

# Research Journal of Pharmaceutical, Biological and Chemical Sciences

## Burning Mouth Syndrome-Retrospective Analysis of 328 Patients.

Vucicevic Boras V<sup>1\*</sup>, Peakic M<sup>2</sup>, Music L<sup>2</sup>, Krpan K<sup>2</sup>, Illes D<sup>3</sup>, and Gabric D<sup>4</sup>.

<sup>1</sup>Department of Oral medicine, School of Dentistry, Gunduliceva 5, University of Zagreb and Clinical Hospital Center Zagreb, Kispaticeva 19, Zagreb, Croatia.

<sup>2</sup>Students of the sixth year at School of Dentistry, University of Zagreb, Croatia.

<sup>3</sup>Department of Prosthodontics, School of Dentistry, Gunduliceva 5, University of Zagreb, Croatia.

<sup>4</sup>Department of Oral surgery, School of Dentistry, Gunduliceva 5, University of Zagreb, Croatia.

### ABSTRACT

Burning mouth syndrome (BMS) is a chronic multifactorial painful condition which primarily affects peril/postmenopausal women. In the published literature there are conflicting data whether local and systemic factors as well as medication intake might contribute to the BMS. The aim of this study was to retrospectively obtain data from the patient charts of 328 BMS patients (270 females and 58 males), median age of the participants was 64 years (age range 17– 88 years) regarding local and systemic disturbances, medication intake and treatment response on the alleviation of oral symptoms. Statistical analysis was performed by use of Chi-square test to assess the differences between categorical variables while Mann Whitney test was used to assess the differences between continuous variables. P values lower than 0.05 were considered significant. Median duration of symptoms was significantly higher in females when compared to males (6 (range 1-180) versus 2 (range 1-54);  $p=0.05$ ). No significant differences in age, chief complaint, site, co morbidities, medication intake, and salivary flow rate and treatment outcome between males and females were found. Follow up data were available for 187 patients. One hundred seventeen patients (62.6%) reported their condition to be unchanged while 70 (37.4%) patients reported improvement compared to the baseline. None of the patients reported complete resolution of the symptoms. It may be concluded that there are no associations between burning mouth syndrome with investigated local and systemic diseases and drug intake as well as tried treatment options such as salivary substitutes, low level laser therapy, chlorhexetidine mouthwash and vitamin B<sub>1</sub>, B<sub>6</sub> and B<sub>12</sub> replacement therapy.

**Keywords:** burning mouth syndrome, vitamins, BMS.

*\*Corresponding author*

**INTRODUCTION**

Burning mouth syndrome (BMS) is probably neuropathic disturbance as opposite to the burning symptoms which might be concomitant to some par functional habits, Candida infection, side effects of drug intake, etc. Despite extensive search in the field, little is known about BMS. Usually, some other symptoms might accompany BMS such as dry mouth and/or altered taste [1]. Quite interestingly, it seems that in some parts of the world, prevalence of burning symptoms is more often than in others. BMS affects more frequently peril/postmenopausal women and tongue is the most commonly affected site. Currently, it is thought that primary burning mouth syndrome reflects neuropathy of the small trigeminal fibers whereas secondary burning mouth syndrome (symptoms) reflects underlying local or systemic pathology. Prevalence of oral burning varies between 0.7%-15percent in the general population [1].

Salivary hypo function has been suggested as one of the main contributory factors for burning mouth syndrome [2]. In the current literature, there are conflicting and not many data regarding relationship between symptoms of dry mouth and oral burning. Some of the systemic conditions such as gastrointestinal and hematological diseases, as well as medication intake have been regarded as a possible cause of oral burning symptoms, albeit with conflicting results. Therefore, the aim of this study was to evaluate local and systemic factors as well as medication intake together with treatment outcome in patients suffering from burning mouth syndrome.

**MATERIALS AND METHODS**

Study was approved by Ethical Committee of the University of Zagreb, Croatia. Retrospective analysis of patient’s charts was performed and burning mouth diagnosis was retrieved. Data were organized in the Excel spreadsheets (Microsoft Excel®, Microsoft Corporation, and U.S.) and coded appropriately for statistical analysis. The statistical analysis was performed by the SPSS® ver.20 software (IBM Corporation, U.S.). Normality of distribution was tested by Smirnov Kolmogoroff test. Chi-square test was used to assess the differences between categorical variables while Mann Whitney test was used to assess the differences between continuous variables. P values lower than 0.05 (p <0.05) were considered as statistically significant.

**RESULTS**

Data were available for 328 patients (270 females and 58 males). Median age of the participant was 64 years (age range 17 – 88 years). Other demographic and clinical characteristics of the patients are presented in Table 1.

**Table 1: Demographic and clinical characteristics of the study participants.**

		Difference between males and females p
Gender (N (%))		
Female	270 (82.3)	
Male	58 (17.7)	
Age years (median (range))	64 (17 – 88)	0.653
Chief complaint (N (%))		
Burning	173 (52.7)	0.485
Burning and xerostomia	141 (43)	
Burning and taste disorder	14 (4.3)	
Duration months (median (range))	4 (1 – 180)	0.05*
Affected site (N (%)) <sup>†</sup>		
Tongue	95 (34.8)	0.711
Whole mouth	163 (59.7)	
Lips	8 (2.9)	
Other	7 (2.6)	
Geographic tongue	17 (5.2)	0.456
Coated tongue	5 (1.5)	

Parafunctional habit	2 (0.6)	
Comorbidities (N (%))		
Chronic pain	63 (19.6)	0.776
Hypothyroidism	29 (8.9)	0.109
Psychiatric disorders	20 (6.1)	0.779
Gastritis	125 (38.1)	0.975
Anaemia	13 (4)	0.335
Drugs (N (%))		
Psychiatric	102 (31.1)	0.825
ACE inhibitors	53 (16.7)	0.498
Gastrointestinal	54 (16.5)	0.339
Salivary flow rate ml/min (median (range))	0.2 (0 – 1.2)	0.715
Treatment (N (%))**		
Salivary substitute	204 (71.6)	0.391
Antiseptic mouthwash	75 (26.3)	0.839
Vitamin B	86 (30.2)	0.640
Laser	14 (4.9)	0.282

<sup>+</sup> - data were available for 273 (83.2%) patients

<sup>\*\*</sup> - percentages do not add up to 100% because most of the patients used more than one therapy

Median duration of symptoms was significantly higher in females when compared to males (6 (range 1-180) vs. 2 (range 1-54); p=0.05). No significant differences in age, chief complaint, site, co morbidities, drugs,

Salivary flow rare and treatment between males and females was found.

Follow up data were available for 187 patients. One hundred seventeen patients (62.6%) reported their condition to be unchanged while 70 (37.4%) patients reported improvement compared to the baseline. None of the patients reported complete resolution of the symptoms. The details on two groups of follow up patients are presented in the Table 2.

**Table 2: Follow up data for patients.**

	Improved	Not improved	p
Gender (N (%))			
Female	58 (37.4)	97 (62.6)	0.993
Male	12 (37.5)	20 (62.5)	
Age years (median (range))	65 (26 – 85)	64 (25 – 88)	0.399
Chief complaint (N (%))			
Burning	36 (51.4)	59 (50.4)	0.895
Burning and xerostomia	34 (48.6)	58 (49.6)	
Duration months (median (range))	3 (1 – 54)	4 (1 – 180)	0.338
Comorbidities (N (%))			
Chronic pain	11 (16.4)	19 (16.2)	0.971
Hypothyroidism	2 (6.8)	8 (2.9)	0.242
Psychiatric disorders	5 (7.1%)	10 (8.5%)	0.732
Gastritis	26 (37.1)	35 (29.9)	0.308
Anaemia	3 (4.3)	4 (3.4)	0.762
Drugs (N (%))			
Psychiatric	23 (32.9)	36 (30.8)	0.766
ACE inhibitors	14 (20)	18 (15.8)	0.464
Gastrointestinal	10 (14.3)	16 (13.7)	0.907
Salivary flow rate ml/min	0.12	0.16	0.349

(median (range))	(0 – 0.64)	(0 – 0.96)	
Treatment (N (%))			
Salivary substitute	42 (66.7)	70 (66.7)	0.999
Antiseptic mouthwash	22 (34.9)	30 (28.6)	0.389
Vitamin B	17 (27)	25 (23.8)	0.645
Laser	5 (7.9)	7 (6.7)	0.757

No significant differences in gender, age, chief complaint, duration, comorbidities, medication intake, salivary flow rate and treatment outcome was found between patients who whose symptoms improved compared to the ones whose symptoms did not.

### DISCUSSION

#### Local factors

Usually tongue is most frequently involved site of burning (75% of cases) as reported by Nett et al [3] This is in contrast to the results of this study which showed that the most frequent place where burning symptoms were present was whole oral cavity.

Ago et al [4] reported that BMS was supported by tongue thrusting habit and lip sucking which is in concordance with the results of Paterson et al [5] and contrary to our results as only 0.6% of our patients with BMS had par functional habit.

Contrary to our results Ago et al [4] found significant relationship between smoking and BMS, a finding which we couldn't confirm as most of our patients with BMS do not smoke. Ching et al [6] reported that BMS is associated with increased prevalence of geographic tongue, a finding which we could not confirm as only 5.2% of the tested patients had geographic tongue.

Palacios Sanchez et al [7] reported that presence of dry mouth, burning feeling, and foreign body sensation in the mouth and cancer phobia are closely related with BMS. Cancer phobia seems to be more prevalent in BMS patients in comparison to the patient with oral lichen planes, a result that has also been published before. On the contrary, Nett et al [3] show that dry mouth and altered taste were not frequently associated with BMS (15.6% and 6.3% respectively). Similarly, de Moure et al [8] found that salivary flow rate among controls was lower than that of BMS patients. Tammiala-Salonen et al [9] on the contrary reported higher flow rates in patients with burning symptoms, but the difference was not significant. Rouleau et al [10] found that patients with burning symptoms had slightly but insignificantly increased unstimulated salivary flow rate and decreased stimulated salivary flow rate when compared with patients without burning symptoms.

Prevalence of dry mouth in patients with BMS ranges from 29.6% till 75%, however, altered taste appears to be less common and prevalence ranges from 11-69%. On the basis of our results it seems that xerostomia was present in 43% of the participants whereas altered taste was present in 4.3% of the studied participants. Rouleau et al [10] reported that 40% (out of 170) of patients with dry mouth had a concomitant complaint of oral burning mouth. Cofactors associated with burning included age and use of herbal medications (reduced burning symptoms). The same authors concluded that oral burning is often concomitant to oral dryness and targeting factors associated with oral dryness may help alleviate an oral burning complaint in select populations. Suh et al [11] reported that out of 78 patients with burning mouth, dry mouth was associated complaint in 78.2% subjects. Soares et al [12] also reported that an association between xerostomia and burning symptoms were seen in 75%.

Pajukoski et al [13] reported that 63% of hospitalized elderly patients and 57% of elderly outpatients complained of dry mouth, whereas 13% and 18% respectively reported burning mouth symptoms. Such et al. [11] reported that out of 78 patients with burning mouth, dry mouth was associated complaint in 78.2% subjects. Soars et al [12] also reported that an association between xerostomia and burning symptoms were seen in 75%. Johansson et al [14] reported that there was a strong association between xerostomia and burning mouth, taste changes and Para- and dysfunction of the masticator system in a sample of 8888 and

8313 Swedish persons, respectively on the basis of self-reported questionnaire. Villa and Abate [15] reported that in a sample of 601 persons on the basis of self-administered questionnaires among tertiary referral dental clinic attendees, they found presence of xerostomia in 19.6% cases and burning mouth symptoms in 9%.

Chukwunneke et al [16] reported higher incidence of globes pharynges in patients with burning mouth syndrome; however, we were unable to confirm this finding as none of the patients with burning symptoms in this study reported globes pharynges.

### **Systemic factors**

Few years ago we made our first retrospective analysis of BMS patients and at the time, Brailo et al [17] found significant difference regarding the presence of gastritis in BMS group (51.3%) compared to the 27.5% in the control group ( $p < 0.05$ ). That finding was previously reported in the literature by Backer et al [18], Lamb et al [19]. These results were confirmed by others such as Nett et al [3] who reported that gastrointestinal disease and urogenital diseases were significantly more prevalent in patients with BMS in comparison to the controls as well as H-2 receptor antagonist intake and proton pump inhibitor drugs. Campisi et al [20] found burning symptoms in 58 out of 120 patients (48.3%) with GERD in comparison to the 19 out of 98 (19.3%) in the control group. Becker et al [21] reported that there is no causal connection between episodes of laryngopharyngeal reflux and oral burning symptoms in 22 patients who suffered from intraoral burning.

However, the same authors found improvement in 55% of patients with LPR treated with Omeprazole. The authors thought that  $pH < 6$  can stimulate the TRPV-receptor which mediated burning sensation, while Omeprazole increases oral pH values and decreases activation of TRPV-receptor. Maresky et al [22] have not found significant correlation between burning symptoms and gastric disturbances.

This study is in contrast to one performed earlier [17] as now we did not find any correlations between local and systemic disturbances as well as medication intake in patients with burning mouth syndrome.

Sun et al [23] concluded that there is a significant association of deficiency of hemoglobin, iron and vitamin B12 in patients with burning mouth syndrome. Gao et al [4] could not find any significant differences in white and red blood cell count as well as platelet count between patients with BMS and controls. Recently, Lin et al [24] concluded that there is a significant association of deficiency of iron, and vitamin B12; abnormally high blood homocysteine level; and serum GPCA positivity with BMS. The same authors did not find differences in folic acid between patients with BMS and controls. The result of this study show that there was no association between burning mouth syndrome and anemia as only 13 persons was anaemic.

Contrary to the results of Femi no [25] that many patients with BMS suffer from hypothyroidism we could not confirm a finding as only 8.9% of the studied patients suffered from hypothyroid disease.

Dangore-Khasbage et al [26] reported that 20.66% out of 150 psychiatric patients had burning mouth syndrome and that the prevalence of BMS was much higher in patients taking psychiatric medication (25%) than in drug-naive patients. This finding is in accordance with our previous study upon BMS patients i.e. they use more psychotropic drugs (mostly benzodiazepines) in comparison to the controls. Also this finding is in contrast to the one of Soars [12] who concluded that there was no association between BMS and use of psychotropics. The results of the present study show that there were no associations between intake of psychotropic medication and burning mouth syndrome.

### **Treatment outcome**

Recently, ad Silva et al [27] concluded that protecting the oral mucosa with topic medication can be useful in the control of BMS and that improvement was higher (60%) than attributable to placebo (30%). This is in contrast to the results of this study as improvement in patients burning symptoms was independent of the therapy used (salivary substitutes, chlorhexetidine mouthwash, vitamin B replacement therapy and low level laser therapy)

One hundred seventeen patients (62.6%) reported their condition to be unchanged while 70 (37.4%) patients reported improvement compared to the baseline. None of the patients reported complete resolution of the symptoms.

### CONCLUSION

It may be concluded that there are no associations between burning mouth syndrome with investigated local and systemic diseases and drug intake as well as tried treatment options such as salivary substitutes, low level laser therapy, chlorhexetidine mouthwash and vitamin B<sub>1</sub>, B<sub>6</sub> and B<sub>12</sub> replacement therapy.

### REFERENCES

- [1] Savage NW, Boras VV, Barker K. *Australas J Dermatol* 2006;47:77-81.
- [2] Jensen JL, Barkvoll P. *Ann N Y Acad Sci.* 1998;842:156–162
- [3] Netto FO, Diniz IM, Grossmann SM, de Abreu MH, do Carmo MA, Aguiar MC. *Clin Oral Investig* 2011;15:571-5.
- [4] Gao J, Chen L, Zhou J, Peng J. *J Oral Pathol Med* 2009;38:24-8.
- [5] Paterson AJ, Lamb AB, Clifford TJ, Lamey PJ. *J Oral Pathol Med* 1995; 24: 289-92.
- [6] Ching V, Grushka M, Darling M, Su N. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2012;114:444-8.
- [7] Palacios Sanchez MF, Jordana Comin X, Garcia Sivoli CE. *Med Oral Patol Oral Cir Bucal* 2005; 10: 388-93.
- [8] De Moura SAB, de Sousa JMA, Lima DF, do Monte Negreiros AN, de Vasconcelos Silva F, da Costa LJ. *Gerodontol* 2007; 24: 173-76.
- [9] Tammiala-Salonen T, Soderling E. *Scand J Dent Res* 1993; 101: 215-8.
- [10] Rouleau TS, Shychuk AJ, Kayastha J, Lockhart P, Nussbaum ML, Brennan MT. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2011;111:720-5.
- [11] Suh KI, Lee JY, Chung JW, Kim YK, Kho HS. *J Oral Rehabil* 2007; 34: 739-44.
- [12] Soares MS, Chimenod-Kustner E, Subira-Pifarre C, Rodriguez de Rivera-Campillo ME, Lopez-Lopez J. *Med Oral Patol Oral Cir Bucal* 2005; 10: 301-8.
- [13] Pajukoski H, Meurman JH, Halonen P, Sulkava R. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2001; 92: 641-9.
- [14] Johansson AK, Johansson A, Unell L, Ekback G, Ordell S, Carlsson GE. *Gerodontol* 2012; 29: e107-e115.
- [15] Villa A, Abati S. *Aust Dent J* 2011; 56: 290-295.
- [16] Chukwunneke F, Akpe J, Okoye L, Ekwueme C, Obiakor A, Amobi E, Egbunike D. *Oral Health Prev Dent* 2014. doi: 10.3290/j.ohpd.a31676.
- [17] Brailo V, Vucicevic-Boras V, Alajbeg IZ, Alajbeg I, Lukenda J, Curkovic M. *Med Oral Patol Oral Cir Bucal* 2006 1;11:E252-5.
- [18] Basker RM, Sturdee DW, Davenport JC. *Br Dent J* 1978; 145: 9-16.
- [19] Lamb AB, Lamey PJ, Reeve PE. *Br Dent J* 1988; 165: 256.
- [20] Campisi G, Lo RL, Di Liberto C, et al. *J Dent* 2008; 36: 268-71.
- [21] Becker S, Schmidt C, Berghaus A, Tschiesner U, Olzowy B, Reichel O. *Eur Arch Otorhinolaryngol* 2011; 268: 1375-81.
- [22] Maresky LS, van der Bijl P, Gird I. *Oral Surg Oral Med Oral Pathol* 1993;75:303-7.
- [23] Sun A, Lin HP, Wang YP, Chiang CP. *J Oral Pathol Med* 2012;41:500-4.
- [24] Lin HP, Wang YP, Chen HM, Kuo YS, Lang MJ, Sun A. *J Formos Med Assoc* 2013;112:319-25.
- [25] Femiano F, Lanza A, Buonaiuto C, Gombos F, Nunziata M, Cucurullo L, Cirillo N. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2008;105:e22-7.
- [26] Dangore-Khasbage S, Khairkar PH, Degwekar SS, Bhowate RR, Bhake AS, Singh A, Lohe VK. *J Oral Sci.*2012; 54: 85-91.
- [27] Da Silva LA, de Siqueira TT, Teixeira MJ, de Siqueira SRDT. *Arq Neuropsiquiatr* 2014; 72: 91-98.