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Efficacy of Alpha-Lipoic Acid for Symptomatic Relief in Burning Mouth Syndrome: A Clinical Study

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ABSTRACT

Objectives: To evaluate the clinical efficacy and tolerability of systemic alpha-lipoic acid (ALA) in patients with primary Burning Mouth Syndrome (BMS), a chronic neuropathic orofacial pain disorder with limited effective treatment options.

Materials and Methods: A retrospective observational pilot study, lacked control group, was conducted on 32 patients clinically diagnosed with BMS and treated with alpha-lipoic acid at a dose of 300 mg twice daily for eight weeks. Symptom severity was assessed using a 10-point Visual Analogue Scale (VAS) at baseline and after treatment. Treatment response was categorized as marked (≥50% VAS reduction), moderate (30–49%), or minimal (<30%). Statistical analysis was performed using the paired Student's t-test., with $p < 0.05$ considered statistically significant.

Results: The mean baseline VAS score was 7.6 ± 1.2. Significant reduction was observed at eight weeks (3.9 ± 1.6) ($p < 0.001$). Marked improvement was recorded in 20 patients (62.5%), moderate improvement in 8 patients (25%), and minimal or no improvement in 4 patients (12.5%). Mild gastrointestinal discomfort was reported by three patients (9.4%), which resolved without treatment discontinuation. No other serious adverse events were observed.

Conclusions: Alpha-lipoic acid demonstrated significant symptomatic improvement with good tolerability in patients with Burning Mouth Syndrome. Its neuroprotective and antioxidant properties support its role as a safe systemic therapeutic option, particularly in patients with neuropathic features or intolerance to centrally acting agents.

Keywords: Burning mouth syndrome, Alpha-lipoid acid, Neuropathic pain, Oral dysesthesia, Antioxidant therapy.

1. Introduction

Burning Mouth Syndrome (BMS) is a chronic orofacial pain condition characterized by a persistent burning or dysesthetic sensation of the oral mucosa, occurring in the absence of identifiable clinical or laboratory abnormalities. According to the International Classification of Orofacial Pain, BMS is defined as a daily intraoral burning pain lasting for at least two hours per day over a period exceeding three months, without an evident local or systemic cause. The condition predominantly affects middle-aged and elderly women and is associated with significant impairment of quality of life (1).

Reported prevalence rates of Burning Mouth Syndrome (BMS) show considerable variability, with estimates of approximately 1.7% in the general population and rising to nearly 8% among patients attending specialized clinical services. A pronounced female predilection has been consistently observed, with an estimated female-to-male ratio of 3:1, particularly

affecting peri-menopausal women and reaching frequencies as high as 18% in post-menopausal individuals (2,3) Clinically, BMS is characterized by a persistent burning or scalding oral sensation, most frequently involving the tongue (glossodynia), and less commonly the lips, palate, and gingival tissues (4). Patients often report associated complaints, such as oral dryness, altered taste perception, paresthetic sensations, and significant psychosocial burden, including elevated rates of anxiety, depressive symptoms, and sleep disorders (5).

The etiology of BMS is complex and multifactorial. While secondary BMS may be associated with nutritional deficiencies, endocrine disorders, xerostomia, or mucosal disease, primary BMS is increasingly recognized as a neuropathic pain disorder. Current evidence supports the involvement of peripheral small-fiber neuropathy, altered trigeminal sensory processing, dopaminergic dysfunction, and impaired descending inhibitory pathways. Oxidative stress and mitochondrial dysfunction have also been implicated in neural degeneration and abnormal pain modulation in BMS (6-8).

Local contributory factors include reduced salivary flow, oral fungal infections, parafunctional activities, hypersensitivity reactions, and post-procedural dental trauma. Certain pharmacological agents with xerogenic or neurotoxic properties may further increase susceptibility. Psychological conditions-particularly anxiety, depressive disorders, and ineffective coping strategies-are frequently implicated in amplifying symptom severity and promoting persistence of pain (9).

Accumulating evidence indicates that primary Burning Mouth Syndrome (BMS) is predominantly neuropathic in origin. Peripheral involvement is characterized by small-fiber dysfunction, diminished Aδ-fiber activity with relative preservation of C-fiber transmission, and upregulation of nociceptive ion channels including TRPV1 and P2X3. At the central level, altered dopaminergic activity within the basal ganglia and dysfunction of descending inhibitory pathways contribute to abnormal pain processing. These mechanisms collectively account for the variable clinical presentation of BMS and its strong association with psychiatric comorbidities (10-13).

Clinically, BMS is broadly classified into two categories. Primary (idiopathic) Burning Mouth Syndrome is regarded as a neuropathic pain condition of neurogenic origin, involving small-fiber neuropathy, altered trigeminal system function, and central pain processing dysregulation. It is diagnosed only after exclusion of identifiable local or systemic etiologies. In contrast, secondary BMS occurs as a manifestation of identifiable underlying conditions, such as hormonal imbalance, nutritional deficiencies, salivary dysfunction, or oral mucosal pathology (14). An additional clinical classification proposed by Lamey and Lewis describes three symptom patterns: Type 1, characterized by absence of symptoms on waking with progressive intensification during the day and commonly linked to systemic or metabolic abnormalities; Type 2, marked by persistent daily symptoms frequently associated with anxiety and sleep disturbances; and Type 3, featuring episodic symptoms with symptom-free intervals, often related to local irritants or allergic triggers (15).

Management of BMS remains challenging (16). Systemic pharmacological therapies, such as antidepressants, anticonvulsants, and benzodiazepines, demonstrate variable efficacy and are often limited by adverse effects, particularly in elderly patients. Topical therapies, including clonazepam mouthwash, have shown benefit in selected patients (17); however, not all individuals respond adequately, and alternative or adjunctive systemic therapies are often required. Recently explored non-drug-based treatment modalities for Burning Mouth Syndrome include low-level laser therapy (LLLT), repetitive transcranial magnetic stimulation (rTMS), and various mechanical aids, such as tongue-shielding devices; however, these approaches are still not routinely implemented in clinical practice. Considering the persistent nature of BMS and its significant effect on patients' quality of life, a comprehensive management strategy that combines pharmacological therapy with psychological and behavioral support is strongly recommended (18-20).

Alpha-lipoic acid is an endogenous antioxidant and mitochondrial cofactor with established neuroprotective properties. It has been widely used in the management of diabetic and idiopathic neuropathies due to its ability to reduce oxidative stress, improve nerve conduction, and enhance microcirculation (21-23). These mechanisms provide a strong biological rationale for its use in Burning Mouth Syndrome. Although previous studies have reported mixed outcomes regarding its efficacy in BMS, differences in study design, dosage,

duration, and patient selection may explain this variability.

The present retrospective study aimed to evaluate the clinical efficacy and safety of alpha-lipoic acid in patients with primary Burning Mouth Syndrome in a real-world clinical setting.

2. Materials and Methods

2.1 Study Design and Setting

This retrospective observational study was conducted at the Department of Dental Surgery, BIRDEM General Hospital, Shahbag, Dhaka, Bangladesh, where electronic medical records of patients diagnosed with Burning Mouth Syndrome (BMS) between August 2024 and October 2025 were reviewed. The sample represents a convenient cohort consisting of all eligible patients identified during the study period. No priority sample size calculation was performed due to the retrospective nature of the study. All patients had previously provided informed consent for treatment and use of anonymized data for research purposes.

2.2 Sample Size and Population

A total of 32 patients fulfilling the diagnostic criteria for primary BMS were included in this analysis. The sample size was determined based on the number of eligible cases available during the study period, which provided sufficient statistical power (>80%) to detect a clinically meaningful change of 2 points on the 10-point Visual Analogue Scale (VAS) for pain intensity, assuming a standard deviation of 2.5 and an α-level of 0.05.

2.3 Inclusion and Exclusion Criteria

Adult patients (≥18 years) clinically diagnosed with BMS after exclusion of identifiable local or systemic causes were included. Eligible subjects must have received oral alpha-lipoic acid 300 mg capsules twice daily after meals for at least eight weeks and completed both baseline and follow-up evaluations. Patients presenting with visible mucosal lesions, oral infections, systemic disorders associated with burning sensations (such as diabetes mellitus, nutritional deficiencies, or hormonal imbalance), history of psychiatric hospitalization, or concurrent systemic benzodiazepine therapy, were excluded.

2.4 Intervention

All patients received oral alpha-lipoic acid 300 mg capsules twice daily after meals for eight weeks. Patients were instructed regarding compliance and advised to report any adverse effects.

2.5 Follow-Up and Data Collection

The primary outcome measure was change in pain intensity assessed using a 10-point Visual Analogue Scale (VAS). Assessments were performed at baseline and eight weeks. Marked improvement was defined as ≥50% reduction in VAS, moderate as 30-49%, and minimal as <30%. Secondary outcomes included patient-reported improvement in oral comfort and documentation of adverse events. Data was extracted from electronic medical records.

2.6 Statistical Analysis

VAS scores were expressed as mean ± SD. Baseline and post-treatment scores were compared using paired Student's t-test ($p < 0.05$). Analyses were performed with SPSS (version 25).

2.7 Ethics

This investigation involved only secondary analysis of previously recorded clinical data generated during standard patient care. As the study did not involve new data collection or any form of clinical intervention, this study was exempt from ethical review.

3. Results

3.1 Patient Characteristics

The observational study included 32 patients with a mean age of 55.2 ± 9.1 years (range 39–71 years). Female predominance was observed (75%). The tongue was the most commonly affected site, followed by the palate and the lips. Pre-treatment baseline severity stratification is provided in Table 1.

Table 1. Pre-treatment baseline VAS severity

Baseline VAS severity	No. of cases
Severe (VAS 7–10)	32
Moderate (VAS 4–6	0
Mild (VAS 1–3)	0

3.2 Treatment Outcomes

The mean baseline VAS score of 7.6 ± 1.2 decreased

significantly to 3.9 ± 1.6 at eight weeks ($p < 0.001$). The mean overall VAS reduction was 3.7 points.

Marked improvement (≥50% VAS reduction) was observed in 20 patients (62.5%), moderate improvement in 8 patients (25%), and minimal or no improvement in 4 patients (12.5%). Figure 1 illustrates comparative mean VAS scores of patients before and after treatment.

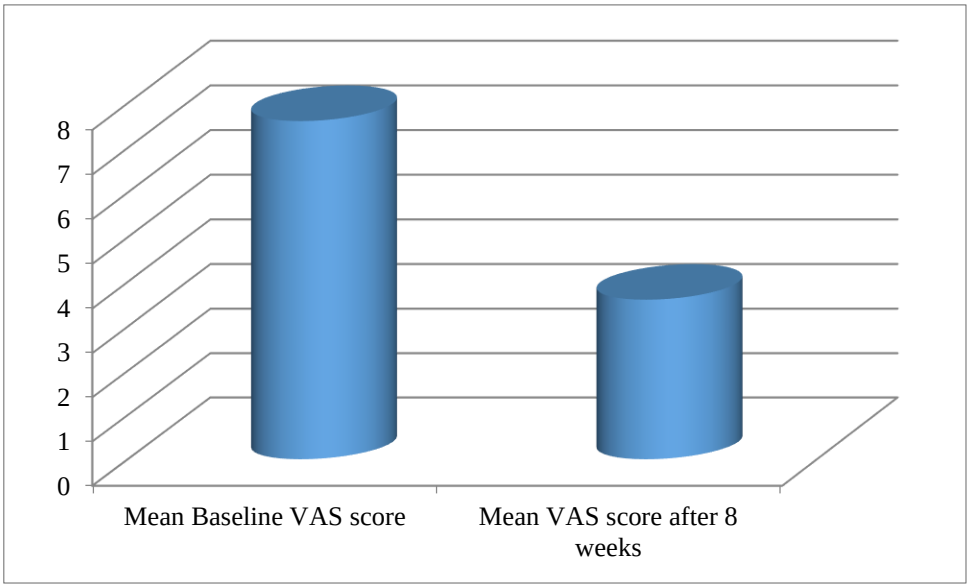

Figure 1: Bar chart showing comparative mean VAS scores

Table 2 represents Summary of patient improvement.

Table 2. Summary of patient improvement (n=32)

Improvement category	Number of patients (%)
Marked	20 (62.5%)
Moderate	8 (25%)
Minimal or No	4 (12.5%)

There was no statistically significant difference in VAS reduction between males and females. Both of the groups notified improvement of quality of life following treatment.

3.3 Safety and Tolerability

Three patients (9.4%) reported mild gastrointestinal discomfort during the first two weeks of therapy, which resolved spontaneously. No patient discontinued treatment, and no other serious adverse effects were recorded.

4. Discussion

This prospective study demonstrates that alpha-lipoic acid provides significant symptomatic relief in a substantial proportion of patients with Burning Mouth Syndrome. The observed reduction in pain intensity was both statistically and clinically meaningful, supporting the role of ALA as an effective systemic therapy for BMS.

The therapeutic benefit of alpha-lipoic acid is likely related to its multifaceted neuroprotective actions. ALA reduces oxidative stress, improves mitochondrial function, enhances endoneurial blood flow, and stabilizes small sensory nerve fibers. These mechanisms are particularly relevant in BMS, where small-fiber neuropathy and oxidative neuronal injury are increasingly recognized as key pathophysiological contributors (21-23)

Compared with centrally acting agents, such as antidepressants or benzodiazepines, alpha-lipoic acid offers several advantages. It has a favorable safety profile, minimal drug interactions, and good tolerability, making it suitable for elderly patients and those with multiple comorbidities. While the magnitude of pain reduction may be modest compared with topical clonazepam in some cases, ALA may serve as a valuable alternative or adjunctive therapy, particularly in patients who do not tolerate or respond to topical agents (24).

Previous studies evaluating ALA in BMS have reported variable outcomes. Differences in dosage, treatment duration, and patient selection likely

contribute to inconsistent findings. The present study supports the concept that sustained treatment over at least eight weeks is necessary to achieve optimal benefit, reflecting the gradual neuroregenerative effects of antioxidant therapy (24,25).

The psychosocial component of BMS should also be considered. While alpha-lipoic acid primarily targets peripheral neuropathic mechanisms, comprehensive management should integrate patient education, reassurance, and psychological support to optimize outcomes.

This study has several limitations. Its retrospective observational design restricts causal inference, and the absence of a placebo-controlled group prevents definitive attribution of symptom improvement to alpha-lipoic acid, particularly given the recognized placebo response in primary Burning Mouth Syndrome. The use of a convenient sample within a defined timeframe, without prior sample size calculation, and the relatively small cohort limit generalizability. Additionally, potential selection bias related to record-based inclusion cannot be excluded. Finally, although pain intensity was assessed using VAS scores, no validated quality-of-life instrument was employed. Prospective randomized controlled trials with standardized outcome measures are required to confirm therapeutic efficacy.

Future research should focus on well-designed, adequately powered randomized controlled trials to determine the true therapeutic efficacy of alpha-lipoic acid in primary Burning Mouth Syndrome. Incorporation of placebo control, predefined sample size calculation, baseline severity stratification, and analysis of symptom duration is recommended. The use of validated quality-of-life instruments alongside standardized pain assessment tools would further enhance clinical relevance and evidence strength.

5. Conclusions

Alpha-lipoic acid appears to be a safe and moderately effective systemic therapy for Burning Mouth Syndrome, providing significant symptomatic relief with minimal adverse effects. Its antioxidant and neuroprotective properties make it a rational therapeutic option, particularly in patients with neuropathic features or intolerance to centrally acting medications. Larger randomized controlled trials are warranted to further define its role in the management of Burning Mouth Syndrome.

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Conflict of Interests

The authors affirm that no financial, professional, or personal relationships existed that could be perceived as influencing the design, execution, or interpretation of this study.

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