Clinical and Histological Manifestations of Chronic Coca Leaf Chewing in a Peruvian Population: A Cross-sectional Study

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Abstract

Aims: This study aimed to determine the possible clinical and histological periodontal effects of long-term coca leaf chewing habit in habitants of the highland region of Peru.

Materials and Methods: A total of 100 residents, were recruited for the study. Fifty individuals were habitual coca leaf chewers and 50 were non-users. Eligibility criteria were: 60-80 years old, ≥20 teeth present (excluding third molars), systemically healthy (controlled systemic disease), not using medication affecting the gingiva. Chronic tobacco smokers were excluded. All participants completed questionnaires, received clinical periodontal examination, and had gingival biopsies harvested for histopathological assessment.

Results: Most coca leaf chewers reported several oral changes resulting from the habit, such as bitterness, numbness and mouth dryness, while none of the non-chewers reported experiencing such changes. Within the clinical periodontal parameters, it was found that there was a significant difference in terms of clinical attachment level loss, with a p value of 0.014 in those who chewed coca leaves, who appeared to have less clinical attachment loss.

Conclusion: Chewing coca leaf produce bitterness, numbness and mouth dryness, and clinical attachment loss. Histologically higher number of inflammatory cells in the stratum spinosum, with more acanthosis, clear cell, and higher number of blood vessels.

Keywords: Periodontal diseases, coca leaf, periodontal health smoking

Introduction

Tobacco smoking is an established risk factor for periodontal disease, associated with increased probing depth, attachment loss, bone loss, and gingival recession (Leite *et al*., 2018). The negative periodontal impact of tobacco smoking appears to be similar regardless of smoking type; cigarettes, pipes, and hookahs all share the same effects (Haber *et al*., 1993). Similarly, chronic use of cannabis has been associated with periodontal manifestations, including increased probing depth and attachment loss (Thomson *et al*., 2008). In contrast, smokeless tobacco does not lead to increased probing depths or interproximal attachment loss (Weintraub and Burt, 1987; Preber and Bergström, 1990). However, chronic smokeless tobacco use, especially when consistently placed in the same vestibular area, leads to localized gingival recession and oral mucosal lesions (Kavitha *et al*., 2014; Lesan *et al*., 2014). Therefore, the periodontal and oral consequences of such environmental factors, typically introduced by the personal and habitual use of various plant products, vary depending on the manner of use and the product itself.

One plant product with a long tradition of habitual daily use in several populations is coca (*Erythroxylum coca*) leaves (Biondich and Joslin, 2016). Among the population of the Peruvian Andes, the habit of chewing coca leaves is a deeply-rooted ancestral tradition; coca use by highland, Amazonian and coastal populations has been traced back more than 6000 years, among diverse

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regional cultures (Bolton, 1976; Rivera *et al.*, 2005). Leaves are chewed, without the need for swallowing, to obtain the desired stimulatory effects on the muscular, digestive and nervous systems (Stolberg, 2011). It has been documented that the habit of consuming natural coca leaves has an impact on periodontal health, with reports describing benign, premalignant and malignant lesions following habitual use (Page and Beck 1997).

The aim of this cross-sectional observational study was to determine the clinical and histological periodontal effects of long-term coca leaf chewing habit in inhabitants of the highland region of Peru.

Materials and Methods

Study design and study population:

This was a cross-sectional observational study. Participants completed questionnaires, received clinical periodontal examination, and had gingival biopsies harvested for histopathological assessment. The study protocol was prepared in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (Von Elm *et al.*, 2008). It was approved by the Ethics in Research Committee of the Cientifica del Sur University Faculty of Dentistry (Protocol #00386) and was conducted in accordance with the 1964 Helsinki Declaration, in its revised (2008) form. Study participants were volunteers who received detailed information regarding the proposed research and provided signed informed consent. The study was conducted among the population of the rural area of Chongos Bajo district, Chupaca province, Junín department, Peru. All participants belonged to the Senior Citizens Club of the Municipality of Chongos Bajo, population 4,409 (2005 census, National Institute of Statistics and Informatics), located at an altitude of 3,275 meters. All study procedures were performed at the Chongos Bajo Health Center.

A total of 100 residents, among members of the local senior citizens' club, were recruited for the study. Fifty individuals were habitual coca leaf chewers and 50 were non-users. Eligibility criteria were: 60-80 years old, ≥20 teeth present (excluding third molars), systemically healthy (controlled systemic disease), not using medication affecting the gingiva. Smokers more than 10 cigarettes per day were excluded.

Questionnaires

Consenting participants completed questionnaires to collect the following information: age and gender; general health status; diagnosed systemic disease; medical treatment received; prescription medication; coca chewing habit history details (starting date; added ingredients); self-reported outcomes (symptoms associated with coca chewing; ability to quit if needed).

Clinical parameters

The following periodontal clinical parameters were recorded on six sites per tooth for all teeth present (excluding third molars), by two trained and calibrated examiners (M.C., A.B): Gingival Index; (Löe, 1967) Quigley-Hein Plaque Index (Turesky modification) (Silness *et al.*, 1964), using disclosing solution (sodium erythrosine and brilliant blue plaque revealer – Ditonos Eufar); Bleeding on probing (BOP); Gingival recession (GR); Probing depth (PD); Clinical attachment level (CAL). In addition, the Periodontal Disease Index (PDI) was recorded using Ramfjord teeth (Ramfjord, 1997). Recessions present were classified according to Miller classification (Miller, 1985). Examiner calibration: the two examiners were calibrated by examining. The intra-examiner kappa intra-class correlation coefficient for both PD and CAL was > 0.82.

Gingival Biopsies

Biopsies of gingival tissues were obtained in 10 participants per group from the distal aspect of the most distal molar in either maxilla or mandible by one investigator (C.P.) during tooth extraction or crown lengthening. Following extraoral asepsis and antimicrobial rinse, local anesthesia was provided, and an incisional biopsy was performed, harvesting a tissue sample of approximately 6x6 mm area. Biopsy samples were immediately placed in 10% buffered formalin and submitted for histopathology. Biopsy sites were sutured with silk sutures, which were removed at 1 week.

Histopathology

Biopsy specimens were routinely processed for histopathology, including dehydration, paraffin embedding and sectioning in a direction from the surface (epithelium) to the base (connective tissue). Sections (20 μm thickness) were hematoxylin& eosin (H&E) stained and digital photomicrographs were obtained Photomicrographs were analyzed using image analysis software (Figures 1 and 2).

Statistical analysis

Statistical analysis was conducted using statistical software (SPSS Statistics Version 21). Descriptive statistics were compiled for quantitative and qualitative variables. In order to compare GR, PD, and CAL between the two groups, the normal distribution of these numerical clinical parameters was first tested (Kolmogorov-Smirnov test). Because the data failed the normality test, between group comparisons were conducted using Mann-Whitney U-test. In order to compare the rest of the clinical variables (qualitative data) between the two groups, Fisher's exact test was employed. Histopathological data between the two study groups were compared by Chi-square and Fisher's exact tests. Significance level was set at 5%.

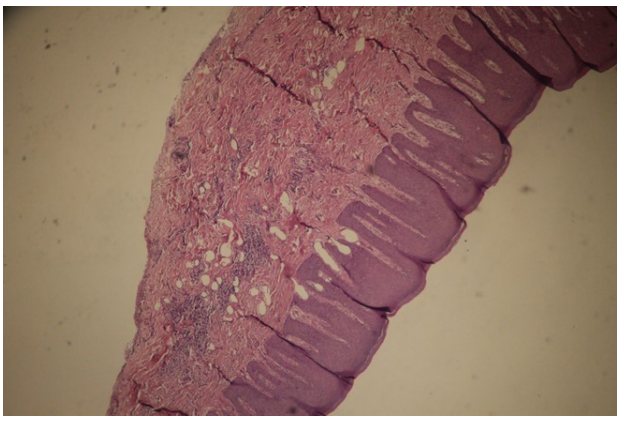

Figure 1.

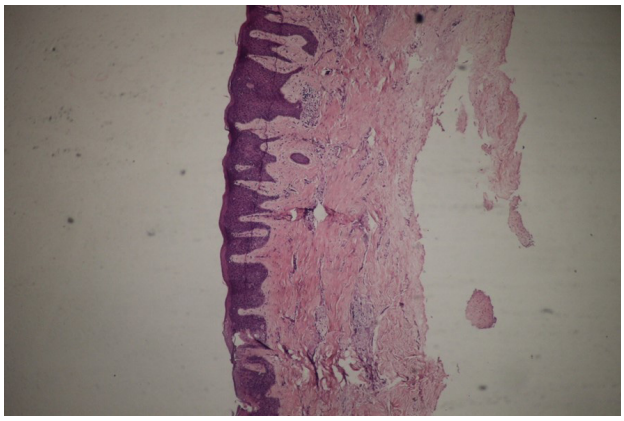

Figure 2.

Results

A total of 100 senior citizens (62 women) were recruited and examined. One group (n=50) was composed of those having the habit of chewing coca leaves and the other group (n=50) was composed of persons who did not have a coca chewing habit. The demographic characteristics of the two groups are reported in (Table 1). Almost half of the participating seniors (49%) did not report any systemic disease (Table 2). Among those reporting a systemic disease history, hypertension was the most common disease. Among these seniors, 94% denied any tobacco smoking habit.

For coca leaf chewers, the average starting age for this habit was 17.8±3.7 years (Table 3). All chewers indicated they could give up the habit if they wished. All of chewers reported mixing the coca leaves with an alkaline product known as *llipta*, consisting of quinoa leaf ashes, which they used together with the coca leaves to sweeten the chewing bolus. Most coca leaf chewers reported several oral changes resulting from the habit, such as bitterness, numbness and mouth dryness, while none of the non-chewers reported experiencing such changes.

Within the clinical periodontal parameters, it was found that there was a significant difference in terms of clinical attachment level loss (p=0.014) in those who chewed coca leaves, who appeared to have less clinical attachment loss (Table 4). A statistically significant difference was also found in the plaque index between those who chewed coca leaves and those who did not. The recession values according to Miller's classification were similar in the two groups, with no alterations reported, and the same was the case for gingival indexes (table 5).

Table 1. Demographics of study population

Characteristics	Chewers (n=50)		Non-chewers (n=50)		P value
Age (in years; mean ± SD*) (Range)	70.4± 5.6 (60-80)		69.8± 4.22 (60-80)		0.522
Gender (females:males)	34:16 (n)	68:32 (%)	28:22 (n)	56:44 (%)	0.216

** SD = Standard deviation*

Table 2. Systemic disease and smoking status

Characteristics	Chewers (n=50)		Non-chewers (n=50)		
	n	%	n	%	P value
Systemic Disease					
None	22	44.0	27	54.0	
Hypertension	7	14.0	8	16.0	0.014
Arthritis	7	14.0	6	12.0	0.330
Arthrosis	3	6.0	3	6.0	1
Gastritis	5	10.0	5	10.0	1
Diabetes	6	12.0	1	2.0	0.101
Smoking Habit					
Yes	2	4.0	4	8.0	0.678
No	48	96.0	46	92.0	

Table 3. Coca leafuse

Characteristics	Chewers (n=50)		Non-chewers (n=50)	
	n	%	n	%
Age of onset/SD*	17.8±3.7		-	
Would cease chewing?				
Yes	50	100.0		
No	0	0		
Changes in mouth				
None	8	16.0	50	100.0
Drymouth	11	22.0	0	0
Bittermouth	18	36.0	0	0
Numbness	13	26.0	0	0

* SD = Standard deviation

Table 4. periodontal clinical parameters

Characteristics	Chewers (n=50)	Non-chewers (n=50)	P value^
GR*(mm)/SD*	1.91±1.18	2.30±1.40	0.186
PD*(mm)/SD*	1.85±0.55	2.24±0.88	0.062
CAL*(mm)/SD*	3.76±1.40	4.51±1.50	0.014

*SD = Standard deviation, *Gingival recession, *Probing depth, *Clinical attachment level
^Mann-Whitney U-tests

Table 5. Periodontal index

CHARACTERISTICS		COCA CHEWER (N=50) 95% CI		NON COCA CHEWER (N=50) 95% CI		P VALUE†
		N	%	N	%	
Gingival Index	0	1	2.0	2	4.0	0.738
	1	8	16.0	6	12.0	
	2	26	52.0	30	60.0	
	3	15	30.0	12	24.0	
Plaque Index	**0**	**0**	**0**	**0**	**0**	**<0.001**
	1	**0**	**0.0**	**7**	**14.0**	
	2	**7**	**14.0**	**26**	**52.0**	
	3	**35**	**70.0**	**13**	**26.0**	
	4	**6**	**12.0**	**3**	**6.0**	
	5	**2**	**4.0**	**1**	**2.0**	
Gingival Recession	1	21	42.0	24	48.0	0.730
	2	9	18.0	10	20.0	
	3	15	30	14	28.0	
	4	5	10	2	4.0	

† Fisher's Exact Test

In the histological assessments, we found differences in inflammatory cells, with a higher number in those who chewed coca leaves. Differences between the two groups were also found in the stratum spinosum, with more acanthosis, clear cell and eosinophils. In addition, in the lamina propria a statistically significant higher number of blood vessels were found in the group of those who chewed coca leaves (Table 6). The soft tissue biopsies were taken after tooth removal to facilitates wound closure and healing.

Discussion

The coca leaf is considered sacred, possessing enormous ritual and religious significance, and it is present in all major ceremonies: offerings to Mother Earth; offerings at sacred sites; offerings made by walkers at cairns (altars or shrines placed at certain crossroads); the first cutting of an infant's hair as part of indigenous baptism; burial practices; marriage proposals; wedding ceremonies; the blessing of a new house; etc. Within the social sphere, it brings people together and forms an indispensable part of collective labor intended to benefit the community as a whole (Martin, 1970).

From a medical perspective, it is useful in the treatment of symptoms of altitude sickness and acts as a local anesthetic. It can be employed to relieve toothache, and as a poultice for alleviating the pain produced by burns, wounds and extensive grazes. It is also used to treat gastrointestinal complaints, stomachache, diarrhea, indigestion and colic (Biondich and Joslin, 2016).

The chewing of coca leaves was practiced in Peru in ancient times, possible before the Incas. Nevertheless, in the opinion of chroniclers of the conquest of Peru by the Spaniards, the cultivation and use of coca was very restricted at that time, so that chewing was a privilege of the Inca aristocracy, who consumed coca during official and religious ceremonies (Zapata-Ortiz, 1970).

This work is important due to the high prevalence of coca leaf chewers in the high Andean regions of Peru. It has been estimated that in Peru about 8,500,000 kg of coca leaves are consumed per year, but taking into consideration that the control of this plant is very difficult due to the fact that it grows in inter-Andes valleys, and that the means of communication are difficult, the real consumption of leaves probably exceeds the indicated amount (Zapata-Ortiz, 1970).

The volunteers chewed raw and unprocessed coca leaves several times a day is an exclusively Andean practice. The nearly universal method of its use involves folding of several plants' leaves into a wad placed between the teeth and the inside of the cheek in the form of a 'quid'. The leave's cocaine content gradually seeps from the quid into the oral cavity's saliva, numbing the oral mucosa by its local anesthetic property. After about an hour, the quid is expelled although occasionally it may be swallowed.

In modern Peruvian Indians, the age at which coca chewing begins typically ranges from 15-24 years, but as people get older, they tend to adopt the habit (Indriati and Buikstra, 2001). In our study, the coca chewing starting age was 17.8 ± 3.7 years.

Cocaine is the most studied and discussed alkaloid in the scientific literature. The most widely cultivated variety has been found to contain approximately 0.6% cocaine in its dried leaves. However, there are a number of other biologically active alkaloids that have been studied. The four cultivated Erythroxylum varieties contain eighteen alkaloids, belonging to the tropanes, pyrrolidines, and pyridines (Biondich and Joslin, 2016).

Table 6. Histopathologic features

HISTOPATHOLOGIC FEATURES*		COCA CHEWER (N=10)	NON COCA CHEWER (N=10)	P VALUE†
Surface Layer	Hyperkeratosis	9	5	0.141
	Inflammatory Cells	**10**	**4**	**0.011**
Spinous Layer	Acanthosis	9	1	**<0.001**
	Clear Cell + Eosinophils	10	0	**<0.001**
	Dyskeratoticcells	0	9	**<0.001**
Epithelialnails	Wavy	0	6	**0.011**
	Elongated + Widened	8	1	**0.005**
Lamina Propria	Inflammatory Cells	8	3	0.070
	Blood Vessels	10	2	**0.001**

* The values indicate the presence of the condition
† Chi-square test and fisher's exact test

An extensive review details the previously studied biological activity of several of the alkaloids found in coca. Compounds reviewed include cinnamoylcocaine benzoylecgonine, methylecgonine, pseudotropine, benzoyltropine, tropacocaine, α- and β-truxilline, hygrine, and cuscohygrine. All compounds were found to be considerably less toxic than cocaine with a lack of the euphoric effects that cocaine is known to have (Jenkins *et al.,* 1996).

Previous studies (Bhat *et al*., 2018; Giovannoni *et al*., 2018) that evaluated the effect of smokeless tobacco and/or chewing tobacco showed that the tobacco itself jeopardize the periodontal status condition compared with no tobacco users (smoking and chewing). Our data presented a similar trend for the oral cavity effect but the coca chewing effect differed from tobacco users. Although the present study did not compare coca chewing versus tobacco chewing, it could be speculated that the anti-inflammatory properties of coca leafed were responsible for such achievement. Previous studies have suggested that chewing tobacco affected locally the area more than the whole cavity (Pandey *et al*., 2016). Taken together, it is suggested that that during chewing process, an alkaline substance from the coca remains in the entire mouth and therefore could impact in the whole periodontal tissues in the same intensity.

Previous research has suggested that coca chewing induces xerostomia, thus causing cervical-root caries on the molar area where the coca quid is typically positioned during chewing. Coca chewing also suppresses salivary glandular activity, decreasing the secretion of saliva and slowing salivary flow, a condition termed xerostomia (dryness of the mouth, caused by the halting of normal salivary release (Indriati and Buikstra, 2001). These results are in concordance with our study where we found that 11 coca leaf chewers reported mouth dryness in comparison with none of the non-chewers.

In one observational study 68.4 % of 150 coca leaf chewers showed in the histologic study yielded hyperparakeratosis and a notable intracellular edema in the spinal cell layer and the surface layer, without any inflammatory signs in the lamina propia (Borghelli *et al*., 1975). In our study, we found 90% coca leaf chewers with hyperparakeratosis and 80% inflammatory cells in the lamina propia.

Conclusion

Chewing coca leaf produce bitterness, numbness and mouth dryness, and clinical attachment loss. Histologically, higher number of inflammatory cells in the stratum spinosum, with more acanthosis, clear cell, and higher number of blood vessels. The most remarkable feature in patients who chew coca leaves, with these histological characteristics, is reflect an increase in the keratinization of the posterior areas, since chewing is generated in these places. Further prospective studies must be conducted to evaluate the impact of this cultural habit on periodontal status, in both healthy and diseased conditions.

Conflict of Interest Statement

The declare that there are no conflicts of interests for any author in the present paper.

References

Biondich A and Joslin J. Coca: The history and medical significance of an ancient Andean tradition. *Emergency Medicine International* 2016; **2016**:1-5.

Bhat M, Do L and Roberts-Thomson K. Risk indicators for prevalence, extent and severity of periodontitis among rural Indian population aged 35-54 years. *International Journal of Dental Hygiene* 2018; **16**:492-502.

Bolton R. Andean Coca Chewing: A metabolic perspective. *Journal of the American Anthropological Association* 1976; **78**:630-634.

Borghelli R, Stirparo M, Andrade J, Barros R, Centofanti M and De Estevez O. Leukoedema in addicts to coca leaves in Humahuaca, Argentina. *Community Dentistry and Oral Epidemiology* 1975; **3**:40-43.

Giovannoni M, Valdivia-Gandur I, Lozano de Luaces V, Varela H, Balasubbaiah Y and Chimenos-Küstner E. Betel and tobacco chewing habit and its relation to risk factors for periodontal disease. *Oral Dis*eases 2018; **24**:829-839.

Haber J, Wattles J, Crowley M, Mandell R, Joshipura K and Kent R. Evidence for cigarette smoking as a major risk factor for periodontitis. *Journal of Periodontology* 1993; **64**:16-23.

Indriati E and Buikstra J. Coca chewing in prehistoric coastal Peru: Dental evidence. *American Journal of Physical Anthropology* 2001; **114**:242-257.

Jenkins AJ, Llosa T, Montoya I and Cone EJ. Identification and quantitation of alkaloids in coca tea. *Forensic Science International* 1996; 77:179-189.

Kavitha P, Supriya M, and Pradeep S. Smokeless tobacco use as a risk factor for periodontal disease. *Frontiers in Public Health* 2014; **2**:1-4.

Leite F, Nascimento G, Scheutz F and López R. Effect of smoking on periodontitis: A systematic review and meta-regression. *American Journal of Preventive Medicine* 2018; **54**:831-841.

Lesan S, Nosratzehi T, Ousia M, Arbabikalati F and Pourmardan E. The correlation between the Frequency of oral lesions and the amount of smokeless tobacco usage in patients referred to oral medicine department of Zahedan dental school. *Journal of Dentistry* 2014; **15**:81-85.

Löe H. The Gingival index, the plaque index and the retention index systems. *Journal of Periodontology* 1967; **38**: 610-616.

Martin R. The Role of Coca in the History, religion, and medicine of South American Indians. *The New York Botanical Garden* 1970; **24**:422-438.

Miller P. A classification of marginal tissue recession. *The International Journal of Periodontics & Restorative Dentistry* 1985; **5**:8-13.

Page R and Beck J. Risk assessment for periodontal diseases. *International Dental Journal* 1997; **47**:61-87.

Pandey A, Desai A, Ostwal V, *et al.* Outcome of operable oral cavity cancer and impact of maintenance metronomic chemotherapy: A retrospective study from rural India. *South Asian Journal of Cancer* 2016; **5:**52-55.

Preber H and Bergström J. Effect of cigarette smoking on periodontal healing following surgical therapy. *Journal of Clinical Periodontology* 1990; **17**:324-328.

Ramfjord S. The periodontal disease index (PDI). *Journal of Periodontology* 1967; **38**:602-610.

Rivera M, Aufderheide A, Cartmell L, Torres C, and Langsjoen O. Antiquity of coca-leaf chewing in the south central andes: A 3,000 Year archaeological record of coca-leaf chewing from Northern Chile. *Journal of Psychoactive Drugs* 2005; **37**:455-458.

Silness J and Löe H. Periodontal disease in pregnancy II. Correlation between oral hygiene and periodontal condition. *Acta Odontologica Scandinavica* 1964; **22**:121-135.

Stolberg V. The use of coca: Prehistory, history, and ethnography. *Journal of Ethnicity in Substance Abuse* 2011; **10**:126-146.

Thomson W, Poulton R, Broadbent J, et al. Cannabis smoking and periodontal disease among young adults. *Journal of the American Medical Association* 2008; **299**:525-531.

Von Elm E, Altman D, Egger M, *et al.* The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Journal of Clinical Epidemiology* 2008; **61**:344-349.

Weintraub J and Burt B. Periodontal effects and dental caries associated with smokeless tobacco use. *Public Health Reports* 1987; **102**:30-35.

Zapata-Ortiz V. The chewing of coca leaves in Peru. *International Journal of Addictions* 1970; **5**:287-294.