Pain Medicine

Pain Medicine 2011; 12: 466–469
Wiley Periodicals, Inc.

CASE REPORT

Burning Mouth Syndrome Responsive to Duloxetine: A Case Report

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Funding Sources, Financial Relationship and Conflict of Interest: No funding sources for this work were provided. Authors have no conflict of interest or financial relationship to declare and all participated in the preparation of the manuscript.

Abstract

Introduction. Burning mouth syndrome (BMS) is a chronic, idiopathic, intraoral mucosal pain condition in the absence of specific oral lesions and systemic disease. Among evidence-based pharmacological treatments for this disorder, topical and systemic clonazepam, levosulpiride, selective serotonine reuptake inhibitors have been used with partial results.

Case. We report a case of a 65-year-old otherwise healthy woman with a 3-year history of oral burning. Clinical and laboratory evaluations allowed us to make a diagnosis of burning mouth syndrome. She was treated with duloxetine (60 mg PO qd), a selective serotonine, and norepinephrine reuptake inhibitor, obtaining a complete remission of symptoms, evaluated via standardized clinical rating scales, and an improvement of her quality of life and level of functioning.

Discussion. The pathogenesis of BMS still remains unclear. Recently, it has been suggested an underlying neurophatic mechanism, demonstrating a dysfunction in the trigeminal nociceptive pathways at peripheral and/or central nervous system level. The rationale behind the administration of duloxetine resides in its central mechanism of action, and analgesic effects previously demonstrated in diabetic peripheral neurophathy, and fibromyalgia. Also, it has been shown to reduce painful physical symptoms associated with depression.

Conclusion. We hypothesize that duloxetine might represent a useful, effective, and additional therapeutic option in the treatment of BMS.

Key Words. BMS; Burning Mouth Syndrome; Duloxetine; Clonazepam; Serotonine

Introduction

Burning mouth syndrome (BMS) is a chronic idiopathic pain condition that affects more than one million individuals in the United States [1].

The International Association for the Study of the Pain has identified it as a distinctive nosological entity, characterized by a diffuse, continuous burning sensation involving intra-oral soft tissue, lasting at least 4–6 months, in the absence of specific oral lesions without alterations in blood tests and/or instruments findings [2]. BMS usually occurs in the fifth-seventh decade of life with an estimated prevalence range from 0.7% to 4.6% in the general adult population [3].

It is more common in females than males and was reported in 1–4% of women attending the centers for menopausal treatment [4].

In almost all patients, BMS is characterized by widespread mucosal symptoms (burning, pain, dysesthesia, hyperesthesia) involving mainly the tongue. Other sites generally affected are the hard palate, lips, alveolar ridges, cheek, and floor of the mouth. Multiple etiological factors of local, systemic, and psychological origin have been suggested.

Although many drugs have been proposed for the treatment of BMS, the management is not yet satisfactory. BMS is commonly treated with systemic anxiolitytics, antidepressants, and anticonvulsivant drugs [5,6].

Duloxetine (DLX) is a selective dual reuptake inhibitor of serotonin and norepinephrine, which has been shown to be efficacious, safe, and well tolerated in the treatment of pain and major depressive disorder (MDD) in patients with

at least moderate pain associated with depression [7]. Clinical studies have also provided evidence for the efficacy of DLX for pain conditions, as diabetic peripheral neuropathic pain (DPNP) [8] and fibromyalgia with or without major depressive disorder [9].

We report a case of a patient with BMS successfully treated with DLX.

Case Report

A 65-year-old woman was admitted to our Department for a burning sensation localized on her tongue and lips, which has lasted for 3 years. Pain was daily continuous but improved by meals. She did not report any worsening factor associated with burning. Over the previous 3 years, the patient saw a general practitioner who made a diagnosis of oral candidiasis and prescribed her topical nystatine (oral suspension, 100,000 units twice a day as mouthwash) and fluconazole (100 mg PO qd) for 7 days, without any improvement of the symptomatology.

On admission, body temperature was 36.5°C, her heart rate was 72 beats per min, and her blood pressure 100/60. The intraoral and extraoral clinical examination did not reveal any abnormalities and the salivary flow rates were normal.

Patient was examined by a complete laboratory work-up, including complete blood cell count, blood urea nitrogen, creatinine, glycemia, glucose tolerance test, glycosylated hemoglobin, alanine transferase, aspartate transaminase, gamma-glutamyl transferase, alkaline phosphatase, human serum albumin, serum total protein, direct, indirect, and total bilirubin, iron, ferritin, trasferrin saturation, tryglicerids, cholesterol, electrolytes: Na^+, K^+, Cl, HCO_3, Ca^{++}. All parameters were within normal limits. She denied other medical antecedents or use of medications.

On physical examination, she appeared otherwise healthy. Other symptoms reported were itching ears and chronic fatigue. Based on clinical, laboratory and anamnestic data we established a diagnosis of BMS.

The psychiatric examination revealed that the patient did not meet DSM-IV TR or ICD-10 criteria for any psychiatric disorder and had no history of depression, anxiety, or any psychiatric diagnosis. Furthermore the patient was negative for any psychiatric therapy. She underwent a battery scale for psychodiagnostic evaluation: Hamilton depression scale (HAM-D), State-Trait Anxiety Inventory Form Y 1-2 form (STAY-Y), visual analog scale (VAS), Pain Numeric Rating Scale (PNRS), Short-form Mc Gill Pain Questionnaire (SF-MPQ), Present Pain intensity (PPI) -VAS, Quality of life Enjoyment and Satisfaction Questionnaire Short Form (Q-LES-Q SF), and Sheehan Disability Scale (SDS). All these tests were performed at baseline after 6 and 12 months except for PNRS, which was carried out at baseline, and after 3, 6, and 12 months.

Table 1 Battery scale for psycho–diagnostic assessment

Scale	Baseline	Six Months	Twelve Months
SF-MPQ	8	4	1
PPI	3	4	1
PNRS	9	4	1
VAS (cm 0–11)	8.3	5.9	1.0
Q-LES-Q-SF	2.62	3.68	3.87
SDS (total mean)*	6.33	3.33	2.66

* The SDS value was calculated by mean of the three parameters: work, social life, and family life.
SF-MPQ = Short form McGill Pain Questionnaire; PPI = Present Pain Intensity-Visual Analog Scale; PNRS = pain numeric rating scale; VAS = visual analog scale; Q-LES-Q SF = Quality of life Enjoyment and Satisfaction Questionnaire Short form; SDS = Sheehan Disability Scale.

HAM-D scale results did not reveal depression (at baseline: 4, at 6 months: 7, and at 12 months: 5; normal range 0–8), STAY-Y scale results revealed a very mild anxiety (at baseline: 45, and at 6 and 12 months: 43; normal range 0–41). The results of SF-MPQ scale, PPI scale, PNRS, VAS, Q-LES-Q SF scale, SDS at baseline, at 6 and 12 months were reported in Table 1.

At baseline, patient started therapy with DLX (60 mg PO qd). After 3 months of treatment she reported a 40% improvement of pain (a decrease from 9 to 5 on PNRS), and then, a tapering of DLX from 60 to 30 mg daily was scheduled. One month later, patient showed a further improvement (a decrease from 5 to 4 on PNRS) but she reported a moderate constipation as side effect, and thus, voluntarily ceased taking DLX. Ten days after withdrawal, oral burning symptom increased by 40% (from 4 to 8 on PNRS), for which DLX was restarted at the dosage of 60 mg daily. Her symptoms reduced again by 40% (from 8 to 4 on PNRS) within a month, then, by 100% within 6 months (from 4 to 1 on PNRS), obtaining a complete remission of symptoms. Likewise, her quality of life showed an improvement either in terms of Q-LES-Q-SF (from 2.62 at baseline to 3.87 after 12 months of therapy) or SDS (from 6.33 at baseline to 2.66 after 12 months of therapy).

A very mild constipation reappeared, but did not require any medical treatment or immediate discontinuation of therapy. DLX was progressively tapered up to its complete withdrawal within 30 days.

The patient was followed-up for 12 months, showing a complete and long-lasting clinical remission.

Discussion

BMS is a quite common disease, which mainly affects postmenopausal women and its prevalence in the general

population ranges from 0.7% to 15%. It is characterized by spontaneous oral discomfort or burning in the tongue or other mucous membrane without organic cause [10,11].

The pathogenesis of BMS still remains poorly understood: both psychological and neurophysiological factors have been involved [12].

Indeed, a psychiatric co-morbidity was reported in many studies, ranging from 19% to 85% [3,4,13–15]. Other investigations have revealed a variety of psychosocial features and personality disorders in BMS patients, such as alexythymic traits, cancerophobia, somatization, obsession-compulsion, personal sensitivity, hostility, psychoticism, and social isolation [5,6,16,17]. In addition, a chronic pain can obviously increase the risk for depression and anxiety even in patients with no history of these problems.

On the other hand, a previous study on a small group of patient with BMS demonstrated a lower density of epithelial nerve fibers and axonal degeneration on biopsy in the anterior two-thirds of the tongue, suggesting that BMS is caused by a trigeminal small fiber sensory neuropathy [18]. In addition, neurophysiological and imaging studies have suggested a dysfunction of the nigrostriatal and mesolimbic dopamine pathways in BMS patients similar to those found in patients with anxiety and other levels of psychological distress. These studies revealed a net brain hypoactivity, which should cause a loss of function in descending inhibitory serotonergic, and noradrenergic pathways, or at least, contribute to chronic pain [19,20].

These hypotheses might explain the efficacy of serotonin and noradrenalin re-uptake-blocking antidepressant in BMS, too. Until now, the mainstay of treatment for BMS has been antidepressant and benzodiazepines [5,21]. This is the first study reporting on the efficacy of DLX in the treatment of BMS.

DLX has been approved by the Food and Drug Administration in the United States for the treatment of MDD [22] and DPNP [23] in 2004, and more recently in 2008, for fibromyalgia too, based on two randomized controlled trials [24]. Notably, it has received the same approval in Italy, except for fibromyalgia. DXL is a mixed serotonin-norepinephrine reuptake inhibitor, and a potent inhibitor of the inactivation by neuronal reuptake of both serotonin and norepinephrine with similarly high affinity for their transporter proteins (SERT and NET) in brain and other tissues. The drug has considerably less affinity for the dopamine transporter, and low affinity or for histaminic, adrenergic, cholinergic, serotoninergic, opioid, and other receptors [25–28].

Since the same deficit of neurotransmission has been detected either in depression or in BMS, we assumed that the efficacy of DLX in treating BMS might be due to its peculiar pattern of modulation of serotonine and norepinephrine neurotransmission, even in the absence of a diagnosis of depression. Also, DLX showed fast acting, few side effects with a good tolerability, and long-term results [29]. We obtained a complete remission of symptoms (PNRS from 9 to; VAS from 8.1 to 1) after 1 year of therapy with DLX, with no relapse during the follow-up. In addition, the treatment with DXT has shown a high improvement of her quality of life (Q-LES-Q SF) and level of functioning (Table 1). Indeed, her work ability, social life, and family life or home responsibilities were highly impaired at baseline and improved to a total of more than 50% after 12 months therapy.

DLX has shown a good compliance: even though a relationship with constipation was described, we noticed a scaling down on intensity of this side effect after restarting the therapy.

In conclusion, the present report suggested that DLX, in a cost/benefit analysis, might be effective for patients with BMS, even without anxiety and depression, due to its efficacy on neuropathic pain but, in order to better confirm our observation, should be proved on a larger cohort of patients in multicentric randomized controlled clinical trials.

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