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PHARMACOLOGICAL MANAGEMENT OF BURNING MOUTH SYNDROME: A MULTIDISCIPLINARY APPROACH

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ABSTRACT

Burning mouth syndrome (BMS) is a poorly understood, ill-defined condition characterized by painful and burning sensations of the oral cavity in the absence of any visible mucosal abnormality or other organic disease. Although the syndrome has been recognized for long, there is no absolute consent on the diagnosis, etiology and treatment of BMS. The current manuscript attempts to unveil the dilemma surrounding pharmacological management of BMS and a brief review of related literature.

Keywords: Burning mouth syndrome, Multifactorial Etiology, Pharmacological Management.

INTRODUCTION

BMS, also known as stomatopyrosis, glossopyrosis, stomatodynia, glossodynia and oral dysaesthesia have been interchangeably adopted to emphasize the quality and/or the location of pain in the oral cavity [1]. Although the condition has been recognized for a long time, but the state of current knowledge and specific treatment protocols are still dilemmatic about this syndrome. This leads to multiple referrals of the patients seeking treatment without any useful results, leading to an increased burden on both the health care system and the patients [2]. The management relies on proper understanding of the pathogenesis of the syndrome and a multidisciplinary approach to treat it. A number of etiologies including psychologic factors have been proposed. Owing to the large variety of associated factors, the protocol for BMS management is complex [3]. An effective approach for these patients should be based on a multidisciplinary collaboration among different

medical specialists. The present manuscript reports a systematic pharmacological approach to make BMS management more predictable and effective.

DISCUSSION

The International Association for the Study of Pain (IASP) defines BMS as a 'distinctive nosological entity including all forms of burning sensation in the mouth, including complaints described as stinging sensation or pain, in association with an oral mucosa that appears clinically normal in the absence of local or systemic diseases or alterations [4].

The true prevalence of BMS is difficult to establish due to the lack of rigorous diagnostic criteria in many of the published series that do not distinguish between the symptom of oral burning and the syndrome itself, including BMS as only a symptom of other diseases. Thus, figures vary widely, with prevalence varying between 0.7 and 4.5% [5]. A number of etiological factors

involving the interaction of biological and psychological systems have been proposed for BMS. Postmenopausal women are most commonly affected with prevalence rates as high as 13% [6]. Based on the etiological factors, BMS has been classified into primary and secondary forms. Any local or systemic organic causes cannot be identified for the primary or essential/idiopathic form. Secondary form has been considered as a variant resulting from local or systemic pathological conditions.

Pharmacological management of Burning Mouth Syndrome

Owing to the large variety of associated factors, the protocol for BMS management is complex. A thorough history and clinical examination are very important along with adequate investigations to formulate the diagnosis of BMS. Patient management involves a differential diagnosis and the discrimination between primary and secondary forms based on the identification of possible etiologic factors for the syndrome. The various factors associated with secondary BMS and the psychological disorders detected in these patients deserve major emphasis at the time of treatment [7].

The current manuscript reviews various drugs belonging to different pharmacological groups: antiepileptic drugs, antidepressants, antipsychotics, analgesics and mucosal protectors for management for BMS.

Anti-epileptic drugs

Antiepileptic drugs act in a way similar to gamma-amino butyric acid (GABA), enhancing its inhibitory effects upon the central nervous system, with a reduction in neuron excitability and pain. Clonazepam and gabapentin are the major antiepileptic drugs that have been used to treat BMS [8].

Clonazepam have been used in both systemic (oral) as well as topical form effectively. In a previous study, the starting dose for Clonazepam was 0.25 mg/day, and was increased at a rate of 0.25 mg/week, to a maximum of 3 mg/day, or until treatment response was elicited. Many patients responded positively to a dose of 0.75 mg/ day or lower [9]. Clonazepam can be used in topical form by breaking up the tablet and retaining saliva in the mouth for three minutes without swallowing - followed by expulsion. The administered dose can be 0.5 to 1 mg, two or three times a day. A combined topical and systemic Clonazepam therapy for management of BMS has also been advocated in earlier studies. The patients were prescribed 0.5 mg Clonazepam, three times daily and changes were made to this regimen based on individual responses. Patients were asked to dissolve the tablet orally before swallowing and were reviewed over a period of 6 months. Pain was assessed by patients on an 11 point numerical scale (0 to 11). A large percentage of patients (80%) obtained more than 50% reduction in pain over the

treatment period. The various published studies provide preliminary evidence that most of the BMS patients record a pain reduction, feel better and wish to continue the treatment with topical and/or systemic Clonazepam. According to the results obtained with gabapentin, it seems to have little or no effect in patients with BMS. The medication was administered at an initial dose of 300 mg/day, increasing by 300 mg/day every two days to a maximum of 2,400 mg/day without any significant relief.

Anti-depressant drugs

Anti-depressants can be considered useful in view of the known psychogenic component present in most cases of BMS. The treatment benefits vary among different population groups for anti-depressant drugs.

The tricyclic antidepressants such as amitriptyline and nortriptyline at low doses are useful in BMS, although some authors contraindicate their use in patients with dry mouth as they can worsen the condition. Studies have been made to evaluate the efficacy and tolerance of amisulpiride (50 mg/day) and selective serotonin inhibitors: paroxetine (20 mg/day) and sertraline (50 mg/day) in the treatment of BMS, over eight weeks, with a reasonably high efficacy (around 70%). However, the effect of amisulpiride manifests early, after one week of treatment. No serious adverse effects are referred in any of the three groups. Serotonin reuptake inhibitors are effective, above all with an associated depression, being better tolerated for the absence of anti-cholinergic effects, particularly in dry mouth [9].

Analgesic drugs

Analgesics have also been used to treat the symptoms of BMS. These drugs were selected in view of their usefulness in treating other chronic pain disorders (topical and systemic capsaicin) or other alterations of the oral mucosa involving pain (benzylamine hydrochloride). Topical capsaicin has been applied as a desensitizing agent in BMS, but it is usually unaccepted by patients due to its taste.¹⁰ Systemic capsaicin (0.25% three times a day, for a period of one month) via oral route has been evaluated in an earlier randomized, triple blind and placebo controlled study. In the treated group, it was seen that 93% of the patients who initially presented VAS scores of 8-10, showed improvement. However its use is not recommended for an extended time since many patients experience gastric pain after four weeks of treatment.

Trials have also been made on rinsing with benzylamine hydrochloride at 0.15%, having an analgesic and anti-inflammatory effect. The affected patients received 15 ml of benzylamine hydrochloride 0.15% as a rinse for one minute, three times a day during four weeks.¹¹ 10% of the treated patients reported partial improvement. Studies have also demonstrated that rinsing with local anesthetic mouthwash such as Lidocaine has

limited therapeutic value due to short duration of analgesic effect [10].

Adjuvant therapeutic modalities

Hormone replacement therapy (HRT) has been found to be effective in a small group of females suffering from BMS, having estrogen receptors in the oral mucosa. However, HRT cannot be considered as an effective treatment modality in the majority of patients.

Trials with antioxidants such as alpha lipoic acid (ALA), Vitamin C and E have found to significantly improve the symptoms of BMS in majority of patients. ALA (200 mg, three times a day) is a powerful neuro-protector that prevents damage to nerve cells by free radicals and reduces symptoms of peripheral neuropathy. The combination of psycho-therapy (one hour session twice weekly, for a period of 2 months) and ALA (600 mg per day for 2 months) was more beneficial than either therapy alone in a previous study, suggesting that ALA can prove to be an acceptable alternative / supplement to psycho-active medication [11,12].

Sucralfate has been used as a therapeutic agent in few trials based on the fact that it has protective role on

digestive mucosa. Sucralfate was used in two pharmacological forms, 20% suspension of sucralfate four times a day during three weeks and chewable tablets containing 1 g of sucralfate. Only a limited number of patients reported improvement in symptoms, thus restricting the application of sucralfate as a standard therapy [13].

CONCLUSION

Despite the fact that numerous studies have been carried out, there is no universal consensus on the diagnosis, etiology and treatment of BMS. The lack of understanding of the exact cause and mechanism behind the syndrome adds to the difficulty in finding a standardized therapeutic management program. Current knowledge of interventions for the treatment of BMS appears to be deficient. Thus, future studies are required, in order to improvise the means in which clinicians diagnose and manage patients suffering from this complex syndrome. Till then, an effective approach for these patients should be based on a multidisciplinary collaboration among different medical specialists.

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