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Efficacy of Clonazepam Mouthwash for Symptomatic Relief in Burning Mouth Syndrome: A Pilot Study

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ABSTRACT

Objectives: To evaluate the clinical efficacy and tolerability of topical clonazepam mouthwash in patients with Burning Mouth Syndrome (BMS), a chronic idiopathic pain disorder that significantly affects quality of life.

Materials and Methods: A retrospective pilot study was conducted on 30 patients clinically diagnosed with BMS and treated with clonazepam mouthwash (0.5 mg/5 mL solution, three times daily). Symptom severity was assessed using the Visual Analogue Scale (VAS) at baseline and after treatment. Statistical analysis was performed using the paired Student's t-test.

Results: The mean age of participants was 54.7 ± 8.9 years, with a female predominance (76.7%). The mean baseline VAS score of 7.8 ± 1.1 decreased significantly to 3.2 ± 1.4 after therapy ($p < 0.001$). Marked improvement was reported in 70% of patients, moderate benefit in 20%, and minimal change in 10%. Two patients (6.7%) experienced transient drowsiness, with no major adverse effects observed.

Conclusions: These findings contribute region-specific data from a South Asian cohort, an under-represented population in BMS research. Clonazepam mouthwash provided significant symptomatic relief with excellent tolerability, suggesting its potential as a safe, locally acting therapeutic option for BMS. Further large-scale, prospective studies are warranted to confirm efficacy and optimize treatment protocols for long-term management.

Keywords: Burning mouth syndrome, Clonazepam, Mouthwash, Oral pain, Retrospective study, Topical therapy.

1. Introduction

Burning Mouth Syndrome (BMS) is a chronic orofacial pain disorder, defined by the International Classification of Orofacial Pain as an intraoral burning or dysesthetic sensation occurring daily for at least two hours over a period exceeding three months, without identifiable local or systemic pathology (1). The reported prevalence varies, affecting around 1.7% of the general population and up to 8% of specialist clinical patients, with a marked female predominance (female-to-male ratio is approximately 3:1), particularly among peri- and up to 18% of post-menopausal women (2,3).

Despite growing international evidence, there is limited data on the efficacy of topical clonazepam in South Asian populations, despite growing, who may exhibit different dietary, cultural, and psychosocial profiles affecting treatment response. BMS typically manifests as a burning or scalding sensation, most commonly affecting the tongue (glossodynia), followed by the lips, palate, and gingiva (4). Accompanying symptoms often include xerostomia, dysgeusia, paraesthesia, and heightened psychosocial distress, with

comorbid anxiety, depression, and sleep disturbance being frequently reported (5).

The condition is multifactorial. Contributory systemic factors include endocrine disorders (diabetes mellitus, thyroid disease), nutritional deficiencies (iron, zinc, folate, vitamin B12), and hormonal changes, particularly estrogen deficiency during menopause (6,7,8). Local factors may include salivary hypofunction, oral candidiasis, parafunctional habits, allergic reactions, or trauma following dental procedures. Medications with xerostomic or neurotoxic effects may also predispose patients. Psychological comorbidities, such as anxiety, depression, and maladaptive coping behaviors, often exacerbate pain perception and disease chronicity (9). Current evidence supports a neuropathic basis for primary BMS. Peripheral mechanisms include small-fiber neuropathy, reduced Aδ fiber activity with preserved C fiber function, and overexpression of nociceptive receptors, such as TRPV1 and P2X3. Central mechanisms involve dopaminergic hypofunction within the basal ganglia and impaired descending inhibitory control, contributing to altered pain modulation. These pathophysiological processes explain the heterogeneous clinical picture and the frequent association with psychiatric morbidity (10-13).

BMS can be categorized into two broad types: Primary (idiopathic) BMS with no identifiable systemic or local cause, representing true neuropathic pain, and secondary (symptomatic) BMS symptoms arising secondary to identifiable conditions, such as endocrine dysfunction, nutritional deficiency, xerostomia, or oral mucosal disease (14). Further clinical sub-categorization was proposed by Lamey and Lewis: Type 1: no symptoms on waking, worsening throughout the day; often associated with systemic/metabolic disturbances, such as diabetes or deficiencies; type 2: Continuous daily symptoms, closely linked to anxiety and poor sleep; type 3: Intermittent symptoms with symptom-free periods, sometimes related to allergic reactions or local irritants (15).

Management of BMS remains challenging due to its multifactorial etiology and neuropathic underpinnings (16). A combination of informative intervention and reassurance, cognitive-behavioral therapy (CBT), and pharmacological or topical agents is recommended. Systemic treatments, including tricyclic antidepressants, serotonin–noradrenaline reuptake inhibitors, gabapentin, pregabalin, and systemic benzodiazepines, demonstrate inconsistent efficacy and may be poorly tolerated. Topical therapies, particularly clonazepam and capsaicin rinses, have shown more consistent efficacy in randomized trials and meta-analyses, with clonazepam demonstrating benefit in both short- and long-term symptom control (17). Emerging non-pharmacological interventions include low-level laser therapy (LLLT), repetitive transcranial magnetic stimulation (rTMS), and mechanical devices, such as tongue protectors, although their use is not yet widespread. Given the chronicity and impact of BMS, a multidisciplinary approach integrating both pharmacological and psychosocial support is widely advocated (18, 19, 20).

This retrospective pilot study therefore aimed to evaluate the efficacy and tolerability of clonazepam mouthwash in a South Asian cohort of patients with BMS, thereby contributing context-specific evidence to guide clinical practice.

2. Materials and Methods

2.1 Study Design and Setting

This retrospective 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 January 2022 and June 2024 were reviewed. All patients had previously provided informed consent for treatment and use of anonymized data for research purposes.

A total of 30 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.

2.2 Inclusion and Exclusion Criteria

Adult patients (≥18 years old) clinically diagnosed with BMS, after exclusion of identifiable local or systemic causes, were included. Eligible subjects must have received topical clonazepam mouthwash for at least two 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.

2.3 Intervention and Communication

All patients were prescribed clonazepam mouthwash (0.5 mg/5 mL solution). They were advised to prepare fresh homemade mouthwash before use by crushing one 0.5 mg clonazepam tablet into fine powder followed by, mixing with 5 mL of sterile or boiled-cooled water to form uniform suspension. They were instructed to retain the solution intraorally for three minutes before expectoration, to be used three times daily. Clear verbal and written instructions were provided regarding dosage, duration (ranging from two to six weeks), and avoidance of swallowing. Patients were counseled regarding potential drowsiness and advised against operating heavy machinery during the treatment period.

2.4 Follow-up and Data Collection

Patients were followed up at 2-week intervals, either in person or through telephonic consultation, to assess symptom progression, treatment adherence, and possible adverse effects. The total follow-up period ranged from two weeks to six weeks, tailored to individual patient response. Marked improvement was defined as ≥50% reduction in VAS, moderate as 30-49%, and minimal as <30%. Data was extracted from electronic medical records using a structured template, including demographic variables (age, sex), duration of symptoms, treatment duration, baseline and follow-up VAS scores, and occurrence of side effects.

2.5 Outcome Measures and Gender Comparison:

The primary outcome measure was the change in pain intensity on a 10-point VAS between baseline and the final follow-up. Secondary outcomes included subjective improvement in oral comfort, along with documentation of adverse events. Data was further analyzed to compare treatment response between male and female patients to identify any potential gender-related variations in therapeutic outcomes.

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).

The research was based solely on secondary analysis of archived data obtained during routine clinical care. Since no new data was collected and no intervention was performed, the study was thus exempted from ethical review.

3. Results

Thirty patients were included (mean age 54.7±8.9 years, range 38-70 years). Female predominance (76.7%) was noted. The tongue was the most frequently affected site (60%), followed by the palate (23.3%) and the lips (16.7%).

The mean baseline VAS score was 7.8 ± 1.1, which declined significantly to 3.2±1.4 post-treatment ($p < 0.001$). The mean reduction of 4.6 points represents a clinically meaningful benefit and is also statistically significant. Figure 1 represents comparative mean VAS scores of patients before and after treatment. Out of 30 participants, 21 recorded marked improvement, 6 recorded moderate improvements, while 3 recorded minimal/no improvements (Table 1).

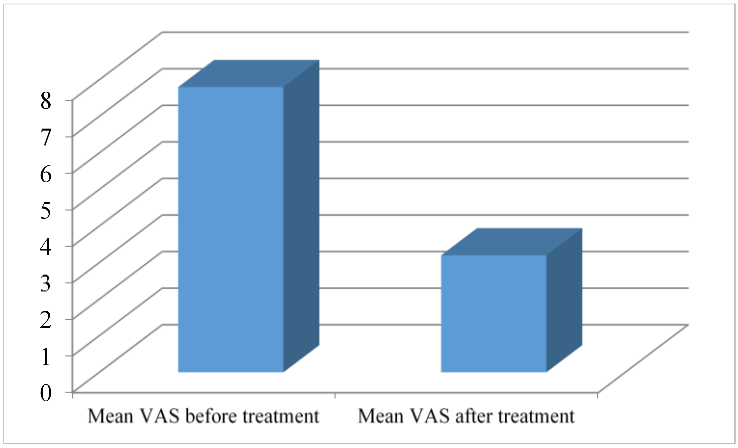

Figure 1: Bar chart showing comparative mean VAS scores

Table 1: Summary of patient improvement (n=30)

Improvement category	Number (%) of patients
Marked	21 (70%)
Moderate	6 (20%)
Minimal	3 (10%)

There was no statistically significant difference in VAS reduction between males and females. Two patients (6.7%) reported mild transient drowsiness, which resolved spontaneously. No major adverse effects were observed.

4. Discussion

This retrospective pilot study demonstrates that clonazepam mouthwash provides a significant symptomatic relief in patients with Burning Mouth Syndrome (BMS), with a mean VAS reduction of 4.6 points and favorable tolerability. The magnitude of improvement observed exceeds the minimum clinically important difference for pain, indicating a clinically meaningful benefit.

BMS is a notoriously challenging disorder to treat because of its multifactorial etiology and complex neuropathophysiology. Conventional systemic treatments—including tricyclic antidepressants, serotonin–noradrenaline reuptake inhibitors, and anticonvulsants—often provide inconsistent benefits and are frequently limited by adverse effects and poor patient adherence. In contrast, clonazepam has emerged as one of the more consistently effective therapeutic options. Several previous studies have reported significant pain reduction with topical clonazepam in BMS, supporting our findings, whereas a few trials have shown variable or short-lived responses, possibly due to differences in dosing, duration, or patient selection. These discrepancies may be explained by heterogeneity in BMS sub-types and underlying psychosocial comorbidities, reinforcing the need for individualized therapy.

The therapeutic effect of clonazepam mouthwash is primarily attributed to its action on peripheral γ-aminobutyric acid type A (GABA_A) receptors located in the oral mucosa. By enhancing inhibitory neurotransmission, clonazepam reduces peripheral nerve hyperexcitability and abnormal nociceptive signaling, which are key mechanisms implicated in BMS. Additionally, topical application may exert a secondary anxiolytic effect through limited systemic absorption, further contributing to symptom relief.

Topical clonazepam offers distinct advantages over systemic administration. Local mucosal application ensures direct delivery to peripheral GABA_A receptors abundant in the tongue, palate, and salivary glands, thereby modulating neuropathic excitability at the site of symptoms. This limits systemic absorption, reducing the risks of sedation, cognitive impairment, and dependence associated with oral benzodiazepine use. In the present study, only two patients reported mild transient drowsiness, consistent with the favorable safety profile reported in previous literature (21,22).

Several other interventions have been evaluated in BMS with variable outcomes. Topical capsaicin has demonstrated efficacy through desensitization of TRPV1 receptors, although its clinical utility is often limited by poor tolerability due to initial burning sensations. Alpha-lipoic acid and gabapentin, either alone or in combination, have shown modest benefit in randomized trials; however, meta-analyses have not confirmed consistent efficacy across studies (23). Duloxetine and venlafaxine may improve symptoms in refractory cases, but their use is frequently constrained by systemic adverse effects.

Non-pharmacological interventions are gaining attention. Low-level laser therapy has demonstrated short- and long-term analgesic benefits through photobiomodulatory and anti-inflammatory mechanisms. Repetitive transcranial magnetic stimulation targeting the dorsolateral prefrontal cortex has provided significant pain reduction in randomized controlled trials, particularly in medication-resistant BMS. Mechanical aids, such as tongue protectors, may reduce local trauma, although long-term compliance remains limited. These findings suggest that multimodal therapy may be advantageous, particularly in refractory or complex cases (17-19).

Clinical characteristics may influence treatment response. Higher baseline pain intensity and irregular pain patterns have been associated with improved response to clonazepam, whereas comorbid depression

appears to attenuate therapeutic efficacy. This underscores the importance of comprehensive clinical evaluation and tailored treatment strategies.

The psychosocial dimension of BMS is increasingly recognized. Anxiety, depression, and pain catastrophization not only exacerbate symptom perception, but also reduce responsiveness to treatment. Evidence indicates that reassurance and patient education can improve quality of life, while cognitive–behavioral therapy has demonstrated both short- and long-term benefits in resistant cases (25). Accordingly, topical clonazepam should ideally be incorporated into a multidisciplinary management approach combining pharmacological, behavioral, and psychological interventions.

Unlike many randomized controlled trials, this study reflects routine clinical practice in a resource-limited, high-burden region, thereby enhancing its real-world and translational relevance.

To the authors' knowledge, this is the first documented report evaluating topical clonazepam mouthwash in a South Asian BMS cohort. Cultural and dietary factors, including frequent consumption of spicy foods, may influence symptom expression and treatment response, highlighting the importance of region-specific clinical data.

4.1 Study Strengths and Limitations

The strengths of this study include its real-world clinical setting, good treatment tolerability, and contribution of novel regional data from an under-represented South Asian population. However, several limitations must be acknowledged. Reretrospective design, small sample size, absence of a *placebo* or comparator group, lack of secondary outcome measures, and reliance on subjective pain scales limit causal inference and may introduce reporting bias. Additionally, secondary outcome measures were not assessed, and the relatively short follow-up period precludes conclusions regarding long-term durability of benefit.

Future research should focus on larger, multicenter randomized controlled trials to validate these findings, determine optimal dosing and duration of topical clonazepam therapy, and evaluate combination strategies integrating pharmacological and psychosocial interventions.

Data from studies, such as the present one, may help inform future clinical guidelines and support evidence-based decision-making for BMS management in resource-limited and high-prevalence settings, where simple, low-cost, and well-tolerated therapies are particularly valuable.

In summary, clonazepam mouthwash appears to be a safe, effective, and well-tolerated therapeutic option for Burning Mouth Syndrome, providing clinically meaningful symptom relief with minimal adverse effects. While being not curative, it represents a valuable component of multidisciplinary BMS management, particularly in populations where high-quality regional evidence remains limited.

5. Conclusions

Clonazepam mouthwash appears to be a safe, effective, and well-tolerated therapy for symptomatic relief in BMS. It offers a practical, locally acting option with minimal systemic risk. These preliminary findings, particularly in a South Asian population, underscore the need for well-designed prospective trials to confirm efficacy and to guide evidence-based management of this challenging condition. These results warrant further prospective investigation and provide early evidence to inform practice in South Asian populations where BMS remains under-recognized.

This study contributes novel, region-specific evidence regarding the efficacy of topical clonazepam in a South Asian cohort—a population in which Burning Mouth Syndrome is often underdiagnosed and under treated, and where dietary and psychosocial factors may alter disease presentation and treatment response.

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Conflict of Interests

The authors declared no conflict of interest.

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