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Clinical evaluation of the efficiency of low-level laser therapy for oral lichen planus: a prospective case series.

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Abstract

Oral lichen planus (OLP) is an inflammatory disease that can be painful, mainly in the atrophic and erosive forms. Numerous drugs have been used with dissimilar results, but most treatments are empirical. However, to date, the most commonly employed and useful agents for the treatment of OLP are topical corticosteroids. The study objective was to detail the clinical effectiveness of low-level laser therapy (LLLT) for the management of OLP unresponsive to standard topical therapy.

The authors studied a prospective cohort of 30 patients affected by OLP, who received biostimulation with a 980-nm gallium-aluminum-arsenide (GaAIAs) diode laser (DM980, distributed by DMT S.r.l., Via Nobel 33, 20035, Lissone, Italy). Outcome variables, statistically evaluated, were: the size of lesions; visual analogue score of pain and stability of the therapeutic results in the follow up period.

Eighty-two lesions were treated. We reported significant reduction in clinical scores of the treated lesions and in reported pain. No detailed complications or therapy side effects were observed during the study.

As previously reported by our group with a preliminary report, this study suggests that LLLT could be a possible treatment choice for patients with unresponsive symptomatic OLP, also reducing the possible invasiveness correlated with other therapies.

Introduction

Oral lichen planus (OLP) is a relatively common chronic inflammatory disease, of unknown aetiology, rarely undergoing spontaneous remission and potentially premalignant [1]. OLP is difficult to palliate and in several cases, most therapies are merely symptomatic [2]; even if the best treatment remains high-potency topical corticosteroids, management is usually empirical, without adequate control groups or corrected study designs [3].

Low-Level Laser Therapy (LLLT) is an approach increasingly used in medicine, which has potential biostimulating effects also if applied to oral tissues by improving wound healing, enhancing epithelization after periodontal surgery, and preventing or healing induced oral mucositis [4-6]. Laser biostimulation can obtain different intracellular biological reactions to stimulate regenerative abilities, without undesired adverse effects, reducing also the pharmacological support and its possible invasiveness. Besides explaining many controversies in the field of low-power laser effects (i.e., the diversity of effects, the variable magnitude or absence of effects in certain studies), the proposed redox-regulation mechanism may be a fundamental explanation for some clinical effects of irradiation, for example the positive results achieved in treating wounds, chronic inflammation, and ischemia, all characterized by acidosis and hypoxia [7].

To date, few reports have been published describing the efficacy of laser irradiation in erosive oral mucosal diseases, such as mucous membrane pemphigoid [8-10], aphthous stomatitis [11, 12], OLP [13] and chronic lichenoid graft-vs.-host disease [14].

The aim of this prospective study was to estimate the effects and the efficacy of LLLT on the outcome of unresponsive OLP, in term of clinical healing and pain control, on a prospective cohort of patients attending an oral medicine clinic.

Patients and methods

Consecutive Caucasian patients, attending the Oral Medicine Section of the Lingotto Dental School, Turin Hospital, Italy, from January 2009 and July 2012, were selected for the present study.

The inclusion criteria were: a) histological diagnosis of OLP on the basis of WHO criteria [15]; b) presence of painful and atrophic-erosive oral lesions, unresponsive to topical corticosteroid therapy (already and previously treated in our department); c) ability to complete the present clinical trial.

The exclusion criteria were: a) presence of histological signs of dysplasia; b) use of lichenoid reaction inducing drugs; c) therapy for OLP in the 2 months prior to the study; d) pregnant or breast-feeding women.

All patients were clinically evaluated by a skilled group of oral health care providers [A.C and P.G.A], who recorded the clinical aspect of the lesions, size and sites of oral involvement.

Different treatment options were discussed with the patients, and they all submitted written informed consent before enrolment, which was carried out in accordance with the declaration of Helsinki.

LLLT was delivered with a 980-nm gallium-aluminum-arsenide (GaAIAs) diode laser (DM980, distributed by DMT S.r.l., Via Nobel 33, 20035, Lissone, Italy). The device was used according to the manufacturer's instructions. A

collimated probe, with a diameter of 0.6 cm and a spot size of 0.28 cm^2, was used. The output power was 300 mW, verified using the calibrating door of the laser device, and the power density was about 1 W/cm^2. A "spot" technique was used, with a slight overlapping in order to evenly distribute energy covering all the mucosal lesions and also the peri-lesional tissues up to 0.5 cm.

Each session was performed delivering a fluence of 4 J/cm^2 *per* lesion, and the probe was held perpendicularly at a distance of about 2 mm. The time of delivery per point of application was calculated using the formula t (time) = D (dose-fluence) x A (area of the spot) / P (output power).

Therefore the calculations are: t (time) = 4 x 0,28/0,3 = 3,73 seconds in continuous wave.

Each patient underwent one laser irradiation sessions weekly until the resolution of signs (*e.g.* the disappearance of all atrophic-erosive lesions, regardless of any persisting hyperkeratotic lesions).

A single skilled examiner [A.C.] performed all the laser sessions, and another one [P.G.A.] recorded site and size of lesion, and reported pain. Clinical measurements were performed one week before the first laser procedure (T0), after each laser session, and 30-90-180 days after the resolution of signs, then every 6 months thereafter. Each patient was examined by means of record chart compilation, oral examination, registration of symptoms and clinical signs, and photo. The clinical data were scored according to the criteria scale used by Thongprasom and co-workers [16]: score 0: no lesions; score 1: hyperkeratotic lesions; score 2: atrophic area $\leq$ 1 cm²; score 3:

atrophic area > 1 cm²; score 4: erosive area ≤ 1 cm²; score 5: erosive area >
1 cm².

Complete response (total resolution of the clinical signs) was defined as the disappearance of all atrophic-erosive lesions, regardless of any persisting hyperkeratotic lesions; scores were either zero or one. Partial response, or persisting of the patient's condition, meant a decrease (score 2, 3 or 4) or no change at all in the patient's score. The difference between baseline and endpoint scores numerically expresses the clinical and symptomatic improvement.

The symptoms score was obtained using a Visual Analogue Scale (VAS). The VAS consisted of a 10 cm-horizontal line marked 0 (= no pain) to 10 (= most severe pain ever experienced). Patients were requested to mark the scale at each visit, before and after laser session. Complete resolution of the symptoms (no symptoms) was defined as the absence of any discomfort, corresponding to a zero VAS score.

The stability of the results in the follow up period was also described.

Describing general information, data was reported as means and standard deviation (SD), unless otherwise described. Wilcoxon's signed rank was used to calculate the significance of the outcome data for clinical score, whereas paired samples T-test to calculate difference in reported symptoms. P-values ≤ 0.05 were considered to be statistically significant. SPSS (SPSS for windows, version 11, SPSS inc, Chicago, IL, USA) statistical software was utilized.

Results

A total of 30 patients took part in the study, of which 19 were women (63.33%); the mean age at presentation was 64.5 years (± 11.27).

Seventeen patients had been previously treated with clobetasol propionate ointment 0.05% (Clobesol®, Glaxo, Verona, Italy), usually applied twice daily for at least 2 months; anti-mycotic treatment was also used as prophylaxis against oropharyngeal candidosis, consisting of miconazole gel (Micotef®, LPB, Cinisello B., Milano, Italy) applied once daily and 0.12% chlorhexidine mouth rinse (Plack-out®, BYK, Gulden Italia, Cormano, Milano, Italy) three times daily. The remain 13 patients did not receive any earlier treatment for oral ulcerations due to OLP.

Eighty-two lesions were treated at the end of the protocol (10 with score 2; 20 with score 3; 37 with score 4 and 15 with score 5). The different sites of involvement are reported in Table 1. The buccal mucosa was the most common site (52.7%), followed by the upper gingiva and the tongue. A complete resolution in clinical signs was obtained in 64 of the 82 lesions treated (78.05%) with a mean number of laser sessions of 11.79 (± 4.32). Moreover, a partial clinical response was found in 14 lesions (17.07%), with a mean number of laser sessions of 13.50 (± 3.91). Only 4 lesions (4.88%) had no change at all in the clinical characteristics, with a mean number of laser sessions of 12.7 (± 4.56) (Figure 1-2). The initial score, gender and age did not influence the results (data not shown). Considering the overall response for each case, 18 patients (60%) obtained a total resolution of the clinical signs, 10 patients (33.3%) a partial resolution and 2 patients (6.6%) did not respond at all.

We calculated the clinical improvement as the difference of clinical score at baseline and at the end of the treatment, reporting significant statistical differences (P=0.003) (Figure 3).

Sixty-five of the 82 treated patients (79.27%) had symptom improvements already after the first 4 sessions of therapy, with significant statistical differences (P=0.001) (Figure 4).

Table 2 provides information about the total dose for session for every treated case. No reported complications or therapy side effects were observed in any of the patients treated. We also examined patient pain perception after each procedure, and the VAS score was 0 in all cases.

The mean duration of follow-up was 26.6 months (± 6.38). During the follow-up period, 15 patients (50%) did not show new atrophic-erosive lesions.

Discussion

Nowadays, among many treatments accessible, high potency corticosteroids remain the most reliable and effective modality for the therapy of symptomatic OLP. For instance, clobetasol propionate appeared to be one of the most effective topical steroids, as in an adhesive base led to complete remission in 56-75% of patients [17-19]. Unfortunately, some patients are refractory to topical corticosteroids.

As previously reported, LLLT is a newly approach increasingly used in medicine, which has potential biostimulating effects also if applied to oral tissues. It is unclear how LLLT works; it has been suggested to reduce inflammation by lowering, in a dose-dependent manner, levels of prostaglandin E2, prostaglandin-endoperoxide synthase 2, interleukin 1

beta, tumour necrosis factor-alpha, the cellular influx of neutrophil granulocytes, oxidative stress, edema, and bleeding; other mechanism may be related to stimulation of mitochondrion to increase the production of adenosine triphosphate, resulting in an increase in reactive oxygen species, which influences redox signalling, affecting intracellular homeostasis or the proliferation of cells [20, 21].

Some recent evidence suggests that LLLT would currently appear to be a possible treatment for some patients with different type of oral erosive lesions, guaranteeing an immediate and notable analgesic effect [8-14]. In particular, in a preliminary report our group reported that LLLT appeared to be a possible treatment for some patients with OLP and can be used as an alternative therapy alongside standard treatment methods, especially for unresponsive patients [13]. Nonetheless controversies about tissues biostimulating with LLLT still remain and missing of homogeneous reporting of physical and biological variables makes summing up of the results particularly difficult.

Our findings might have a significant clinical impact since LLLT is easy to perform, but does not increase morbidity or presents side effects.

Before starting this study, we reported some preliminary data about LLLT for olp patients in which most of the patients reported an immediate pain relief after the first sitting, and all of them reported a complete resolution of symptoms at the end of the laser sessions, even if some lesions had only a partial clinical response [13]. For those cases, we initially used a 904-nm pulsed infrared laser (4 J/cm^2 energy density per minute, spot size 0.8 cm); in this new prospective study we decided to deliver the same energy density using a 980-nm gallium-aluminum-arsenide (GaAIAs) diode laser that has a

more superficial action, from an optical point of view if compared to 810 nm and to 904 nm [22], and this could be more useful for managing atrophic-erosive oral lesions, also possibly explaining the better results reported in this new group of patients.

We showed a statistical significance in the different of clinical scores after laser treatment. Only 4 lesions (4.88%) had no change at all in the clinical characteristics. Similar to previous limited published data, the number of laser sessions necessary for the tissues to heal was different, in relation to the characteristics of the lesions; the gingiva seemed to be more resistant but without statistical significance (data not shown). Usually, the clinical remission was obtained in a period of approximately 5 to six week; if the lesions do not show any clinical improvement after 6 to 8 laser sessions, this means that that type of patient does not respond clinically.

More than resolution of clinical scores, in this new series, pain score had a highly statistical improvement, quickly improving the quality of life of patients, even in the absence of complete resolution of all oral signs.

In conclusion, this study confirmed our previously data; LLLT appears to be a possible treatment for OLP patients and a diode laser seems to be the more effective wave length. To date, no data are available comparing LLLT with standard therapies, and it could be interesting in the future to test this statement, also if considering that it is a minimally invasive therapy and that invasiveness is not an absolute concept, depending on many factors such as age, illness, disability and/or psychological conditions [23].

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