

Real-Time PCR was used to detect high and low-risk HPV both in cytobrush and biopsy specimens. Descriptive and analytical statistics were performed. Fisher's exact test was performed for the analysis of contingency tables.

RESULTS: We studied 17 oral dysplastic lesions classified as mild (13 cases; 76,5 %) and severe (4 cases; 23,5 %) from 14 subjects. The study group was composed of 6 males (42,9 %) and 8 females (57,1 %); the age of patients ranged from 48 to 78 years with a mean age of 63,76 years (DS±10,72). Nine (52,9 %) samples were collected from tongue mucosa. As regard to smoking habits, 47,1 % of patients were non-smokers, 35,3% smokers and 17,6 % ex-smokers. 64,7 % of samples were derived from alcohol consumers.

Clinically, 9 of the 17 (52,9 %) oral lesions were described as leukoplakia, 2 (11,8 %) erythroplakia, 4 (23,5 %) verrucous lesions and 2 (11,8 %) ulcerative lesions.

HPV DNA was detected in 2/17 (11,8 %) of oral dysplastic lesions; both were oral severe dysplasia.

One case was positive to HPV 6; the other one has a triple infection by HPV 11, 16, 53.

Biopsy and cytological sampling by brushing were not statistically significant correlated ($p = 0.99$); the two tests were not overlapped.

CONCLUSION: Although the analysed cases were small, our study reveals a low prevalence (11,8 %) of HPV in oral dysplasia. Statistical analysis reveals that two tests can not be considered superimposed. The cytobrush technique has many advantages such as easy execution, it is less expensive, and it is less invasive. However, it does not allow analysis of deep cells layer and it seems to be less accurate than biopsy. Viral DNA presence in premalignant or malignant oral mucosal lesions may only be expression of secondary viral infection; immunohistochemical studies highlights signal expressed by cell following the integration of HPV into the host cell.

Therefore, immunohistochemical studies would be needed to assess the real integration of the HPV into the oral mucosal cells.

Tens effects on salivary stress markers: a pilot study

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BACKGROUND: The objective of this pilot study is to evaluate salivary alpha amylase (sAA) as a marker of stress in two groups of healthy subjects, one receiving ultra-low frequency transcutaneous electrical nerve stimulation (ULF-TENS) and one without stimulation.

METHODS: Sixty healthy people were enrolled. The test group consisted of 30 participants (15 men, 15 women). The control group consisted of 30 participants (15 men, 15 women).

RESULTS: Statistical analysis showed that sAA levels were statistically different between men and women independently from TENS; we hypothesize that treatment could influence sAA levels because it is thought to activate μ opioid receptors. The results of this study seem to indicate that the analysis of sAA, through a non-invasive saliva sample, could be an efficient aid for understanding the functions of the autonomic nervous system.

CONCLUSIONS: The results seem to indicate that women have a lower ability to relax both in spontaneous conditions and with TENS stimulation, compared to men, in both the test and control groups. In particular, TENS stimulation increases relaxation, especially in men. This result may prove that TENS could reduce stress, as other scientific studies have already reported.

Oral lesions as primary manifestations of acute agranulocytosis related to metamizole: a case report

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BACKGROUND: Metamizole (dipyrone) is a non-opioid compound with potent analgesic, antipyretic and spasmolytic effects. Its prolonged administration could be related to severe condition called "acute agranulocytosis": a potentially fatal event already discovered in the early 1930s but only in the 1980s recognized as a possible drug-related adverse reaction by the International Agranulocytosis and Aplastic Anemia Study (IAAAS). Agranulocytosis was characterized by neutrophil granulocyte count below 100 cells/mm³ and normal values of other blood cell lines. The main clinical manifestation of agranulocytosis are fever, tonsillitis, pharyngitis, sepsis, pneumonia and, in the oral cavity, periodontitis, alveolar bone loss, ulcerations and local supra-infections (i.e. oral candidosis). If underdiagnosed, the mortality rate is 10%. On the contrary, with early diagnosis and appropriate management, this rate is tending to drop significantly and complete recovery is expected in over 80% of patients.

We present a case of a woman with primary oral manifestation of neutropenia related to metamizole administered for dental pain.

CASE REPORT: A 55-year-old woman was referred to the Department of Surgical, Oncological and Oral Sciences, with worsening diffuse oral pain. Clinically, ulcer and pseudomembranous lesions on the mouth floor and alveolitis post 3.6 extraction were recognized. Oral hygiene was poor. No significant medical history was distinguished. The patient reported dental pain before and after 3.6 extraction, and took metamizole for 2 weeks; moreover, she had hematological investigations positive for severe neutropenia (neutrophil granulocyte count: 20 cells/mm³). In accordance with hematologist, the diagnosis of acute agranulocytosis related to metamizole was made. During hospitalization for appropriate neutrophils replacement and antimicrobial therapies (by intravenous administration of antibiotics, antifungal drugs and bone marrow growth factors), the management of oral manifestation was performed by antiseptic topical treatment (chlorhexidine gel, thrice daily for 10 days). Furthermore, the patient was educated to oral hygiene. One month after hematological therapy, the intra-oral examination showed resolution of all oral manifestations.

CONCLUSIONS: Acute agranulocytosis is a severe disease potentially associated with the use of the drugs (i.e. metamizole). Although rarely, the oral manifestations could be

the first signs of this adverse reaction and must be promptly diagnosed/treated by a multidisciplinary approach.

Use of *in vivo* reflectance confocal microscope for evaluation of oral cavity lesions: a systematic review of the literature

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BACKGROUND: Since the early 2000s, several authors have studied the application of reflectance confocal microscopy (RCM) to the oral cavity. This technology offers the opportunity to carry out a “real time” inspection at a microscopic level during the clinical examination, obtaining horizontal (en face) images of the scanned region. In addition, RCM can examine both soft and hard tissues of the oral cavity. Being an *in vivo* method, RCM could in theory bypass all of the difficulties and problems related to a biopsy and the subsequent histological examination, which still represents the gold standard for definitive diagnosis. Aims of this review are to provide an overview of the literature on RCM analysis of the oral cavity *in vivo* and to identify any flaws in the studies, providing guidance to improve RCM applications and the design of future studies of RCM.

METHODS: We performed a systematic literature search using three search engines: PubMed, Web of Science, and Cochrane Library. The search strategy included the use of “reflectance confocal microscopy” and “RCM” in combination with “mouth” and other terms related to the topic of interest. Selection criteria for studies to include were as follows: RCM studies performed on the human oral cavity, *in vivo*, published in English, for which the full text was available. In the first examination of the search results, the reviewers eliminated studies based solely on reading the titles and abstracts, if the abstracts showed that the studies did not meet the selection criteria. This first step also served to exclude all duplicate publications. Subsequently, the reviewers read the full text of the remaining papers for more accurate screening.

RESULTS: The search gave 419 results. Only 32 were related to *in vivo* RCM analysis of the human oral cavity. After reading the full texts, 16 of the 32 articles met our criteria. We decided to organize the selected articles according to four topics: healthy mucosa, autoimmune diseases, cancer and precancerous lesions, and hard dental tissues.

CONCLUSIONS: This systematic review identified some flaws in *in vivo* RCM studies of the oral cavity. However, there are still too few publications on this topic. Moreover, most of the studies concern subjects with healthy mucosa. The paucity of work conducted in patients with autoimmune diseases or precancerous and neoplastic lesions suggests that more RCM analyses of these patients are indispensable. In addition, the small size of the examined samples must be considered. A further problem, regarding studies of soft tissues, is the absence of comparison with histological studies. Consequently, it is difficult to establish criteria for a viable differential diagnosis based on the use of RCM, which cannot be a substitute for histology. In conclusion, although RCM is a promising device for diagnosing and monitoring oral pathology, there are shortcomings with RCM. Future studies need to consider these guidelines to increase the quantity and quality of the results, to translate research into clinical practice.

White Sponge Nevus: two case reports and a review of the literature

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BACKGROUND: The aim of this paper is to describe two new cases of White Sponge Nevus (WSN) and perform a critical review of the literature.

METHODS: Two patients, one fourteen and the other nineteen years old, were referred to our Clinic for the diagnosis of white spongy asymptomatic diffuse oral lesions.

RESULTS: After a thorough medical history, an incisional biopsy was performed in both cases and pathology revealed a hyperparakeratotic epithelium with acanthosis and spongiosis. No dysplasia was found in the specimens, so a final diagnosis of WSN was performed. Even if WSN is due to a genetic mutation, no parents of the two patients presented oral lesions. **CONCLUSIONS:** White lesions in the oral cavity are common and have multiple etiologies. While most intraoral white lesions are benign, some are premalignant or malignant at the time of diagnosis, thus it is extremely important to accurately identify and appropriately manage these lesions. Due to the similar clinical appearances, it may be difficult, sometimes, to differentiate benign white lesions from their premalignant/malignant counterparts. Between hereditary white lesion leukoedema and WSN are the most common to find. White Sponge Nevus is an autosomal-dominant condition that is due to point mutations for genes coding for keratin 4 and/or 13. It is an asymptomatic, white lesion that may affect several mucosal sites. Lesions tend to be thickened and have a spongy consistency. The presentation intraorally is almost always bilateral and symmetric and usually appears early in life, typically before puberty. The characteristic clinical manifestations of this particular form of keratosis are usually best observed on the buccal mucosa, although other areas such as the tongue and vestibular mucosa may also be involved. Also esophageal and genital mucosa may be affected.

The differential diagnosis includes leukoedema, hereditary benign epithelial dyskeratosis, lichen planus, lichenoid drug reaction, lupus erythematosus, cheek chewing and candidiasis. A correct diagnosis can be made combining clinical with pathological features; WSN does not disappear when stretched so it can be differentiated from leukoedema; the absence of an inflammatory infiltrate, dysplasia and hyphae help in the differential diagnosis toward OLP, leukoplakia and candidiasis. A final diagnosis of WSN is necessary because the lesion is benign and no further biopsies or specific treatments are required.

Medication-related osteonecrosis of the jaw (MRONJ): proposal of non-surgical treatment protocols

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BACKGROUND: The research aim is to describe a complete protocol centred on a non surgical approach to man-