RBCS ARTIGOS ORIGINAIS

# BURNING MOUTH SYNDROME: TOPICAL APPLICATION OF 0.002% CAPSAICIN (Capsicum frutescens L)

SÍNDROME DA ARDÊNCIA BUCAL: APLICAÇÃO TÓPICA DE 0,002% CAPSAICINA (Capsicum frutescens L)

# Juliana Cassol Spanemberg<sup>1</sup>, Alberto Rodriguez-Archilla<sup>2</sup>, Alejandro Ceballos-Salobreña<sup>3</sup>, Mário Caputo Coppola<sup>4</sup> e Lenita Maria Aver de Araújo<sup>5</sup>

- <sup>1</sup> Post-graduate student Stomatology and Bucomaxillofacial Cancer Prevent Division, São Lucas Hospital Pontifical Catholical University of Rio Grande do Sul PUC/RS (Brazil).
- <sup>2</sup> DDS, PhD. Oral Medicine. School of Dentistry. University of Granada (Spain).
- <sup>3</sup> MD, PhD. Oral Medicine. School of Dentistry. University of Granada (Spain).
- <sup>4</sup> DDS, MSc, PhD. Associate Professor, School of Dentistry, Federal University of Pelotas (Brazil).
- <sup>5</sup> DDS, MSc, PhD. Associate Professor, Department of Semiology and Clinic. Coordinator of the Center for Diagnosis of Diseases of the Mouth, School of Dentistry, Federal University of Pelotas (Brazil).
- <sup>4</sup> DDS, MSc, PhD. Associate Professor. School of Dentistry, Federal University of Pelotas (Brazil).
- <sup>5</sup> DDS, MSc, PhD, Associate Professor, Department of Semiology and Clinic. Coordinator of the Center for Diagnosis of Diseases of the Mouth, School of Dentistry, Federal University of Pelotas (Brazil).

# **ABSTRACT**

**Aim:** To evaluate the effectiveness of topical application of capsaicin (*Capsicum frutescens L*) at a concentration of 0.002% for the Burning Mouth Syndrome (BMS) treatment. **Study design:** Forty patients diagnosed with BMS were evaluated at the Center for Diagnosis of Diseases of the Mouth, School of Dentistry, Federal University of Pelotas (Brazil). Clinical characteristics such as type of BMS, time to express the BMS symptoms and most affected site were evaluated. Patients were oriented to mouth rinse for 1 minute, 20 drops of diluted substance in 50 ml of water, 3 times a day, during 7 days. All the data obtained were transferred to a data bank and analyzed statistically using SPSS 14.0.1. The chi-square test, t-test were used for mono factor analysis. A probability of  $P \le 0.05$  was accepted as significant. **Results:** The BMS type II was the most prevalent and the most affected site was the tongue. Twenty-two patients obtained partial reduction of symptoms (up to) 50% of remission) and 9 (22,5%) individuals showed complete reduction of symptoms. **Conclusion:** Topical application of capsaicin as mouthwash proved itself as an alternative for the treatment of symptoms in patients with BMS. It is necessary to conduct new studies to identify the causes of BMS and, mainly, to identify an effective and cheap treatment for patients, helping the approach to this pathology.

**Keywords:** Burning mouth syndrome; Capsaicin; Topical application.

## RESUMO

**Objetivo:** Avaliar a efetividade da aplicação tópica de capsaicina (Capsicum frutescens L) na concentração de 0,002% para o tratamento da síndrome da ardência bucal. Metodologia: Foram avaliados 40 pacientes diagnosticados com SAB no Centro de Diagnóstico de Doenças da Boca da Faculdade de Odontologia da Universidade Federal de Pelotas - UFPel, no Rio Grande do Sul, Brasil. Características clínicas, tais como tipo de SAB e sítio mais acometido, foram avaliadas. Orientouse os pacientes a bochecharem, por um minuto, 20 gotas da substância em referência, diluídas em 50ml de água, três vezes ao dia, durante sete dias. Todos os dados obtidos foram transferidos para um banco de dados e analisados estatisticamente com o programa SPSS 14.0.1. Utilizou-se o teste t de Student para a comparação de duas médias; já para a comparação de variáveis qualitativas, fez-se uso do teste Qui-quadrado. Aplicou-se o teste exato de Fischer bilateral. Considerou-se como nível mínimo de significância o valor de p ≤ 0.05. **Resultados:** A SAB tipo II foi a evidência mais prevalente, e o sítio de eleição mais afetado foi a língua. Vinte e dois pacientes obtiveram redução parcial dos sintomas (até 50% de remissão) e nove (22,5%) indivíduos apresentaram remissão completa dos sintomas. Conclusão: A aplicação tópica de capsaicina na forma de colutório mostrou-se uma alternativa para o tratamento da sintomatologia presente nos pacientes portadores da SAB. Faz-se necessária a realização de novos estudos que busquem identificar as causas da SAB e, principalmente, um tratamento eficaz e barato para os pacientes, auxiliando, desta forma, na abordagem desta doença.

Palavras-chave: Síndrome da ardência bucal; Capsaicina; Tratamento tópico.

# 1. INTRODUCTION

Burning Mouth Syndrome (BMS) is a chronic disturbance characterized by constant complain of burning and even pain on oral mucosa without causes or systemic and oral signs identified<sup>(3, 5, 7, 19)</sup>. BMS could be considered an expression of atypical facial pain. This condition affects primarily females with prevalence increasing with age, particularly following menopause, at 55-60 years and being rare under 30 years<sup>(5)</sup>.

According to Lamey and Lewis (14), BMS can be classified into three subtypes, depending on clinical history:

- Type I: burning sensation starts in the morning and its intensity increase as day passes, being at night the major discomfort;
- Type II: symptoms are present in the hole day long in same intensity;
- Type III: patients present intermittent symptoms that disappear and appear after days or months.

In BMS, it is common that the intensity of symptoms gradually changes as time passes, despite of suddenly arise and precipitated in some patients. The most affected burning local are anterior regions of tongue and hard palate and lower<sup>(10, 16)</sup>. Besides many researches have been realized, the etiology of BMS is still unknown, making hard the handling of these individuals and many times it can become frustrated.

The recent neuropathological findings in BMS may suggest the need for alternative therapies. Studies relate the use of topical capsaicin (*Capsicum frutescens L*) to neuropathic pain treatment. It acts on sensorial neurons and can be used as analgesic<sup>(8, 9, 11, 20)</sup>. The prolonged capsaicin application promotes depletion of P substance reservoir and others neurotransmitters of sensitive nervous terminations, reducing or eliminating the painful stimulus transmission<sup>(11)</sup>. The administration of high doses of capsaicin can reduce neurotoxicity<sup>(18)</sup>, while low doses, as a cream of 0.025%, is well tolerated in temporomandibular joint area pain treatment<sup>(22)</sup>.

To use capsaicin as collutory, it is necessary to evaluate the burning sensation related by the patient, since the active principles of fruit of *Capsicum frutescens L* produce, in not controlled doses, burning sensation, making it unbearable to the individual<sup>(21)</sup>. This study aimed to evaluate the effectiveness of topical application of capsaicin (*Capsicum frutescens L*) in a concentration of 0,002% to the Burning Mouth Syndrome treatment.

#### 2. PATIENTS AND METHODS

The sample was of intentional type, 40 patients were selected alleatory from data bank of Center for Diagnosis of Diseases of the Mouth, School of Dentistry, Federal University of Pelotas (Brazil). All participants agreed to participate in the study and authorized the use of their data to the study. This research was approved by Research Ethics Committee of the Federal University of Pelotas.

The resinous oil of Capsicum frutescens L (Lot 9910243; 25g; Riq = 8,4% da Roig Farma S.A/Barcelona-Spain), was extracted from red pepper, 1mg/50 ml of bi-distilled water, corresponding to 0,002% concentration of capsaicin. The patients received orientation about how to proceed during treatment: dilute 20 drops of the substance in 50 ml of water, rinse for 1 minute, 3 times a day (in the morning, in the evening and at night) during 7 days. The intensity of symptoms was evaluated before and after the treatment with topical capsaicin, by the numerical visual scale.

All the data obtained were transferred to a data bank and analyzed statistically in SPSS 14.0.1 for Windows (SPSS® Inc. Chicago, Illinois, USA). The chi-square test and t test were used for monofactor analysis. A probability of p  $\leq 0,05$  was accepted as significant.

#### 3. RESULTS

Of the 40 patients with burning mouth syndrome, 90% were women, mean age was 60.27  $\pm$  11,54 years. The most prevalent BMS was type II with 19 (47,5%) patients. The total distribution is represented in Table 1.

Comparing the average ages of patients with SAB type I 61.07 ( $\pm$  8,11) years and II 64,05 ( $\pm$ 10,95) years did not show statistically significant differences (p = 0,39). Patients with SAB type I and II had a mean age of 62.78 ( $\pm$  9,82) years, while the average age of patients with SAB type III was 48,42 years ( $\pm$  12,39), 14,36 lesser years (p = 0,0017).

There was a large period of symptoms variation presented by the patients before diagnostic of BMS, some cases taking more than 5 years to express symptoms (Table 2). The anatomical local most affected was the tongue (27,5%), with apex and edge being the most affected regions (53%). Areas as buccal mucosa and gingiva were not very frequent. Considering the used treatment, 22 patients obtained partial reduction of symptoms (unitl 50% of remission) and 9 (22,5%) showed complete remission (Table 3).

**Table 1:** Distribution of patients according to the type of BMS. Pelotas-RS, Brazil, 2009

	Frequency (%)
Туре І	35,0
Type II	47,5
Type III	17,5
Total	100%

**Table 2:** Distribution of time to express the BMS symptoms in patients. Pelotas-RS, Brazil, 2009

	Frequency (%)
Between 1 and 6 months	35
Between 7 and 12 months	20
Between 2 and 3 years	10
Between 3 and 4 years	12,5
Between 4 and 5 years	7,5
More than 5 years	15
Total	100

**Table 3:** Distribution of number of patients according to symptoms remission after topical treatment with capsaicin. Pelotas-RS, Brazil, 2009

	Frequency (%)
Until 50% of remission	55
More than 50% of remission	20
Complete remission	22,5
There was no improvement	2,5
Total	100

#### 4. DISCUSSION

Although the Burning Mouth Syndrome is a disease of relatively high prevalence, its etiology follows unknown. The therapeutic methods aim to eliminate local factors that can aggravate the symptoms<sup>(5)</sup>.

According to Lamey and Lewis<sup>(14)</sup> classification, the most prevalent type in our study was the type II (47,5%), while type III (17,5%) was the least found. Classifying patients confers specific characteristics to the study permitting to reproduce it. When comparing ages of patients with types of BMS, it was obtained a significant statistical difference, pointing that type III patients are the youngest of our sample. This may be related to the psychological factor of the patients and stressful events experienced by them.

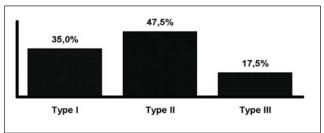
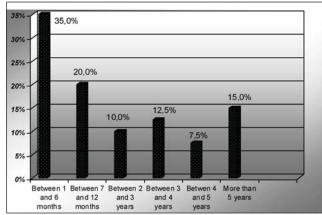
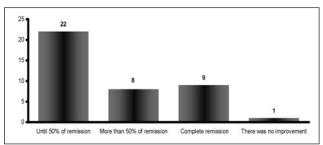


Figure 1: Distribution of patients according to the type of BMS. Pelotas-RS, Brazil, 2009



**Figure 2:** Distribution of time to express the BMS symptoms in patients. Pelotas-RS, Brazil, 2009



**Figure 3:** Distribution of number of patients according to symptoms remission after topical treatment with capsaicin. Pelotas-RS, Brazil, 2009

Observing the local of described symptoms by patients, the most frequent was tongue, agreeing with Bergdahl and Bergdahl<sup>(2)</sup> and Amenábar *et al.*<sup>(1)</sup>. To Just, Steiner and Pau<sup>(13)</sup> pain-related sensitivity and gustatory function are strongly decreased in BMS, suggesting that the syndrome influences both gustatory and peripheral trigeminal sensitivity. The results from Ito *et al.*<sup>(12)</sup> indicated that pain of the patients is strongly affected not only at a sensory component but also at an affective/motivational component.

Capsaicin, the active component of chilli pepper, is an agonist of the transient receptor

ARTIGOS ORIGINAIS SAUDE

potential vanilloid type 1 receptor (TRPV1). It opens the channel and causes membrane depolarization of sensory neurons, which release CGRP, SP and other pain peptides; excitation is followed by a refractory state, causing inactivation<sup>(6)</sup>.

According to Lauritano, Petruzzi and Baldoni<sup>(15)</sup>, systemic capsaicin can be considered a successful therapeutical approach for BMS patients. Eighty-four patients were divided in 2 groups: the first group received 3 capsules of capsaicin (50 mg of powder of red pepper with 0,25% of capsaicin) a day for one month and the second group, the control, received 3 capsules of placebo a day for the same period. Petruzzi *et al.*<sup>(17)</sup>. reported, in a pilot study, successful use a short-term of systemic capsaicin 0,25% for the management of BMS. Yet, systemic administration of capsaicin was associated with significant gastric pain and the number of complaints relating to this side-effect increased with time on treatment.

Epstein and Marcoe<sup>(8)</sup> used topical capsaicin in gel 0,025% to treat 2 patients with BMS. To the authors, the topical use of capsaicin shows

limitations, because of little effectiveness and bitter taste, reducing the adhesion of patient to topical treatment. In this study, the capsaicin in a 0,002% concentration was evaluated, showing that 22,5% of patients observed complete remission of symptoms.

The capsaicin, as mouthwash, has advantages: topical application, easy use, low cost and little collateral effects. In this study, neither patient related any adverse effect. It was verified, however, that adhesion is fundamental to the treatment, since the drug is used as mouthwash, and the use is controlled by individual itself.

## 5. CONCLUSION

The results suggest that the topical application of capsaicin in a concentration of 0,002% 3 times a day during 7 days showed to be an alternative to the treatment of BMS. Controlled studies are necessary to prove the effectiveness of capsaicin in BMS treatment and the physiopathology mechanisms of this multifactorial character must be elucidated.

RBCS ARTIGOS ORIGINAIS

# **REFERENCES**

- 1. Amenábar JM, Pawlowski J, Hilgert J, Hugo FN, Bandeira DR, Lülher F, et al. Anxiety and salivary cortisol levels in patients with burning mouth syndrome: case-control study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008 Apr;105(4): 460-5.
- 2. Bergdahl M, Bergdahl J. Burning mouth syndrome: prevalence and associated factors. J Oral Pathol Med 1999 Sep;28(8):350-4.
- 3. Brailo V, Vuéiaeeviae-Boras V, Alajbeg IZ, Alajbeg I, Lukenda J, Aeurkoviae M. Oral burning symptoms and burning mouth syndromesignificance of different variables in 150 patients. Med Oral Patol Oral Cir Bucal 2006 May;11(3):E252-5.
- 4. Cavalcanti DR, Silveira FRX. Alpha lipoic acid in burning mouth syndrome a randomized double-blind placebo-controlled trial. J Oral Pathol Med 2009 March;38(3):254-61.
- 5. Cherubini K, Maidana JD, Weigert KL, Figueiredo MAZ. Síndrome da ardência bucal: revisão de cem casos. Rev Odonto Ciênc 2005 abr/jun;20(48):109-13.
- 6. Cianchetti C. Capsaicin jelly against migraine pain. Int J Clin Pract 2010 Mar; 64(4):457-9.
- 7. Danhauer SC, Miller CS, Rhodus NL, Carlson CR. Impact of criteria-based diagnosis of burning mouth syndrome on treatment outcome. J Orofac Pain 2002 Fall;16(4):305-11.
- 8. Epstein JB, Marcoe JH. Topical application of capsaicin for treatment of oral neuropathic pain and trigeminal neuralgia. Oral Surg Oral Med Oral Pathol 1994 Feb;77(2):135-40.
- 9. Espinosa LS, López JP, Frutos RR. Síndrome de boca ardiente. Eficacia de la aplicación tópica de capsaicina. Estudio piloto. Av Odontoestomatol 2004 Dic;20(6):297-304.
- 10. Evans RW, Drage LA. Burning mouth syndrome. Headache 2005 Sep;45(8):1079-81.
- 11. Grushka M, Epstein JB, Gorsky M. Burning mouth syndrome. Am Fam Physician 2002 Feb;65(4):615-20.
- 12. Ito M, Kurita K, Ito T, Arao M. Pain threshold and pain recovery after experimen-

- tal stimulation in patients with burning mouth syndrome. Psychiatry Clin Neurosci 2002 Apr;56(2):161-8.
- 13. Just T, Steiner S, Pau HW. Oral pain perception and taste in burning mouth syndrome. J Oral Pathol Med 2010 Jan;39(1):22-7.
- 14. Lamey PJ, Lewis MAO. Oral medicine in practice: burning mouth syndrome. Br Dent J 1989; 167(6):197-200.
- 15. Lauritano D, Petruzzi M, Baldoni M. Preliminary protocol for systemic administration of capsaicin for the treatment of the burning mouth syndrome. Minerva Stomatol 2003 Jun; 52(6):273-8.
- 16. Ortiz RA. Diagnóstico diferencial del dolor orofacial I. Asociado a estructuras intracraneanas, extracraneanas y desordenes psicogénicos. Rev Fac Odontol Univ Antioq 2001 jul/dic;13(1):5-16.
- 17. Petruzzi M, Lauritano D, De Benedittis M, Baldoni M, Serpico R. Systemic capsaicin for burning mouth syndrome: short-term results of a pilot study. J Oral Pathol Med 2004 Feb; 33(2):111-4.
- 18. Ritter S, Dihn TT. Capsaicin induced degeneration in rat brain and retina. *In*: Wood JN, ed. Capsaicin in the study of pain. San Diego, CA: Academic Press, 1993. p. 105-38.
- 19. Salort-Llorca C, Mínguez-Serra MP, Silvestre FJ. Drug-induced burning mouth syndrome: a new etiological diagnosis. Med Oral Patol Oral Cir Bucal 2008 Mar;13(3):E167-70.
- 20. Scala A, Checchi L, Montevecchi M, Marini I, Giamberardino M. Update on burning mouth syndrome: overview and patient management. Crit Rev Oral Biol Med 2003;14(4):275-91.
- 21. Szallasi A, Blumberg PM. Vanilloid (capsaicin) receptors and mechanisms. Pharmacol Rev 1999 Jun;51(2):159-211.
- 22. Winocur E, Gavish A, Halachmi M, Eli I, Gazit E. Topical application of capsaicin for the treatment of localized pain in the temporomandibular joint area. J Orofac Pain 2000 Winter;14(1):31-6.

#### Correspondence to:

**Juliana Cassol Spanemberg.** Hospital São Lucas, da PUC/RS. Av. Iiranga, n. 6.690, sala 231, 2º andar – CEP 90610-000 – Porto Alegre – Rio Grande do Sul – Brazil. Tel.: +55 51 8498-8370. E-mail: jcs.odonto@yahoo.com.br