

disease definition, and diagnostic criteria can be improved and clarified.

USE OF PRESCRIPTION SIALOGOGUES FOR MANAGEMENT OF XEROSTOMIA IN CHRONIC GRAFT-VS-HOST DISEASE

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Objectives: The objective of this study was to analyze use patterns of prescription sialogogues for management of xerostomia in patients with chronic graft-vs-host disease (cGVHD) after allogeneic hematopoietic cell transplant (allo-HSCT).

Methods: A retrospective chart review was conducted of patients who were diagnosed with cGVHD and prescribed sialogogue therapy from 2005 to 2019. Data collected included patient demographic characteristics, date of transplant, date of oral cGVHD diagnosis, concurrent immunosuppressive medication, sialogogue regimen including start and end dates, worst xerostomia score reported, and patient-reported percentage improvement.

Results: This study included 67 patients with a median age of 64 years (range, 25-78 years) diagnosed with oral cGVHD at a median of 8.2 months after allo-HSCT. Most patients were prescribed pilocarpine (81%) at 5 mg (88.5%) or, less frequently, 7.5 mg (3.8%), 10 mg (5.8%), or 15 mg (1.9%). Cevimeline was prescribed less frequently (19%), always at 30 mg. The median worst xerostomia score was 6.5 (range, 1-10). Pilocarpine dose was increased in 2 patients (4%) with no subsequent change in worse xerostomia score or percentage improvement. Overall median duration of therapy was 7.4 months (range, 1-152). For patients receiving pilocarpine, the median duration on therapy was 7 months (range, 1-152), and for patients on cevimeline, the median duration was 10 months (range, 1-111 months). The overall median patient-reported percentage improvement was 20% (range, 0-100%). Most common side effects were diarrhea (1.6%) and nausea (2.9%); excessive sweating was infrequent (1.4%).

Conclusions: The median duration of sialogogue therapy was 7.4 months, and most patients were prescribed pilocarpine at 5 mg. The median overall reported improvement was 20%, and side effects were infrequent and did not lead to therapy discontinuation. Patients receiving higher dosages of pilocarpine had a higher worst xerostomia score and a lower percentage improvement in symptoms. The prolonged duration of therapy suggests perceived benefits; however, prospective studies are needed.

ASSOCIATION OF CANDIDA AND FLUCONAZOLE THERAPY WITH PROINFLAMMATORY CYTOKINES IN ORAL LEUKOPLAKIA: A PILOT STUDY

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Objectives: Chronic inflammation caused by infection may lead to the production of proinflammatory cytokines (PICs) that can cause DNA damage and cell proliferation, thus playing a role in carcinogenesis. *Candida* infection has been reported to be increased in oral leukoplakia (OL) and is associated with an increased rate of malignant transformation into oral squamous cell carcinoma (OSCC). In vitro studies have demonstrated that the interactions between *Candida* and the oral epithelium lead to the release of PICs (interleukin [IL]-6, IL-8, IL-17, tumor necrosis factor [TNF]- α) that have also been found to be upregulated in OSCC and OL. This study aims to determine the correlation between *Candida* infection and PICs and their response to fluconazole therapy in OL.

Methods: Immunocompetent adult patients with OL (30 homogenous leukoplakia [HL], 30 nonhomogenous leukoplakia [NHL]) and 30 age- and sex-matched healthy control subjects (C) with no predisposing factors for oral candidal infection were recruited. Sterile cotton swabs and polyvinyl alcohol ophthalmic sponges were used to take samples from the lesional surface in OL and from the buccal mucosa in C for direct microscopy and culture for *Candida* and to determine levels of PICs (IL-6, IL-8, IL-17, TNF- α) by enzyme-linked immunosorbent assay, respectively. Sampling for PICs was repeated from the same sites in OL after treatment with tablet fluconazole 100 mg (oral rinse for 2 minutes and swallow) once daily for 14 days. Chi-square and Mann-Whitney *U* tests were used to estimate the difference between the groups.

Results: Forty percent of patients with NHL and 30% of patients with HL had positive findings for *Candida albicans*. Levels of IL-6, IL-8, and IL-17 were observed to be significantly higher ($P < .05$) in patients with NHL than in those with HL and in C. Patients with NHL and HL showing the presence of *C. albicans* had significantly ($P < .05$) higher levels of IL-6, IL-8, IL-17, and TNF- α than C and showed reduction in their levels and clinical improvement (decrease in size, thickness, and erythema) after fluconazole therapy.

Conclusions: Candidal infection is common in OL and causes release of PICs. There is a decrease in levels of these PICs and clinical improvement after fluconazole therapy in both NHL and HL. Hence, antifungal therapy in the management of OL can reduce the inflammatory milieu in which carcinogenesis can occur.

IN VIVO ECTOPIC OSTEOGENESIS OF ADIPOSE-DERIVED MESENCHYMAL STEM CELLS/OSTEOBLASTS COMBINED WITH PLLA/HAP NANOSTRUCTURED AEROGEL SCAFFOLDS

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Objectives: Osteoblast deficiency is a key problem in bone tissue engineering, and transplant of mesenchymal stem cells combined with osteoblasts can achieve ideal results. We sought to investigate the in vivo ectopic osteogenesis of adipose-derived mesenchymal stem cells (ADSCs) and osteoblasts (OBs) combined with poly(L-lactic acid) (PLLA)/hydroxyapatite (HAP) nanostructured aerogel scaffolds.

Methods: We tested a new supercritical fluid-assisted technique for the formation of nanostructured aerogel scaffolds. We obtained PLLA aerogel scaffolds and PLLA/HAP aerogel

scaffolds with high level of porosity (>90%), interconnectivity, and mechanical properties (compressive modulus up to 2 kPa). The fibrous nanostructure of these scaffolds was joined to micronic cells of controllable size. ADSCs and OBs were obtained by using an adherent method and an enzymatic digestion method. ADSCs, OBs, and the mixture of ADSCs and OBs (at a ratio of 1:1) were cultured with PLLA/HAp nanostructured aerogel scaffolds, respectively. After 48 hours of in vitro culture, cell-scaffold complexes were subcutaneously implanted into the back of Sprague-Dawley rats in corresponding groups, and PLLA/HAp nanostructured aerogel scaffolds without cells were implanted in a control group. The rats in each group were killed at 8 weeks post-operatively. The macroscopic and histopathological observations were performed to assess the ectopic osteogenesis potential.

Results: After adipogenic, chondrogenic, and osteogenic induction, ADSCs were positive for Oil Red O, toluidine blue, and alizarin red staining. Results of flow cytometry showed that ADSCs were positive for CD147, CD90, CD105, and CD44, with the rate of positivity being >80%, but negative for CD117, CD34, CD131, and CD45, with the rate of positivity being <5%. Passage 3 OBs were positive for both alizarin red staining and alkaline phosphatase staining. At 8 weeks after implantation, soft tissues grew into the complexes under gross observation. At 8 weeks after implantation, ectopic bone formation was visible in each group. The bone formation was more visible in the ADSC-PLLA/HAp nanostructured aerogel scaffold group than in the other groups with a significant difference ($P < .05$).

Conclusions: To conclude, ADSCs can promote the ectopic bone formation of OBs in vivo in combination with PLLA/HAp nanostructured aerogel scaffolds.

CLINICAL IMPACT OF DIRECT-ACTING ANTIVIRAL TREATMENT ON PATIENTS WITH HEPATITIS C VIRUS-RELATED ORAL

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Objectives: Oral lichen planus (OLP) is a chronic inflammatory mucocutaneous disease. It has been related to hepatitis C virus (HCV) infection as one of the extrahepatic pathologic manifestations. The current treatment for HCV infection with direct-acting antivirals (DAAs) is highly effective and safe. This study aimed to evaluate the impact of HCV eradication on OLP clinical manifestations.

Methods: Patients with a histologic diagnosis of OLP and HCV chronic infection were recruited from the oral medicine and internal medicine units of the University of Campania "Luigi Vanvitelli." All patients received DAA treatment and were monitored at baseline and during and after treatment for liver function and antiviral response. Patients underwent an oral clinical examination before receiving DAAs (T0) and 8 weeks after the end of treatment (T1), and they were observed periodically in follow-up (FU). Statistical analysis was performed using Mann-Whitney and Wilcoxon tests, chi-square tests, and Fisher exact tests.

Results: Eighteen patients (13 females and 5 males; median age, 75 years) with chronic HCV infection of different genotypes were enrolled. All patients cleared HCV RNA with a

sustained virologic response at FU. No adverse events were reported. The median FU was 92 weeks at T2. At T0, 5 patients presented with reticular and bilateral white lesions; 7 patients presented with erosive OLP; and 6 patients presented with a mixed form. The mean percentages of oral sites involved were 30% (± 13.9) at T0, 20.8% (± 12.9) at T1, and 16.2% (± 15.2) at T2, showing improvement from T0 to T1 ($P = .007$) and T2 ($P = .005$). One patient developed oral cancer during the treatment and was excluded. Oral lesions have improved in 9 cases (52.9%) at T1 and in 10 cases (55.6%) at FU (T2); among these, 6 (60%) showed complete remission. However, statistical analysis did not reveal a significant correlation between oral improvement and HCV genotype ($P = .64$), viral load ($P = .27$), liver status ($P = .60$), isolated HBcAb positivity ($P = .633$), and type of DAA received ($P = .103$).

Conclusions: DAA treatment leading to HCV eradication can improve OLP symptoms. However, a causative relationship between HCV infection and OLP pathogenesis is difficult to establish. Further studies are necessary.

SELENIUM: A SOLE TREATMENT FOR ERO-SIVE ORAL LICHEN PLANUS (RANDOM-IZED CONTROLLED CLINICAL TRIAL)

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Objectives: Oral lichen planus (OLP) is a chronic disease with immune-mediated pathogenesis. Selenium (Se), an antioxidant, plays a role in modulating immunity. The aim of this clinical trial was to evaluate 2 Se forms (novel topical hydrogel and oral capsules), solely, in treating erosive OLP based on clinical evaluation and salivary oxidative stress markers. To date, to our knowledge, this is the first study to evaluate the role of Se solely in treating erosive lesions associated with erosive OLP. This clinical trial has been registered in the Cochrane Database under registry number PACTR201901531815403.

Methods: Patients were allocated into 1 of 3 groups: group I, topical corticosteroids and topical antifungal as an adjunctive therapy; group II, novel topical Se hydrogel; or group III, systemic Se. Treatment lasted for 6 weeks. Patients were clinically evaluated at baseline and at 6 and 12 weeks for reduction in pain scores and clinical lesion size. Biochemical analysis was performed for salivary malondialdehyde (MDA) and total antioxidant capacity (TAC) levels at baseline and 6 weeks. Correlation between clinical signs and symptoms and salivary oxidative stress markers was measured at 6 weeks. Two-way analysis of variance (ANOVA) followed by a post hoc Tukey test was performed to assess for significant differences in mean pain scores, clinical lesion size, and salivary MDA and TAC levels at 6 weeks. One-way ANOVA was used to test for significant variations in clinical parameters at 12-week follow-up. Principal component analysis and nonmetric dimensional scaling were performed to test for correlation and possible relationships between clinical parameters and salivary oxidative stress markers.

Results: There was a significant reduction in signs and symptoms in response to all treatment modalities. However, there was no significant difference among the 3 groups at 6 weeks. At 12 weeks, group II had significantly lower pain scores than group I. Salivary MDA levels showed a significant decrease