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Potential of optical coherence tomography in patients with oral lichen planus treated by photobiomodulation: experimental study.

PhD Program in Bioengineering and Medical-Surgical Sciences

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Introduction.
Oral lichen planus (OLP) is a relatively common chronic inflammatory disease (1-2% of the total population), of unknown aetiology. To date, the gold-standard treatment remains high-potency topical corticosteroids. In oral medicine, clinical studies have demonstrated the effectiveness of PBM in patients with OLP, whenever poorly responsive to first-line approaches. Optical Coherence Tomography (OCT) could repeat, in real time, an image of architecture of epithelial and sub-epithelial tissues and surrounding structures. To date, OCT has been scarcely used in oral medicine, with no study focusing on ultrastructural changes in patients with OLP undergoing different treatments.

Aims of the study.
AIM 1: to compare OCT scan of healthy mucosa and of atrophic-erosive OLP to the traditional histopathology, in order to create a preliminary pattern between pathologist and clinician. *AIM 2*: to evaluate, through OCT, the morphometric changes of the oral tissues of patients with erosive and painful OLP that have performed the topical steroid therapy (Group A), compared to Photobiomodulation - PBM (Group B).

Materials and Methods.
Patients: Two groups (Group A and B) of 20 patients each, selected from a random original sample of 100 patients affected by erosive and painful OLP, referred to the Department of Oral Medicine, CIR Dental School, Turin untreated in the previous eight weeks.
Optical coherence tomography: a recent variant (OCT oral instrument: a variant (OCT oral instrument, version 2.1) of a commercial frequency domain swept source OCT dermatological instrument (SS-OCT, VivoSight® Michelson Diagnostics Ltd, version 2.0, Orpington, Kent, UK) was deployed. Length of the probe was 124 mm, probe shaft diameter was 15 mm; field of view of 6 mm^2. OCT (enface and dynamic) scans were obtained before and after treatment, and six months after the end of the eight-weeks treatment.
Study design: Group A would undergo a eight weeks "gold-standard" treatment with two daily application of clobetasol dipropionate 0.05% in an aqueous gel of 4% hydroxyethyl cellulose (100 g) in equal parts (50:50). Group B would undergo eight PBM sessions – once a week for eight weeks - with "Raffaello diode laser" 980/645 nm, used with the following parameters: output power = 300 mW, power density = 1 W/cm^2, fluence = 4 J/cm^2, collimated probe of 0.6 cm in diameter and spot size of 0.28 cm^2, kept perpendicularly at 2 mm from the area of irradiation. A "spot" technique with a slight overlapping would be carried out in each site, in order to distribute energy evenly on the mucosal lesions and the peri-lesional tissues up to 0.5 cm.

Results.
AIM 1: the following OCT features were commonly registered among the patients affected by erosive OLP belonging to both groups: epithelium (EP) at enface scan revealed less width, and higher hyper-reflectiveness than EP of a healthy mucosa, indicative of either hyper-

keratosis or hyperparakeratosis. At dynamic scans EP scattered red dots emerged within EP, which might be attributed to the concurrent intra and inter-cellular oedema, as expected in cases of acanthosis and spongiosis, commonly encountered in OLP. Lamina Propria (LP) revealed loss of integrity and hyper-reflectiveness at enface scans, with an increased, denser red pattern of vascularization at dynamic scans.
AIM 2: EP and LP width showed significant fluctuation after treatment, both in Group A and Group B. Specifically, paired t-student test showed a significant increase of EP width ($p < 0.01$) for both groups after eight-weeks treatment, indicative of a partial healing of the atrophic epithelium. On the other hand, paired t-student test displayed a significant decrease ($p < 0.01$) of LP width in both groups, indicative of a possible reduction of the activity of the band-like inflammatory infiltrate. Unpaired t-student test revealed a significantly higher increase of EP width in Group A, when compared to Group B ($p < 0.01$), at the end of treatment; on the contrary, no significant decrease of LP was detected between the two groups ($p > 0.05$). After six months, these variations were not preserved, with LP and EP width in both groups returning to be not significantly different from pre-therapy pattern ($p > 0.05$).

Conclusions.
This is the first project that would analyze and show significant ultrastructural changes of the oral mucosa after PBM and clobetasol with OCT. No significant differences were found between the two groups. The main limitation of this study is the operator-dependent approach required for an innovative technique, since no probe for a thorough analysis of the oral cavity has been standardized yet. Although biopsy remains the gold standard for OLP in oral medicine, OCT seemed to be a helpful tool for the clinician and the pathologist. Further studies on larger samples are needed, ideally with a designated probe for the necessities of the oral physician. Further clinical entities, such as other premalignant disorders, or autoimmune bullous-erosive diseases requiring constant follow-up or/and therapy, should be investigated, to fully understand the true scope of action of OCT in oral medicine.