Clinical effect of Non-Thermal CO₂ Laser Therapy (NTCLT) on Pain Relief of Oral Aphthous Ulcers of Behçet's Disease

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Abstract

Introduction: Behçet's disease (BD) is a debilitating and chronic vasculitis which can affect multiple organs. Recurrent oral aphthosis is the most common clinical feature of BD. The remarkable pain associated with painful oral ulcers can exert a major impact on the patients' quality of life. Relieving pain of these oral ulcers is an essential approach in the management of mucocutaneous lesions of BD. Non-thermal CO₂ laser therapy (NTCLT) as a novel photobiomodulative approach has recently been used for significant and immediate pain reduction of some types of painful oral lesions such as recurrent aphthous stomatitis, pemphigus vulgaris, and so on. In this procedure by some considerations, the conventional CO₂ laser is used as a non-surgical, non-thermal, photobiomodulative laser without any visible thermal adverse effects. In this article, we report our experiences about the analgesic effects of NTCLT on painful oral aphthous ulcers of BD.

Case Presentation: We report four cases of BD, whose painful oral aphthous ulcers were irradiated with NTCLT. Immediately after NTCLT, the pain of the lesions was significantly relieved with no visible complications.

Conclusion: The results of this study suggest that NTCLT could be proposed as a hopeful procedure for significant and instant pain relief of oral aphthous ulcers of BD without any visible thermal adverse effects.

Keywords: Behçet's disease; Non-thermal CO₂ laser therapy (NTCLT); Oral aphthous ulcers; Pain relief; Photobiomodulation.

Introduction

Behçet's disease (BD) is a chronic, relapsing, multisystem vasculitis which can affect vessels of all sizes of various organs. Oral ulcers, genital ulcers, skin lesions, and articular and ocular involvement are the most common manifestations of BD.¹⁻⁸ BD has global distribution; however, it is particularly prevalent along the "ancient Silk Road", with the highest prevalence in Turkey, Iran, Japan, China and Korea. In Iran, the prevalence of BD has been estimated to be 16-80 patients per 100 000 residents.²

Recurrent oral aphthosis which often precedes other clinical signs is the most common mucocutaneous manifestation of BD observed in more than 90% of cases.⁸⁻¹¹ The frequency of oral aphthosis in a large

series of patients within the Iranian nationwide registry was 97.3%.³ These lesions with a diameter of 1-20 mm are painful, punched-out ulcers with grayish yellow necrotic base, surrounded with a bright red halo.¹⁻⁸ The ulcers usually subside within 1 to 4 weeks spontaneously and recur at intervals from days to months.^{2, 4} The considerable pain of these ulcers may cause difficulty during eating, drinking and performing routine oral hygiene and may exert a major impact on the patients' quality of life.⁹⁻¹¹ Since the definite mechanisms of oral ulcers in BD are poorly understood, the treatment of oral ulcers (without any other organ involvement) is mainly aimed at pain relief, the promotion of the healing process and the reduction of the recurrence rate.⁹⁻¹¹ These lesions

are usually painful, hindering the patients from eating, drinking and speaking. Due to the relationship between pain and quality of life, obtaining new pain-relieving approaches for the symptomatic management of these painful ulcers during conventional treatment is rational.

Over the past decades photobiomodulation (PBM) has gained increasing acceptance as a beneficial, non-pharmacological therapeutic modality to relieve pain, reduce inflammation and stimulate the healing process. The most common wavelengths employed in PBM are in the red and near-infrared spectral regions. However, recent studies have indicated that by some measurements, the CO₂ laser (10 600 nm) can be used as a low-level, non-thermal, photobiomodulative laser to achieve remarkable and immediate pain relief on some oral and mucosal lesions with no visible adverse effects. This process is non-thermal, smokeless, and pain-free with no need for anesthetic agents.¹²⁻²⁰ Afterwards this procedure was termed NTCLT (non-thermal CO₂ laser therapy). In our previous studies, we reported the significant and instant pain-relieving effects of NTCLT on some types of painful oral and mucosal lesions such as recurrent aphthous stomatitis, oral lesions of pemphigus vulgaris and genital ulcers of BD.^{14-16,19-20} In this paper, we report 4 cases of BD, whose painful oral ulcers immediately responded to the pain-relieving effects of NTCLT without any visible thermal complications.

Clinical Cases

Case 1

A 36-year-old female patient with BD presented to the laser clinic of Medical Laser Research Center, Yara Institute, for relieving the pain of her oral aphthous ulcer by NTCLT. She fulfilled the International Criteria for Behçet's disease (ICBD), with a 10-year history of recurrent oral aphthosis with high frequency, histopathologically proven genital aphthous ulcers and a positive pathergy test. She was treated with sulfasalazine and colchicine. On clinical examination, there was an aphthous ulcer in her upper lip (Figure 1), posing difficulty in her eating and speech. She was requested to grade and record the contact VAS (visual analog scale) pain scores of her ulcer on a horizontal 10-cm line before and immediately after NTCLT, 4 and 8 hours after the operation and then daily for the next 5 days.

Before NTCLT, the ulcer and its surrounding tissue were covered with a thick layer (3-4 mm) of transparent gel (Abzar Darman Co., Iran) with high water content (87.5%) with no anesthetic effects. The surgical staff and the patient used protective eyeglasses during the procedure. The CO₂ laser ($\lambda = 10\,600\text{ nm}$; Lancet-2, Russia) was operated (power: 1 W) with a de-focused handpiece, scanning the surface of the lesion with rapid circular motion of the handpiece. Immediately after NTCLT, the contact VAS pain score of the ulcer showed a

Figure 1. Case 1: Aphthous Ulcer of the Upper Lip Before NTCLT.

significant improvement from 6 to 0. No kind of thermal side effects or aggravation of the lesion was observed after NTCLT. The procedure was pain-free and no kind of anesthetic agent was needed. The pain-relieving effect of NTCLT continued during the four-day healing period. The patient was visited every other day for four days and then two and four weeks after NTCLT. No kinds of visible complications such as burn or aggravation of the ulcers were detected during the patient's follow-up periods.

Case 2

A 34-year-old male patient with known BD was referred to our clinic for a palliative care consult and NTCLT of his painful oral ulcer. He fulfilled the ICBD, with a 12-year history of recurrent oral aphthous ulcers with high frequency, genital aphthous ulcers and a positive pathergy test.

On clinical examination, there was an aphthous ulcer in his lower lip (Figure 2). The contact and non-contact VAS pain scores of the ulcer were 7 and 4 respectively.

Figure 2. Case 2: Aphthous Ulcer of the Lower Lip Before NTCLT.

The patient's aphthous ulcer was treated with NTCLT (with the same protocol as the first case). Immediately after NTCLT, the pain of the ulcer was relieved completely; therefore, he was able to drink and eat easily. No visible adverse effects were observed after NTCLT. The technique was pain-free with no need for anesthetic agents. The pain-relieving effect of NTCLT continued throughout the four days of the recovery period.

Case 3

A 34-year-old male patient with known BD was referred to our clinic for relieving the pain of his oral aphthous ulcer by NTCLT. He fulfilled the ICBT criteria for diagnosis of BD, with a 12-year history of recurrent oral aphthosis with high frequency, a history of erythema nodosum, ocular lesions, clinically consistent with BD, and a positive pathergy test.

The contact and non-contact VAS pain scores of his ulcer in the upper lip (Figure 3) were 7 and 3 respectively. Immediately after NTCLT both the contact and non-contact pains of the ulcer were completely relieved. However, after an hour the contact pain recurred (VAS contact pain score: 3), although it was less than the pre-treatment level. The VAS contact pain score of the lesion remained 4 at 4 and 12 hours post-operatively. The patient recorded the contact VAS pain scores 3, 2, 2 and 0 on the 2nd, 3rd, 4th and 5th days post-laser respectively. After NTCLT the non-contact pain score of the lesion was zero during the five-day healing period. No kind of complications was reported within the follow-up periods.

Case 4

A 47-year-old male patient with known BD was referred to our clinic for a palliative care consult and NTCLT of his painful oral ulcer. He met the ICBT criteria for diagnosis of BD, with a history of recurrent oral and genital aphthous ulcers and a positive pathergy test. On clinical examination, there was an aphthous ulcer in his lower lip (Figure 4). The contact and non-contact VAS pain scores of his ulcers were 6 and 2 respectively. Immediately after NTCLT the pain of the ulcer was relieved completely. The

lesion pain did not recur during the four-day healing time.

Discussion

The results of NTCLT in these patients suggest that NTCLT as a photobiomodulative procedure could be potentially considered a hopeful procedure for the immediate pain management of oral ulcers of BD without any visible thermal adverse effects. The application of NTCLT was painless and smokeless and no kind of anesthesia was required.

Over the past decades PBM (low-level laser therapy) has gained increasing acceptance as an efficient, non-pharmacological and safe therapeutic procedure for pain relief, inflammation reduction and improving and accelerating the wound healing process. A growing number of reports have demonstrated promising outcomes of PBM for the pain management of diverse acute and chronic painful conditions.

The most popular wavelengths applied for photobiomodulation therapy (PBMT) are in the red and near-infrared spectrum. However, some studies have pointed out that the far infrared wavelength (CO₂ laser, 10 600 nm) can be applied as a non-ablative, non-thermal laser for PBM,¹²⁻²⁰ a technique which was termed NTCLT afterwards.^{19,20}

In addition to traditional photobiomodulative low-power lasers, high-power surgical lasers can also be used for PBMT. As Tuner stated, "When high power lasers are used for biomodulation, one only need to make the beam wide enough not to burn. An alternative is to scan rapidly over the lesion with a narrow beam. Therefore, the power density or average power is kept low enough to avoid burning, and their incident energy and power density are set within the low intensity laser therapy range."²¹

For the application of the CO₂ laser for NTCLT as a photobiomodulative (low-level laser therapy) procedure, in addition to the rapid scan of the lesion with a defocused beam, illumination of the lesion is performed through a thick layer of a gel with high water content. By these measurements the final beam power significantly drops (200-500 times) on the surface of the gel to the level of

Figure 3. Case 3: Aphthous Ulcer of the Upper Lip Before NTCLT.

Figure 4. Case 4: Aphthous Ulcer of the Lower Lip Before NTCLT.

low-intensity photobiomodulative lasers¹⁴ and can be successfully applied for the pain management of some oral lesions without any visible thermal adverse effects. This laser technique which was initially termed as non-ablative laser therapy, after proving its non-thermal nature, was renamed as NTCLT to avoid misunderstanding with surgical fractional nonablative CO₂ lasers used by dermatologists for cosmetic purposes.^{19,20}

In this article, we reported known cases of BD, whose painful oral aphthous ulcers were illuminated with NTCLT and immediately after the procedure, the pain of the lesions was relieved dramatically without any visible side effects even erythema. As we guessed before, none of the patients reported warmth sensation in their ulcers throughout NTCLT, and the procedure was pain-free and did not require anesthesia.

During the performance of NTCLT procedure, we highly recommend the application of eyeglasses not only matched to the CO₂ laser (10 600 nm) wavelength but also to the wavelength of the guiding beam to protect the physician's eyes against the reflected beam from the surface of the gel.

Since BD is a serious systemic disease with considerable morbidity and even mortality, the patients should be informed that they should stay on their prescribed systemic drugs for BD in spite of the significant and instant analgesic effects of NTCLT. This report can be valuable for dentists, dermatologists and rheumatologists. There is a clear need for well-designed high quality controlled studies with large sample sizes to prove the pain-relieving effects of NTCLT on oral aphthous ulcers of BD. In addition, these kinds of clinical trials will be able to demonstrate whether NTCLT can improve and accelerate the wound healing process of these lesions or not.

Conclusion

The results of this report suggest that NTCLT could be potentially proposed as a hopeful procedure for instant and considerable pain relief of oral aphthous ulcers of BD without any visible complications.

Ethical Considerations

Informed consent for the execution of the procedure and for the scientific use of images was obtained from the patients.

Conflict of Interests

The authors declare no conflict of interest.

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