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The Effects of Gabapentin in Treatment of Burning Mouth Syndrome: Retrospective Pilot Study

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Purpose: The objective of this retrospective pilot study was to evaluate the effectiveness of Gabapentin in patients with primary burning mouth syndrome (BMS).

Methods: Ten subjects were diagnosed with primary BMS (8 women and 2 men). The mean age was 60.1 years. They had clinical examination to exclude local factors such as the presence of *Candida* species, xerostomia, lichen planus, etc. They also underwent hematological examination to exclude secondary BMS due to systemic disorders. Pain was assessed by patients on an 11-point numerical rating score system (0 to 10). Gabapentin was administered at a starting dose of 300 mg/day, slowly titrated up to maximum of 1,800 mg/day. All patients were treated for 4 weeks.

Results: One half of the patients (n=5) obtained reduction in pain over the treatment period. Four patients reported no reduction in pain symptoms. One patient reported that symptoms were worsening. The average pain score before the treatment was 6.3 and after the treatment was 5.25. No significant relationship was detected between pretreatment and posttreatment pain score. Only one patient noted mild side effect (dizziness).

Conclusions: This retrospective pilot study provides no preliminary evidence that Gabapentin has effect in the management of BMS. However, further research (well-designed, randomized, and controlled trial with large sample) would be needed to investigate the efficacy of Gabapentin in treatment of BMS.

Key Words: Burning mouth syndrome; Gabapentin

INTRODUCTION

Burning mouth syndrome (BMS) is a condition that is diagnosed based on the presence of an oral burning or similar dysesthesia in the absence of other dental or medical causes.[1)] Its true prevalence is uncertain, which an estimated incidence of the condition of 0.7%-4.6% in the general population and a predominance among women.[2-5)] The tongue is the primary location of the burning complaint in the majority of cases, but BMS can also involve the lips, palate, and gingival.[6)] BMS be classified into 2 clinical forms: "primary BMS" and "secondary BMS."[7)] The primary BMS for which organic local or systemic causes cannot be identified and a neuropathological cause is likely.[8)] No precise information pertaining to the natural history of BMS is available. However, according to based on a single study, spontaneous and complete remission is rare and reported to occur in 3% of patients within 5 years after the onset of BMS.[9)]

To date, the treatment of BMS has largely been empirical and depends on the patient's condition and physician's preference. There is no effective treatment applicable to most patients with BMS.[10)] However, currently employed therapies for the treatment of BMS include hormone replacement therapy, anticonvulsants, antidepressants, capsaicin, benzodiazepines, analgesics, alpha-lipoic acid (ALA),

and congnitive therapies.[11] In spite of the many behavioral and medication-based treatment, the management of BMS is still not satisfactory.

Gabapentin was approved by the U.S. Food and Drug Administration in 2002 for the treatment of postherpetic neuralgia. Even before this, Gabapentin has been used off-label for many types of neuropathic pain disorders including BMS.[12]

The objective of this pilot study was to evaluate the effectiveness of Gabapentin in patients with primary BMS.

MATERIALS AND METHODS

The study was approved by the Institutional Review Board of Pusan National University Dental Hospital.

1. Subjects and Treatment Methods

This study was conduted at the Department of Oral Medicine, Pusan National University Dental Hospital during the period from April to September 2012. Consecutive outpatients complaining of burning mouth pain were screened for inclusion in the study by clinical examination to exclude local factors, such as the presence of *Candida* species, parafunctional habits, allergic contact stomatitis, xerostomia, and lichen planus. In addition, they underwent hematological examinations to exclude systemic disorders including determination of serum levels of iron, zinc, folic acid, vitamin B_{12}, and blood glucose (Table 1). Ultimately, 10 patients (8 women and 2 men) met the inclusion criteria with definitive diagnosis of primary BMS according to the criteria of Scala et al.[7] also the exclusions criteria were as follows:

- Use of certain medications associated with BMS (for example, angiotensin converting enzyme inhibitors)
- Patients treated and being treating with psychological therapies
- History of an allergy to dental materials

2. Dose Escalations and Pain Assessment

Gabapentin was administered at a starting dose of 300 mg/day, slowly titrated up to maximum of 1,800 mg/day. The mean dose was 900±374.16 mg/day. All patients were treated for 4 weeks. Pain was assessed by patients on an 11-point numerical rating score system (0 to 10) before and after treatment.

3. Statistical Analysis

The categorical variables were summarized as counts and percentages; numerical variables as the mean±standard deviation. The treatment outcomes were statistically analyzed by Wilcoxon signed rank test using SPSS 12.0 for Windows (SPSS Inc., Chicago, IL, USA). p-values less than 0.05 were considered to be statistically significant.

RESULTS

Of the 10 subjects included in this study, 8 were female and 2 were male. The mean age was 60.1±11.56 years, ranging from 49 to 79 years. The mean symptom duration was 27.2±31.13 months. Average treatment course was 2.7 visits (range, 2-4 visits). One half of the patients (n=5) obtained reduction in pain over the treatment period. Four

Table 1. Clinical and laboratorial evaluations

Laboratory tests	Complete blood cell count	As normal values we considered;
	Blood glucose level	Glucose (fasting), plasma 75-99 mg/dL
	Serum iron level	Iron, serum (male) 65-175 μg/dL, (female) 50-170 μg/dL
	Serum vitamin B_{12}	Vitamin B_{12}, serum 200-950 pg/mL
	Folic acid levels	Folic acid, serum 145-590 ng/mL
	Zn	Zn, serum 66-110 μg/dL
Salivary flow rate measurement	Whole unstimulated saliva and stimulated saliva collected into a graded glass tube for 5 minutes	As normal values we considered; US ≥0.1 mL/min SS ≥0.7 mL/min
Exfoliative cytology	Scarpes from oral mucosa	As normal we considered absence of yeast or *Candida* species
Detection of local abnormalities	Clinical evaluation	Exclusion criteria: presence of visible mucosal lesions, inadequate prosthesis, periodontal diseases, clinical signs and symptoms of temporomandibular joint disturbances

US, unstimulated saliva; SS, stimulated saliva.

Table 2. Effect of Gabapentin in the 10 subjects

Clinical outcomes	Subject, n (%)
Improve	5 (50)
No effect	4 (40)
Worsening	1 (10)

Table 3. Summary of pain scores recorded during treatment

Pain score	Mean±SD	Range	Significant change
Pretreatment	6.3±2.26	4-10	No (p=0.168)
Posttreatment	5.25±2.68	4-8.5	

SD, standard deviation.
Statistical analysis by Wilcoxn signed rank test.

patients reported no reduction in pain symptoms. One patient reported that symptoms were worsening. After treatmet, only 2 patients obtained more 50% reduction of pain score (Table 2).

Average pain score before treatment was 6.3±2.26 (range, 4-10). The average pain score after treatment was 5.25±2.68 (range, 4-8.5). Since data did not turn out to have normal distribution because of small sample size, the Wilcoxson signed rank test was applied to analyze the difference after treatment. No significant relationship was detected between pretreatment and posttreatment pain score (p=0.168) (Table 3). Side effects were recorded by patient history. All subjects completed testing without major side effects. Only one patients noted mild side effect (dizziness).

DISCUSSION

Although there are several etiologic factors (including local, systemic, or psychological factors) in BMS patients, the exact mechanisms of BMS are not elucidated.[13] Recent neurophysiologic, psychophysical, neuropathological, and functional imaging studies have provided evidence that primary (idiopathic) BMS may be a chronic neuropathic pain disorder.[8] Therefore, for primary BMS treatment, various drugs for chronic neuropathic pain therapy have been used in clinics.[11] According to Cochrane database of systematic review in 2005, only three interventions demonstrated a reduction in BMS symptoms: ALA, clonazepam, and congnitive behavioral therapy.[1] Also, based on expert opinion and common clinical practice, topical capsaicin, systemic tricyclic antidepressants, anticonvulsant and benzodiazepine are used for managemant of BMS.[14] Although there is no one accepted treatment of for BMS, BMS should be treated as a neuropathic pain. However, management of BMS is difficult and challenging.

Gabapentin is used to manage many neuropathic pains for example postherpetic neuralgia, trigeminal neuralgia and diabetic neuropathies.[15] The mechanisms of action of Gabapentin is still uncertain but most likely it acts to affect voltage-dependent L-type CA^{2+} channels. For neuropathic pain therapy, starting dose is 300 mg/day. The dose is gradually increased to 3,600 mg/day (the maximum dose). Advantage of Gabapentin are that it has good tolerability and lower drug-drug interactions. General side effects of Gabapentin include edema, drousiness, nausea, dizziness, fatique, etc.[16] However, these side effects are not serious and self-limiting. A recent case report showed that Gabapentin was beneficial at reducing oral burning symptoms.[17] Also, Heckmann et al.[18] reported pilot study. According to the authors, Gabapentin has little or no effect for BMS. However, this study is an open-label study with small sample. Therefore, before randomized controlled study with sufficient sample, we conducted retrospective pilot study.

The results of this pilot study also suggest that Gabapentin are not beneficial for BMS treatment. Only 2 patients (20%) obtained more 50% reduction in BMS symptoms. Such results may be explained as follows: first, possible explanation that the dosage was too small or that the duration of treatment was too short. And the number of patients was too small to detect a significant treatment effect. Second, such results also may be explained by the ambiguity of the cause of BMS: primary BMS cannot be caregorized into a single pain type (neuropathic pain).

This pilot study provides no preliminary evidence that Gabapentin has effect in the management of BMS. However, further research (well-designed, randomized and controlled trial with large sample) would be needed to investigate the efficacy of Gabapentin in treatment of BMS.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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