RESEARCH LETTER

Clinical evaluation of dental hard tissues in an adult population with cystic fibrosis

Tamara Pawlaczyk-Kamieńska[1], Maria Borysewicz-Lewicka[1], Renata Śniatała[1], Halina Batura-Gabryel[2]

1 Department of Pediatric Dentistry, Poznan University of Medical Sciences, Poznań, Poland
2 Department of Pulmonology, Allergology and Respiratory Oncology, Poznan University of Medical Sciences, Poznań, Poland

Introduction In recent decades, mainly due to multidisciplinary healthcare, life expectancy of patients with cystic fibrosis (CF) has increased,[1] and nowadays new aspects of medical care, including dental care, ought to be considered. Dental issues do not seem to be receiving sufficient attention from multidisciplinary CF teams, whereas research shows that among patients with CF, compared with healthy controls, an equal or higher prevalence of developmental enamel defects in permanent dentition is observed and the defects are more severe.[2] Not only does it pose an aesthetic problem but it may also increase caries susceptibility.

On the one hand, dental enamel is a unique body tissue because it is the hardest and most mineralized tissue, which is exposed to external influences, such as food and air. On the other hand, molecular identification of enzyme proteins associated with transepithelial ion transport in enamel formation (amelogenesis) is similar to that described in other organs. The biology of the enamel is a part of the biology of an integrated system and can be affected by the same anomalies.[3-5] Enamel-forming cells (ameloblasts) are highly sensitive, even to relatively minor changes in their microenvironment, such as temperature increases, hypocalcemia, and acidic pH.[4,6] Factors that may interfere can be either local (trauma or infection of a primary predecessor of a permanent tooth) or systemic (systemic pathologies, toxic factors, nutritional disorders; these may affect the process directly or indirectly through complications of an underlying disease or the use of any pharmacotherapy).[3,5] Researchers suggested that the disruption of cystic fibrosis transmembrane conductance regulator (CFTR) may also have a negative impact on enamel phenotype in patients with CF.[3,5,7-10]

The aim of this study was to determine the dental status of adult patients with CF, namely, the prevalence and severity of enamel defects as well as caries incidence.

Patients and methods The ethical principles expressed in the World Medical Association Declaration of Helsinki were followed in this study. The study approval was requested and obtained from the Ethical Committee of the Poznan University of Medical Sciences, Poland (no. 427/16).

The study involved 22 patients 18 years of age or older with a confirmed diagnosis of cystic fibrosis, treated at the Department of Pulmonology, Allergology and Respiratory Oncology of the Poznan University of Medical Sciences, Poznań, Poland. The control group included 22 generally healthy individuals matched for sex and age. The age of patients in each group ranged from 20 to 43 years. Both study groups lived in the same region and, as a result, under the same environmental conditions. After being informed of the aim of the study and its procedure, all individuals gave informed consent to participate in the study.

Dental clinical examinations were carried out by 2 professionals in the same room and under the same lighting conditions, using a dental mirror and dental probe, according to the recommendation for oral epidemiological surveys by the World Health Organization.[11] The examiners were calibrated (enamel defects, $\kappa = 0.85$; dental caries, $\kappa = 0.82$). To assess the presence of enamel defects, teeth surfaces were examined and scored using the modified Developmental Defects of Enamel index.[12] When 2 different defects were found in the same tooth, the more severe was registered. To determine dental caries, the decayed, missing, and filled permanent teeth index (DMFT) was used, where decayed permanent teeth (DT) meant the number of teeth with carious lesions; filled permanent teeth (FT), the presence of dental fillings; and missing

Correspondence to:
Tamara Pawlaczyk-Kamieńska, DDS, PhD, Department of Pediatric Dentistry, Poznan University of Medical Sciences, ul. Bukowska 70, 60-812 Poznań, Poland, phone: +48 61 854 70 53, email: tpawlaczyk@ump.edu.pl
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TABLE 1 Prevalence of enamel defects and dental caries in adult patients with cystic fibrosis and controls

Parameter		Patients with CF (n = 22)	Controls (n = 22)	*P* value
Caries, n (%)		22 (100)	19 (86.36)	0.07
Caries free, n (%)		0 (0)	3 (13.64)	0.07
Enamel defects, n (%)	Total	12 (54.55)	5 (22.73)	0.03
	White/cream colored opacity	3 (13.64)	3 (13.64)	0.98
	Yellow/brown colored opacity	2 (9.09)	2 (9.09)	0.98
	Diffused opacities	4 (18.18)	0 (0)	0.04
	Hypoplasia	3 (13.64)	0 (0)	0.07
Dental caries, median (Q1; Q3)	PT	27 (25; 28)	28 (27; 28)	0.12
	DT	2 (2; 6)	0 (0; 2)	0.01
	MT	1 (0; 3)	0 (0; 1)	0.01
	FT	9 (2; 11)	4 (2; 6)	0.31
	DMFT	14 (9; 18)	5 (4; 10)	0.001

Abbreviations: CF, cystic fibrosis; DMFT, decayed missing filled teeth (index for dental caries); DT, decayed teeth; FT, filled teeth due to caries; MT, missing teeth due to caries; PT, number of present teeth; Q1, first quartile; Q3, third quartile

permanent teeth (MT), missing teeth caused by complications of dental caries.

Statistical analysis Statistical analysis was carried out using the Statistica program, version 12 (StatSoft, Inc., Tulsa, United States). The difference between the test and control groups in relation to the parameters of the DMFT index and its components (DT, MT, FT) was tested using the Mann–Whitney test and the prevalence of enamel defects was tested by the difference test between 2 proportions. The Spearman rank correlation analysis was used to evaluate the relationship between dental status and predicted forced expiratory volume in one second and between dental status and CFTR mutation class. *P* values of less than 0.05 were considered significant.

Results In patients with CF, as compared with the control group, the prevalence of enamel defects was higher ($P = 0.03$) (TABLE 1), the defects were more severe, and more teeth were affected (patients with CF, 7.41%–100%, and healthy individuals, 7.14%–36%). In patients with CF, defects were noted in all types of teeth, and in the control group only in the incisors and first molars.

Caries experience (DMFT) in patients with CF was higher comparing with the controls. Moreover, in patients with CF, higher decayed (DT) and missing (MT) indices were reported. In the control group, the first molars were 66.7% of all teeth extracted, while in patients with CF, the percentage of extracted incisors, premolars, and molars was the same.

In CF adults, there was no statistically significant correlation neither between dental status and predicted forced expiratory volume in one second nor between dental status and CFTR mutation class ($P \geq 0.05$).

Discussion Available publications on the dental status of patients with CF have been concerned mainly with children and adolescents.[2] To the best of our knowledge, ours is the first report on the dental condition in adults with CF. It was difficult to compare our results with other authors' reports because many patient variables were different, for example, age, number of erupted permanent teeth, disease duration, and pharmacotherapy. The above-mentioned publications showed equal or higher prevalence of enamel defects of the permanent dentition in patients with CF compared with healthy individuals.[2] Although our patients differed in age from those in the cited publications, our results confirmed the significantly higher prevalence and increased severity of enamel defects in patients with CF compared with a healthy population.

The published reports are inconsistent with regard to dental caries in adults with CF. They show an equal or lower caries risk in patients with CF in comparison with controls.[2] The results of the present study indicate not only poor dental status (DMFT) in adults with CF but, most of all, medical negligence. With definitely higher caries experience (DT, MT), there was no difference in the treatment levels (FT) between the patients with CF and healthy controls.

Enamel defects only in the incisors and first molars of the control group suggest that these anomalies meet the Molar Incisor Hypomineralization criteria, in which the etiology is multifactorial and related to general factors, such as premature birth, general health problems, and systemic conditions in the first 3 years of life. In patients with CF, theses anomalies were not related to any specific dental group and were equally distributed in all of them, suggesting a continuing insult of the causative factor.

For a long time, the etiology of enamel defects in patients with CF was attributed mainly to the adverse effects of antibiotic therapy and complications of the underlying disease.[2] But laboratory studies carried out in animal models[4,7,8,10] suggest the CFTR disruption in amelogenesis, during which a large number of H^+ protons are formed. Buffering these protons to neutrality is essential for mineral deposition and further enamel formation.[4,5,7-9] The function of CFTR in amelogenesis is poorly understood, but at the present state of knowledge, it is likely to be for controlling the activity of the bicarbonate-chloride (Cl^-/HCO_3^-) exchanger channel in the cell membranes; this regulator thus neutralizes the H^+ protons and provides the optimal pH necessary for the transport of Ca^{2+} ions.[3,4,7-10] The CFTR protein is localized in the apical plasma membrane of epithelial cells, also in the ameloblasts, where it is located on

the apical side in proximity to the growing enamel crystals.[3,8] The elemental analysis and investigation of enamel pH carried out by Sui et al[4] and Bronckers et al[8] showed lower pH, fewer Cl^- ions, and diminished HCO_3^- concentration in the enamel of mice with CF compared with healthy controls. Moreover, Arquitt et al[7] and Bronckers et al[8] confirmed the thesis on the unfavorable effect of low pH on Ca^{2+} transport through the cell membrane. The authors showed a lower calcium level, similar phosphate level, and lower calcium-to-phosphate ratio in the mature enamel of unerupted teeth in mice with CF than present in healthy individuals.

Tooth enamel is a protective layer for other tooth tissues, and abnormalities in its structure and chemical composition arising during development are irreversible. These irregularities significantly affect the physical and chemical properties of the tissue, making it less resistant to damaging factors. Reduced enamel hardness and increased porosity promote penetration of cariogenic bacteria into the tissues and the development of carious lesions. Therefore, it is necessary to implement early dental care and develop an individual long-term prophylaxis and treatment program to prevent complications such as pulpitis and periapical infection—conditions that could be a source of autoinfection for CF patients.

Conclusions Due to the high prevalence of enamel defects in patients with CF, it is necessary to implement early systemic preventive dental care in children. Pediatric dentists should be members of a CF multispecialty team. Poor dental status in adults with CF indicates the lack of proper dental care as well as not meeting prevention needs regarding oral health. It is necessary to develop and implement targeted caries prophylaxis and treatment programs for patients with CF.

ARTICLE INFORMATION

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CONFLICT OF INTEREST None declared.

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