients with BMS based on sound scientific principals. Efforts should be directed toward different pathogenetic mechanisms, including the possible neuropathic origin of BMS.

Burning mouth syndrome is a treatable syndrome. Considering BMS as a form of local oral neuropathy, the authors propose some new pharmacological approaches, which include the use of local anesthetic through a systemic route of administration (mexiletine in doses of up to 10 mg/kg) and use of newer SNRI antidepressant, Duloxetine (Cymbalta; Eli Lilly), 30–60 mg/day with slow titration in order to reach maximum decrease of adverse events in patients with BMS. We also propose the continuous use of the gabapentinoid ($\alpha^2\gamma$ subunit VGCC-ligands) group of drugs (Gab-
pentin and Pegabalin) prescribed alone or as an add-on treatment. These drugs suggest an additional therapeutic option for BMS patients in whom other treatments have failed or are contraindicated. In our opinion, these new approaches may enable clinicians to better manage this challenging disorder. Treatment should be individually tailored to each patient and may best be conducted in a multidisciplinary set-up.

New and future developments promise a better quality of life for patients with BMS. Emphasis must be placed, therefore, upon educational efforts in order to improve clinicians’ awareness of BMS. This should increase attentiveness for the appropriate referral to pain centers for patients with chronic orofacial pain because of BMS.

REFERENCES


