Research, Society and Development, v. 14, n. 2, e3614248159, 2025
(CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v14i2.48159

Effectiveness of Photobiomodulation in pain associated with Burning Mouth Syndrome: A systematic review

Eficácia da Fotobiomodulação na dor associada à Síndrome da Boca Ardente: Uma revisão sistemática

Efectividad de la Fotobiomodulación en el dolor asociado al Síndrome de Boca Ardiente: Una revisión sistemática

Received: 01/27/2025 | Revised: 02/06/2025 | Accepted: 02/07/2025 | Published: 02/11/2025

Aylla de Lima Leal
ORCID: https://orcid.org/0009-0005-5930-4118
Universidade Estadual de Feira de Santana, Brazil
E-mail: ayllaleal@gmail.com
Almira Oliveira Pereira
ORCID: https://orcid.org/0000-0003-0888-8449
Universidade Estadual de Feira de Santana, Brazil
E-mail: oliveirapereiraalmira@gmail.com
Lais Karuline Silva Costa
ORCID: https://orcid.org/0009-0004-0142-8807
Universidade Estadual de Feira de Santana, Brazil
E-mail: laiskaruline@hotmail.com
Serena de Oliveira Guimarães Passos
ORCID: https://orcid.org/0009-0006-6236-5656
Universidade Estadual de Feira de Santana, Brazil
E-mail: serenadeog@gmail.com
Juliana Monteiro Azevedo
ORCID: https://orcid.org/0000-0001-5009-9115
Universidade Estadual de Feira de Santana, Brazil
E-mail: jscmonteiro@uefs.br
Valéria Souza Freitas
ORCID: https://orcid.org/0000-0002-7259-4827
Universidade Estadual de Feira de Santana, Brazil
E-mail: vsfreitas@uefs.br
Michelle Miranda Lopes Falcão
ORCID: https://orcid.org/0000-0002-0929-2324
Universidade Estadual de Feira de Santana, Brazil
E-mail: mmlfalcao@uefs.br

Abstract
Objective To evaluate the effectiveness of low-level laser in reducing pain associated with Burning Mouth Syndrome. Method A systematic review was carried out, analyzing randomized clinical trials (RCTs) that compared the use of low-level laser with another treatment strategy to reduce pain in patients with BMS. The studies were selected through search in the databases PubMed (including Medline), Scopus, Embase, SciELO, Web of Science, Latin American and Caribbean Health Sciences (LILACS) and Cochrane until November 30, 2022, and updated on October 30, 2023. Results Eight RCTs which included 183 study participants and 150 controls were identified. The studies showed a higher percentage of women affected by BMS in relation to men. The predilection sites were the tongue, buccal mucosa and lip. Individuals irradiated with the laser showed improvement at the end of the intervention. Conclusion The use of low-level laser can be a therapeutic option for controlling the painful symptoms caused by BMS, as well as, indirectly, the associated emotional aspects. However, according to the diversity of photobiomodulation protocols found, new studies need to be developed to standardize laser therapy parameters for BMS and, thus, evaluate the control of painful symptoms longitudinally.
Keywords: Photobiomodulation; Pow-level laser; Burning Mouth Syndrome; Pain.

Resumo
Objetivo Avaliar a eficácia do laser de baixa intensidade na redução da dor associada à Síndrome da Boca Ardente. Método Foi realizada uma revisão sistemática, analisando ensaios clínicos randomizados (ECR) que compararam o uso do laser de baixa intensidade com outra estratégia de tratamento para redução da dor em pacientes com SBA. Os estudos foram selecionados por meio de busca nas bases de dados PubMed (incluindo Medline), Scopus, Embase,

SciELO, Web of Science, Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS) e Cochrane até 30 de novembro de 2022, e atualizados em 30 de outubro de 2023. Resultados Foram identificados oito ECRs que incluíram 183 participantes do estudo e 150 controles. Os estudos apresentaram maior percentual de mulheres acometidas pela SBA em relação aos homens. Os locais de predileção foram língua, mucosa bucal e lábio. Os indivíduos irradiados com o laser apresentaram melhora ao final da intervenção. Conclusão O uso do laser de baixa intensidade pode ser uma opção terapêutica para o controle dos sintomas dolorosos causados pela SBA, bem como, indiretamente, dos aspectos emocionais associados. Entretanto, diante da diversidade de protocolos de fotobiomodulação encontrados, novos estudos precisam ser desenvolvidos para padronizar os parâmetros da laserterapia para SBA e, assim, avaliar o controle dos sintomas dolorosos de forma longitudinal.
Palavras-chave: Fotobiomodulação; Laser de baixa intensidade; Síndrome da Boca Ardente; Dor.

Resumen
Objetivo Evaluar la efectividad del láser de baja intensidad en la reducción del dolor asociado al síndrome de boca ardiente. Método Se realizó una revisión sistemática, analizando ensayos clínicos aleatorizados (ECA) que compararon el uso de láser de baja intensidad con otra estrategia de tratamiento para reducir el dolor en pacientes con SBA. Los estudios fueron seleccionados mediante búsqueda en las bases de datos PubMed (incluyendo Medline), Scopus, Embase, SciELO, Web of Science, Ciencias de la Salud de América Latina y el Caribe (LILACS) y Cochrane hasta el 30 de noviembre de 2022 y actualizada al 30 de octubre de 2023. Resultados Se identificaron ocho ECA que incluyeron 183 participantes del estudio y 150 controles. Los estudios mostraron un mayor porcentaje de mujeres afectadas por SBA en relación a los hombres. Los sitios de predilección fueron la lengua, la mucosa bucal y el labio. Los individuos irradiados con el láser mostraron mejoría al final de la intervención. Conclusión El uso de láser de baja intensidad puede ser una opción terapéutica para el control de los síntomas dolorosos ocasionados por el SBA, así como, indirectamente, los aspectos emocionales asociados. Sin embargo, de acuerdo a la diversidad de protocolos de fotobiomodulación encontrados, es necesario desarrollar nuevos estudios que permitan estandarizar los parámetros de la terapia láser para el SBA y, de esta manera, evaluar longitudinalmente el control de los síntomas dolorosos.
Palabras clave: Fotobiomodulación; Láser de baja intensidad; Síndrome de Boca Ardiente; Dolor.

1. Introduction

Burning Mouth Syndrome (BMS) is characterized by a burning sensation accompanied by pain in most cases, without the presence of any dysfunction or apparent organic cause. These characteristics associated with burning sensation, dry mouth and altered taste comprise the set of symptoms that define it as a syndrome. Any location in the oral cavity can be affected, however, the most reported sites are the tongue, hard palate, gums, lips and buccal mucosa (Afonso et al., 2011; Maltsman-tseikhin et al., 2007; Monteiro et al., 2011).

The prevalence of this syndrome varies from 0.01% to 40% (ben Aryeh A' et al., 1996; Jääskeläinen & Woda, 2017; van der Waal, 1990) in the general population. A case-control study carried out at the Oral Lesions Reference Center (CRLB) at the State University of Feira de Santana (UEFS) between 2005-2015 reported 41 cases of BMS (Cerqueira et al., 2015). Although the number may seem small, BMS is related to a worse quality of life for those affected (Saintrain et al., 2011).

The etiopathogenesis of BMS is still unknown and the multifactorial nature that may be involved in the process of triggering and maintaining symptoms makes its diagnosis and treatment difficult. The symptoms of BMS may vary among individuals. Patients usually report a burning sensation, pain, numbness and tingling possibly accompanied by loss or change in taste, dry mouth, headaches, and muscle pain (Pastana et al., 2013).

Some studies (Cerchiari et al., 2006; Scarabelot et al., 2011; Soares et al., 2008) have reported that patients with BMS generally present changes in their psychological profile in relation to the general population. It is believed that these individuals tend to develop depression and anxiety. The sensation of burning mouth, with no apparent cause, associated with several other symptoms in the mouth, works as a trigger for exacerbating one's mental state. As a result, their quality of life is directly affected, establishing a bidirectional relationship (Pastana et al., 2013).

There are several treatments proposed for BMS, but they are considered empirical and ineffective due to the complexity of the diagnosis, requiring the adaptation of several therapeutic modalities in most cases (Soares et al., 2008). Given the normality of clinical and laboratory findings, several proposals are used to improve the quality of life of the affected

person, ranging from the elimination of local irritants to the prescription of drugs and nutritional supplements (Cherubini et al., 2005; Soares et al., 2008).

There are studies that address the importance of therapy for cases with chronic pain using antidepressants, benzodiazepines, topical capsaicin, clonazepam, and even combinations of herbal medicines and cognitive behavioral therapy (Braga, 2010; Monteiro et al., 2011; Serra et al., 2007).

Low-level laser therapy (LLLT), known as photobiomodulation, has been used as an alternative for treating BMS symptoms due to the absence of side effects, as well as the analgesia promoted throughout the sessions (Pandeshwar et al., 2016). The low-level laser is a beam of light irradiated in different locations that promotes tissue regeneration, relieves pain and reduces inflammation (Huang et al., 2011). Given the variability of results associated with LLLT, this study was proposed to systematize the published information and, thus, seek scientific evidence for the use of this therapy in pain associated with BMS.

Therefore, the objective of this review is to evaluate the effectiveness of low-level laser in reducing pain associated with Burning Mouth Syndrome, analyzing the relationship between the protocol used and its effect on this symptomatology.

2. Methodology

A quantitative study in terms of article quantity, and quality and in terms of articles analysis, and of a systematic literature review was carried out (Pereira et al., 2018).

A systematic literature review (Gomes & Caminha, 2014) was carried out using the PICO strategy to answer the question: “Is the use of low-level laser capable of stopping or reducing the pain associated with Burning Mouth Syndrome?”

Before the search and selection of studies began, the protocol for this systematic review was registered in the International Prospective Register of Systematic Reviews – PROSPERO under number CRD42021281911.

Data collection and analysis procedure

-Eligibility criteria

The inclusion criteria used were randomized clinical trials— without restrictions on period or language of publication—addressing the evaluation of the use of low-level laser therapy in pain associated with Burning Mouth Syndrome. The exclusion criteria were experimental studies in vitro, in silico, carried out on animals, case reports, letter to the editor, literature review, books, book chapters, pilot studies, annals, course conclusion works, dissertations or theses. Studies that used laser therapy concomitantly with any other therapeutic resource for BMS in the same individual were also not included.

- Search and selection of articles

The search and selection of articles was carried out by two independent reviewers previously trained in the methodology for searching and selecting articles. The databases used for research were PubMed (including Medline), Scopus, Embase, SciELO, Web of Science, Latin American and Caribbean Health Sciences (LILACS) and Cochrane. The descriptors used in the search were indexed in MeSH (Medical Subject Headings), DeCS (Health Sciences Descriptors) and Emtree (Embase Subject Subject Headings). The Boolean operators “AND” and “OR” were used to leverage the search strategy through various combinations of descriptors: laser therapy, pain, burning mouth syndrome (Table 1). There were no restrictions on language or period. After applying the filters for the search strategy, the articles obtained were imported into the Rayyan application (https://rayyan.ai/reviews/364838) to remove duplicates.

Table 1 - Table with search string form in databases.

Databases	**String**
PubMed, Scopus, Embase, SciELO, Web of Science, Latin American and Caribbean Health Sciences (LILACS) and Cochrane	"Burning Mouth Syndrome" OR "Burning pain" AND "Biostimulation, Laser" OR "Laser Irradiation, Low Power" "Burning Mouth Syndrome" OR "Burning pain" AND "Low-Level Light Therapy" OR "Laser Phototherapy" "Burning Mouth Syndrome" OR "Burning pain" AND "Laser Therapies, Low-Level" OR "LLLT" "Burning Mouth Syndrome" OR "Burning pain" AND "Photobiomodulation Therapies" "Pain, burning" OR "glossalgia" AND "Biostimulation, Laser" OR "Laser Irradiation, Low Power" "Pain, burning" OR "glossalgia" AND "Low-Level Light Therapy" OR "Laser Phototherapy" " Pain, burning" OR "glossalgia" AND "Laser Therapies, Low-Level" OR "LLLT" "Pain, burning" OR "glossalgia" AND "Photobiomodulation Therapies"

Source: Authors.

The first stage of selecting articles included the analysis of titles and abstracts. Papers with titles unrelated to the topic of the systematic review were eliminated at this stage. Abstracts whose titles met the main objective of the review were analyzed. Abstracts not available at that time of the search were analyzed in full in the second stage.

The eligible studies in the first stage of the search were selected for further complete reading and evaluation of compliance with the article's eligibility criteria in the second stage. At this stage, for the purpose of detecting works that might not have been included in the first phase of the search, the references of eligible articles were analyzed individually. The excluded studies were recorded in a separate spreadsheet with the corresponding reasons for exclusion (Table 2).

Table 2 - Table with list of articles excluded after reading in full.

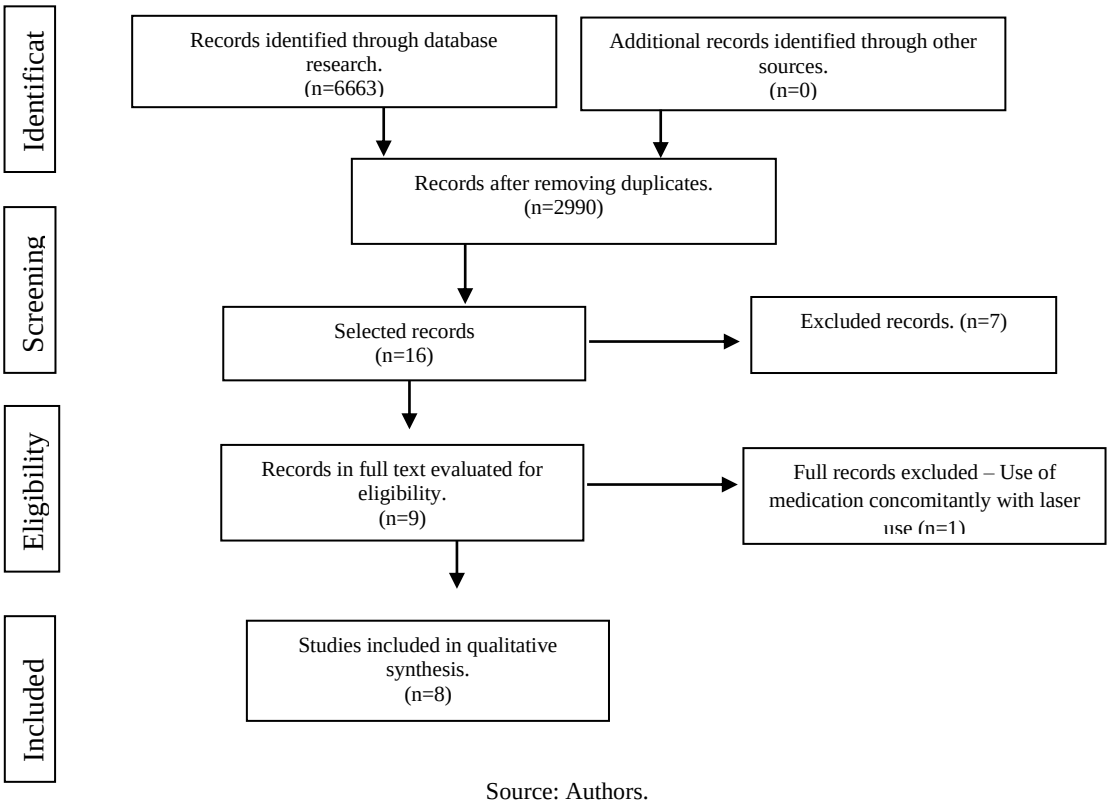
Author, year, article title	**Reason for exclusion**
Spanenberg, JC *et al.*, 2019Low-level laser therapy in patients with Burning Mouth Syndrome: A double-blind, randomized, controlled clinical trial. DOI:10.4317/jced.55517	Used other therapies concomitantly with laser application
Valenzuela, S. *et al.*, 2016 Effect of a 2% topical chamomile application for treating burning mouth syndrome: a controlled clinical trial. DOI: 10.1111/jop.12412	Did not use laser as the main treatment
Barker, K.E.; Batstone, MD; Savage, NW, 2009 Comparison of treatment modalities in burning mouth syndrome. DOI: 10.1111/j.1834-7819.2009. 01154.x	Did not use laser as the main treatment
Acharya, S. *et al.*, 2018 Clinical characterization of women with burning mouth syndrome in a case-control study. DOI: 10.1080/00016357.2017.1420226	Not an intervention study
Kato et al., 2010 Low-Level Laser Therapy in Burning Mouth Syndrome Patients: A Pilot Study DOI: 10.1089/pho.2009.2630	Study pilot

Santos et al., 2015 Phototherapy on the Treatment of Burning Mouth Syndrome: A Prospective Analysis of 20 Cases DOI: 10.1111/php.12490	Used other therapies concomitantly with laser application
Sikora et al., 2018 The efficacy of low-level laser therapy In burning mouth syndrome – a pilot study DOI: 10.20471/acc.2018.57.02.12	Study pilot
Pezelj-Ribarić et al., 2013 Proinflammatory cytokine levels in saliva in patients with burning mouth syndrome before and after treatment with low-level laser therapy. DOI: 10.1007/s10103-012-1149-5	Did not assess the pain of study participants

Source: Authors.

Disagreements regarding the findings were resolved by discussion with a third reviewer in search of consensus. During the initial phase of the research, 6663 articles were found in the various databases selected for the study. After removing the duplicates, 2990 remained and were moved on to the titles and abstracts reading phase. After the initial reading, 16 works were selected for full reading. After detailed analysis, eight articles that met the study's eligibility criteria were selected (Figure 1).

Figure 1 - Results from searching the databases PubMed (including Medline), Scopus, Embase, SciELO, Web of Science, Latin American and Caribbean Health Sciences (LILACS), and Cochrane.



Source: Authors.

- Data collection and analysis

After the study selection phase, information was extracted about the identification of the work (author, year, country, and location of research), sample characteristics (number of individuals in each study, distribution by sex, average age, laser parameters and analogue pain scale), and quality of life. The results found were critically analyzed in a descriptive manner, evaluating the homogeneity or heterogeneity between the selected studies.

To assess the risk of bias in the quality of each study included in this work, the RoB 2 tool was used. The risk of bias in the study was considered high when 49% of positive responses were obtained; moderate when the study reached 50% to 69% positivity; and low when the study reached 70% or more of positive responses.

3. Results

The selected studies (n=08) were carried out in Spain (25%), Brazil (25%), Italy (25%), Croatia (12.5%) and Iran (12.5%) between 2015 and 2023. The general characterization of the articles is described in Table 3.

Table 3 - Characterization of studies on the use of low-level laser in the painful symptoms of Burning Mouth Syndrome.

Author	Year	Country	Sample	Mean age (SD)
Spanenberg *et al.*	2015	Brazil	67 women (85.8%) 11 men (14.2%)	GL1= 63.6 (9.61) GL2= 60.5 (6.42) GL3= 63.2 (6.91) GC= 61.5 (8.76)
Arbabi-Kalati *et al.*	2015	Iran	20 women (100%)	GL= 47.2 (5.3) GC= 46.6 (4.6)
Valenzuela and Lopez-Jomet	2016	Spain	41 women (93.1%) 03 men (6.9%)	65.5 (10.6)
Sugaya *et al.*	2016	Brazil	21 women (91.3%) 02 men (8.7%)	59.7 (29-83)
Bardellini *et al.*	2019	Italy	85 women (100%)	GL= 59.76 (9.51) GC= 60.86 (10.02)
From Pedro *et al.*	2020	Spain	16 women (80%) 04 men (20%)	GL= 60.30 (15.19) GC= 67.60 (10.68)
Skrinjar *et al.*	2020	Croatia	20 women (87%) 03 men (13%)	GL= 61 (47-70) GC= 62 (50-69)
Scardina *et al.*	2020	Italy	20 women (50%) 20 men (50%)	62.06 (3.1)

Legend: GL= laser group; CG = control group; SD= Standard Deviation. Source: Authors.

Use of low-level laser in bms

Spanemberg et al. (2015) presented a study with three intervention groups: two with an infrared laser— each with a difference in laser parameters, and one with a red laser. The results presented showed a significant difference in pain assessment scores in the infrared laser groups. The less satisfactory results in the red laser group were attributed to the lower dosage, energy and output power used compared to those in the infrared group.

The irradiated areas varied in the studies, with the laser being applied to all areas where participants reported symptoms. Four studies did not specify the irradiated sites, one without delimiting the area (Škrinjar et al., 2020), two covering the oral mucosa (Sugaya et al., 2016; Valenzuela & Lopez-Jornet, 2017) and one covering painful areas (Bardellini et al., 2019).

The study by Bardellini et al. (2019) irradiated the most affected areas of the oral cavity with a discontinuous wavelength between 660-970 nm. The average power used was 3200 mW with an irradiation time of 3'51". This study showed a significant reduction in BMS symptoms. The parameters used in each study can be seen in Table 4.

Pedro et al. (2020) irradiated 56 points in total, 3 points on the vestibular mucosa of the 4 quadrants, 4 points on each labial mucosa, 6 on each of the two buccal mucosae, 6 on the hard palate, 4 on each lateral edge of the tongue, 6 on the dorsum of the tongue and 4 sublingual points. All patients in the intervention group had reduced pain associated with BMS. Arbabi-

Kalati, Bakhshani e Rasti (2015) applied the laser to 10 areas of the oral mucosa, 2 areas of the oral mucosa on each side, 2 areas of the tongue, 2 areas of the floor of the mouth, 1 area of the soft palate, and 1 area of the hard palate, showing a significant improvement in the Visual Analogue Scale scores (VAS) and quality of life after treatment.

In the study developed by Scardina et al., 2020, the laser was focused on the upper lip mucosa, buccal mucosa, dorsal surface of the tongue and lower lip mucosa. Individuals showed a reduction in pain sensation after laser application. Spanemberg et al. (2015) applied the treatment to 44 points in total, distributed across the tongue (17 points), buccal mucosa (8 points), lip mucosa (5 points), hard palate (8 points), soft palate (3 points), gingival mucosa and alveolar border (3 points). All study groups achieved a significant improvement in symptoms (Table 4).

Table 4 - Low-intensity laser parameters used in studies to control the painful symptoms of Burning Mouth Syndrome.

Author/Year	Laser type/ Model/Manufacturer	Wavelength	Fluency	Power	Power density	Time(s)	Dose (J)	Irradiation frequency
Spanenberg *et al* , 2015	diode laser (Thera Lase™, DMC Equipamentos LTDA)	GL1: 830nm GL2: 830nm GLV: 685nm	GL1: 176 J/cm ^{2} GL2: 176 J/cm ^{2} GLV: 72 J/cm ^{2}	GL1:100mW GL2:100 mW GLV: 35 mW	-	GL1: 50s/pt. GL2: 50s/pt. GLV: 58s/pt.	-	Continuous
Arbabi-Kalati *et al.*, 2015	diode laser (Mustange laser- Russia)	630nm	1 J/cm2	30 mW	-	10s	3J	-
Valenzuela and Lopez-Jornet, 2016	diode laser (LaserSmile ® Biolase Technology. Inc. Irvine. USA)	815nm	GL1:133.3 J/cm ^{2} GL2: 200 J/cm ^{2}	1000mW	-	GL1: 4s GL 2: 6s	GL1: 4 J GL2: 6 J	Continuous
Sugaya *et al.*, 2016	Diode laser (QTUM00A/ QUANTUM - Ecco Fibras Opticas e Dispositivos LTDA)	790nm	6 J/ ^{cm2}	120 mW	4W/ ^{cm2}	50s/pt.	6J	Continuous
Bardellini *et al.*, 2019	K Laser Cube $^{3®}$	660-970nm	-	3200 mW	-	231s	-	Pulsed
From Pedro *et al.*, 2020	diode laser (Fox ARC Laser, Italy)	810nm	12 J/cm²	60 mW	1.2W/cm²	6s/pt.	6J	Continuous
Skrinjar *et al.*, 2020	Ga-Al-As LED Laser Light	685nm	60 J/ ^{cm2}	30mW	0.003W/cm²	381s	2J	-
Scardina *et al.*, 2020	diode laser (Biolase Epic 10)	800nm	50 J/ ^{cm2}	60 mW	180mW/ ^{cm2}	300s	1200 J	Continuous

Source: Authors.

The study by Spanemberg et al. (2015) presented the idea of the relationship between the effective improvement of painful symptoms and the frequency of weekly sessions, showing that the number of sessions can influence the result. The study by Sugaya et al. (2016) reported that the protocol used did not offer significant results, attributing this fact to the low frequency of sessions and the laser parameters.

Symptom assessment

Six studies used the Visual Analogue Scale (VAS) to determine pain levels before and after treatment protocols, one study used the Numerical Rating Scale (Arbabi-Kalati et al., 2015), and another used both scales (Scardina et al., 2020). In general, there was a reference to improvement in pain in all studies. Table 5 shows the scale scores of the studies before and after treatment, as well as their results.

Sugaya et al. (2016) presented the VAS values characterized by each patient as a percentage of the reported symptoms. It considered 0 as absence of burning (0%), 1 as excellent reduction (1-25%), 2 as good reduction (26-50%), 3 as regular reduction (51-75%), 4 as unchanged pain (76-100%), and 5 as worsening of the symptoms (> 100%). The intervention group showed improvement, reaching 18% in the excellent reduction category.

Table 5 - Comparison of pain assessment scores before and after treatment with low-level laser (LLLT) for burning mouth syndrome.

Author/year	Before LLLT (average/SD)	After LLLT (average/SD)	Frequency of sessions	Conclusion
Spanenberg *et al.*, 2015	GL 1 = 82.15 (14.47) GL 2 = 78.90 (15.25) GLV = 80.68 (18.63) GC = 85.26 (14.25)	GL 1= 28.20 (27.24) GL 2= 30.85 (24.08) GLV= 44.87 (28.32) GC= 66.37 (19.81)	GL 1 = 10 sessions 1x per week GL 2 = 9 sessions 3x per week GLV = 9 sessions 3x per week GC = 9 sessions 3x per week	Improvement at the end of treatment. The effects of improvement remained for the following months.
Arbabi-Kalati *et al.*, 2015	GL = 8 (2.3) GC = 8.2 (1.7)	GL= 3.6 (3) GC= 8 (1.5)	4 sessions 2x per week	The study reports the effectiveness of the LLLT but presents limitations in relation to the sample. It also suggests further research.
Valenzuela and Lopez-Jornet, 2016	GL 1 = 7.56 (1.5) GL 2 = 8.38 (1.7) GC = 7.83 (1.3)	GL 1= 6.38 (1.6) GL 2= 7.06 (1.8) GC = 7.65 (1.2)	4 sessions 1x per week	There was an improvement in symptoms. There was no difference between the protocols used.
Sugaya *et al.*, 2016	-	-	4 sessions 2x per week	There was complete remission in some GL patients at some irradiation sites.
Bardellini *et al.*, 2019	-	-	10 sessions 1x per week	Improvement at the end of treatment. The effects of improvement remained for the following months.
From Pedro *et al.*, 2020	GL = 6.8 GC = 7.1	GL= 3.4 GC= 7.6	10 sessions 2x per week	Pain decreased in the GL and increased in the CG. The effects of improvement remained for the following months.
Skrinjar *et al.*, 2020	GL = 5.5 (4~9) GC = 5 (0~8)	GL= 4 (3~7) GC= 3 (1.5~6.5)	10 sessions consecutive	LLLT can lower stress levels.
Scardina *et al.*, 2020	-	-	8 sessions 2x per week	There was a significant decrease in pain scores. In relation to the thickness of the capillary bed, there was a reduction.

Legend: GL = laser group; GLV = red laser group; CG = control group. Source: Authors.

Quality of life

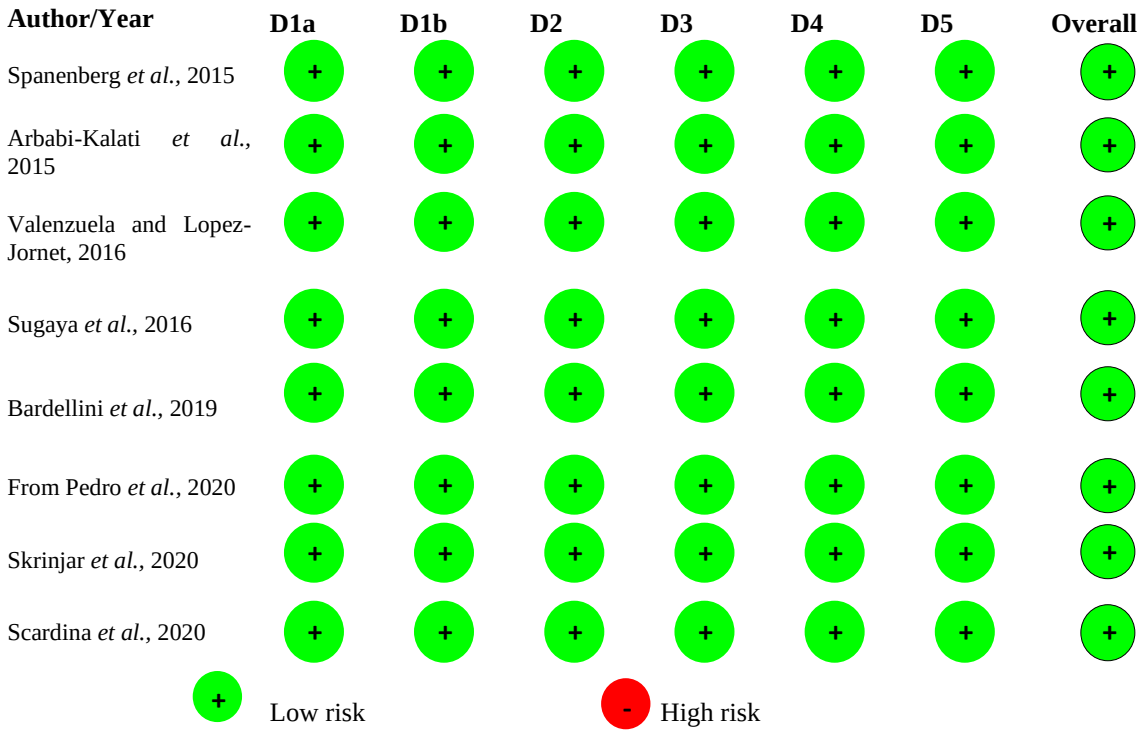
To assess quality of life, four studies (Bardellini et al., 2019; Pedro et al., 2020; Spanemberg et al., 2015; Valenzuela & Lopez-Jornet, 2017) used the Oral Health Impact Profile (OHIP) questionnaire, while one study used a validated questionnaire (Arbabi-Kalati et al., 2015).

In the study by Pedro et al., (2020) OHIP-14 scores reduced in the study group and increased in the control group, showing an improvement in quality of life. A study demonstrated that there was an improvement in quality of life in both groups (Spanemberg et al., 2015). Bardellini et al. (2019) showed that LLLT had a positive effect on improving the quality of life of individuals after the 7th week of treatment. Valenzuela e Lopes-Jornet (2017) demonstrated a significant improvement in individuals in the study group after treatment.

Two articles suggested that the reduction of symptoms associated with BMS using laser had a positive impact on the individual's psychological aspects (Pedro et al., 2020; Škrinjar et al., 2020).

The assessment of the risk of quality bias indicated a high level of reliability of the studies included in this systematic review (Figure 2).

Figure 2 - Risk of bias in studies reviewed according to RoB 2 Caption: D1a: Randomization process; D1b: Moment of identification or recruitment of participants; D2: Deviations from intended interventions; D3: Lost data; D4: Measurement of results; D5: Selection of the reported result.



Source: Adapted from the Risk of Bias 2.0 Tool.

It was only possible to perform the heterogeneity test based on the results from Arbabi-Kalati *et al.* (2015), Spanenberg *et al.* (2015), Pedro *et al.* (2020) and Valenzuela and Lopez-Jornet, (2016). The data from the articles by Sugaya *et al.* (2016) and Scardina *et al.* (2020) were qualitative. The article by Skrinjar *et al.* (2020) did not present sufficient statistical data for the calculation, while the article by Bardelini *et al.* (2019) did not present data for the same variable used in other

studies. For these reasons, these four studies did not participate in the heterogeneity calculation, the result of which was I^2 = 89%. Given the heterogeneity above 65%, it was not possible to proceed with the meta-analysis.

4. Discussion

The use of laser is considered a promising alternative for controlling BMS and it has been widely used for this purpose. However, the lack of a single protocol that defines, among other things, dosimetry, number of sessions, and number of application points, makes it difficult to analyze the effectiveness of the therapy. This suggests the conduction of new clinical trials capable of overcoming the limitations presented by the works included in this systematic review. Despite there being a difference in parameters in the protocols, the studies present in this review displayed satisfactory results in relation to the reduction of painful symptoms associated with BMS.

The low frequency laser, unlike other laser procedures, is a mechanism that does not release heat or promote the removal of material. It acts as an energy modulator, with light energy being absorbed and transformed into chemical energy (Pandeshwar et al., 2016). The laser's mechanism of action is still being studied and is believed to have three basic effects: analgesia, anti-inflammatory and promotion of wound healing (Arbabi-Kalati et al., 2015; Bardellini et al., 2019). These characteristics justify the use of photobiomodulation in BMS.

One of the ideas behind the laser's mechanism of action is that it acts on tissues, due to the presence of photoreceptor cells. Light is absorbed by the mitochondria, which accelerates the metabolism, increasing ATP synthesis in addition to increasing the production of endorphins and serotonin. Therefore, to achieve the desired effects of photobiomodulation it is necessary to observe the ideal therapeutic window for each case. This is because the use of doses lower than necessary will not produce an effect, while the use above the limit will inhibit it (Bardellini et al., 2019; Pandeshwar et al., 2016). In this regard, defining the ideal dosimetry for the control of BMS is necessary. As exposed by this review, the variation between the parameters used in the studies may justify the difference in results between them.

Most of the studies in this review used the Visual Analogue Scale (VAS) to evaluate the evolution of painful symptoms related to BMS before and after the use of the laser. The VAS is a one-dimensional scale that assesses the intensity of pain at the time of its application. Even though this scale has the limitation of considering only the intensity aspect of the pain, its simplicity, easy understanding for the participants, and speed of application are advantages that support its use (Martinez et al., 2011).

When adding the number of participants in each study, it can be observed that BMS affected 87.08% women and 12.92% men, corroborating the literature on the higher prevalence of the syndrome in females (Scardina et al., 2020). Furthermore, the average age of individuals was related to the post-menopausal period, which raises questions about the hormonal influence on the etiology of BMS (ben Aryeh A' et al., 1996).

Regarding laser parameters, the red and infrared wavelengths in the literature range from 390 to 1100 nm (Mussttaf et al., 2019), while the works in this review used the 630~970 nm range with power ranging from 20 mW to 6400 mW. Currently, wavelengths of 800~900 nm and power above 100mW have been most used in therapeutic devices, due to their ability to penetrate deeper tissues (Pandeshwar et al., 2016). Only one study (Sugaya et al., 2016) used power below what has been found in the literature and, nevertheless, obtained significant results in reducing BMS symptoms.

The low-frequency laser has an analgesic effect, acting differently depending on the degree of pain. Acute pain requires daily treatment, whereas treatment for chronic pain can be done two to three times a week during three to four weeks (Pandeshwar et al., 2016). Two studies carried out monitoring for four sessions only, obtaining little reduction in pain assessed

by the VAS scale, suggesting the need to increase the number of sessions (Arbabi-Kalati et al., 2015; Valenzuela & Lopez-Jornet, 2017).

An individual's quality of life is characterized by the balance between biological, mental and social functions (Pastana et al., 2013). It is noticeable that BMS leads to a decrease in the quality of life of individuals, as its symptoms can be accompanied by effects on the oral mucosa, such as loss of taste and dry mouth (Scardina et al., 2020). Of the eight studies presented, six demonstrated that low-level lasers have a positive impact on the quality of life of patients with BMS. The other two studies did not present data on the participants' quality of life (Škrinjar et al., 2020; Sugaya et al., 2016).

This systematic review was limited by the heterogeneity of the studies: there were many differences between the LLLT irradiation protocols, which made it impossible to carry out a meta-analysis of the results obtained. Most studies used a different protocol regarding laser parameters. Additionally, the weekly frequency of irradiation between studies varied from one to five sessions per week between studies.

The main advantage of LLLT is the absence of side effects after its administration. This characteristic encourages its use in BMS therapy. However, given the variability of protocols used by the studies in this review, it is necessary to perform randomized clinical trials with adequate blinding and standardization of the therapeutic protocol based on the available clinical findings. This is essential to a better understanding of the use of laser in BMS, and to allow for the control of selection and observation biases, avoiding bias in the evaluation of study results.

The current review went through the PRISMA checklist. After analyzing the data, it was found that of the 42 questions evaluated, 39 were addressed, while three were left unanswered. This outcome stemmed from the impossibility of carrying out the meta-analysis given the heterogeneity of the studies included.

5. Conclusion

From this review, it can be concluded that the use of low-level laser can be a therapeutic device to control the painful symptoms caused by BMS, as well as its effects on the psychological aspect of those affected. Given the methodological diversity presented among the studies, it is not possible to state that this therapy can stop the symptoms of BMS. Thus, it is necessary to carry out new studies that standardize the parameters of laser therapy for BMS and evaluate the effect on the associated symptoms longitudinally.

References

Afonso, A., Montandon, B., Pinelli, L. A. P., Rosell, F. L., & Fais, L. M. G. (2011). Síndrome da Ardência Bucal : avaliação e tratamento. *Revista de Odontologia Da Universidade Cidade de São Paulo*, 23(1), 59–69.

Arbabi-Kalati, F., Bakhshani, N. M., & Rasti, M. (2015). Evaluation of the efficacy of low-level laser in improving the symptoms of burning mouth syndrome. *Journal of Clinical and Experimental Dentistry*, 7(4), e524–e527. https://doi.org/10.4317/jced.52298

Bardellini, E., Amadori, F., Conti, G., & Majorana, A. (2019). Efficacy of the photobiomodulation therapy in the treatment of the burning mouth syndrome. *Medicina Oral Patologia Oral y Cirugia Bucal*, 24(6), e787–e791. https://doi.org/10.4317/medoral.23143

Ben Aryeh A', H., Gottlieb, I., Ish-Shalom, S., David, A., Szargep, H., & Laufer, D. (1996). Oral complaints related to menopause. In Maturitas (Vol. 24).

Braga, F. do P. (2010). Síndrome de ardência bucal: estudo dos fatores clínicos associados ao diagnóstico e avaliação da acupuntura como modalidade terapêutica. Faculdade de Odontologia da Universidade de São Paulo.

Cerchiari, D. P., Moricz, R. D., Rapoport, P. B., Moretti, G., & Guerra, M. M. (2006). Burning mouth syndrome: etiology. *Revista Brasileira de Otorrinolaringologia*, 72(3), 419–424. https://doi.org/https://doi.org/10.1590/S0034-72992006000300021

CERQUEIRA, I. S., EUFRÁZIO, A. N., EÇA, J. F., OLIVEIRA, M. C., & FALCAO, M. M. L. (2015). Conhecendo o perfil epidemiológico da síndrome da ardência bucal em mulheres. Anais Concurso e Painéis Científicos 22o CIORJ, 22, 377–377.

Cherubini, K., Maidana, J. D., Weigert, K. L., & Figueiredo, M. A. (2005). Síndrome da ardência bucal: revisão de cem casos. *Revista Odontologia Ciência*, 20(48), 109–113.

Gomes, I. S., & Caminha, I. de O. (2014). Guia para estudos de revisão sistemática: uma opção metodológica para as Ciências do Movimento Humano. Movimento, 20, 395–411.

Huang, Y. Y., Sharma, S. K., Carroll, J., & Hamblin, M. R. (2011). Biphasic dose response in low level light therapy - an update. *Dose-Response*, 9(4), 602–618. https://doi.org/10.2203/dose-response.11-009.Hamblin

Jääskeläinen, S. K., & Woda, A. (2017). Burning mouth syndrome. *Cephalalgia*, 37(7), 627–647. https://doi.org/10.1177/0333102417694883

Maltsman-tseikhin, A., Moricca, P., & Niv, D. (2007). Burning Mouth Syndrome: Will Better Understanding Yield Better Management? *World Institute of Pain*, 7(2), 151–162.

Martinez, J. E., Centola Grassi, D., & Marques, L. G. (2011). Análise da aplicabilidade de três instrumentos de avaliação de dor em distintas unidades de atendimento: ambulatório, enfermaria e urgência. *Revista Brasileira de Reumatologia*, 51(4), 299–308.

Monteiro, A. D., Sousa, A. C. V. de, Matos, F. Z., Carvalhosa, A. A. de, França, D. C. C., & Aguiar, S. M. H. C. Á. de. (2011). Síndrome da ardência bucal, correlações fisiopatológicas, medicamentosas: revisão de literatura. *Revista de Odontologia de Araçatuba* (Online), 32(2), 33–37. http://apcdaracatuba.com.br/revista/v322jd2011/6-.pdf

Mussttaf, R. A., Jenkins, D. F. L., & Jha, A. N. (2019). Assessing the impact of low level laser therapy (LLLT) on biological systems: a review. In *International Journal of Radiation Biology* (Vol. 95, Issue 2, pp. 120–143). Taylor and Francis Ltd. https://doi.org/10.1080/09553002.2019.1524944

Pandeshwar, P., Roa, M. D., Das, R., Shastry, S. P., Kaul, R., & Srinivasreddy, M. B. (2016). Photobiomodulation in oral medicine: a review. *Journal of Investigative and Clinical Dentistry*, 7(2), 114–126. https://doi.org/10.1111/jicd.12148

Pastana, S. da G., Cantisano, M. H., Mariano, B. O., & Bianchini, E. M. G. (2013). Queixas orais e verificação da fala de indivíduos com síndrome da ardência bucal. *Revista CEFAC*, 15(4), 904–912. https://doi.org/10.1590/s1516-18462013000400019

Pedro, M., López-Pintor, R. M., Casañas, E., & Hernández, G. (2020). Effects of photobiomodulation with low-level laser therapy in burning mouth syndrome: A randomized clinical trial. *Oral Diseases*, 26(8), 1764–1776. https://doi.org/10.1111/odi.13443

Pereira, A. S., Shitsuka, D. M., Parreira, F. J., & Shitsuka, R. (2018). *Metodologia da pesquisa científica*. UFSM.

Saintrain, maria vieira de lima, Braga, janaina de oliveira, Carlos, márlio ximenes, & Maia, maria cristina germano. (2011). Perfil epidemiológico de mulheres idosas com sintomas de ardência bucal. *Revista Brasileira de Pesquisa Em Saúde*, 24(3), 238–244.

Scarabelot, V. L., Gutierrez, L. M., Souza, A., Oliveira, M. G., Chaves, A. C. M., Munerato, M. C., Hidalgo, M. P., Caumo, W., & Torres, I. L. (2011). Avaliação de fatores associados ao diagnóstico de queimação bucal um estudo preliminar. *Clinical and Biomedical Research*, 31(3), 318–325.

Scardina, G. A., Sofia, C., Giuseppa, B., & Pietro, M. (2020). Photobiomodulation therapy in the managemente of burning mouth syndrome: morphological variations in the capillary bed. *Dental Journal*, 8, 99. https://doi.org/10.20944/preprints202007.0635.v1

Serra, M. P. M., Salort Llorca, C., & Donat, F. J. S. (2007). Pharmacological treatment of burning mouth syndrome: A review and update. *Medicina Oral Patologia Oral e Cirurgia Bucal*, 12, 299–304.

Škrinjar, I., Brzak, B. L., Vidranski, V., Boras, V. V., Rogulj, A. A., & Pavelić, B. (2020). Salivary cortisol levels and burning symptoms in patients with burning mouth syndrome before and after low level laser therapy: A double blind controlled randomized clinical trial. *Acta Stomatologica Croatica*, 54(1), 44–50. https://doi.org/10.15644/asc54/1/5

Soares, M. S. M., Lima, J. M. C., & Pereira, S. C. C. (2008). Avaliação do fluxo salivar, xerostomia e condição psicológica em mulheres com Síndrome da Ardência Bucal. *Revista de Odontologia Da UNESP*, 37(4), 315–319.

Spanemberg, J. C., López, J. L., de Figueiredo, M. A. Z., Cherubini, K., & Salum, F. G. (2015). Efficacy of low-level laser therapy for the treatment of burning mouth syndrome: a randomized, controlled trial. *Journal of Biomedical Optics*, 20(9), 098001. https://doi.org/10.1117/1.jbo.20.9.098001

Sugaya, N. N., da Silva, É. F. P., Kato, I. T., Prates, R., de Barros Gallo, C., & Pellegrini, V. D. (2016). Low Intensity laser therapy in patients with burning mouth syndrome: a randomized, placebo-controlled stud. *Brazilian Oral Research*, 30(1), 1–9. https://doi.org/10.1590/1807-3107BOR-2016.VOL30.0108

Valenzuela, S., & Lopez-Jornet, P. (2017). Effects of low-level laser therapy on burning mouth syndrome. *Journal of Oral Rehabilitation*, 44(2), 125–132. https://doi.org/10.1111/joor.12463

van der Waal, I. (1990). *The burning mouth syndrome* (1st ed., Vol. 1). Wiley–Blackwell.