Oral health in patients with cystic fibrosis

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The oral health in patients with cystic fibrosis (CF) is not well studied. **Aim:** Our aim was to describe the frequency of dental problems and to perform the description of plaque index and gingival index in patients with CF. **Methods:** We performed a descriptive study about oral health enrolling 94 patients with CF. **Results:** The CF diagnosis was done considering the sweat test with chloride values ≥ 60 mmol/L. The permanent dentition was predominant in 57/94 (60.64%) patients with CF – 28/57 (49.12%) caries, 57/57 (100%) filled teeth and 1/57 (1.75%) missing tooth. Deciduous teeth occurred in 37/94 (39.36%) patients with CF – 22/37 (59.46%) carious, 29/37 (78.38%) exfoliated teeth, 20/37 (54.05%) filled teeth. Also, the plaque index and gingival index had scored less than one in many cases (≥ 50% of the cases). **Conclusions:** Patients with CF showed oral health problems with prevalence comparable to that of the normal population and low values in the plaque index and gingival index.

**Keywords:** Cystic fibrosis. Dental caries. Dental plaque index. Periodontal index. Oral health.
Introduction

A high prevalence of enamel defects is seen in cystic fibrosis (CF) (OMIM: #219700), and it is associated with the disease severity (metabolic and nutritional disorders) and its chronic therapy$^{1,2}$. Also, patients with CF have higher prevalence of dental calculus, probably due to the high saliva calcium and phosphate associated with the disease, contributing to tartar formation$^3$. However, caries occurs at lower to equal rates in patients with CF than healthy controls subjects$^{4,5}$. Long-term use of antibiotics and pancreatic enzymes could protect the patients against caries. Finally, the presence of enamel defects can be classified as opacity (qualitative defect: white or discolored enamel with a smooth surface and normal thickness) and hypoplasia (quantitative defect: pits or rows of pits, grooves, partial or complete absence of enamel) and should be studied in patients with CF$^{2,6}$. In this context, our primary objective (outcome) was investigating the oral health from patients with CF and the secondary objective (outcome) was verify the values of plaque index and gingival index.

Materials and methods

A descriptive study was carried out on 94 patients with CF (Chloride ≥ 60 mmol/L) from University of Campinas. The sweat test is the gold standard for the CF diagnosis. The interpretation of the sweat test should be concomitant to the clinical context, and when possible, molecular analysis of the CFTR gene. For the CF diagnosis it is necessary to perform at least two sweat tests with a chloride concentration ≥ 60 mmol/L. When the value is < 30 mmol/L, the CF diagnosis is considered unlikely. Concentrations of chloride in sweat with values between ≥ 30 and < 60 mmol/L are considered doubtful and should be repeated$^{7,8}$.

Dental plaque accumulation, caries and dental enamel defects were examined to determine the oral health in patients with CF. Also, a baseline score of the oral hygiene was done using the plaque index of Silness and Loe$^9$ (1964) and the gingival health using the gingival index of Silness and Loe (1964).

Plaque index was assigned as follow: 0- no plaque; 1- a film of plaque adhering to the free gingival margin and adjacent area of the tooth. The plaque may be seen in situ only after application of disclosing solution or by using the probe on the tooth surface; 2- moderate accumulation of soft deposits within the gingival pocket, or the tooth and gingival margin which can be seen with the naked eye; 3- abundance of soft matter within the gingival pocket and/or on the tooth and gingival margin.

Gingival index was assigned as follow: 0- normal gingiva; 1- mild inflammation – slight change in color and slight edema but no bleeding on probing; 2- moderate inflammation – redness, edema and glazing, bleeding on probing; 3- severe inflammation – marked redness and edema, ulceration with tendency to spontaneous bleeding$^{10}$.

Use of dornase alfa (recombinant human deoxyribonuclease I) and antibiotics was obtained from patients’ healthcare records. Chronic use of antibiotics was defined as the use of antibiotics for at least two years in last five years.

The study was approved by Ethics Committee of the University of Campinas (#157/2010).
Results

In our sample, we included 94 patients with CF with mean age of 12.74 years, and 45/94 (47.87%) were male.

The permanent teeth dentition was more frequent in 57/94 (60.64%) patients: 28/57 (49.12%, mean of 0.50 lesions/patient) had caries, 57/57 filled teeth (100%, mean of 1 tooth/patient) and only 1/57 patient (1.75%) had a missing tooth. Deciduous teeth occurred in 37/94 (39.36%) patients: 22/37 (59.46%, mean of 0.59/patient) had carious, 29/37 (78.38%, mean of 0.78/patient) had exfoliated teeth and 20/37 (54.05%, mean of 0.54/patient) had filled teeth. In our casuistic, we observed few (36.57%) defects in the dental enamel. Finally, regarding the oral health in patients with CF, it was observed a higher percentage of caries in the permanent dentition, while the defects of the enamel were more prevalent in the primary dentition.

Plaque index and gingival index are shown in Table 1, and both indexes had a scored less than one in many cases (≥ 50% of the cases). Also, the drugs used were set in the same table.

Discussion

We need to treat the patients with CF; taking care of their oral health equates taking care of their other problems related to CF disease11. In this context, we performed the first study regarding the oral health in patients with CF from Brazil.

While children with CF may be at lower risk for dental caries, adolescents with CF may not be at lower caries than those without CF12-17. This fact can be associated with the use of some antibiotics, which targets Pseudomonas aeruginosa, and do not affect the Streptococcus mutans. Although there are no studies about this issue, one hypothe-
esis is that although the antibiotic does not affect *S. mutans*, the continuous use this medicament alters the oral microbiome and consecutively, the components from oral cavity\(^\text{18}\). Therefore, adolescents with CF would lose the benefits of caries protection afforded in childhood\(^\text{19}\).

Moreover, in a study to identify the relationship between the number of caries and the *S. mutans* and lactobacilli, a lower amount of caries occurred in p.Phe508del homozygotes when compared to heterozygous patients\(^\text{20}\). Also, previously, a study compared patients with CF and healthy control subjects and no difference was observed regarding the number of caries\(^\text{21}\). In this context, the Cystic fibrosis transmembrane conductance regulator (CFTR) genotype should be considered to evaluate the oral health in patients with CF because the pathogenic variants in *CFTR* gene can alter the components from oral cavity, and consecutively, the prevalence of some bacteria. Also, severe CFTR genotypes are a risk group to use wide spectrum and aggressive antibiotic therapy causing alteration in the human microbiome, including the oral cavity microbiome.

The development of caries is a complex process related to environmental and hereditary factors. The low prevalence of caries in patients with CF, observed in some studies, can be attributed to several factors. Maybe, the effects of pH by consuming a diet with a high content of dairy products protect the teeth from deterioration\(^\text{1-3,19}\). Also, the reduced amount of caries in CF patients could be related to a higher pH and storage capacity of saliva\(^\text{22}\). In this way, the incorporation of salivary calcium and phosphate into the enamel may be a post-eruption maturation process that gives the tooth greater resistance to demineralization. The CFTR protein is expressed in the salivary glands, but its effects on salivary gland and oral health, including caries, are inconsistent.

The results regarding caries are controversial and in literature the following information can be identified: (i) no association between salivary flow rate or buffering capacity and caries prevalence; (ii) negative association between salivary pH and caries prevalence, but this association was no longer significant after adjusting for age; (iii) no significant interaction between salivary flow rate and buffering capacity or between antibiotic use and the salivary factors. This issue should be studied at CF disease, because at CF we had ionic alterations at saliva and in salivary glands functions, causing an abnormal ionic environmental at oral cavity. Also, we had the chronic use of antibiotic therapy promoting a “chronic” adaptation from oral cavity microbiome regarding the CF treatment.

In this context, as previously discussed, the patients with CF make use of antibiotics due to chronic lung infection and this fact could reduce the prevalence of caries, since it alters the oral microbiome\(^\text{15,16}\). Azithromycin is often prescribed and it affects gram-positive bacteria. Also, it penetrates dental biofilm, with good absorption in periodontal tissue, and can be retained in the periodontal pocket for up to 14 days\(^\text{23}\). Moreover, patients with CF and their parents tend to be motivated to health care and therefore, in general, show adherence to dental treatment. In addition, the majority of patients with CF use pancreatic enzyme replacement, that reduce the incidence of caries\(^\text{24}\), although our study was not comparative we observed a low frequency of caries lesions.
In addition, changes in salivary pH, oxidation-reduction reactions or continuous use of antibiotics may cause imbalance in the oral microbiome with increase of pathogenic or potentially pathogenic bacteria, triggering diseases that may be a non-serious condition such as gingivitis or caries, or being severe and give rise to infections\textsuperscript{25,26}.

In CF, it is possible that the \textit{CFTR} gene mutations that causes the disease could be responsible for the high incidence of enamel defects\textsuperscript{27}. Molecular studies have shown that the \textit{CFTR} gene is expressed in developing teeth and other mineralized tissues. The \textit{CFTR} gene mutations cause an alteration in the pH during enamel development, which results in a lack of calcium influx during enamel maturation, hypomineralization, and alteration of the normal crystal growth and of the protein processing functions necessary for optimal enamel formation\textsuperscript{28,29}.

Abnormal enamel mineralization, ion concentrations and molecular evidence of \textit{CFTR} mRNA expression by odontogenic cells strongly suggest that \textit{CFTR} plays an important role in enamel formation\textsuperscript{2,29}. Although our study demonstrated a low incidence of enamel defects and opacities, the absence of a group of healthy subjects (control) prevents a comparison with the general population without CF.

Enamel and dentin have chemical components that participate in ion exchanges and demineralization and remineralization processes\textsuperscript{30}. Since \textit{CFTR} is present in teeth and CF is basically characterized by ion transport defect and ion channels are related to the biological functions of dental development, perhaps this explains a considerable frequency of tooth enamel defects in our sample.

Finally, Azevedo et al. (2006) evaluated patients with CF and showed that more than 90% of subjects had at least one enamel defect (demarcated opacities, diffuse opacities and enamel hypoplasia)\textsuperscript{31}. The previous prevalence was greater than the observed in our data sample (~40%).

In conclusion, patients with CF showed oral health problems with prevalence comparable to that of the normal population. Also, dental plaque accumulation, caries and dental enamel defects were examined and presented problems similar to healthy control subjects from other studies. In addition, plaque index and gingival index had low values. Future studies should investigate cariogenic bacteria levels, salivary conditions, medication use and \textit{CFTR} genotype to give a better conclusion about health condition at oral cavity in patients with CF.

References


