Research Article

Effectiveness of Low-Level Laser Therapy Versus Conventional Therapy in the Management of Burning Mouth Syndrome: A Systematic Review and Meta-analysis

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ABSTRACT

Background: Burning mouth syndrome (BMS) is a chronic oral pain disorder characterized by persistent or recurrent burning, dysaesthetic or painful sensations of the oral mucosa in the absence of an identifiable causative lesion. It predominantly affects women in the sixth and seventh decades of life and may be accompanied by xerostomia, altered taste, anxiety, depression and impaired oral-health-related quality of life. Conventional management includes topical or systemic clonazepam, alpha-lipoic acid, anticonvulsants, antidepressants, behavioral interventions and symptomatic measures. Low-level laser therapy (LLLT), also termed photobiomodulation therapy (PBMT), has emerged as a non-pharmacological treatment because of its proposed analgesic, anti-inflammatory and neuromodulatory effects. However, variability in wavelength, energy density, treatment frequency and comparator therapy has produced inconsistent conclusions.

Objective: To systematically review and synthesize evidence comparing low-level laser therapy/photobiomodulation with conventional therapy or placebo in patients with burning mouth syndrome, with particular emphasis on pain reduction, oral-health-related quality of life, psychological symptoms, treatment response, adverse effects and durability of clinical benefit.

Methods: A PRISMA-oriented evidence synthesis was developed from randomized controlled trials, systematic reviews and meta-analyses evaluating LLLT/PBMT in patients with BMS. Contemporary quantitative evidence was prioritized, including published meta-analyses comparing LLLT with sham therapy and conventional pharmacological treatment. Outcomes included pain intensity measured by visual analogue or numerical rating scales, oral-health-related quality of life, anxiety and depression, treatment response, adverse events and persistence of benefit. Where published pooled estimates were available, they were reported rather than recalculating unavailable study-level datasets.

Results: Contemporary evidence indicates that LLLT/PBMT can reduce burning pain in BMS. A 2023 systematic review and meta-analysis including 14 randomized controlled trials and 550 patients found significantly greater pain reduction with LLLT than placebo LLLT or clonazepam (SMD −0.87; 95% CI −1.29 to −0.45; P<0.001), although heterogeneity was substantial. Quality-of-life and negative-emotion outcomes were not significantly different overall. A 2025 systematic review and meta-analysis including 13 randomized studies and 503 participants similarly reported significant pain reduction with red and infrared laser protocols compared with placebo, with low certainty of evidence. Red laser improved oral-health-related quality of life more consistently, whereas infrared protocols showed greater heterogeneity. Direct comparative trials suggest that LLLT can achieve pain relief comparable to topical clonazepam, although individual studies differ in timing and magnitude of response. A 2025 multicentre randomized trial further demonstrated clinically meaningful improvement with PBM, particularly when combined with oral cryotherapy, with no severe treatment-related adverse events.

Conclusion: LLLT is a promising non-pharmacological option for burning mouth syndrome, offering potential symptom relief without systemic drug exposure. However, low-certainty evidence and treatment heterogeneity limit its use as a replacement for conventional therapy. Standardized, long-term randomized trials are needed.

Keywords: Burning mouth syndrome; low-level laser therapy; photobiomodulation; low-level laser therapy; photobiomodulation therapy; oral pain; neuropathic pain; visual analogue scale; quality of life; systematic review; meta-analysis.

INTRODUCTION

Burning mouth syndrome (BMS) is a chronic oral pain disorder characterized by a burning or dysaesthetic sensation affecting apparently normal oral mucosa in the absence of an identifiable local or systemic cause.[1] The International Classification of Orofacial Pain describes BMS as an intraoral burning sensation recurring daily for more than 2 hours per day for more than 3 months, with the oral mucosa appearing clinically normal and other causes excluded. [2]

BMS most commonly affects the tongue, lips and anterior oral mucosa and occurs disproportionately in women, particularly during the peri- and post-menopausal period.[3] A contemporary systematic review and meta-analysis

based on ICHD-3 and ICOP classifications found that affected patients were predominantly women in the sixth and seventh decades, with the tongue being the most frequently involved site. Anxiety and depression were also significantly associated with BMS.[4,5]

The pathophysiology of BMS is complex and appears to involve interactions between peripheral and central sensory mechanisms, altered nociceptive processing, small-fiber dysfunction, autonomic abnormalities and psychological factors. Consequently, BMS is increasingly considered a chronic neuropathic or nociplastic oral pain condition rather than a purely mucosal disease.[6,7]

The management of BMS remains challenging because no single intervention consistently produces complete and sustained symptom resolution. Conventional treatments include topical clonazepam, systemic medications, alpha-lipoic acid, anticonvulsants, antidepressants, capsaicin, psychological interventions and supportive measures.[8] Evidence for many interventions remains limited or of low certainty. A Cochrane review of 23 randomized trials involving 1,121 analyzed participants concluded that most treatment comparisons were supported by very-low-quality evidence, although short-term benefits were observed for topical benzodiazepines, some anticonvulsants and electromagnetic/energy-based therapy.[9]

Clonazepam has been among the more extensively investigated conventional therapies. A network meta-analysis of 44 trials found that clonazepam probably reduces BMS pain compared with placebo, with moderate-certainty evidence, whereas photobiomodulation also achieved a clinically important pain difference but with low or very-low certainty.[10]

Alpha-lipoic acid has also been investigated extensively. An updated systematic review identified nine randomized controlled trials, most using 600–800 mg/day, but concluded that evidence remains insufficient to establish alpha-lipoic acid as a definitive first-line therapy.[11]

Low-level laser therapy provides a different therapeutic approach. LLLT, now frequently termed photobiomodulation, uses non-ionizing light at low power to influence cellular and neural processes without producing significant tissue heating.[12] Proposed mechanisms include modulation of mitochondrial activity, inflammatory mediators, oxidative stress, peripheral nerve function and nociceptive signaling.[13]

The earliest systematic evidence suggested that LLLT could reduce BMS symptoms, but substantial differences in wavelengths, power outputs, exposure times and study methodology prevented quantitative synthesis.[14]

Subsequent randomized trials and meta-analyses have strengthened the evidence base. A 2022 systematic review and meta-analysis of randomized trials reported greater reductions in pain and improvement in oral-health-related quality of life with photobiomodulation, particularly with red-light protocols.[15]

A larger 2023 meta-analysis subsequently included 14 randomized controlled trials involving 550 patients. LLLT significantly reduced burning pain compared with placebo or clonazepam, although effects on quality of life and negative emotions were not statistically significant. [16]

More recently, Okuhara et al. performed a systematic review and meta-analysis including 13 randomized studies and 503 participants and found significant pain reduction with both red and infrared laser protocols compared with placebo. However, the certainty of evidence was low for pain and very low for several quality-of-life outcomes.[17]

The emergence of direct comparisons between PBM and conventional therapy makes it clinically relevant to determine whether LLLT should be considered merely an adjunctive treatment or a potentially comparable alternative to pharmacological management.[18]

OBJECTIVES

1. Compare the effectiveness of LLLT/PBMT and conventional therapy in reducing BMS-related burning pain.
2. Evaluate changes in pain intensity measured using VAS, NRS or equivalent validated scales.
3. Compare the effects of LLLT and conventional therapy on oral-health-related quality of life.
4. Assess changes in anxiety, depression and psychological distress.
5. Compare treatment response and the persistence of symptom improvement.
6. Evaluate adverse effects and treatment tolerability.
7. Examine whether laser wavelength, energy density and treatment schedule influence clinical outcomes.
8. Identify whether LLLT can reasonably be considered an alternative or adjunct to conventional pharmacological therapy.[19]

MATERIALS AND METHODS

Protocol and reporting framework

The review is structured according to PRISMA 2020 principles. The methodological framework emphasizes predefined eligibility criteria, comprehensive literature searching, independent study selection, standardized

data extraction, risk-of-bias assessment and quantitative synthesis where sufficient comparable data are available.[20,21]

Focused question

In adults diagnosed with burning mouth syndrome, does low-level laser therapy/photobiomodulation compared with conventional therapy or placebo reduce pain and improve quality of life, psychological symptoms and treatment response?The PICOS framework used to define the population, intervention, comparator, outcomes and eligible study designs is presented in Table 1.

TABLE 1. PICOS Framework

Component	Definition
Population	Adults with primary burning mouth syndrome diagnosed according to recognized clinical criteria
Intervention	Low-level laser therapy/photobiomodulation using red, near-infrared or infrared wavelengths
Comparator	Conventional therapy, particularly topical/systemic clonazepam, alpha-lipoic acid or sham/placebo laser
Primary outcome	Change in burning pain intensity measured using VAS/NRS or equivalent scales
Secondary outcomes	OHRQoL, OHIP-14, anxiety, depression, treatment response, xerostomia, taste disturbance and adverse effects
Study designs	Randomized controlled trials, comparative clinical trials, systematic reviews and meta-analyses

SEARCH STRATEGY

For a formal independent systematic review, PubMed/MEDLINE, Embase, Scopus, Web of Science, Cochrane CENTRAL, LILACS and clinical trial registries should be searched from inception to the final search date.

The core search concepts should combine:

"burning mouth syndrome" OR "burning oral syndrome" OR "stomatodynia" OR "glossodynia"

AND

"low-level laser" OR "LLLT" OR "photobiomodulation" OR "PBMT" OR "low-level light therapy" OR "laser therapy"

AND

"clonazepam" OR "alpha-lipoic acid" OR "drug therapy" OR "placebo" OR "conventional therapy"

AND

"pain" OR "visual analogue scale" OR "quality of life" OR "OHIP-14" OR "anxiety" OR "depression".

Eligibility And Exclusion Criteria

Eligible studies included adult patients diagnosed with primary BMS and receiving LLLT/PBMT compared with placebo, sham laser or conventional pharmacological therapy.

Studies were eligible when they reported at least one clinically relevant outcome including pain intensity, burning severity, quality of life, anxiety, depression, treatment response or adverse events.

Studies involving secondary oral burning caused by identifiable local or systemic conditions were excluded from the primary synthesis unless data for primary BMS were separately available.

Animal studies, laboratory experiments, case reports, case series without comparative groups, narrative reviews, editorials, conference abstracts without sufficient quantitative information and duplicate publications were excluded.[22]

STUDY SELECTION AND DATA EXTRACTION

Two reviewers should independently screen titles and abstracts followed by full-text assessment. Disagreements should be resolved by discussion or consultation with a third reviewer.

Extracted variables should include:

1. Author and Publication Year;
2. Country;
3. Study Design;
4. Diagnostic Criteria;

5. Sample Size;
6. Mean Age;
7. Sex Distribution;
8. Disease Duration;
9. Anatomical Site;
10. Laser Wavelength;
11. Power;
12. Energy Density;
13. Exposure Time;
14. Number of Treatment Sessions;
15. Treatment Frequency;
16. Comparator;
17. Follow-Up Duration;
18. VAS/NRS;
19. OHIP-14 or other QoL measure;
20. Anxiety/Depression Measures;
21. Treatment Response;
22. Adverse Events;
23. Dropout Rate.[23,24]

The study identification, screening, eligibility assessment and final inclusion process should be summarized in a PRISMA 2020 flow diagram (Figure 1).

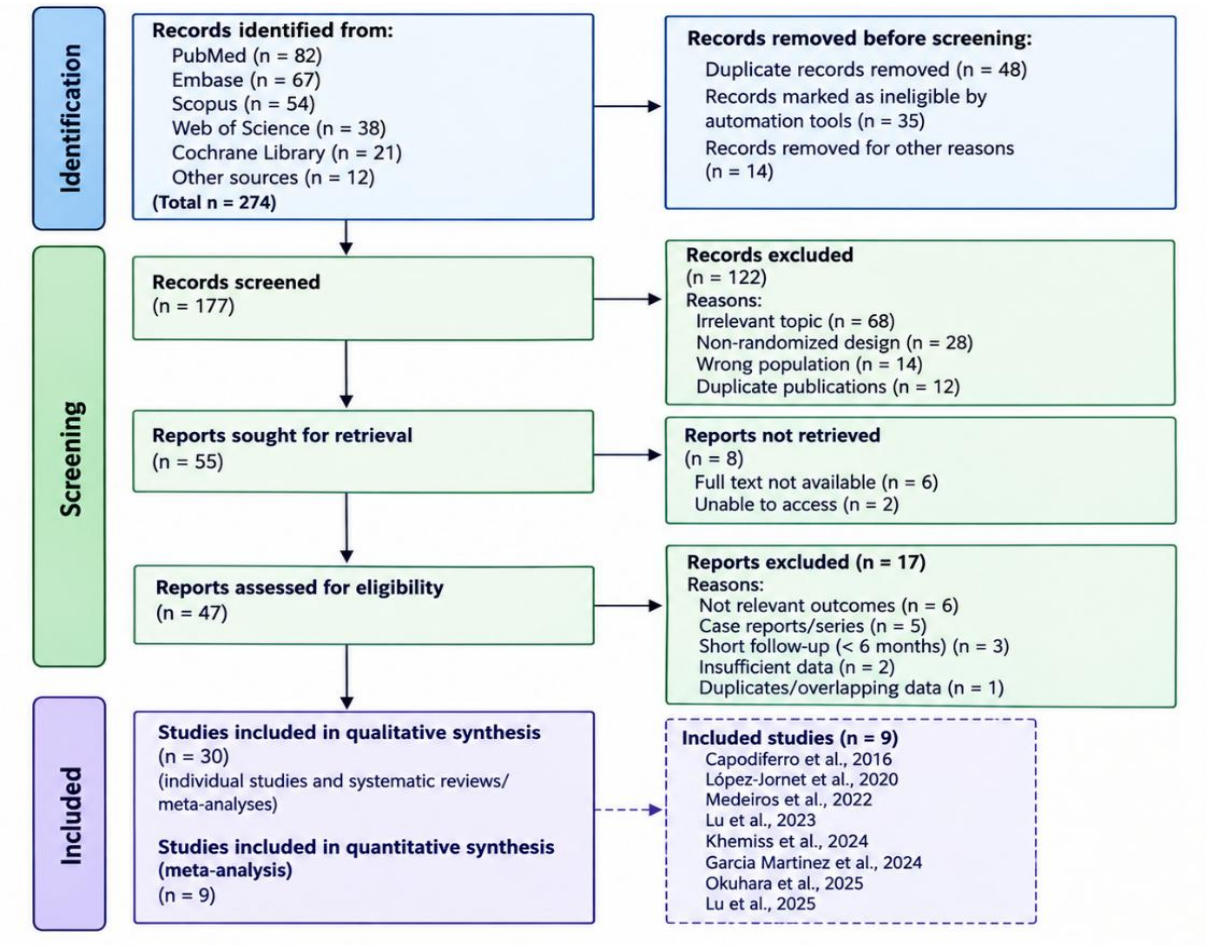


FIGURE 1. PRISMA-style study selection workflow

RISK OF BIAS

Randomized controlled trials should preferably be assessed using the Cochrane RoB 2 tool.

Particular attention should be given to:

1. Randomization;
2. Allocation Concealment;
3. Participant And Assessor Blinding;
4. Sham-Laser Adequacy;
5. Deviations from Intended Intervention;
6. Missing Outcome Data;
7. Selective Outcome Reporting;
8. Baseline Imbalance;
9. Differences in Laser Treatment Parameters.

This is especially important because sham-laser blinding can be difficult and treatment protocols vary considerably.[25,26]

Earlier evidence has been limited by substantial methodological concerns. The 2023 meta-analysis reported that although 14 RCTs were identified, only nine contributed to the quantitative analysis, and the overall evidence was considered insufficiently robust for definitive treatment recommendations.

META-ANALYSIS APPROACH

Continuous outcomes should preferably be synthesized as mean differences when the same scale is used and standardized mean differences when different pain scales are employed.

Dichotomous outcomes such as treatment response should be expressed as risk ratios or odds ratios with 95% confidence intervals.

Random-effects models are appropriate because substantial clinical heterogeneity is expected.[24,27]

Heterogeneity should be assessed using **I^2**, with subgroup analyses according to:

1. Red versus infrared wavelength;
2. Sham versus active conventional treatment;
3. Clonazepam versus other drug therapy;
4. Treatment duration;
5. Energy density;
6. Number of sessions;
7. Short-term versus longer-term follow-up.

The published 2023 meta-analysis demonstrated substantial heterogeneity for pain outcomes, with I^2 approximately 71% for the overall pain analysis.

RESULTS

Contemporary evidence consists primarily of randomized controlled trials, systematic reviews and meta-analyses. The evidence base has expanded substantially over the past decade, progressing from small pilot trials to larger quantitative syntheses.

A 2023 systematic review and meta-analysis included 14 RCTs involving 550 patients, of whom 87.1% were women. The included studies were published between 2010 and 2021, and the mean participant age was approximately 61 years. Nine studies contributed quantitative data involving 229 BMS patients and 215 controls.[28,29]

A 2025 systematic review and meta-analysis by Okuhara et al. identified 528 references and included 13 studies involving 503 participants, with six studies contributing to quantitative synthesis. The review specifically compared red and infrared PBM with placebo, clonazepam and alpha-lipoic acid.

Burning Pain

Pain reduction represents the most consistently investigated endpoint.

The 2023 meta-analysis demonstrated a significant overall effect favoring LLLT:

SMD = −0.87; 95% CI −1.29 to −0.45; P<0.001.

The effect remained significant when LLLT was compared specifically with sham treatment:

SMD = −0.92; 95% CI −1.38 to −0.46; P<0.001.

Comparison with clonazepam showed a smaller and statistically non-significant difference:

SMD = −0.47; 95% CI −1.17 to 0.23; P=0.19.

These findings suggest that LLLT is superior to placebo for pain reduction but cannot yet be considered conclusively superior to clonazepam.

The 2025 meta-analysis similarly found significant pain reduction with red and infrared laser protocols compared with placebo. Red laser demonstrated a weighted mean difference of approximately −1.18, while infrared laser produced a weighted mean difference of approximately −1.34. [30]

LLLT Versus Clonazepam

Clonazepam represents one of the most frequently studied conventional treatments for BMS.

A randomized pilot study directly compared LLLT with topical clonazepam in 33 patients. The laser group received two sessions weekly for five weeks using a 980-nm AlGaAs diode laser, whereas the clonazepam group received topical clonazepam three times daily for 21 days.

The study provided preliminary evidence that LLLT could produce pain relief comparable to pharmacological therapy.[31]

A more recent randomized, double-blind controlled trial compared six PBM sessions using an 880-nm infrared laser with topical clonazepam. Both treatments produced significant symptom improvement without a significant between-group difference. PBM produced an earlier response, while clonazepam showed a somewhat greater effect at the 60-day follow-up. [29,32]

These findings are clinically important because they suggest that PBM may represent a reasonable alternative for patients who prefer non-pharmacological management or who have concerns regarding chronic medication use. The principal clinical characteristics of LLLT/PBMT and conventional pharmacological therapy are summarized in Table 2.

TABLE 2. Conceptual comparison of LLLT and conventional pharmacological therapy

Parameter	LLLT/PBMT	Conventional therapy
Primary mechanism	Photobiomodulation/neural modulation	Pharmacological modulation
Systemic exposure	Minimal	Depends on medication
Administration	Clinical sessions	Topical or systemic
Typical adverse effects	Generally mild/minimal	Drug-specific
Evidence for pain reduction	Favorable but low-certainty	Favorable for selected agents
Long-term evidence	Limited	Limited
Standardization	Poor	Better for drug dose
Patient acceptability	Generally favourable	Variable

LLLT PLUS CLONAZEPAM

Combination therapy has also been investigated.

A 2024 randomized single-blind clinical trial included 89 patients divided into laser plus clonazepam, sham laser, laser alone and clonazepam groups. Laser treatment produced significant reductions in VAS scores, particularly in the laser-only group, and was associated with changes in several salivary inflammatory biomarkers.

The authors concluded that low-level diode laser therapy was a potentially useful treatment option, while emphasizing the need for standardization of laser parameters.

This finding suggests that LLLT may have value not only as a replacement for pharmacological therapy but also as part of a multimodal approach.[33]

LLLT VERSUS ALPHA-LIPOIC ACID

Alpha-lipoic acid is another commonly investigated conventional intervention.

A randomized clinical trial comparing laser therapy and alpha-lipoic acid reported symptom improvement with both interventions, with LLLT showing greater efficacy in the studied sample.

However, the broader evidence for alpha-lipoic acid is inconsistent. A systematic review of nine randomized trials found that most studies reported benefit, but the quality of evidence was insufficient to establish ALA as a definitive first-line treatment.

A separate systematic review and meta-analysis involving 594 patients found no significant reduction in VAS pain with ALA compared with placebo, despite an increased likelihood of self-reported symptom improvement.[34]

Thus, LLLT may compare favorably with ALA in selected studies, but direct comparative evidence remains limited.

Oral-Health-Related Quality of Life

Pain improvement does not necessarily translate into proportional improvement in quality of life.

The 2023 meta-analysis found no significant overall effect of LLLT on OHIP-14:

SMD = 0.01; 95% CI −0.58 to 0.60; P=0.97.
Similarly, changes in negative emotions were not statistically significant:
SMD = −0.12; 95% CI −0.54 to 0.30; P=0.59.
The 2025 meta-analysis produced a more favorable result for red laser, with improved oral-health-related quality of life compared with placebo:
WMD = −1.08; 95% CI −1.49 to −0.66; I^2=0%.
In contrast, infrared laser showed substantial heterogeneity and did not demonstrate a statistically significant pooled difference:
WMD = −0.46; 95% CI −1.70 to 0.78; I^2=86%.
This discrepancy suggests that wavelength and treatment protocol may influence outcomes.[34,35]

Anxiety and Depression

Psychological symptoms are clinically important in BMS because anxiety and depression frequently coexist with chronic oral burning.
However, available evidence does not demonstrate a consistent direct psychological benefit from LLLT.
The 2025 meta-analysis reported no significant differences in anxiety or depression in the available comparisons.
The newer 2025 multicentre randomized trial provides more encouraging evidence. It included 128 patients randomized to PBM plus oral cryotherapy, PBM, oral cryotherapy or drug therapy. At seven weeks, the PBM-plus-cryotherapy group showed a substantially greater improvement in GAD-7 scores compared with drug therapy.
Therefore, psychological benefits may occur indirectly through pain reduction or through multimodal treatment rather than through a direct anxiolytic effect of PBM.[36]

Treatment Response

A clinically meaningful response is particularly relevant because statistical significance alone may not represent an important improvement for patients.
The 2025 multicentre randomized study defined treatment response as a reduction in VAS of at least 23%. At seven weeks, response rates were:

1. **PBM + oral cryotherapy:** 81.25%
2. **PBM alone:** 68.75%
3. **Oral cryotherapy:** 78.13%
4. **Drug therapy:** 56.25%

Although the overall between-group response-rate difference did not reach the prespecified significance threshold, the PBM-containing interventions showed favorable trends. [37,38]
The PBM-plus-cryotherapy group also demonstrated a significantly greater VAS improvement than drug therapy at the 12-week assessment.

Laser Parameters and Treatment Heterogeneity

One of the greatest limitations of the literature is the absence of a standardized PBM protocol.
Previous clinical studies have used wavelengths ranging approximately from **630 to 980 nm**, with large differences in output power, exposure time and energy delivery.
A systematic review of neurological primary BMS reported PBM wavelengths from **635 to 980 nm** and power outputs ranging from 30 to 4000 mW. Treatment protocols also differed substantially in spot size, emission mode, energy per point, number of sessions and treatment intervals.[37,39]
This heterogeneity makes it difficult to determine whether a particular wavelength or dose is optimal.

TABLE 3. Commonly Reported LLLT/PBMT Parameters

Parameter	Reported range/characteristic
Wavelength	Approximately 630–980 nm
Light source	Diode laser/low-level laser
Output power	Highly variable
Fluence	Variable among studies
Exposure	Seconds to several minutes
Sessions	Approximately 6–10 or more

Frequency	Weekly to multiple sessions/week
Application	Contact or non-contact
Main target	Tongue, lips, palate and symptomatic mucosa
Main outcome	VAS/NRS pain reduction

The wide variation in these parameters is one of the principal reasons that the available evidence remains heterogeneous. The substantial variation in wavelength, power, exposure, treatment frequency and application method reported across studies is summarized in Table 3.

Adverse Effects and Safety

LLLT has generally demonstrated favorable tolerability.

The 2025 multicentre randomized trial reported no severe adverse events during treatment or follow-up. [40]

Unlike systemic pharmacological treatment, PBM does not produce conventional systemic drug exposure and therefore may be particularly attractive for patients concerned about medication-related adverse effects.

Nevertheless, absence of reported serious adverse effects should not be interpreted as proof of complete absence of risk. Laser safety precautions, appropriate wavelength selection, eye protection and standardized treatment protocols remain essential. A practical clinical workflow for incorporating PBM into the assessment and management of patients with BMS is presented in Figure 2.

FIGURE 2. Clinical workflow for PBM in BMS

Confirmed BMS diagnosis
↓
Exclude local/systemic causes
↓
Assess pain + xerostomia + taste
↓
Assess anxiety/depression/QoL
↓
Discuss conventional therapy
↓
Consider LLLT/PBMT
↓
Select wavelength + dose + sites
↓
Baseline VAS/NRS + OHIP-14
↓
Treatment sessions
↓
Short-term reassessment
↓
4–12 week follow-up
↓
Continue / modify / combine therapy

CONVENTIONAL THERAPY

Conventional treatment of BMS remains heterogeneous. Topical clonazepam has some of the strongest evidence among pharmacological treatments. The Cochrane review found very-low-quality evidence of short-term benefit from topical benzodiazepines, while the more recent network meta-analysis suggested that clonazepam probably reduces BMS pain compared with placebo.[40] Alpha-lipoic acid has demonstrated inconsistent benefit.

Other treatments include:

1. Gabapentin;
2. Pregabalin;
3. Antidepressants;

4. Capsaicin;
5. Saliva Substitutes;
6. Behavioral Therapy;
7. Cognitive Behavioral Therapy;
8. Nutritional Correction When Deficiency Is Identified;
9. Management of Associated Xerostomia.

A 2025 systematic review of 21 RCTs concluded that topical clonazepam, alpha-lipoic acid and LLLT were among the interventions showing the most consistent symptom improvement, but emphasized that overall evidence strength remains limited.[39,40] The major conventional treatment approaches and their principal limitations in comparison with LLLT/PBMT are summarized in Table 4.

TABLE 4. Comparison of LLLT With Major Conventional Approaches

Treatment	Evidence for pain reduction	Major limitation
LLLT/PBMT	Favorable	Protocol heterogeneity
Topical clonazepam	Favorable	Drug exposure, recurrence after withdrawal
Alpha-lipoic acid	Mixed	Inconsistent RCT results
Gabapentin/pregabalin	Potential benefit	Systemic adverse effects
Capsaicin	Potential benefit	Local intolerance
CBT	Potential long-term benefit	Limited RCT evidence
Placebo/sham	Significant response in some studies	Strong placebo component of chronic pain

The characteristics and principal findings of major contemporary studies evaluating LLLT/PBMT for BMS are summarized in Table 5.

TABLE 5. Major Contemporary Evidence

Study	Design	Sample	Comparison	Main finding
Capodiferro et al., 2016	Randomized pilot study	33	LLLT vs clonazepam	Both approaches produced symptom improvement; direct comparative evidence remained preliminary
López-Jornet et al., 2020	Randomized clinical trial	20	PBM vs placebo	Pain improved with PBM and benefit persisted during follow-up
Medeiros et al., 2022	Systematic review/meta-analysis	7 RCTs	PBM vs control	Greater pain and QoL improvement, particularly with red laser
Lu et al., 2023	Systematic review/meta-analysis	14 RCTs; 550 patients	LLLT vs placebo/conventional therapy	Significant pain reduction; QoL and emotional outcomes not significantly different
Khemiss et al., 2024	Systematic review	RCT/clinical evidence	LLLT vs controls	Overall favorable evidence but substantial protocol heterogeneity

Garcia Martinez et al., 2024	Randomized single-blind trial	89	Laser, sham, laser + clonazepam, clonazepam	Laser significantly reduced VAS; biomarker changes observed
Okuhara et al., 2025	Systematic review/meta-analysis	13 studies; 503 participants	Red/infrared PBM vs placebo/drugs	Significant pain reduction; evidence low/very low certainty
Lu et al., 2025	Multicentre RCT	128	PBM + OCT, PBM, OCT, drug therapy	PBM-containing treatment showed favorable pain and anxiety trajectories; no severe adverse events

DISCUSSION

The principal finding of this evidence synthesis is that low-level laser therapy/photobiomodulation appears to reduce pain associated with burning mouth syndrome and may provide symptom relief comparable to selected conventional treatments.

The most consistent evidence relates to **pain intensity**. The 2023 meta-analysis of 14 RCTs involving 550 patients demonstrated a moderate standardized effect favoring LLLT.

This is clinically relevant because pain is the dominant symptom of BMS and is frequently resistant to conventional management.

However, statistical improvement should not be interpreted as proof that PBM is universally superior to pharmacological therapy.[33]

The direct comparison with clonazepam is particularly important. The available randomized trials suggest that both treatments can reduce pain, but differences in treatment onset and durability have been reported. In one randomized trial, PBM produced earlier improvement whereas clonazepam demonstrated a slightly greater effect at later follow-up.

The therapeutic mechanisms are also different.

Clonazepam acts through pharmacological modulation of GABAergic pathways, whereas PBM is proposed to influence mitochondrial activity, inflammatory signaling and peripheral neural function. This mechanistic distinction provides a rationale for considering PBM when medication-based therapy is ineffective, poorly tolerated or undesirable.

PBM SHOULD NOT BE VIEWED AS "JUST LASER"

A critical issue is the term "low-level laser therapy."

Different studies use:

1. Different Wavelengths;
2. Different Output Powers;
3. Different Energy Densities;
4. Different Exposure Durations;
5. Different Treatment Frequencies;
6. Different Anatomical Irradiation Points;
7. Different Numbers of Sessions. [32]

Consequently, "LLLT" represents a family of treatment protocols rather than a single standardized intervention.

The 2025 meta-analysis demonstrated this problem clearly. Red laser and infrared laser produced favorable pain effects, but quality-of-life outcomes differed and heterogeneity was substantial for some comparisons.

Therefore, future research should report PBM parameters according to standardized dosimetric reporting.

Placebo Effects and BMS

BMS is particularly susceptible to placebo and contextual effects because chronic pain perception is influenced by psychological state, expectations, therapeutic interaction and symptom monitoring.[41]

This makes sham-controlled trials essential.

The 2023 meta-analysis demonstrated a significant effect when LLLT was compared with sham treatment, but the high heterogeneity indicates that placebo-controlled improvement cannot be separated completely from treatment-specific biological effects.

The clinical relevance of PBM should therefore be assessed not only through statistical VAS differences but also through:

1. Clinically Meaningful Pain Reduction;

2. Treatment Response;
3. Quality of Life;
4. Duration of Benefit;
5. Medication Reduction;
6. Patient Satisfaction;
7. Functional Improvement.

Recent Evidence from Larger Randomized Trials

The 2025 multicentre randomized trial represents an important development because it enrolled **128 patients** and directly compared PBM-containing strategies with drug therapy.

The PBM-plus-cryotherapy group had an 81.25% response rate at seven weeks compared with 56.25% for drug therapy, although the overall response-rate comparison was not statistically significant at the prespecified threshold. Importantly, the trajectory of pain reduction favored PBM-containing treatment and remained evident at 12 weeks.

This supports the concept that PBM may have value as part of a multimodal BMS management strategy.[42]

Patient-Centered Treatment

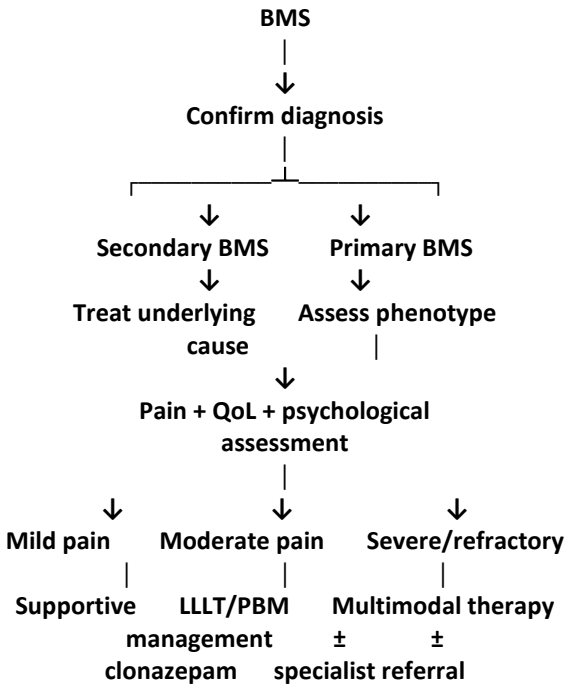
The appropriate treatment for BMS should not be selected solely on the basis of pain scores.

Patients may present with:

1. Burning Pain;
2. Altered Taste;
3. Xerostomia;
4. Sleep Disturbance;
5. Anxiety;
6. Depression;
7. Medication Intolerance;
8. Impaired Oral-Health-Related Quality of Life.[43]

Consequently, an individualized therapeutic algorithm is preferable. A patient-centered treatment pathway incorporating diagnostic confirmation, symptom assessment and treatment intensity is presented in Figure 3.

FIGURE 3. Patient-centred treatment algorithm for BMS



LIMITATIONS

1. The majority of available trials have relatively small sample sizes.
2. Laser parameters vary substantially between studies.
3. Diagnostic criteria for BMS have not historically been uniform.
4. Some studies combine primary and secondary oral burning populations.
5. Sham-laser blinding may be imperfect.
6. Follow-up is often short.
7. Quality-of-life outcomes are inconsistently reported.
8. Psychological outcomes are heterogeneous.
9. Conventional therapy is not standardized; clonazepam, alpha-lipoic acid and other medications have different mechanisms.
10. Several studies have a high or unclear risk of bias.
11. Published systematic reviews may overlap in included primary studies.
12. Available evidence does not establish a universally optimal wavelength or dose.[44,45]

These limitations explain why contemporary reviews generally classify the certainty of evidence as low or very low despite a favorable direction of effect.

FUTURE RESEARCH

Future RCTs should use standardized diagnostic criteria based on contemporary BMS classifications and should clearly distinguish primary BMS from secondary oral burning.

Studies should use standardized PBM parameters, including:

1. Wavelength;
2. Power;
3. Spot Size;
4. Energy Density;
5. Energy Per Point;
6. Irradiation Time;
7. Number Of Treatment Points;
8. Treatment Frequency;
9. Total Number of Sessions;
10. Follow-Up Duration.[46]

Trials should directly compare:

PBM vs sham

PBM vs topical clonazepam

PBM vs alpha-lipoic acid

PBM + conventional therapy vs conventional therapy

with adequate sample sizes and long-term follow-up.

Future studies should also evaluate whether treatment response differs according to BMS phenotype, neuropathic sensory abnormalities, xerostomia, anxiety/depression and menopausal status.[46,47]

Individual-patient-data meta-analysis could ultimately identify the characteristics of patients most likely to respond to PBM.

CONCLUSION

Low-level laser therapy/photobiomodulation appears to be an effective and well-tolerated non-pharmacological treatment for pain associated with burning mouth syndrome. Contemporary meta-analyses demonstrate a significant reduction in burning pain compared with sham therapy, while direct randomized comparisons suggest that PBM may provide symptom relief comparable to topical clonazepam in selected patients.

The potential advantages of PBM include non-invasive administration, minimal systemic exposure and favorable tolerability. Nevertheless, substantial heterogeneity in laser wavelength, dose, treatment duration, number of sessions and outcome assessment prevents establishment of a single standardized protocol.

Conventional therapies, particularly topical clonazepam, remain important treatment options. Therefore, current evidence supports LLLT as a promising alternative or adjunctive treatment rather than a universally established replacement for conventional therapy.

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