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Impact of crack cocaine use on the occurrence of oral lesions and micronuclei

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Abstract. The aim of this study was to investigate the occurrence of oral lesions and micronuclei in crack cocaine users. A cross-sectional study was conducted involving 106 crack users and 106 non-users matched for age, sex, and tobacco use. Socio-demographic characteristics, the consumption of psychoactive substances, and the occurrence of fundamental lesions were investigated. Cellular changes in the oral mucosa (karyolysis, karyorrhexis, 'broken egg' events, and micronuclei) were determined by exfoliative cytology for 54 participants in each group. Crack users had a greater occurrence of fundamental lesions ($P = 0.001$). Furthermore, they had higher mean occurrences of micronuclei (17.25 vs. 3.80), karyolysis (12.39 vs. 9.46), and karyorrhexis (30.39 vs. 10.11) (number per 1000 cells) than non-users (all $P < 0.05$). No difference between the groups was found with regard to broken egg events ($P > 0.05$). After controlling for confounding variables, fundamental lesions were 2.02-fold more frequent and micronuclei were 3.54-fold more frequent in crack users. Crack use was found to be associated with clinical and cellular changes in the oral mucosa. These findings can contribute to the planning of health care for individuals who are dependent on street drugs.

Key words: crack cocaine; drug users; mouth diseases; oral mucosa; micronuclei; exfoliative cytology.

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Users of psychoactive substances, especially crack cocaine, have a greater occurrence of systemic problems, such as cardiovascular, respiratory, neurological, and gastrointestinal complications[1–3]. Considering the consequences to general health and systemic effects, it is plausible that such individuals also have a greater occurrence of changes in the oral mucosa. The biological mechanism that supports a possible association between crack use and changes in the oral mucosa is based on the local effects related to the extreme heat of the smoke, the harmful effects of the chemical content of the drug, tissue necrosis caused by friction over the gingival surface, insufficient blood supply due to vasoconstriction, and diminished salivary flow, as well as the harmful effects on the immune response[4–6]. The consequences of this habit could determine cellular changes and the subsequent development of lesions in the oral mucosa[7–10].

Studies have been conducted to evaluate the harmful effects of crack use on oral epithelial cells. Crack smoke appears to be able to induce inflammatory changes in the oral epithelium, such as an increase in keratinization[7], decrease in the area of nuclei[8], and increase in the number of nucleolar organizer regions[10]. Some studies have shown crack use to be associated

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with a greater frequency of micronuclei in comparison to non-users[9,11,12]. These markers enable the detection of damage to the cellular genome before the emergence of any clinical manifestation of a pathological condition[11].

Associations between oral lesions and inadequate oral hygiene, periodontal disease, a low level of schooling, low socioeconomic status, and drug use (such as alcohol and tobacco), have been demonstrated[13]. However, it appears that no study investigating the association between crack use and clinical oral lesions has yet been published. Knowledge and a better understanding of factors associated with the occurrence of oral lesions are essential to the establishment of adequate prevention and health promotion measures.

The aims of this study were to evaluate the prevalence of fundamental lesions in the oral mucosa and frequency of cell damage in crack users, as well as to investigate the association between crack use and these outcomes after controlling for confounding variables.

Materials and methods

Subjects and study design

A cross-sectional study was conducted in the city of Santa Maria, Brazil, between August 2012 and December 2013. This study received approval from the Institutional Review Board of Centro Universitário Franciscano and all volunteers signed a statement of informed consent after agreeing to participate in the study.

Data were collected from two facilities with chemical dependency treatment programmes (code F14.2, International Classification of Diseases 10th Revision; ICD-10). The eligibility criteria were crack dependency, hospitalization in one of the two facilities, crack use for at least 1 year, and the absence of cognitive impairment. Control individuals with history of street drug use were recruited from public schools or from a list of patients scheduled for treatment at the dental school who required an examination before undergoing treatment. The crack and control groups were matched 1:1 for age (± 3 years), sex, and tobacco smoking habit (non-smoker or smoker). Individuals with a systemic disease that affects the immune system, those taking medication that can increase gingival tissue volume, and those wearing an orthodontic appliance were excluded from the study. Further details on the recruitment process have been published elsewhere[14,15].

Sample size

The difference in the occurrence of periodontal disease between heavy tobacco smokers (67.6%) and mild/moderate tobacco smokers (41.2%) (prevalence ratio 2.98; $n = 212$) was used to calculate the sample size[16]. This sample is compatible with the difference in mean micronuclei (MN) (4.2 ± 3.75 per 1000 cells analysed) between groups in the study by Almeida et al.[9]. Considering a 0.1% significance level, 90% power, a paired design, and 30% increase to compensate for possible dropouts, a minimum of 51 participants was required in each group to assess the outcome (MN).

Data collection

Data on socio-economic and socio-demographic characteristics, oral health status, and psychoactive substance use (tobacco, alcohol, marijuana, cocaine, crack, heroin, etc.) were collected using a validated questionnaire adapted to the Brazilian population administered in the form of an interview[17]. Two researchers who had undergone a training exercise conducted the interviews in an isolated location to ensure the privacy of the respondents. For the test–retest analysis, the substance use questionnaire was administered again after a 4-month period to 10% of the sample, and reliability was determined using the kappa statistic ($\kappa = 0.81$ to 1.0).

The oral examinations were standardized, with the participants seated in a chair under natural and artificial light. The examiner's head lamp provided additional light[18]. After relative isolation, the decayed, missing, and filled teeth (DMFT) index was determined[18]. Traumatic dental injury and the marginal bleeding index (MBI) were also determined[19,20]. Plaque (dental biofilm) was removed prior to the evaluation of tooth loss and traumatic dental injury.

Examiner reproducibility

The identification of fundamental lesions in the oral mucosa was performed by a single examiner trained with computer images. Thirty photographs were evaluated, and the evaluation was repeated after 1 week to determine the examiner reproducibility using the kappa statistic; this was 0.95 prior to the study and 0.93 at 7 months after the onset of the study, when reproducibility was tested again.

Cell analyses were performed by two blinded examiners who had undergone training and were experienced in the MN assay for exfoliated cells. The evaluation of the cells was performed separately for each subject, observing an average of 1000 cells per slide (3 slides per subject). The mean value for all subjects was then determined.

Clinical evaluation of fundamental lesions of the oral mucosa

The presence of the following fundamental lesions was determined clinically: spot (i.e., a focal area with a change in colouration and no elevation or depression in relation to the surrounding tissues), plaque (i.e., a slightly raised lesion with a flat surface), nodule (i.e., a solid raised lesion measuring ≥5 mm in diameter), papule (i.e., a solid raised lesion measuring <5 mm in diameter), vesicle (i.e., a surface lesion with liquid content measuring <5 mm in diameter), blister (i.e., a surface lesion with liquid content measuring ≥5 mm in diameter), erosion (i.e., a surface lesion with partial loss of the epithelial surface), ulcer (i.e., a lesion characterized by the loss of epithelial surface with exposure of the underlying connective tissue), fissure (i.e., a narrow ulceration similar to a groove), pseudomembrane (i.e., an ulcer covered by a removable membrane), and hyperplastic lesion (i.e., an elevation with colouration similar to the surrounding mucosa)[21]. The clinical characteristics of these lesions were evaluated, including the anatomical location, size, colour, past history, and associated aetiological factors. The examination of the oral mucosa was performed in the following sequence: labial mucosa and vestibular sulcus (upper and lower), labial portion of the commissures and oral mucosa (right and left), tongue (dorsal and ventral surfaces and edges), floor of the mouth, hard and soft palates, and finally alveolar ridge/gingiva (upper and lower)[22]. Lesions were recorded and photographed with an intraoral camera (Nikon D40X; Nikon, Tokyo, Japan). Cases for which complementary examinations were needed for the determination of the diagnosis were sent to the dentistry school of the Centro Universitário Franciscano.

Collection of oral mucosa cells

The participants were instructed to remove any dentures and gargle with water for 1 min to remove any detritus that could compromise the analysis. Cells were collected with swabs from the right and left sides of the buccal mucosa. The material was placed in a Falcon tube containing 3 ml of cooled 0.9% saline solution. The samples were centrifuged at 3000 rpm for 10 min. The supernatant was discarded and the remaining sample was re-sus-

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