Int. J. Oral Maxillofac. Surg. 2017; 46: 1505–1511
http://dx.doi.org/10.1016/j.ijom.2017.03.032, available online at http://www.sciencedirect.com

International Journal of Oral & Maxillofacial Surgery

Clinical Paper
Oral Medicine

Pain-relieving effects of clonazepam and amitriptyline in burning mouth syndrome: a retrospective study

M. Fenelon[1,2], E. Quinque[1], E. Arrive[1,2,3], S. Catros[1,2], J. C. Fricain[1,2]

[1]Department of Dentistry, University of Bordeaux, Bordeaux, France; [2]University of Bordeaux, 16 à 20, cours de la Marne 33082 Bordeaux France; [3]University of Bordeaux, ISPED, Centre INSERM U897–Epidémiologie-Biostatistique, Bordeaux, France

M. Fenelon, E. Quinque, E. Arrive, S. Catros, J.C. Fricain: Pain-relieving effects of clonazepam and amitriptyline in burning mouth syndrome: a retrospective study. Int. J. Oral Maxillofac. Surg. 2017; 46: 1505–1511.

Abstract. This retrospective study aimed to evaluate the efficacy of clonazepam and amitriptyline in the treatment of burning mouth syndrome (BMS). A single-centre retrospective cohort study was performed among patients diagnosed with BMS. Either clonazepam or amitriptyline was administered. Patients were asked to evaluate their pain using a 10-point verbal numerical scale (VNS) at baseline, and at 6 weeks and 3 months of treatment. Mean pain-relief values were assessed according to the treatment received using the Kruskal–Wallis test. Thirty-nine patients (85% female) were included. The mean age was 65 ± 10.5 years. The mean VNS score at baseline was 7.1 ± 2.0 in patients treated with clonazepam and 7.5 ± 1.1 in those treated with amitriptyline. The mean VNS scores in the clonazepam and amitriptyline groups were 4.9 ± 2.4 and 6.1 ± 2.6, respectively, after 6 weeks of treatment ($P = 0.498$) and 4.4 ± 2.0 and 4.1 ± 2.7, respectively, after 3 months ($P = 0.509$). There was no difference between the two treatments in terms of pain reduction. Clonazepam as well as amitriptyline may be an effective treatment for BMS.

Key words: burning mouth syndrome; stomatodynia; amitriptyline; clonazepam.

Accepted for publication 29 March 2017
Available online 2 May 2017

Introduction

Stomatodynia or burning mouth syndrome (BMS) is a chronic pain condition characterized by a spontaneous burning sensation in the oral mucosa, usually with a normal clinical examination. In 2013, the International Headache Society classified BMS as ''an intraoral burning or dysaesthetic sensation, recurring daily for more than two hours per day over more than three months, without clinically evident causative lesions''[1]. BMS is often associated with other sensory disorders such as dry mouth (xerostomia) and taste alterations (dysgeusia, hypogeusia) despite normal salivation[2,3].

The main location affected is the tongue (tip and lateral borders), but the lips and the hard and soft palate can also be involved[2,4,5]. In a Swedish study on BMS reported in 1999, a prevalence of 3.7% was found (1.6% of men and 5.5% of women)[6]. This complex chronic disorder mainly affects post-menopausal women[2,7]. Two forms of stomatodynia can be distinguished: primary burning mouth syndrome for which no local or systemic cause has been identified, and

secondary burning mouth syndrome related to local or systemic conditions[3]. There is no specific diagnostic test for BMS[8].

The aetiology of primary BMS remains unclear. Several factors could be involved, including psychopathological factors, hormonal changes, and neuropathic disorders[9–11]. There is no consensus as to the treatment of BMS and there is no definitive cure[10]. Numerous treatments have been used, including benzodiazepines (clonazepam)[12,13], tricyclic antidepressants (amitriptyline)[14], anticonvulsants (gabapentin)[15], capsaicin[16], alpha-lipoic acid[16,17], cognitive behavioural therapy[18], transcranial magnetic stimulation[19], and low-level energy diode lasers[20]. The efficacy of topical clonazepam (Roche(Bâle, Suisse) Teofarma (Valle Salimbene, Italia)) has been demonstrated since it was found to reduce BMS-associated pain in a randomized placebo-controlled study[21]. Furthermore, a recent meta-analysis established that both topical and systemic administration of clonazepam is effective for symptom relief in patients with BMS[22].

Due to its side effects (withdrawal syndrome and misuse), the prescription of clonazepam in France has been restricted to neurologists and paediatricians since January 2012. It is therefore impossible to prescribe this medication in oral medicine. Since a neuropathic origin seems to be involved in the development of BMS, amitriptyline (Roche(Bâle, Suisse) Teofarma (Valle Salimbene, Italia)) could be a good alternative. Amitriptyline is a tricyclic antidepressant that is administered widely to treat chronic neuropathic pain and fibromyalgia[23,24]. It has been demonstrated that amitriptyline has an analgesic action, independent of its antidepressant effect[25–27]. Few authors have mentioned amitriptyline as a treatment for BMS, and there is no single study assessing the efficacy of amitriptyline or clonazepam in the reduction of BMS-associated pain[14,28].

The primary objective of this study was to evaluate the pain-relieving effects of clonazepam and amitriptyline for the treatment of BMS at 6 weeks and at 3 months of treatment. The secondary objectives were to assess the time delay from the beginning of symptoms to the first visit, and the adverse reactions observed with both treatments.

Materials and methods

Approval for this single-centre retrospective study was granted by the ethics review board.

Patients

The study was performed within a single specialized oral medicine consultation centre at the University Hospital of Bordeaux. The files of all patients diagnosed with stomatodynia between 2006 and 2013 were screened (Fig. 1).

Patient files were included if they met the following criteria: diagnosis of primary BMS; treatment with clonazepam or amitriptyline; follow-up visit after the initiation of treatment; availability of verbal numerical scale (VNS) scores for the evaluation of initial pain and pain at 6 weeks and 3 months of treatment in the patient's chart. Primary BMS was defined as chronic pain lasting more than 3 months, characterized by a spontaneous burning sensation in the intraoral soft tissues, for which no local or systemic cause was found.

Patients with a local condition (rough prosthesis, geographic tongue, lichen planus, candidiasis, hyposalivation) or systemic condition (diabetes, nutritional deficiencies, Sjögren's syndrome) that could be considered as a causative factor were not included. Such local or systemic conditions were sought through laboratory examinations only when suspected during the clinical approach[21]. A blood count was done for 10% of the patients, and levels of vitamins B6, B9, and B12, and ferritin were also evaluated in the case of atrophic tissue. Hyposalivation was evaluated using Saliva-Check Buffer (GC America Inc., Alsip, IL, USA), as described previously[29]. Determination of the quantity of stimulated saliva was done after chewing a piece of paraffin wax. Saliva was expectorated into a spittoon each 30 s for 5 min. The quantity of the saliva was measured by checking the millilitre markings on the side of the cup and noted down. Patients were excluded when stimulated salivation was less than 3.5 ml after chewing wax for 5 min. Unstimulated salivary flow of the minor salivary glands was assessed visually by everting the lower lip and observing droplets of saliva formed at the orifices of the minor salivary glands. If the time taken was greater than 60 s then resting flow was considered low and if the time was less than 60 s then resting flow was considered normal[29]. Patients with low unstimulated salivary flow were excluded.

The records of patients with BMS associated with a local or systemic causative condition, those who received treatment other than clonazepam or amitriptyline, and records that did not contain a pain assessment were not included.

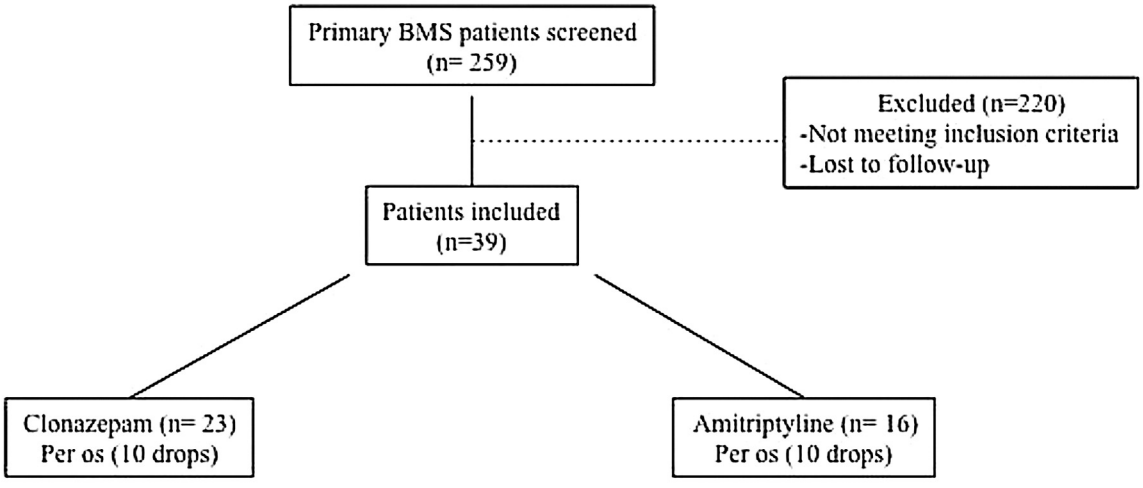

Fig. 1. Flow diagram showing patient inclusion in this retrospective study on burning mouth syndrome.