Low-level laser therapy in cases of burning mouth syndrome

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Abstract. Burning mouth syndrome is an intraoral burning sensation which develops in the absence of mucosal changes. It is a chronic condition and, in most of the cases, it is idiopathic – no cause or mechanism can be identified and no effective treatment can be prescribed. A variety of therapeutic approaches have been applied – cognitive-behavioral therapy, different drugs and supplements, acupuncture, lasers – none of them has achieved a definitive solution of the problem. This leads to anxiety, altered pain perception, and, therefore, reduced quality of life of the affected patients. The aim of this study is to present low-level laser therapy as a pain control option in patients with burning mouth syndrome. We reveal the potential of a diode laser to reduce the unpleasant burning sensation. We also apply laser therapy on patients with primary burning mouth syndrome. The affected sites on the oral mucosa in the selected cases are various – tongue, lower lip, upper lip, palate, cheeks. They are irradiated 10 times (two or three times a week) by an infrared laser (λ = 904 nm) and a red laser (λ = 658 nm). The probe is kept in contact with the tissue and the mucosal surface is scanned during the irradiation. The burning intensity is evaluated through a visual analogue scale before and after the treatment. The low-level laser illumination decreases significantly and for a longer period the burning sensation. The low-level laser therapy is a valuable alternative for BMS treatment and can be combined with other treatment methods.

1. Introduction
According to the definitions of the International Association for the Study of Pain (IASP), the burning mouth syndrome (BMS) is "a distinctive nosological entity characterized by unremitting oral burning or similar pain in the absence of detectable mucosal changes “and "burning pain in the tongue or other oral mucous membranes" [1]. A number synonyms exist for this state – stomatopyrosis, glossopyrosis, stomatodynia, glossodynia, orodynia, sore mouth, sore tongue, oral dysesthesia, and oral galvanism.

The overall prevalence of BMS is about 4%, and it affects mostly middle aged or elderly (50 – 70 years of age) women, as they are 3 – 7 times more likely than men of a similar age to experience the symptoms. No racial or ethnic predilections have been reported. BMS is associated with a higher incidence of gastro-intestinal and urogenital disease, yet the relation is unclear. Burning and pain are often accompanied by subjective xerostomia, oral paresthesia (e.g. tingling) and altered taste or smell (dysgeusia and dysosmia). Sometimes slight changes or normal variations like fissured tongue or geographic tongue can be detected [2].

The etiology of BMS is still debatable. The disorder is rarely attributed to a single cause. It has most commonly a multifactorial origin, in which systemic factors, local factors and psychological factors like stress, anxiety and depression play a role [3]. Other problem is that about 50% of cases of burning
sensation in the mouth have no identifiable cause and mechanism. So, for the better understanding and descriptions of the cases, the BMS is classified into “primary”, when symptoms are idiopathic, and “secondary”, when symptoms can be linked to various medical and dental conditions.

Burning pain follows unclear mechanisms also – it has lately been considered that its pathogenesis is complex and implicates neural and psychological factors and cytokines [4]. Psychiatric and personality disorders, like depression, social phobia and different pathologic personality characteristics usually precede the onset of BMS. Increased parafunctional habits, steroid dysregulation, central disinhibition due to taste dysfunction, and low dopamine levels in the brain may also act like psychological factors [5, 6]. Neuropathic mechanisms include damage of small somatosensory fibers in the tongue epithelial and Aδ taste afferents, lesions of the trigeminal system and decreased inhibition within the central nervous system. These mechanisms combine in different ways and cause three subclinical neuropathic pain states, which can also overlap – peripheral fiber neuropathy, lingual, mandibular or trigeminal system pathology, and central pain [7, 8, 9]. Up-regulation or down-regulation of specific cytokines (IL-2, IL-6, IL-8 and TNF-α) and autoimmune predisposition (low levels of CD28+) may also contribute to the etiopathogenesis of BMS [4, 10, 11].

If we accept that BMS is of neuropathic nature, its treatment should be similar to other neuropathic pain conditions. First line medications include alpha-lipoic acid (ALA), an antioxidant and potent nerve regeneration agent, and gabapentin – anticonvulsant drug whose molecular structure is similar to that of the neurotransmitter γ-aminobutyric acid (GABA) and acts by inhibiting certain calcium channels. They can be combined for potentiating the effect. Clonazepam, a tranquilizer of the benzodiazepine class, acts as a GABA receptor agonist and decreases anxiety levels, but has a lot of side effects. Capsaicin regulates oral symptoms by inducing desensitization of nociceptors – it is applied topically, but may induce dyspepsia. Other treatment modalities, like low-level laser therapy (LLLT) and acupuncture, are also used to reduce the pain [6, 12]. The low-level laser light penetrates tissues and acts like a bio-modulators, i.e., induces analgesic, anti-inflammatory and repairing effects. The analgesic effect is due to inhibition of nociceptive mediators and release of endogenous analgesic substances, such as endorphins, by the central nervous system, which stops the transmission of painful stimuli [3]. The anti-inflammatory effect of LLLT has been confirmed to result from a reduction of the TNF-α and IL-6 salivary levels [13].

The existing state of subclinical pain determines the treatment strategy – the peripheral type responds to peripheral lidocaine blocks and topical clonazepam, whereas the central type does not respond to local treatments and associates often with psychiatric comorbidity (depression or anxiety). A better and more sustainable effect is achieved through integration of medications and other treatment modalities.

The aim of this study is to present the low-level laser therapy as a pain control option in patients with burning mouth syndrome.

2. Patients and methods

2.1. Patients

The object of our study were patients with primary burning mouth syndrome. Both genders and all age groups were included. Only patients with uncontrolled systemic diseases, pregnant women and aggressive patients with psychiatric disorders were excluded. All participants in the study signed an informed consent form.

Burning pain may have single or multiple localization, which may be constant or changing. In this study, various affected sites on the oral mucosa were treated – tongue, lower and upper lip, palatal and buccal mucosa.

2.2. Methods

The “primary BMS” diagnosis was established after rejecting all the other possibilities – systemic and local diseases. For this purpose, general medical history was obtained, blood tests, fungal cultures and allergy tests were used, and the galvanic currents in the mouth were measured. The burning intensity
was evaluated through visual analogue scale (VAS) before and after the treatment. A diode laser system (Six Laser TS C, Atlantis, Bulgaria) was used to reduce the unpleasant burning sensation. The protocol included ten irradiations (two or three times a week) with infrared laser light ($\lambda = 904$ nm, 30 W output power, 24 mW average power, 36.5 Hz repetition rate and 82 seconds application time) and red laser light ($\lambda = 658$ nm, 30 mW average power, 36.5 Hz repetition rate and 76 seconds application time). The spot tip area of the tool was $1 \text{ cm}^2$. The probe was kept in contact with the tissue and the mucosal surface was scanned during the irradiation. In the cases with extensive localizations, the multi-diode head was also used combining the effects of the red and infrared lasers. The dose achieved was $1 - 4 \text{ J/cm}^2$.

A statistical analysis was performed by using SPSS for Windows, version 19.0. The accepted critical level of significance was $\alpha = 0.05$; the corresponding zero hypothesis was rejected for $p < \alpha$.

3. Results and discussion

In all, 14 patients were treated – 12 of them completed the protocol, and 2 stopped for different reasons (poor result and COVID-19 pandemic). Males and females were equal in number. The average age was 49.79 ± 22.10 (range of 27 – 78) – the age distribution was not normal. The gender distribution was interesting, especially when considering that earlier studies have shown the female-to-male ratio of BMS sufferers to be 5:1. Also, the male patients were of lower average age. These facts demonstrate that younger males are more open to new technologies and more easily undergo laser treatment. Females prefer to try pharmacological agents first.

The most common localization of pain was on the tongue, followed surprisingly by gums and lips, palatal and buccal mucosa being affected equally (figure 1). In the majority of studies involving LLLT, the pain localization is not mentioned, while in others the tongue is quoted as the most affected [3].

![Figure 1. Distribution of pain localization in BMS patients.](image)

The burning sensation and pain were reduced significantly in most of the cases, however, there were cases with a 1-2 points decrease only (VAS values). The average value of the initial VAS was 8; after the treatment it dropped to 2.86. Other studies have shown similar results – Spanemberg et al. described a slightly worse result (VAS decrease from 8.9 to 5.5), while Arbadi-Kalati et al. calculated better results (NRS decrease from 8 ± 2.3 to 3.6 ± 3) [3, 14].

It is difficult to compare results from different studies, because of the large variations in the type of devices and wavelengths used and in the number of sessions; however, they all demonstrated some improvement of symptoms. Spanemberg et al. applied eight procedures using a semiconductor GaAlAs laser with a wavelength of 808 nm ± 5 nm (IR), 200 mW output power, 1.97 W/cm² power density, 3 J energy per point and application time of 15 seconds per point. The LLLT was applied punctually in
continuous emissions on each affected site. The two-month follow-up showed better results than in the control group [3]. Valenzuela and Lopez-Jornet completed four sessions (four weeks) of LLLT with a GaAlAs laser with wavelength of 815 nm, 1 W output power, continuous emissions, 4 s and 4 J per point at a fluence of 133.3 J/cm²; alternatively, they used 1 W output power, continuous emissions, 6 s and 6 J at a fluence of 200 J/cm². They described a slight reduction of symptoms [15].

Our patients usually reported an improvement after the third procedure. Arduino et al. used similar parameters (980 nm AlGaAs diode laser, 300 mW output power, 10 J/cm² fluence, 1 W/cm² power density; the probe was held perpendicularly at a distance of about 2 mm from the mucosa; two irradiations weekly for five weeks) and reported a reduction of symptoms even after the first application [16].

The effect of LLLT is quick, but we cannot comment on a long-term improvement, because of the limited amount of data accumulated. A relapse of symptoms was not common – we have only one case of a 78-year-old lady who discontinued the therapy after the sixth procedure because of COVID-19 pandemic; the symptoms re-appeared in one month.

In some cases we combined LLLT with pharmacological agents – alpha-lipoic acid and gabapentin. As a rule, the ALA potentiated the LLLT effect in the studied patients; however, we could not find other publications reporting similar results. There are articles that compare the efficacy of LLLT and ALA and determine LLLT as being the better treatment [17].

When comparing the different treatment approaches, one very important aspect is the safety of the therapy. LLLT is the best one from this point of view – as confirmed by all researchers it has no side effects.

4. Conclusions
The low-level laser therapy is an easily-applicable and relatively non-expensive method for pain control in disorders such as burning mouth syndrome. It is effective in most of the cases and it is safe. Males are more easily convinced to undergo laser therapy, but the results in both genders are comparable. The LLLT is a valuable alternative for BMS treatment, which can also be combined with other treatment methods.

Acknowledgements
The study was supported and financed by the Medical University – Varna, Project No 17016.

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