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Oral Health Status in Adults with Cystic Fibrosis – Dental and Microbiological Assessment

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Abstract

Oral health status during cystic fibrosis may have an influence on respiratory system infections in the group of cystic fibrosis (CF) patients. This important clinical problem was taken in research in the Department of Medical Biology, Medical University of Warsaw, in cooperation with Institute of Tuberculosis and Lung Diseases in Warsaw. In this project an oral health status in the group of adult CF patients was examined. The aim of the current study was to report a case of 33-year old woman, treated in the Institute of Tuberculosis and Lung Diseases. The woman was qualified to the dental and microbiological examinations because of the particularly intensified lesions in her oral cavity. Research included a dental history, evaluation of the dentition and a microbiological analysis. The dental study involved an oral hygiene and a previous treatment. During examination of an oral cavity, attention was paid to: enamel and mucosa defects, dental and periodontal condition, decay intensity, dental plaque index and bleeding index. Saliva properties were analysed, using Saliva Check Buffer test. CRT Bacteria test was used to evaluate presence of cariogenic bacteria. What is more, the Cone Beam Computed Tomography was performed. Basing on the research, it was demonstrated that CF may influence reduced saliva secretion and microbiological changes, resulting in a development of intensified dental caries. Reported case may contribute to formulate a dental care program in CF patients.

Key words: *oral health status, cystic fibrosis.*

Introduction

Cystic fibrosis (CF) is a congenital, incurable, multi-system genetic disease. In the Caucasian population, cystic fibrosis is the most common autosomal recessive inherited disease [1,2]. The highest incidence of cystic fibrosis is observed in northern European countries – 1:2500/3500 births in which every 25th person is a carrier of the cystic fibrosis gene [3].

In Poland, the CF group is estimated at around 2,000 patients [4,5]. In contrast, the Polish Cystic Fibrosis Registry only covers 1,600 patients. The survival of patients with CF in Poland is much shorter (median death 22 years) than in other countries. In Western Europe, the median death increases >40 years [3,6]. 1/3 of Polish patients with CF are adults [4]. With the progress of medicine, this group is constantly growing.

Cystic fibrosis is caused by mutations in the CFTR (cystic fibrosis transmembrane conductance regulator) gene located on the long arm of chromosome 7. The mutations lead to disorders in transport of chloride ions and increase in absorption of sodium ions and water in the membranes of epithelial glands of exocrine glands. As a result, the secretion thickens and increases, which causes disorders of the functioning of many organs. Thick secretions and mucous plugs are mainly found in the lungs, pancreas, liver and gastrointestinal tract [4].

Dysfunctions occurring in both respiratory and digestive systems may predispose cystic fibrosis patients to the development of oral diseases, in particular caries and periodontal disease. Dental problems and antibiotic therapy undertaken in the course of cystic fibrosis may affect the incidence of respiratory infections in this group of patients [1,3]. Invasive respiratory tract infections are the main cause of hospitalisation and premature deaths of CF patients [5,6]. In cystic fibrosis, good oral health can have a significant impact on a patient's overall well-being.

Aim of the research

Dental and microbiological assessment of oral health in adults with cystic fibrosis.

Material and methods

Research was carried out at the Department of Medical Biology in cooperation with the Department of Dental Surgery of the Medical University of Warsaw. The study involved 10 adults with cystic fibrosis (7 women and 3 men, average age 30.1±6.52), treated at the Institute of Tuberculosis and Lung Diseases in Warsaw. Patients with particularly severe lesions in the mouth were qualified for the study.

The project involved subject tests, including general and dental history. The subject tests were dental procedures in the oral cavity and microbiological development of clinical samples taken from patients.

Dental examinations and lesions were evaluated in the structure of enamel, changes on the mucosa, the state of teeth and periodontium, the presence of caries. The DMFT (Decayed, Missing, and Filled Permanent Teeth) index was determined. The API oral hygiene index (*Approximal Plaque Index*) indicating the level of dental plaque and the BoP (bleeding on probing) index were determined. The biochemical properties of saliva samples were determined using the Saliva Check Buffer (*Vivadent*) test.

Microbiological tests included the assessment of the presence of cariogenic bacteria *Lactobacillus* spp. and *Streptococcus mutans* in the mouth with the use of the CRT Bacteria test (*Vivadent*). In addition, studies were performed on the occurrence of *Staphylococcus aureus* strains in samples of patients' saliva as a potential respiratory pathogen.

Results

General history

Subjective studies found that patients were chronically taking a number of primary therapy medications. Mucus-reducing preparations such as Pulmozyme® were mainly used in nebulisation. Patients were taking bronchodilators, including Sabumalin®. In patients with diagnosed asthma, Salmex® was additionally used in therapy. Patients were supplemented with enzyme preparations (Kreon 25,000®, Proursan®).

In hormonal disorders i.e. diabetes or hypothyroidism or hyperthyroidism, insulin and/or thyroid hormones have been used. Patients were subjected to constant antimicrobial therapy. Bactericidal antibiotics were used, mainly against Gram-negative bacteria, including Colistin® from the polymyxin group. Subjective tests showed a reduced value of forced expiratory volume in one second (FEV1), on average 57.4% of the value due. Continuous inhalations with 3% sodium chloride were conducted as a support.

Dental history

Information was obtained on regular attendance for follow-up and therapeutic visits to the dentist. The patients performed hygienic activities properly. Most patients brushed their teeth twice a day, using a manual and electric brush alternately, using toothpaste with a high abrasion rate. Five patients (50%) reported subjective discomfort in the mouth. The main causes of discomfort reported by patients were the occurrence of dry mouth, gum and tooth pain, and a feeling of too little saliva. In one case, the patient experienced increased salivation (Table 1).

Table 1. Characteristics of the studied group of patients with cystic fibrosis

Patient No.	Age	Enamel lesions	Other changes	Subjective discomfort
1	57	-	-	dryness sore gums toothache
2	33	hypoplasia hypomineralisa-tion	-	dryness little saliva
3	27	hipoplazja	-	-
4	31	-	bruxism abraded chewing surfaces	-
5	22	hypoplasia hypomineralisa-tion	-	-
6	22	hypoplasia	-	dryness
7	27	-	-	-
8	21	discoloration	-	dryness
9	32	-	gingivitis	large amount of saliva
10	29	hypoplasia	-	-

Dental examination

In the intraoral examination, in 6 patients (60%) changes in the structure of hypoplasia, hypomineralisation and discoloration of enamel were found. No changes in the enamel structure were observed in 4 patients (40%). Additional changes were found in 2 patients, including abraded chewing surfaces (bruxism) and gingivitis (Table 1). The oral mucosa of patients was faded.

The dentition of the patients was assessed. One patient (32 teeth) presented the full dentition. Other patients had shortages, respectively: 31 teeth – 2 patients, 30 – 3, 29 – 1, 25 – 1, 24 – 1 and 21 teeth – 1 patient (Table 2).

In half of the patients (5 patients) ≥50% of dentition was affected with caries, including two people where caries was observed in all

teeth (100%). The above data allowed calculating the caries severity index (DMFT) in the range of 3-27. In one case a very low DMFT index of 3 was observed. The patient had twenty-nine teeth in his mouth, he lost three teeth due to complications of caries. In the remaining four patients, the DMFT index ranged from 9-15. Of 24-31 teeth present in the oral cavity, 37.5%-48.4% of them had cavities, teeth were affected by caries or filled teeth during treatment because of this (Table 2).

Table 2. Dental indicators of oral health of patients with cystic fibrosis

Index name	Index values obtained in patients with cystic fibrosis	Interpretation
DMFT	3-27: 27 – 1 patient (10%) 25 – 1 patient (10%) 21 – 1 patient (10%) 17 – 1 patient (10%) 15 – 2 patients (20%) 12 – 2 patients (20%) 9 – 1 patient (10%) 3 – 1 patients (10%)	significant number of teeth with carious changes
API norm: <39% sufficient condition <25% – optimal hygiene	16-61%: <25% – 1 patient (10%) <39% – 2 patients (20%) >45% – 7 patient (70%)	sufficient or poor oral hygiene, to be improved
BoP norm: <10%	3-68,9%: >10% – 9 patients (90%) within norm – 1 patient (10%)	moderate and high extent of gingivitis
pH norm: 6,8-7,8	5,8-7,8: <6,8 – 5 patients (50%) within norm – 5 patients (50%)	too low, enamel demineralisation possible
Buffer capacity norm: 10-12	2-12: <10 – 7 patients (70%) within norm – 3 patients (30%)	reduced acid neutralisation capacity

The API oral hygiene index revealed the presence of dental plaque in the range of 16% to 61% of interdental spaces examined. An optimal API rate of <25% was obtained for only one patient. A fairly good oral hygiene index <39% was obtained for two patients. Seven patients showed a sufficient and poor level of hygiene (API> 45%), with a recommendation for improved hygiene (Table 2).

According to the BoP index, between 90% and 68.9% of bleeding sites were observed in 90% of patients due to gum probing. Only one patient's BoP result was within the norms and was 3% (Table 2).

Saliva buffer capacity and pH were also assessed in dental tests using the Saliva Check Buffer test. Normal buffer capacity was obtained in three patients. Seven patients had low results, which meant a reduced ability to neutralize acids. 50% of patients had normal pH values in the range of 6.8-7.8. In the second half of the group of patients low pH values compared to normal values (5.8-6.6) were obtained, which reduced the possibility of enamel demineralisation (Table 2).

Microbiological tests of the oral cavity

The conducted microbiological tests with the use of CRT Bacteria tests allowed to determine the level of cariogenic bacteria in samples of stimulated saliva taken from patients. In five patients (50%), very numerous (≥105cfu/ml) granulosa of *Streptococcus mutans* type, acid-forming streptococci involved in the development of caries were grown. The amount of *S. mutans* in saliva from 104 to 105cfu/ml, promotes the deposition of these microorganisms in the plaque and initiates caries. Other patients (50%) were in a group of low risk of developing caries: <105 cfu/ml or no growth in *S. mutans* (Table 3).

the next isolates from patients were *Lactobacillus* bacteria. 4 patients (40%) who were cultured with ≥105 cfu bacteria per ml of saliva were classified as high risk of caries. This type of bacteria is acidophilic and acid-forming, constituting the second important group of pathogens involved in the development of caries. Low levels of these cariogenic bacteria were found in six patients (60%) (Table 3).

Table 3. The level of cariogenic bacteria in the saliva of patients with cystic fibrosis

Caries-causing bacteria	Number of colonies (CFU/ml)	Number of patients	Interpretation of bacterial levels
Streptococcus mutans	≥105	5(50%)	high
	<105	1(10%)	low
	brak wyhodowania	4(40%)	-
Lactobacillus spp.	≥105	4(40%)	high
	<105	6(60%)	low

During microbiological tests, saliva samples were cultured for *Staphylococcus aureus* strains. This species is the most common etiological factor in respiratory tract infections in patients with cystic fibrosis. Very numerous and numerous colonies of *S. aureus* (≥105-104 cfu/ml) were cultured from three patients (30%). Single S. aureus colonies were isolated from four patients (40%). The growth of these bacteria was not determined in three patients (30%) (Table 4).

Table 4. Appearance of Staphylococcus aureus in saliva samples of patients with cystic fibrosis

Cultured Staphylococcus aureus	Number of patients
≥105 – 104 cfu/ml	4 (40%)
Single colonies (102 cfu/ml)	3 (30%)
Lack of growth	3 (30%)

Discussion

The oral health status of cystic fibrosis is a significant clinical problem. Dental disorders, including caries and periodontitis, may deregulate the microbiome of the mouth. Oral conditions, bacterial imbalance and cystic fibrosis persistent antibiotic therapy predispose to the development of invasive, fatal infections in the respiratory and digestive systems. The topic of infection in children with cystic fibrosis is constantly raised in the literature. In contrast, research on the adult patient population, both glo-

bally and in Poland, is much less common. The available literature lacks a comprehensive assessment of the oral condition of a group of adults with CF. In addition, available data often leads to contradictory conclusions [13]. Therefore, the research presented in this paper is a very important report, especially in the aspect of prophylaxis of invasive respiratory tract infections.

Many authors dealing with the subject of cystic fibrosis point to a constantly growing population of patients with cystic fibrosis. According to the results of the Burgel et al study, by 2025 the number of patients may increase by up to 50%. According to estimates, up to 75% will be adults. The research concerned a large group of patients treated in 34 European countries. According to researchers' estimates, in Poland in 2025, nearly 78% of patients will be adults [15]. That is why research conducted in this group of patients is so important. New diagnostic and therapeutic problems are emerging that still pose a challenge to medicine. New CFTR protein mutations are diagnosed, in which the combination of clinical symptoms, including dental ones, is constantly changing.

The results of many Polish and world studies indicate poor oral condition and great importance of dental treatment in the group of patients with cystic fibrosis, both children and adults. Some researchers indicate that CF patients are at risk of developing periodontal and oral mucosa diseases due to frequent upper respiratory tract infections and oral respiration [15]. Similar conclusions are presented by Ferrazzano et al. who estimated a larger number of tartar in CF patients, usually on the surface of the lower front teeth [11].

In the literature, you can also find studies showing good oral health in this group of patients [14]. According to Peker et al., continuous intake of antibiotics may reduce the number of bacteria in the oral cavity, in particular cariogenic ones, i.e. *Streptococcus mutans*. These studies have shown that chronic antibiotic therapy can be an inhibitor of bacterial biofilm development in the oral cavity and thus reduce tooth decay [14].

The presented clinical case of an adult patient with cystic fibrosis confirms the relationship between the state of oral health and the develop-

ment of infection and the general well-being of patients. The patient had dental disorders, high caries, dental plaque and bleeding gums as well as a high percentage of caries. At the same time, the patient was diagnosed with chronic infections of bacterial and fungal aetiology requiring antimicrobial therapy.

Analysing the given clinical case and available literature data, it seems reasonable to undertake further dental and microbiological tests in people with cystic fibrosis. In addition, it seems necessary to compare the results of tests performed in both groups of patients, children and adults. The basis of preventive and therapeutic measures is the development of a long-term dental management plan for CF patients, which can translate into reduction in the percentage of invasive respiratory infections, more effective primary and antimicrobial therapy, higher percentage of successful, uncomplicated infections, lung transplantation and longer patient survival.

Results

Enamel lesions, hypoplasia, discoloration and hypomineralisation were observed in patients. Four patients had particularly advanced lesions. The average bleeding index was 33.28%, which proved a moderate extent of inflammation. Nearly half of the respondents (45.38%) showed a high plaque index. Significant advancement of caries was observed in the majority of patients. The DMFT index was on average 16.2, which accounted for more than half of the teeth affected by carious lesions. Studies have shown a reduced saliva buffer capacity, on average at 6.8 and normal saliva pH values (6.8). A high percentage of caries-forming bacteria of the *Lactobacillus* and *Streptococcus mutans* types. In terms of the number of cariogenic bacteria in saliva, patients were classified in classes 2 and 3 – with a high level of cariogenic bacteria (>105 CFU/ml of saliva). At the same time, patients were diagnosed with chronic infections of bacterial and fungal aetiology requiring antimicrobial therapy.

Summary

The oral health condition is worse or without significant differences compared to the oral cavity of healthy patients, there is a need to continue research with the extension of the research group.

The results of the research are an introduction to the development of a scientific program on the principles of dental management in patients with cystic fibrosis.

The basis of preventive and therapeutic measures is the development of a long-term dental management plan for CF patients, which can translate into a reduction in the percentage of invasive respiratory infections, more effective primary and antimicrobial therapy, a higher percentage of successful, uncomplicated infections, lung transplantation and longer patient survival.

The condition of oral health may affect the survival rate and improve the quality of life of patients with cystic fibrosis. The results of global and Polish scientific research indicate a significant relationship between the state of oral health and oral microbiome in the pathogenesis of invasive respiratory infections of bacterial and fungal aetiology [7-10].

In the light of the above-mentioned studies, the most common oral health disorders in CF patients are: developmental defects, enamel defects and discolouration, reduced salivation, high levels of caries and an increase in oral colonisation with *Streptococcus mutans* streptococci and other cariogenic bacteria [1,11-13]. It seems that the development of these diseases is influenced by CFTR protein dysfunction, regulating the level of mineralisation and enamel pH, as well as the use of long-term antibiotic therapy, mainly from the tetracycline and carbapenem groups [6,9,13-16]. Other oral disorders in this group of patients are periodontal and mucosal diseases, mainly inflammation and an increased amount of tartar, usually found on the surface of the lower front teeth [16-19].

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