

The role of xerostomia in burning mouth syndrome: a case-control study

O papel da xerostomia na síndrome da ardência bucal: estudo caso controle

Luciana Alvarenga da Silva¹, José Tadeu Tesseroli de Siqueira², Manoel Jacobsen Teixeira³,
Sílvia Regina Dowgan Tesseroli de Siqueira⁴

ABSTRACT

Objective: To assess the efficacy of anti-xerostomic topical medication (urea 10%) in patients with burning mouth syndrome (BMS). **Method:** Thirty-eight subjects diagnosed with BMS according to the International Association for the Study of Pain guidelines were randomized to either placebo (5% sodium carboxymethylcellulose, 0.15% methyl paraben, and 10% glycerol in distilled water qsp 100 g) or treatment (urea 10%) to be applied to the oral cavity 3-4 times per day for 3 months. The patients were evaluated before and after treatment with the following instruments: the EDOF-HC protocol (Orofacial Pain Clinic – Hospital das Clínicas), a xerostomia questionnaire, and quantitative sensory testing. **Results:** There were no differences in salivary flow or gustative, olfactory, or sensory thresholds ($P > 0.05$). Fifteen (60%) patients reported improvement with the treatments ($P = 0.336$). **Conclusion:** In conclusion, there were no differences between groups, and both exhibited an association between reported improvement and salivation.

Keywords: xerostomia, salivary flow, orofacial pain, quantitative sensory testing, burning mouth syndrome.

RESUMO

Objetivo: Avaliar a eficácia do uso de medicação tópica anti xerostômica (ureia 10%) em pacientes com síndrome de ardência bucal. **Método:** Trinta e oito sujeitos diagnosticados com síndrome de ardência bucal de acordo com os critérios da Associação Internacional para Estudo da Dor foram randomizados para grupo placebo (5% de carboximetilcelulose de sódio, 0,15% de metilparabeno e 10% de glicerol em água destilada qsp 100g) ou grupo tratamento (ureia 10%) para ser aplicada na cavidade oral 3-4 vezes ao dia, durante três meses. Os pacientes foram avaliados antes e depois do tratamento: protocolo EDOF-HC, questionário de xerostomia, testes sensitivos quantitativos. **Resultados:** Não houve diferenças no fluxo salivar, limiares gustativos, olfativos e somestésicos (Mann-Whitney $P > 0,05$). Quinze (60%) dos pacientes tiveram melhora com o tratamento ($P = 0,336$, oneway ANOVA). **Conclusão:** Em conclusão não houve diferenças entre os grupos, ambos apresentaram uma associação entre melhora e salivação.

Palavras-chave: xerostomia, fluxo salivar, dor orofacial, teste sensitivo quantitativo, síndrome ardência bucal.

Burning mouth syndrome (BMS) is a continuous intraoral pain characterized by burning mouth in the absence of a primary etiological lesion or disease¹⁻³. The main affected sites are the tongue, palate, and/or the gingiva⁴⁻⁶. It is considered idiopathic, and current evidence has classified it as neuropathic. One of the most widely accepted theories is that there is disinhibition of the trigeminal nerve due to partial or total loss of chorda tympani (facial) nerve function⁶. However, recent findings also

showed that trigeminal neuropathy may be directly involved, and that gustatory abnormalities can be secondary³.

It is known that BMS is eventually associated with reduced salivary flow⁷⁻⁹ and abnormal saliva composition (increasing concentrations of K⁺, Na⁺, Cl⁻, Ca²⁺, immunoglobulin A [IgA], amylase)¹⁰. Even in the absence of hyposalivation, patients may complain of xerostomia and dry mouth^{7-9,11} and loss of taste and smell^{3,12}.

Departamento de Neurologia, Faculdade de Medicina, Universidade de São Paulo, São Paulo SP, Brazil.

¹Postgraduation Student, Departamento de Neurologia, Faculdade de Medicina, Universidade de São Paulo, São Paulo SP, Brazil;

²PhD, DDS, Head of the Orofacial Pain Team, Dentistry Division, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, São Paulo SP, Brazil;

³PhD, MD, Full Professor, Interdisciplinary Pain Center, Hospital das Clínicas and Departamento de Neurologia, Faculdade de Medicina, Universidade de São Paulo, São Paulo SP, Brazil;

⁴PhD, DDS, Associate Professor, Departamento de Neurologia, Hospital das Clínicas, Escola de Medicina, Universidade de São Paulo, São Paulo SP, Brazil.

Correspondence: Luciana Alvarenga da Silva; Av. Niterói 127 / Parque Paraíso / Itapeverica da Serra; 06850-200 São Paulo SP - Brasil; E-mail: lucianaa@usp.br

Conflict of interest: There is no conflict of interest to declare.

Support: FAPESP - Foundation of the State of São Paulo - for the financial support for this research (2009/08697-5).

Received 28 June 2013; Received in final form 18 October 2013; Accepted 25 October 2013.

The treatments for BMS include antidepressants, benzodiazepines, anticonvulsants, local or systemic capsaicin, and alpha lipoic acid. However, the collateral effect of these drugs on decreased saliva secretion can exacerbate the symptoms¹³. Two studies have described the use of anti-xerostomic topical medications as an adjuvant to treat BMS, and urea has been shown to be effective in skin-surface hydration^{14,15}. Thus, the objective of this study was to evaluate xerostomia and salivary flow in patients with BMS treated with amitriptyline before and after the use of anti-xerostomic topical medication.

METHOD

This was a randomized, double-blind clinical trial conducted between August 2011 and February 2012. We enrolled 38 patients with BMS diagnosed according to the International Association for the Study of Pain (*IASP*) guidelines¹⁶, which are followed at the Craniofacial Pain Clinic of Hospital das Clinicas, School of Medicine of the University of Sao Paulo. All subjects were informed about the purposes of the study and provided written informed consent. The protocol was approved by the local Ethics Committee. No patient exhibited hyposalivation at the time of diagnosis with the quantitative evaluation. All patients had been treated with 25-50 mg of amitriptyline within the last 3 months. They underwent laboratory tests and a careful examination to exclude other causes of burning mouth¹⁰.

The exclusion criteria were other facial pain syndromes, other causes of abnormal salivation, other neuropathies or primary diseases associated with burning mouth, or inability to answer the questions and/or perform the tests.

The subjects were randomly divided into two groups:

1. Study Group: 19 patients received topical medication comprised of urea 10% to be applied at the oral cavity 3-4 times per day for 3 months.
2. Control Group: 19 patients received placebo (5% sodium carboxymethylcellulose, 0.15% methyl paraben, and 10% glycerol in distilled water qsp 100 g) to be applied to the oral cavity 3-4 times per day for 3 months.

The patients were evaluated before and after the 3-month treatment period with the following instruments:

1. EDOF-HC protocol (Orofacial Pain Clinic - Hospital das Clinicas): a standardized orofacial pain questionnaire to detail the following: 1) chief complaint, 2) general pain characteristics (location, quality, duration, pain relief, pain triggering), 3) headache and/or body pain complaints, and 4) patient's medical history and co-morbidities¹⁷;
2. Xerostomia questionnaire¹⁸;
3. Quantitative sensory testing (QST). All subjects underwent a standardized QST protocol¹⁹ comprised of 12 tests grouped as follows:
 - salivary flow and gustative and olfactory thresholds;

- thermal detection thresholds for cold and warm sensations;
- mechanical detection thresholds for touch, vibration, and electrical perception;
- mechanical pain sensitivity, including superficial and deep pain thresholds;
- electrical pain threshold at the teeth;
- corneal reflex.

The neuropathic nature of BMS and the impairment of sensory function were the reasons to use a QST protocol in this study. We evaluated bilateral skin areas innervated by the three trigeminal branches. The evaluation started with the quantitative non-stimulated salivary flow by the following method: two pieces of cotton were placed into a plastic device and weighed on a calibrated balance (Acculab® V1200). The patient was oriented to swallow the saliva inside the mouth, and the cotton was placed inside and kept below the tongue for 5 minutes, during which time the patient was instructed not to swallow. Then, the cotton was removed, placed in the plastic device, and weighed, and the difference in weight (before and after the evaluation) was divided by 5 to calculate the salivary flow in mL/min; this technique was previously validated for basal salivation^{20,21}.

Gustative thresholds: The following four substances, corresponding to the four basic tastes, were tested: sweet (glucose): 0.01 M, 0.032 M, 0.1 M, 0.32 M, 1.0 M; sour (citric acid): 0.00032 M, 0.001 M, 0.0032 M, 0.01 M, 0.032M; salty (sodium chlorate): 0.01 M, 0.032 M, 0.1 M, 0.32 M, 1.0 M; bitter (urea): 0.1 M, 0.32 M, 1.0 M, 3.2 M, 10.0 M. For each test, one drop of the substance was placed on the tongue, beginning with the low concentration, and alternated with one drop of distilled water. The concentration was increased until the stimulus was detected by the subject^{3,22,23}.

Olfactory threshold: Using isopropanol solutions (0.09%, 13.0%, 23.0%, 35.0%, 53.0%, 70.0%)^{3,12,19,23,24}, two bottles were offered to the patient: one containing the solution and another containing water, and the patient had to indicate the bottle containing the solution. If this was done correctly for three trials, the threshold was identified. If not, a bottle with the solution at the next concentration was offered along with the bottle of water.

Thermal detection: The thermal test was performed with the modular sensory analyzer (MSA) thermo test device (Somedic, Sweden). The baseline temperature was 32°C and the contact square area of the thermode was 9×9 mm. Cold and warm detection thresholds were assessed using ramped stimuli at 1°C/s. The range was from 10°C to 50°C. First, cold was tested, then warm. The evaluation consisted of five measurements for each thermal threshold, and the means and standard deviations were considered for the analysis.

Mechanical detection threshold: Touch perception was assessed with a set of standardized von Frey filaments with rounded 0.5-mm diameter tips, applied with an electronic device (IITC, Woodland Hills, CA, USA). The probes were used in the

perpendicular position on the area to be tested. The subject was asked to report the detection of the probes, and if they could not after 30 seconds in the second trial, the next filament was used. Three measurements in g/mm² were performed, and the means and standard deviations were considered for the analysis.

Vibration detection threshold: The vibration test was performed with an electronic Vibrometer device (Somedic) with a vibrator of 650 g in weight and a contact area of 1 cm² that was perpendicularly applied and ramped stimuli at 1 Hz/s. The vibration threshold was calculated as the mean between the appearance and disappearance thresholds detected by the patient.

Electrical detection threshold: The electrical threshold test was performed with a Pulpotest electrical device (Sybronendo, Orange, CA USA) with a contact area of 1 cm² for the perception and a metallic device localized 2 cm away from the evaluation area to close the electrical circuit. The electrical stimuli started at 0 and were increased with ramped stimuli at 1 A/s. The stimulus was increased at this speed until detected by the subject, with a maximum value of 80 A.

Pressure pain perception: Deep algometry was measured with an electronic pressure algometer (Somedic) with a probe area of 1 cm² that was pressed on the skin at a ramp rate of 50 kPa/s. The stimulus was increased at this speed until it was detected by the subject.

Superficial pain perception: Superficial algometry was tested with disposable needles of 8×10×0.5 mm, applied with an electronic device (IITC). Three measurements were made in g/mm², and the means and standard deviations were considered for the analysis. The needles were tested in the

perpendicular position on the area to be investigated. The stimulus was increased until it was detected by the subject.

Electrical pain threshold for the teeth: The electrical pain threshold for the teeth was performed with a Pulpotest electrical device (Sybronendo), with a contact area of 1 cm² for perception and a metallic device localized 2 cm away from the area of evaluation to close the electrical circuit. The electrical stimuli started at 0 and were increased with ramped stimuli at 1 A/s. The stimulus was increased at this speed until its detection by the subject, with a maximum value of 80 A.

Corneal reflex: A von Frey filament with a 0.5-mm diameter rounded tip was used in both eyes. This probe was applied on the corneal area of each subject with their vision focused to the opposite side, and the subject was asked to report whether or not they detected the stimulus.

Statistical analysis

All data were tabled, and the tests used were one-way analysis of variance (ANOVA), Fisher's exact test, Mann-Whitney U test, Chi-square, Student's *t*-test and Spearman's correlations²⁵. All statistical calculations were performed using SPSS 17.0 (SPSS Inc., Chicago, IL, USA). The level of significance was P<0.05.

RESULTS

The groups were similar in gender distribution, age, color, marital status, occupation, height, weight, comorbidities, and

Table 1. Comparison of demographic data between groups (N=38).

	Study group (n=19)	Control group (n=19)	P*
Gender	Women 18 (94.7%)	Women 17 (89.5%)	0.500
Age (years)	66.32±12.01 (47-88)	58.42±13.70 (37-82)	0.068
Color	White 16 (84.2%) Black 2 (10.5%) Mulatto 1 (5.3%)	White 16 (84.2%) Black 1 (5.3%) Mulatto 2 (10.3%)	0.717
Occupation	Housekeeper 7 (36.8%) Retired 6 (31.6%) Domestic 2 (10.5%) Seamstress 2 (10.5%) Biomedical 1 (5.3%) Unemployed 1 (5.3%)	Housekeeper 9 (47.4%) Retired 5 (26.3%) Unemployed 2 (10.3%) Nanny 1 (5.3%) Secretary 1 (5.3%) Seller 1 (5.3%)	0.332
Marital status	Married 8 (42.1%) Widowed 6 (31.6%) Single 4 (21.1%) Divorced 1 (5.3%)	Married 8 (42.1%) Widowed 6 (31.6%) Single 3 (15.8%) Divorced 1 (5.3%)	0.974
Height (m)	1.55±0.08 (1.45-1.77)	1.60±0.09 (1.46-1.78)	0.111
Weight (kg)	61.82±14.41 (46-95)	66.22±11.66 (49-85)	0.327
Comorbidities	Hypertension 9 (47.4%) Hypothyroidism 4 (21.1%) Depression 4 (21.1%)	Hypertension 12 (63.2%) Hypothyroidism 1 (5.3%) Depression 8 (42.1%)	0.140
Smoking habits	No smoking 19 (100.0%)	No smoking 15 (78.9%)	0.107

*Pearson's Chi-square, Fisher's exact test, or Student's *t*-test.

Table 2. Orofacial pain characteristics between groups (N=38).

	Study group (n=19)	Control group (n=19)	P**
Main complaint	Oral burning 17 (89.5%) Tongue pain 1 (5.3%) Face and mouth pain 1 (5.3%)	Oral burning 17 (89.5%) Tongue pain 1 (5.3%) Itching tongue 1 (5.3%)	0.553
Duration (years)	6.97±4.93 (1.0-15.0)	2.78±2.61 (0.1-10.0)	0.014
Periods of pain	Variable 15 (78.9%) At night 3 (15.8%) Morning 1 (5.3%)	Variable 16 (84.2%) Morning 1 (5.3%) Afternoon 1 (5.3%) Continuous 1 (5.3%)	0.362
Main descriptors	Burning 19 (100.0%) Twinge 3 (15.8%) Shock-like 1 (5.3%) Formication 1 (5.3%)	Burning 17 (89.4%) Twinge 2 (10.5%) Shock-like 2 (10.5%) Weight 1 (5.3%) Formication 1 (5.3%) Itching 1 (5.3%)	0.397
Intensity (VAS*)	7.58±2.27 (3-10)	7.58±2.74 (1-10)	1.000
Worsening factors	Emotional stress 6 (31.6%) Bitter or sour foods 4 (21.1%) Feed 1 (5.3%) Hot food 1 (5.3%)	Emotional stress 1 (5.3%) Sour foods 3 (15.8%) Feed 3 (15.8%) Cold food 2 (10.5%) Hot food 1 (5.3%)	0.356
Alleviating factors	Medication 4 (21.1%) Resting 1 (5.3%) Removing the prosthesis 1 (5.3%) Cold water 1 (5.3%) Candy 1 (5.3%)	Medication 5 (26.4%) Resting 1 (5.3%) Feed 4 (21.1%) Mouthwash 3 (15.8%) Other 1 (5.3%)	0.365
Causal factor	Spontaneous start 13 (68.4%) Oral surgery 2 (10.5%) Medication 2 (10.5%) Emotional stress 1 (5.3%) Coffee 1 (5.3%)	Spontaneous start 8 (42.1%) Oral surgery 8 (42.1%) Medication 1 (5.3%) Oral infection 1 (5.3%) Coffee 1 (5.3%)	0.236
Previous treatments	Medication 11 (57.9%) No treatment 5 (26.3%) Others 2 (10.5%) Laser 1 (5.3%)	Medication 5 (26.4%) Mouthwash 3 (15.8%) Physical therapy 2 (10.5%) Acupuncture 1 (5.3%)	0.571

*VAS: visual analog scale; **Pearson's Chi-square or Mann-Whitney U test.

smoking habits (Table 1), as well as orofacial pain characteristics (Table 2). The patients were evaluated according to the presence of bruxism, earache, headache, generalized pain, chewing quality, and other orofacial complaints. Four (21.1%) patients and 3 (15.8%) controls had bruxism (Chi-square, $P=0.444$), 5 (26.3%) patients and 4 (21.0%) controls had earache (Chi-square, $P=0.741$), 13 (68.4%) patients and 11 (57.9%) controls had headache (Fisher's exact test, $P=0.288$), 12 (63.2%) patients and 10 (52.6%) controls had generalized pain (Fisher's exact test, $P=0.372$), 11 (57.9%) patients and 8 (42.2%) controls had good chewing quality, and 8 (42.1%) patients and 11 (57.9%) controls had poor or very poor chewing (Chi-square, $P=0.495$).

The evaluation of xerostomia and associated complaints identified 14 (73.7%) patients and 14 (73.7%) controls with dry mouth sensation (Fisher's exact test, $P=0.643$), 2 (10.5%) patients and 7 (36.8%) controls with difficulty of chewing due to xerostomia (Fisher's exact test, $P=0.062$), 4 (21.1%) patients

and 5 (26.3%) controls with difficulty talking due to xerostomia (Fisher's exact test $P=0.500$), 2 (10.5%) patients and 5 (26.2%) controls who drank fluids at meals (Fisher's exact test, $P=0.500$), 8 (42.1%) patients and 9 (47.4%) controls who drank liquids during the night (Fisher's exact test, $P=0.212$), 7 (36.8%) patients and 5 (26.3%) controls with halitosis (Fisher's exact test, $P=0.364$), 6 (31.6%) patients and 4 (21.1%) controls with throat ache (Fisher's exact test, $P=0.357$). Other digestive complaints were: 7 (36.8%) patients and 3 (15.8%) controls with stomach ache (Fisher's exact test, $P=0.135$), 9 (47.4%) patients and 8 (42.1%) controls with abnormal intestinal flow (Chi-square, $P=0.717$), 13 (68.4%) patients and 17 (89.5%) controls with normal digestion (Fisher's exact test $P=0.116$), and 5 (26.4%) patients and 7 (36.9%) controls with food-related digestion problems. These patients reported complaints associated with the following: sour and acid flavors, breads, milk and dairy products, sugars and fats, and vegetables and beans (Chi-square, $P=0.495$).

Post-treatment evaluation

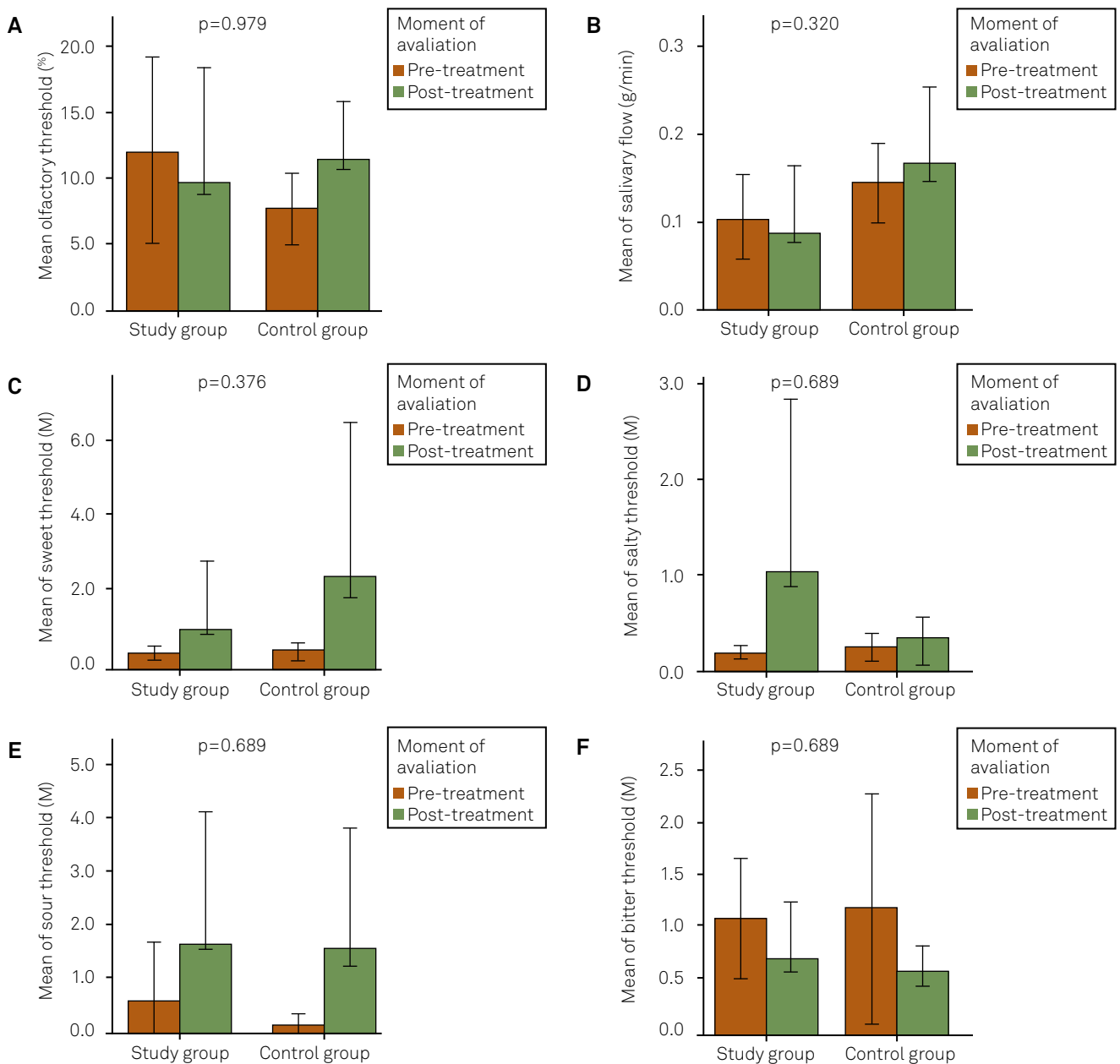
Among the 38 patients that were included in this sample, 25 (65.9%) returned for the re-evaluation (12 from the study and 13 from the control group). Fifteen (60.0%) of them reported improvement with the treatments (7 from the study and 8 from the control group) (ANOVA, $P=0.336$). Overall, there were no differences before and after treatment with regard to orofacial pain, xerostomia, or digestive abnormalities. However, significant improvements in mastication quality (Mann-Whitney, $P=0.041$) and generalized body pain complaints were observed (Fisher's exact test, $P=0.014$).

Pain duration was longer in the study group than in the control group (Mann-Whitney $P=0.014$) and there were

no differences in pain intensity after treatment (Mann-Whitney, $P=0.882$). There were also no differences in salivary flow (Mann-Whitney, $P=0.320$) or thresholds for gustation (Mann-Whitney; sweet $P=0.376$, salty $P=0.689$, sour $P=0.689$, and bitter $P=0.689$) or olfaction (Mann-Whitney, $P=0.979$) (Figure 1). The groups exhibited similar corneal reflex abnormalities (Fisher's exact test: right $P=0.202$, left $P>0.999$).

Somatosensory thresholds

Thermal detection: There were no differences at the trigeminal branches or distant areas in cold detection (Mann-Whitney, $P>0.05$), except at the maxillary branch (Mann-Whitney, $P=0.019$), in which the study group showed



A: Olfactory thresholds; B: Salivary flow; C: Sweet thresholds; D: Salty thresholds; E: Sour thresholds; F: Bitter thresholds. Statistical tests: Mann-Whitney U tests.

Figure 1. Salivary flow, olfactory, and gustative thresholds between groups (N=38).

lower thresholds after treatment than controls. Warm detection did not show differences at the re-evaluation (Figure 2).

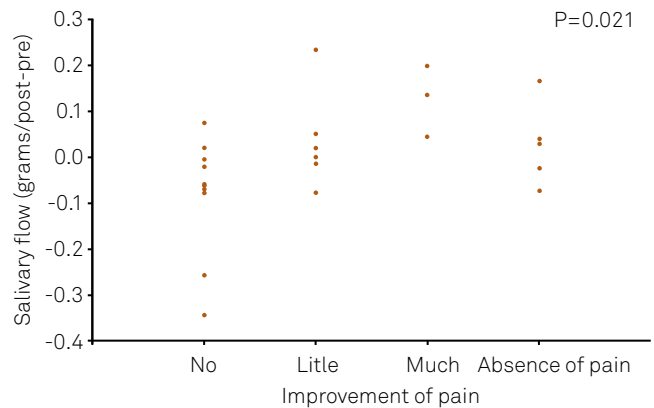
Mechanical thresholds (tactile and vibration): There were no differences at the trigeminal branches or distant areas in tactile detection (Mann-Whitney, $P>0.05$, Figure 2) except at the ophthalmic branch (Mann-Whitney, $P=0.035$), in which the study group showed lower thresholds after treatment than the controls. The vibration detection results did not reveal differences at the re-evaluation.

Electrical skin and teeth thresholds: There were no statistical differences in electrical thresholds between the groups at any place investigated (Mann-Whitney, $P>0.05$).

Pressure and superficial pain perception: Pressure pain detection showed higher thresholds in the study group than in controls at right temporalis (Mann-Whitney, $P=0.010$), bilateral masseters (Mann-Whitney, $P=0.002$ and $P=0.040$), bilateral tibiae (Mann-Whitney, $P=0.007$ and 0.004) and means (Mann-Whitney, $P=0.004$), after the treatment. There were no statistical differences in superficial pain thresholds between the groups at any place investigated (Mann-Whitney, $P>0.05$, Figure 2).

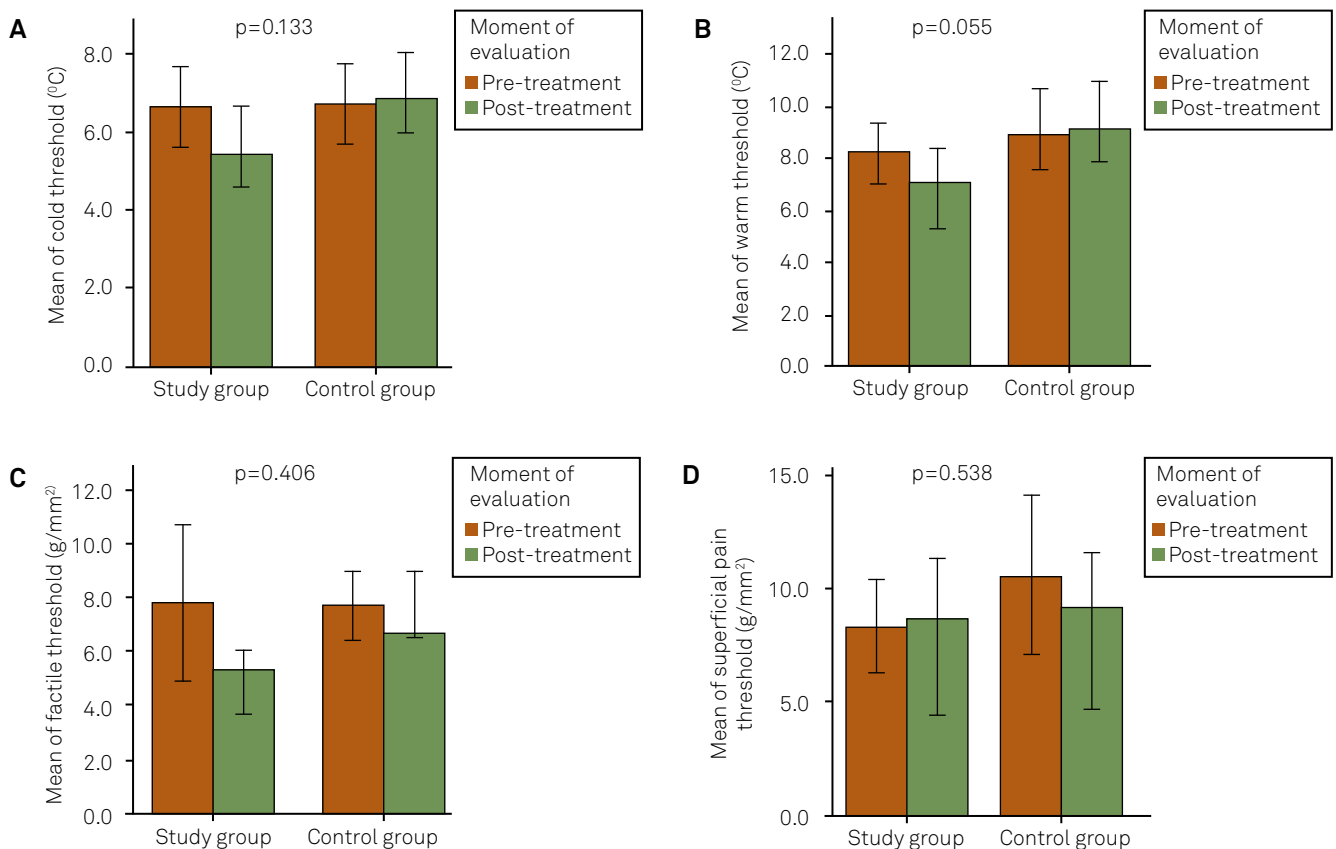
Associations and correlations: There was an association between improvement and higher salty thresholds (Spearman's, $P=0.048$), higher pressure pain thresholds in the right masseter (Spearman's, $P=0.004$), tibia (Spearman's, $P=0.008$ and $P=0.016$) and maxillary branch (Spearman's,

$P=0.036$) in the control group. The improvement of pain in both groups was associated with increased salivary flow (Spearman's $P=0.021$) (Figure 3), increased pressure pain thresholds at the tibia (Spearman's $P=0.040$), and increased electrical teeth thresholds (Spearman's, $P=0.039$). The pain duration of the study group was negatively correlated with vibration thresholds at maxillary, mandibular branches, right hand, and total means (Spearman's, $P=0.007$, 0.023 , 0.032 , and 0.016 respectively). Pain duration in the control group



Statistical tests: Spearman's.

Figure 3. Correlation analysis between salivary flow and pain improvement (N=38).



A: Cold thresholds; B: Warm thresholds; C: Tactile thresholds; D: Superficial pain thresholds
Statistical tests: Mann-Whitney U tests.

Figure 2. Somatosensory thresholds: comparison between groups (N=38).

was negatively correlated with trigeminal cold thresholds (Spearman's, $P=0.046$), tibia tactile threshold (Spearman's, $P=0.044$), superficial pain thresholds at the maxillary branch (Spearman's $P=0.009$), and electrical mandibular threshold (Spearman's $P=0.008$). There was also a negative correlation between pain duration and means of pressure pain thresholds (Spearman's $P=0.020$), mean tactile threshold (Spearman's $P=0.026$), maxillary superficial pain threshold (Spearman's $P=0.043$), and mandibular electrical threshold ($P=0.043$).

Pain intensity was negatively correlated with tibia tactile threshold in the study group (Spearman's, $P=0.030$) and mandibular tactile threshold in the control group (Spearman's, $P=0.046$). For both groups, there was a positive correlation between pain intensity and electric thresholds at ophthalmic and maxillary right branches (Spearman's, $P=0.022$ and $P=0.028$, respectively), left mandibular branch (Spearman's, $P=0.009$), right tibia (Spearman's, $P=0.036$), and mean electrical skin and teeth thresholds (Spearman's, $P=0.005$ and $P=0.012$, respectively).

DISCUSSION

This paper reports the results of a randomized clinical trial of topical medication for xerostomia. The study group received the active substance urea, and the control group received placebo. We observed similar improvement in both groups (60.0%), which probably means that regardless of the vehicle used, oral cavity hydration results in an anti-xerostomic effect noticed in the association between improvement and salivation. This result confirms that protecting the oral mucosa with topic medication can be useful in the control of BMS, a chronic complex condition with a poor prognosis, and that improvement was higher than that attributable to placebo (30%), showing that the vehicle in placebo was also effective.

In general, there were no differences in socio-demographic characteristics between the groups, and this corresponds to the literature (elderly women are the majority of patients)^{26,27}. Pain characteristics (burning, moderate to severe, continuous) and abnormal salivary flow were the most common symptoms reported in previous studies²⁹. There was a high

prevalence of headache and generalized pain in this sample, which had been previously described in trigeminal neuralgia²⁸. It is possible that these complaints and the high prevalence of temporomandibular joint dysfunction (TMD) in these patients are reflexes of pain chronification, affecting the primary pain cause among the reported symptoms by the patient, and suggested that they also need appropriate treatment for TMD²⁸. In this study, there was an improvement in chewing and generalized pain complaints, supporting the role of saliva in oral health and the pathophysiological effects of local chronic pain²⁸.

In general, there were no statistical differences between the groups in sensory thresholds or xerostomia complaints ($P>0.05$). QST tests were performed to verify similar neuropathic impairment in the BMS groups and revealed that the study group had a longer pain duration, which could affect sensory findings in chronic pain patients, and this could compromise the results of this study. Because of the double-blinded design, we could not match pain duration between the groups, which could have prevented this difference. A previous study reported a negative correlation between pain duration and sensory thresholds, which means that patients with longer histories of pain had lower thresholds than other patients, suggesting the presence of a sensory interaction²⁹.

There were several correlations and associations between sensory thresholds and pain improvement, as well as with higher levels of salivary flow. These findings are interesting because they indicate a dynamic influence of pain in neurological responses and perceptions, according to its intensity³⁰. This influence was not only in sensory thresholds but also in efferents (salivation), and these data, which were objectively measured with instruments, are reliable.

The limitations of this study are the loss of part of the sample, which was small. In addition, it would be helpful to match the groups for all pain characteristics, including pain duration, to avoid the effect of the pain history on sensory thresholds and the results.

In conclusion, there were no differences between the groups; both showed an association between improvement and salivation following oral cavity hydration, regardless of the makeup of the treatment.

References

1. Ship JA, Grushka M, Lipton JA, Mott AE, Sessle BJ, Dionne RA. Burning mouth syndrome: An update. *J Am Dent Assoc* 1995;126:842-853.
2. Nasri C, Teixeira MJ, Siqueira JTT. Ardência bucal. Avaliação de uma amostra clínica. *Rev Simbodor* 2000;1:75-82
3. Siviero M, Teixeira MJ, Siqueira JT, Siqueira SR. Central mechanisms in burning mouth syndrome involving the olfactory nerve: a preliminary study. *Clinics* 2011;66:509-512.
4. Grushka M, Sessle BJ. Burning mouth syndrome. *Dent Clin North Am* 1991;35:171-184.
5. Siqueira JTT, Turbino CL, Nasri C. Dor orofacial em pacientes com disfunção temporomandibular e secura bucal: necessidade de diagnósticos diferencial - discussão clínica. *J Bras Ortodont Ortop Facial* 1998;3:39-45.
6. Nasri-Heir C, Gomes J, Heir GM, et al. The role of sensory input of the chorda tympani nerve and the number of fungiform papillae in burning mouth syndrome. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2011;112:65-72.
7. Cho MA, Ko JY, Kim YK, Kho HS. Salivary flow rate and clinical characteristics of patients with xerostomia according to its aetiology. *J Oral Rehab* 2010;37:185-193.
8. Kho HS, Lee JS, Lee EJ, Lee JY. The effects of parafunctional habit control and topical lubricant on discomforts associated

- with burning mouth syndrome (BMS). *Arch Gerontol Geriatr* 2010;51:95-99.
9. Marino R, Torretta S, Capaccio P, Pignataro L, Spadari F. Different therapeutic strategies for burning mouth syndrome: preliminary data. *J Oral Pathol Med* 2010;39:611-616.
 10. Patton LL, Siegel MA, Benoliel R, deLaat A, Hill C, Lauderdale F. Management of burning mouth syndrome: systematic review and management recommendations. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007;103(Suppl 1):S39.
 11. Thomson WM. Issues in the epidemiological investigation of dry mouth. *Gerodontology* 2005;22:65-76.
 12. Siqueira SR, Nóbrega JCM, Teixeira MJ, Siqueira JT. Olfactory threshold increase in trigeminal neuralgia after balloon compression. *Clin Neurol Neurosurg* 2006;108:721-725.
 13. Maltsman-Tseikhin A, Moricca P, Niv D. Burning mouth syndrome: will better understanding yield better management? *Pain Practice* 2007;7:151-162.
 14. Ademola J, Frazier C, Kim SJ, Theaux C, Saudez X. Clinical evaluation of 40% urea and 12% ammonium lactate in the treatment of xerosis. *Am J Clin Dermatol* 2002;3:217-222.
 15. Serup J. A double-blind comparison of two creams containing urea as the active ingredient. Assessment of efficacy and side-effects by non-invasive techniques and a clinical scoring scheme. *Acta Dermato Venereol Suppl (Stockholm)* 1992;177:34-43.
 16. Merskey H, Bogduk N. Classification of chronic pain. Seattle, Washington: IASP Press, 1994.
 17. Siqueira JTT, Ching LH, Nasri C, et al. Clinical study of patients with persistent orofacial pain. *Arq Neuropsiquiatr* 2004;62:988-996.
 18. Korn GP, Pupo DB, Quedas A, Filho IB. Correlation between xerostomia degree and sialometry in patients with Sjogren Syndrome. *Rev Bras Otorrinolaringol* 2002;68:1-2.
 19. Siviero M, Teixeira MJ, de Siqueira JT, Siqueira SR. Somesthetic, gustatory, olfactory function and salivary flow in patients with neuropathic trigeminal pain. *Oral Dis* 2010;16:482-487.
 20. Pupo DB, Bussoloti Filho I, Liquidato BM, Korn GP. Proposta de um método prático de sialometria. *Rev Bras Otorrinolaringol* 2002;68:219-222.
 21. Da Silva LA, Teixeira MJ, Siqueira JTT, Siqueira SRDT. Xerostomia and salivary flow in patients with orofacial pain compared with controls. *Arch Oral Biol* 2011;56:1142-1147.
 22. Bartoshuk L. Clinical evaluation of the sense of taste. *Ear Nose Throat J* 1989;68:331-337.
 23. Davidson TM, Murphy C. Rapid clinical evaluation of anosmia. *Arch Otolaryngol Head Neck Surg* 1997;123:591-594.
 24. Cain WS. Testing olfaction in a clinical setting. *Ear Nose Throat J* 1989;68:316-328.
 25. Kirkwood BR, Sterne JAC. *Essential Medical Statistics*. 2nd ed. Maiden, Massachusetts: Blackwell Science, 2006.
 26. Mignogna MD, Pollio A, Fortuna G, et al. Unexplained somatic comorbidities in patients with burning mouth syndrome: a controlled clinical study. *J Orofacial Pain* 2011;25:131-140.
 27. Silvestre-Rangil J, Silvestre FJ, Tamarit-Santafé C, Bautista D. Burning mouth syndrome: correlation of treatment to clinical variables of the disease. *Med Oral Patol Oral Cir Bucal* 2011;16:e890-894.
 28. De Siqueira SR, da Nóbrega JC, Teixeira MJ, de Siqueira JT. Masticatory problems after balloon compression for trigeminal neuralgia, a longitudinal study. *J Oral Rehabil* 2007;34:88-96.
 29. Melzack R, Wall PD. Pain mechanisms: a new theory. *Science* 1965;150:971-979.
 30. Melzack R. Phantom limbs and the concept of a neuromatrix. *Trends Neurosci* 1990;13:88-92.