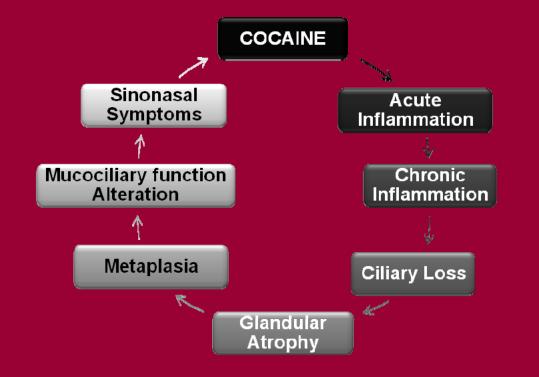


## **ABSTRACT**

Objectives: To analyze the structural changes on the nasa mucosa and the sinonasal symptoms associated with the time of exposure to cocaine. **Methods:** Over the period of two years (January 2006-January 2008), 17 cases of patients with history of cocaine-use were studied at the Hospital Español de México The sinonasal symptoms were asked through a self-applied questionnaire: SNOT-20. The saccharin test was used to evaluate the mucociliary function and nasal mucosa biopsy was taken on five patients. The results were analyzed using the Pearson's correlation coefficient. Results: 17 cases studied. 12 men, 5 women. Median age 30 years old, (13-57 years old) The time of cocaine-use ranged between 6 months and 18 years (median 3 years). Symptoms were referred as mild or some patients referred some items as severe to intolerable. The median of SNOT-20 scores was 0.75. The quality of life was the least affected. The median for the mucociliary test was 11 minutes. The correlation for mucociliary clearance to symptomatology was r=0.53, p<0.05, the correlation for time of exposure to symptoms was r=0.29 and to mucociliary clearance was r=0.84, both statistically significant (p<0.05). The constant histopathologic changes were epidermoid metaplasia, gland atrophy and chronic inflammation Conclusion: There is a statistically significant correlation between time of exposure to cocaine and the progression of nasal mucosa damage, as seen with the mucociliary function the symptoms and histopathologic changes.



EFFECTS OF COCAINE OVER THE NASAL MUCOSA

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# "EFFECTS OF COCAINE OVER THE NASAL MUCOSA"

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#### INTRODUCTION

Cocaine is a central nervous system stimulator, a vasoconstrictor and topical anesthetic. It is derived from the coca plant Erythroxylum. Its use goes back as far as 3000 B.C. in South America.

The most common form of use is the cocaine hydrochloride, an odorless crystalline white powder with a bitter taste that causes numbness. The route of administration is by inhaling it, to be absorbed through the nasal

The mechanism of action is through inhibition of the reuptake of dopamine, serotonine, norepinephrine and epinephrine. It blocks sodium channels producing anesthesia and diminishes the frequency and harmony of ciliary

Inhaling cocaine can cause sinonasal complications at a rate of 4.8%. (3,6) Street cocaine is usually impure; it can be mixed with a variety of ingredients such as manitol, lactose, dextrose, inositol, quinidine amphetamines and anesthetics like lidocaine and procaine. The presence of these substances can cause additional symptomatology.

Pathogenesis of the nasal destruction is the result of combining chemical irritation from the adulterants, ischemic necrosis from the intense small vessel vasoconstriction and the direct trauma, self-inflicted or from forced sniffing.

#### **HYPOTHESIS**

Cocaine produces damage to the nasal mucosa due to chemical irritation ischemic necrosis from vasoconstriction and direct trauma.

The longer the time of exposure, the larger the structural damage, function disturbance and increased sinonasal symptomatology.

# **OBJECTIVE**

To analyze the structural changes on the nasal mucosa, the mucociliary function disturbances and the symptomatology associated to the time of exposure to cocaine.

## METHODS AND MATERIALS

17 cases with history of cocaine-use where analyzed during the period of January 2006 – January 2008 at the Hospital Español de México in Mexico

Sinonasal symptoms where inquired through the validated, self-applied questionnaire of SNOT-20 (20-item Sino-Nasal Outcome Test),(24) which explores the degree of symptomatology and its impact on the quality of life. It contains 20 items qualified in intensity from 0 to 5 by the patient. The final score is the average of all item scores.

To evaluate the mucociliary function, the saccharin test described by Anderson et al,(23) was used: approximately 1mm<sup>2</sup> of saccharin particles are placed over the nasal floor, 1cm away from the anterior border of the inferior turbinate. The time in seconds at which the patient senses a sweet taste is then recorded.

Structural damage was evaluated through inferior turbinate tissue biopsy included in 10% formol and tainted with Hematoxilin and Eosin stain for histopathologic study.

All saccharin tests and biopsies were performed by the same examiner and all the biopsies processed and reviewed by the same Pathologist.

The results were analyzed using the Pearson's correlation coefficient, which measures the lineal relation between two quantitative variables (if the variation of one influences the value of the other).

#### **RESULTS**

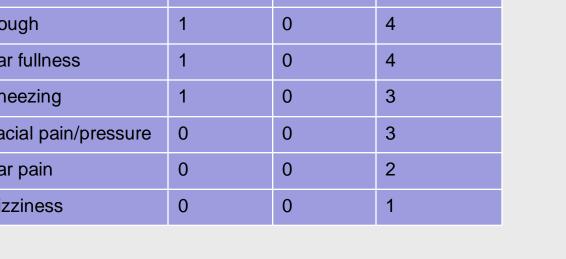
17 cases were reviewed, out of which 12 (70.5%) were men and 5 (29.5%) were women. The age range was 13 to 57 years old (median of 30 years old). The time of consumption varied between 6 months and 18 years (median of 3 years). The average sinonasal symptomatology was mild to moderate, with a median of SNOT-20 score of 0.75. corresponding to absence of or tolerable symptoms (minimum of 0.15 and maximum of 2.65). Quality of life was the least affected. The most frequent symptoms were runny nose, thick nasal discharge and postnasal discharge. The most intense symptoms were the need to blow the nose, followed by thick nasal discharge, cough and ear fullness. All of them consistent with an altered mucociliary clearance. (Table 1a) Regarding quality of life, the most frequent symptom was fatigue and the most intense symptom was sadness followed by fatigue, difficulty to fall asleep, waking up tired and feeling frustrated/restless/irritable. (Table 1b)

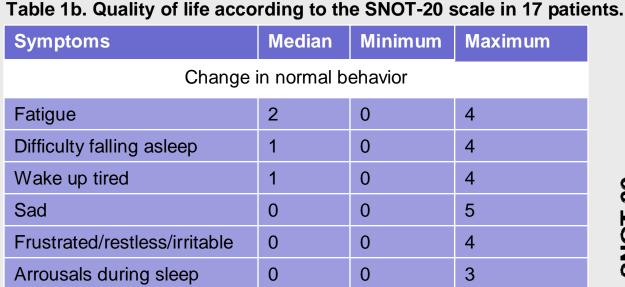
The median time of saccharin test was 11 minutes (range: 1 to >20minutes) By correlating mucociliary function with symptomatology, an r=0.53, p<0.05 was found. (Chart 1) By correlating the time of consumption with these two progression indicators, an r=0.29 was found for the association with symptomatology and an r=0.84 for mucociliary function, both statistically significant with a p<0.05 (Charts 2, 3)

Biopsy was performed only on five patients: constant findings were epidermoid metaplasia, glandular atrophy and chronic inflammation. (Figure 1)

Table 1a. Sinonasal symptoms according to the SNOT-20 scale in 17 patients.

Symptoms	Median	Minimum	Maximum
Clinical Data			
Thick nasal discharge	2	0	4
Runny nose	2	0	3
Postnasal discharge	2	0	3
Need to blow nose	1	0	5
Cough	1	0	4
Ear fullness	1	0	4
Sneezing	1	0	3
Facial pain/pressure	0	0	3
Ear pain	0	0	2
Dizziness	0	0	1



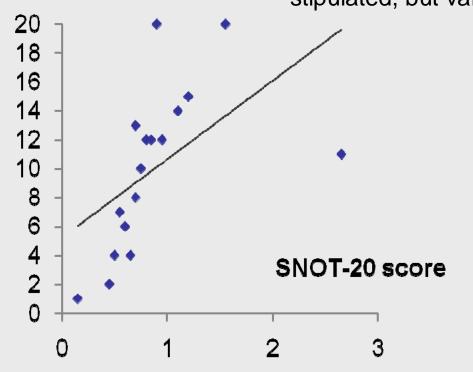


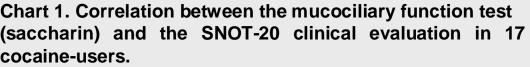
ack of good night's sleep

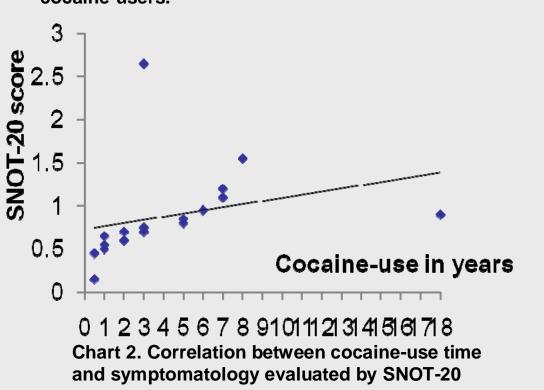
Reduced productivity

Reduced concentration

Embarassed







# DISCUSSION

According to the World Health Organization (WHO), there were 13,300,000 cocaine-users worldwide by the year 2000. It is the most demanded drug in America and the 2<sup>nd</sup> most common drug. In Mexico, 1.44% of the urban population consumes it regularly. It is more frequent among men (4:1) between ages 18 and 34.(26) In Mexico, the average age to begin using is 14. The results of this study correspond to the world's tendencies for gender and age.

Cocaine-use has a great impact in Otorhinolaryngology, where most patients are first seen. They represent a hostile surgical environment with major bleedings and complications. (43) It constitutes a differential diagnosis for nasal cavity damaging pathology and resistance to medical treatment.

Cocaine-users present nasal mucosa and mucociliary function disturbances due to the vasoconstrictive and irritative effect of cocaine: ultrastructurally with partial or total loss of ciliae and disruption between the epithelium and basal membrane, and absence of ciliary and secretory cells. Normal tissue is replaced by fibrous tissue that causes loss of normal function. This translates into sinonasal symptomatology. Based on this data, it is not possible to determine when these alterations begin. Nevertheless, we can infer that they appear as early as after 6 months of use.

The saccharin clearance time test described by Anderson et al. in 1974<sup>(23)</sup> is simple, non-invasive, inexpensive and reproducible. The normal values have not been standardized yet, but average parameters are 4-8 minutes in healthy controls, 11 minutes at sea level and 13 minutes according to a meta-analysis. The cut limit has not been stipulated, but values between 15-30 minutes are accepted. (30,31,32,34,35)

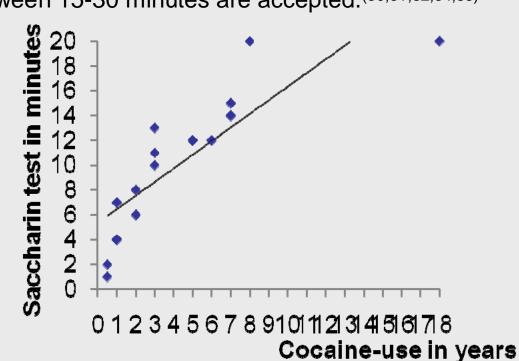


Chart 3. Correlation between cocaine-use time and mucociliary function measured by saccharin test.

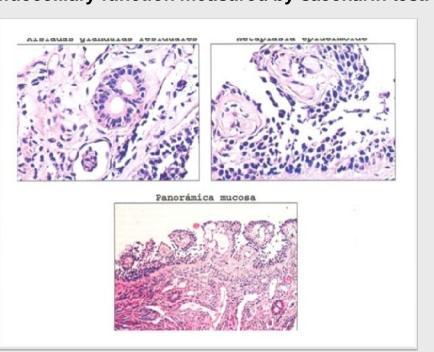


Figure 1. Male, 13yo, 6mo of cocaine-use. SNOT-20 0.15, saccharin test 1min. Biopsy: epidermoid metaplasia, few ciliary cells and mucous glands, atrophy and chronic inflammation.

### DISCUSSION

There is information available on saccharin clearance in healthy subjects and for other pathologies, not for cocaine-use. The degree of damage on the histopathology is consistent with the epithelial atrophy and the decrease on mucous glands. These results validate the clinical use of the saccharin test for cocaine-users assessment. In this study, symptoms were inquired with the SNOT-20 questionnaire, which is a validated and specific measure of quality of life and illness status for patients with sinonasal disease, (24) there is not a specific instrument for cocaine, but the SNOT-20 can be routinely used in clinical practice to assess the patient on his first visit and measure his response to treatment. (27)

The symptoms found on this study are consistent with disturbed mucociliary function, albeit the presence of symptomatology caused by adulterants. (42)

#### CONCLUSIONS

This study represents the first available information in the literature regarding progression of changes on the nasal mucosa due to cocaine use indicating a relation between time of consumption, histopathologic changes, function disturbance and symptomatology.

This information is useful to detect high risk patients at surgery and to understand failures to medical/surgical treatment.

There is a statistically significant correlation between the time of cocaine use and the damage progression as observed through the mucociliary function, symptomatology and histopathologic changes.

There is a statistically significant correlation between the progression indicators (histologic damage, function and symptoms).

Pathologic changes are present as early as after 6 months of use.

Effects of cocaine over the nasal mucosa: "Structural irreversible changes that affect the normal function, and which could cause complications even without major symptoms".

"Every sinonasal inflammatory condition of the upper respiratory tract that persists or remains refractory to treatment could be the first manifestation of a potentially lethal drug addiction".

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