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Evidence of chorda tympani dysfunction in patients with burning mouth syndrome

Eli Eliav, DMD, PhD; Batya Kamran, DMD; Rachel Schaham, DMD; Rakefet Czerninski, DMD; Richard H. Gracely, PhD; Rafael Benoliel, BDS

Burning mouth syndrome (BMS)—also known as stomatodynia, oral dysesthesia or stomatopyrosis—is an intra-oral disorder characterized by a burning mucosal pain without major visible signs typically of spontaneous onset. The condition is most prevalent in post-menopausal women. Reported prevalence rates in general populations vary from 0.7 to 15 percent.¹⁻³ More than one site usually is involved; the anterior two-thirds of the tongue is the most frequently affected site, followed by the hard palate, lips and gingivae.⁴⁻⁸

BURNING MOUTH SYNDROME

True BMS is a chronic pain syndrome that cannot be attributed to any systemic or local cause, lasting from months to several years.^{3,5,7,9,10} Pain can be as severe as a toothache, though pain quality differs. The pain has been described as burning and not sharp or pulsating.⁴ More than two-thirds of patients complain of altered taste sensation (dysgeusia)

ABSTRACT



Background. More than two-thirds of patients with burning mouth syndrome (BMS) have altered taste sensation. The authors conducted a study to assess chorda tympani and trigeminal nerve function in these patients.

Methods. The study was composed of 48 patients; 22 were diagnosed as having BMS, 14 had burning symptoms related to other diseases and were diagnosed as having secondary burning mouth syndrome (SBMS), and 12 were healthy volunteers. The authors evaluated the electrical detection thresholds of the infraorbital and mental nerves and the electrical taste and electrical detection/tingling thresholds in the anterior two-thirds of the tongue for all patients. Electrical taste threshold is thought to be dictated by chorda tympani nerve function while electrical detection/tingling thresholds are regulated by trigeminal nerve function.

Results. The mean electrical taste/tingling detection thresholds ratio and the taste detection thresholds were significantly higher in patients with BMS than in patients with SBMS and in control subjects, indicating chorda tympani nerve dysfunction. Eighteen (82 percent) of the 22 patients with BMS demonstrated chorda tympani dysfunction (13 unilateral and five bilateral).

Conclusions. Chorda tympani hypofunction may play an important role in BMS pathology. Unilateral hypofunction may be sufficient to produce generalized burning sensation exceeding the affected nerve area.

Clinical Implications. Elevated taste detection threshold levels determined via electrogustatory testing and an elevated taste/tingling detection thresholds ratio may assist clinicians in the diagnosis of BMS. More studies are needed to validate these findings.

Key Words. Burning mouth syndrome; dysgeusia; quantitative sensory testing; chorda tympani.

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accompanying the burning sensation; in many cases, the alteration is described as a spontaneous metallic taste.¹¹⁻¹⁴

Although some patients with BMS exhibit evidence of anxiety, depression and personality disorders, it is unclear if the pain led to the psychological disorder or vice versa.¹⁵⁻¹⁹

Secondary burning mouth syndrome.

Alternatively, oral and perioral burning can be a symptom of local factors (such as dentures) or systemic and local diseases; in such cases, the condition can be considered to be secondary burning mouth syndrome (SBMS), not primary BMS.²⁰ Local factors and diseases known to induce SBMS include oral candidiasis, galvanism, dermatologic diseases (such as lichen planus), allergies, hyposalivation and xerostomia. Systemic disorders known to induce SBMS include hormonal changes, nutritional abnormalities such as vitamin B₁₂, folic acid or iron deficiencies, diabetes mellitus and emotional stress, as well as the use of drugs (directly or indirectly).^{1,2,4,7,11,21-26} Successful treatment aimed at the primary disease usually will alleviate the burning sensation in patients with SBMS.

In contrast, clinicians diagnose patients as having BMS if they experience chronic oral and perioral burning pain not accompanied by any of the above. To date, there are no universally accepted inclusion criteria for BMS, and the diagnosis depends on the reported presence of chronic oral and perioral pain and the exclusion of disorders and diseases that may induce chronic oral and perioral pain.

Treating BMS. Treatment options for patients with BMS are limited and, in many cases, insufficient. Several authors have reported pain reduction after treatment with the benzodiazepines chlordiazepoxide and diazepam,²⁷⁻³⁰ a low dosage of tricyclic antidepressants,^{31,32} selective serotonin reuptake inhibitors³³ or lipoic acid.³⁴

Inconclusive study results. The results of previous studies applying sensory assessment in patients with BMS have been inconclusive. Mechanical detection threshold, two-point discrimination test results and thermal detection threshold were similar in patients with BMS and in healthy volunteers.^{35,36} Grushka and colleagues³⁵ reported that thermal pain tolerance was significantly lower in patients with BMS. Svensson and colleagues³⁷ found that pain and detection thresholds to argon laser stimuli were significantly higher in patients with BMS and the

ratios between pain and sensory thresholds were significantly lower in these patients in all examined oral regions. These results suggest a perceptual deficit unrelated to the painful site. A neuropathic etiology was suggested by findings of an altered blink reflex and/or thermal hypoesthesia in 89 percent of patients with BMS.^{38,39} Grushka and Sessle¹² reported a higher sweet taste detection threshold in patients with BMS, suggesting an altered taste sensation. Application of dyclonine (a local anesthetic solution) on patients' tongues reduced phantom dysgeusia but did not reduce the burning sensation; moreover, in 40 percent of cases, the pain was aggravated.^{40,41}

On the basis of accumulated data, Bartoshuk and colleagues¹⁴ and Grushka and colleagues¹⁷ suggested an interesting hypothesis supporting the general concept that BMS is a neuropathic pain syndrome. Taste sensation of the anterior two-thirds of the tongue is supplied by the chorda tympani nerve, a branch of the facial nerve. Other sensory modalities, such as mechanical and thermal sensations, are supplied by the lingual nerve, a branch of the mandibular division of the trigeminal nerve. Inhibitory influences between the two systems are thought to maintain a "sensory balance" in the tongue.^{14,17} Hypothetically, chorda tympani dysfunction can disrupt the equilibrium with the lingual nerve, leading to lingual nerve hyperfunction and a burning sensation.

The purpose of this study was to assess chorda tympani and lingual nerve function using electrical taste and electrical detection (tingling) thresholds in patients with BMS and SBMS, as well as in asymptomatic patients.

PATIENTS AND METHODS

We included in the study patients who were referred to the departments of Oral Medicine, Hadassah University Medical Center, Jerusalem, and Oral and Maxillofacial Surgery, Barzilai Medical Center, Ashkelon, Israel. The attending dentist (E.E.) asked patients with a major complaint of oral and/or perioral burning sensation of at least three months' duration to participate in the study. The patients underwent the sensory evaluation before receiving a final diagnosis and before undergoing any treatment. One of us

ABBREVIATION KEY. **BMS:** Burning mouth syndrome. **ION:** Infraorbital nerve. **MN:** Mental nerve. **SBMS:** Secondary burning mouth syndrome.

(B.K.) performed a routine evaluation that included a dental and an intraoral examination, a complete blood cell count and determination of serum levels of B₁₂, folic acid, iron, glucose and autoantibodies. Patients with local or systemic factors known to induce a burning sensation were diagnosed as having SBMS, whereas an absence of these factors pointed to the diagnosis of BMS.

For the electrical detection threshold, continuous trains of constant current electrical stimuli were delivered to the skin or mucosa through 8-millimeter diameter spherical gold-plated electrodes spaced 20 mm apart. The stimulus frequency was 200 hertz with a 50 percent duty cycle. The electrical stimulator randomized the polarity of the electrodes.

We assessed the electrical detection and taste thresholds via an ascending method of limits. The operator increased the stimulating current at a fixed rate until the subject indicated that he or she detected the current. We evaluated three detection thresholds for each location and calculated the mean threshold, which we used for data analysis.

We assessed the infraorbital nerve (ION) and the mental nerve (MN) bilaterally for electrical detection thresholds. We assessed the left and right anterior two-thirds of the tongue for electrical taste and electrical detection (tingling or itch sensation) thresholds.

We compared the detection thresholds between the three groups via an overall analysis of variance followed by a pairwise comparison relative to the control subjects using Fisher's probable least-squares difference (PLSD) and planned paired *t* tests between the nerves. We computed the electrical taste and electrical detection (tingling) ratio and compared it between the groups via an overall analysis of variance followed by a pairwise comparison with the control subjects using Fisher's PLSD. We used paired *t* tests to analyze differences between the left and right sides within patients. We considered the taste/tingling ratios to be normal when they were within the 95 percent confidence intervals (CIs) calculated from the control group. Values lying below or above the respective limits indicated hypofunction or hyperfunction, respectively.

The authors assessed the left and right anterior two-thirds of the tongue for electrical taste and electrical detection (tingling) thresholds.

RESULTS

We included 48 patients in this study. Two of us (E.E., R.C.) diagnosed 22 of the patients as having BMS (mean ± standard deviation [SD] age, 61.16 ± 2.93 years; 16 women and six men) and 14 as having SBMS (mean ± SD age, 56.86 ± 3.72 years; 11 women and three men); 12 subjects were healthy volunteers (mean ± SD age, 58.00 ± 4.01 years; 10 women and two men).

Control group. Electrical detection thresholds obtained for the control subjects in the MN and ION areas did not differ significantly and the side-to-side ratio did not differ significantly from an expected mean of 1 (*P* > .05). For these values, we

calculated 95 percent CIs. (For the ION, the mean side-to-side ratio = 1.034 and CI = 0.954 to 1.114; for the MN, the mean ratio = 0.970 and CI = 0.856 to 1.068, demonstrating a high degree of consistency in the data.) The electrical taste threshold for the right and left sides of the tongue was at least 15 percent lower than the tingling detection threshold in 11 (92 percent) of the 12 control

subjects. Only one subject had an electrical taste threshold (left side) that was higher than the tingling detection threshold. The mean taste/tingling ratio (0.602; CI = 0.224 to 0.980) did not differ significantly between the right (0.571; CI = 0.180 to 0.962) and left (0.646; CI = 0.208 to 1.084) sides.

BMS and SBMS groups. We detected no significant differences in electrical detection thresholds between the groups in either the ION or MN areas (mean [± SD] BMS MN: 20.04 ± 3.28 microamperes; BMS ION: 16.36 ± 1.77 μA; SBMS MN: 21.94 ± 5.67 μA; SBMS ION: 18.03 ± 2.60 μA; control group MN: 18.54 ± 2.44 μA; control group ION: 21.00 ± 3.40 μA).

The mean (± SD) taste threshold (Figure 1) in the BMS group was significantly elevated (146.558 ± 33.353 μA) compared with that in the SBMS group (63.727 ± 15.795 μA; *P* = .036) and the control group (31.988 ± 5.053 μA; *P* = .007).

The mean (± SD) electrical taste and tingling detection thresholds ratio (Figure 2) was significantly higher in patients with BMS (1.373 ± 0.154 μA) compared with that in patients with SBMS (0.617 ± 0.087 μA, *P* < .001) and control subjects (0.602 ± 0.087 μA; *P* < .001).

We found taste hypofunction on at least one

side (taste/tingling detection thresholds ratio exceeded the 95 percent CI for the healthy control subjects) in 18 (82 percent) of the 22 patients with BMS (seven left side, six right side and five bilateral) and in four (29 percent) of the 14 patients with SBMS (two left side, two right side, 0 bilateral).

DISCUSSION

The most prominent feature of this study is the chorda tympani nerve dysfunction in patients with BMS. We believe that clinicians may be able to use an elevated taste/tingling ratio to support a diagnosis of BMS.

The method we used to assess chorda tympani function—the electrical taste detection threshold (via the electrogustatory test)—is well-established as a clinical tool.⁴²⁻⁴⁵ Typical sensations evoked by stimulating the anterior two-thirds of the tongue are sour and “metallic” taste, conducted by the chorda tympani nerve, or tingling, conducted by the lingual nerve.⁴⁶ However, this testing method has a number of limitations that we need to take into account. The mechanism involved in stimulating electrical taste is complex. In addition to the direct nerve fiber activation, pH changes induced by the electrical current may contribute to the taste sensation. The electrical current causes hydrogen ion discharge from the anode, leading to a reduction in the pH of adjacent saliva, and the acidic saliva activates ionic receptors, which trigger the perception of sour taste.^{47,48} Hence, hyposalivation or variations in saliva composition may alter electrical taste thresholds. Moreover, electrode size, composition and material and distance between the electrodes also may affect electrical taste.^{49,50} All of the above can contribute to unpredictability and inconsistency in the testing results.

To minimize intersubject variability with regard to electrical detection thresholds, previous studies expressed results as a ratio for each tested area (that is, the electrical detection threshold of the affected side divided by the electrical detection threshold of the contralateral side).⁵¹⁻⁵⁴

Use of side-to-side ratios for the tongue is pointless given that BMS and, therefore, the suspected pathology often are bilateral. However, because the anterior two-thirds of the tongue is innervated by two sensory nerves (chorda tympani nerve for taste and lingual nerve for other modalities), the electrical taste/tingling detection

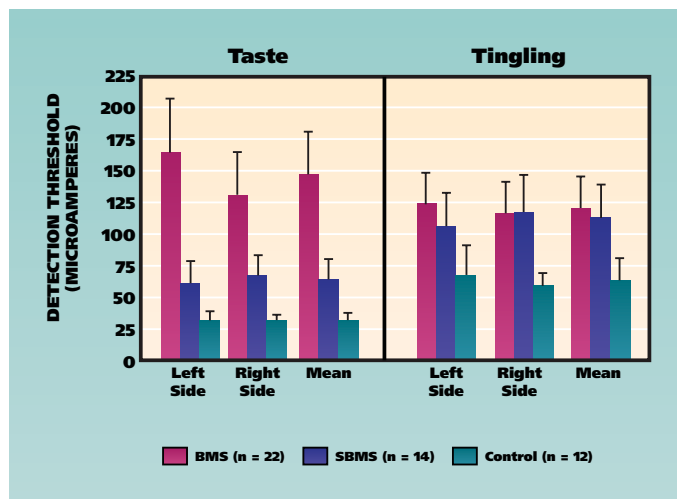


Figure 1. Electrical current was applied bilaterally to the anterior two-thirds of the tongue in patients with burning mouth syndrome (BMS) and secondary burning mouth syndrome (SBMS), as well as in control subjects. The mean taste threshold in the BMS group was elevated significantly compared with that in the SBMS group ($P = .036$) and the control group ($P = .007$). In the SBMS and control groups, the taste detection threshold was significantly lower than the tingling detection threshold.

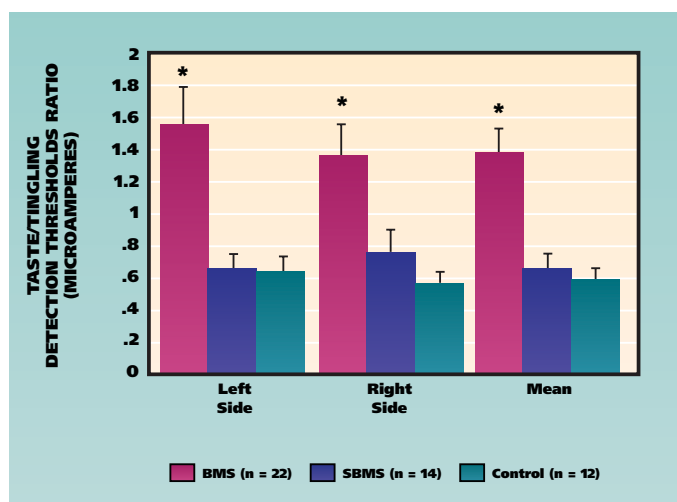


Figure 2. The mean electrical taste/tingling detection thresholds ratio was significantly higher in patients with BMS than in patients with SBMS and in control subjects ($P < .001$). Taste hypofunction on at least one side of the tongue was found in 18 (82 percent) of 22 patients with BMS, four (29 percent) of 14 patients with SBMS and only one (8 percent) of 12 control subjects. Asterisks represent significant differences between patients with BMS and control subjects.

thresholds ratio may be a repeatable and reliable parameter. Therefore, we favor the use of a taste/tingling ratio as a clinical diagnostic tool. The mean taste detection threshold also was significantly elevated in patients with BMS; however, the heterogeneity of the results (range, 6.25-700.00 μ A) makes it an imprecise measure.

Electrical stimulation is not used commonly for sensory assessment, though it offers unique prop-

erties. Unlike other assessment methods that stimulate nerve receptors, electrical stimuli may bypass the receptor to stimulate the primary afferent axon. Owing to this property, electrical stimuli are not affected by changes in receptor sensitivity, such as in sensitization, suppression or receptor fatigue. At sites other than the tongue, altered electrical sensitivity alone indicates processes beyond the receptor level, while altered responses to natural stimuli cannot distinguish between a receptor and processes beyond the receptor level. As mentioned above, the pH changes induced by the electrical current may have affected the taste receptors in the tongue and not only the chorda tympani nerve.

Our findings suggest that unilateral chorda tympani dysfunction, as reflected by an elevated taste/tingling (itch) ratio is sufficient to produce a bilateral burning sensation (13 of the patients with BMS had unilateral dysfunction with bilateral symptoms). The mechanisms can be related to central nervous system processing. Ongoing disruption of equilibrium induced by chorda tympani dysfunction (either unilateral or bilateral) leads to lingual nerve hyperfunction. The continuous input may generate central sensitization leading to pain that spreads beyond the affected nerve distribution. In addition, in approximately 2 centimeters of the tongue tip, the chorda tympani nerve crosses over and innervates the opposite side.⁵⁵ This may explain the high frequency of involvement of the tip of the tongue,^{4,7,11} particularly in the early stages of the disease before the initiation of central sensitization.

CONCLUSION

The results of this study support the hypothesis that BMS is a form of neuropathic pain, which may be related to chorda tympani nerve dysfunction. Elevated taste detection threshold levels (via electrogustatory testing) and an elevated taste/tingling detection thresholds ratio have the potential to assist clinicians in the diagnosis of BMS. However, more studies are needed to confirm these findings. ■

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