International Journal of Research In Pharmacovigilance and Pharmacotherapeutics

Burning mouth syndrome (stomatodynia) sensile to duloxetine-a case report

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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 serotonin reuptake inhibitors have been used with partial results. **Case:** We report a case of a 65-year-old 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 (DLX) (60 mg PO qd), a selective serotonin, and norepinephrine reuptake inhibitor, obtaining a complete remission of symptoms, evaluated via standardized clinical rating scales (BPRS), 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 neuropathic 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 neuropathy, 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.

Keywords: Burning Mouth Syndrome; Duloxetine; Clonazepam; Serotonin

ISSN: Awaiting
Case Report

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Article Info

Received on: 20-04-2020
Revised on: 12-05-2020
Accepted on: 21-05-2020

DOI: https://doi.org/10.33974/ijrpp.v1i1.193

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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 origins 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 STUDY

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 q.i.d) for 7 days, without any improvement of the symptoms. 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 extra oral 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. All other 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 scale for psycho diagnostic 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). 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. 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). 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 in Sheehan disability scale (SDS) based on 3 parameters work, social life and family life (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 neuro physiological factors have been involved[12] Indeed, a psychiatric co-morbidity was reported in many studies, ranging from 19% to 85%[3, 4] Other investigations have revealed a variety of psychosocial features and personality disorders in BMS patients, such as alexythymic traits, somatization, obsession-compulsion. and social isolation[5, 6] In addition, a chronic pain can obviously increase the risk for depression and anxiety even in patients with no history of these problems. 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 hypo activity, which should cause a loss of function in descending inhibitory serotonergic and noradrenergic pathways, or at least, contribute to chronic pain[13] These hypotheses might explain the efficacy of serotonin and noradrenalin reuptake-blocking antidepressant in BMS, too. Until now, the mainstay of treatment for BMS has been antidepressant and benzodiazepines.[5] 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 and DPNP in 2004, and more recently in 2008, for fibromyalgia. Notably, it has received the same approval in Italy, except for fibromyalgia. DXL is a mixed serotoninnorepinephrine 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. We assumed that the efficacy of DLX in treating BMS might be due to its peculiar pattern of modulation of serotonin 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. 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 and 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.

CONCLUSION

The present report suggested that DLX, in a 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 the observation, should be proved on a larger cohort of patients in multi center randomized controlled clinical trials.

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