Oral health and related factors in a group of children with cystic fibrosis in Istanbul, Turkey

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Abstract

Background: Cystic fibrosis (CF) patients can be considered as high caries risk patients because they frequently consume sugar-rich food between meals and they have a high intake of sugar containing syrups, aerosols, and salivary flow reducing medication. Variable caries prevalences were reported in CF patients in previous studies. There are no studies related to CF and salivary thromboplastic activity, which can be presented as a marker of wound healing and bleeding tendency of oral cavity.

Objective: The aim of this study was to compare oral health status and salivary pH, flow rate, and thromboplastic activity in children with CF and healthy controls.

Materials and Methods: A sample of 35 children with CF (23 girls and 12 boys), and 12 healthy control subjects (6 girls and 6 boys) were selected. Caries experience, oral hygiene, and dental erosion were assessed. Salivary flow rate, pH, thromboplastic activity, and total protein content were determined. Differences between the groups were evaluated using Chi-square test with a significance level set at 0.05.

Results: The differences between children with CF and healthy controls in tooth brushing frequency, use of fluoride tablets, caries experience, dental erosion index, oral hygiene index, salivary flow rate and total protein levels were not statistically significant ($P > 0.05$). Salivary thromboplastic activity of the CF group was significantly lower than the healthy controls ($P < 0.01$).

Conclusion: Large population studies may be necessary to establish the role of salivary thromboplastic activity in children with CF considering our findings related to the decreased salivary thromboplastic activity, which may indicate delayed oral wound healing process.

Key words: Caries, children, cystic fibrosis, saliva, salivary thromboplastic activity

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Introduction

Cystic fibrosis (CF) is the most common lethal autosomal recessive inherited disease in Caucasians with prevalence of 1 in every 2000 live births affecting both sexes equally. It is caused by mutations of the gene situated on the long-arm of the seventh chromosome coding CF Transmembrane Conductance Regulator (CFTCR), which is responsible for the synthesis of cyclic adenosine monophosphate-dependent membrane chloride channel located on the top surface of epithelial cells of exocrine glands. Accumulation of the secretion in the outlet ducts caused by a dysfunction or lack of CFTCR proteins leads to abnormal activity of exocrine glands, especially in the respiratory and alimentary tracts. Fundamentally, the disease is caused by a defective sodium reabsorption and as a consequence all exocrine glands, including the salivary glands, are affected.[1,2]

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Carbohydrates are the main dietary components that supply energy to the body, but at the same time are the major cariogenic agents. CF patients can be considered as high caries risk patients; they frequently consume sugar-rich food between meals and they have a high intake of sugar containing syrups, aerosols, and salivary flow reducing medication. Salivary dysfunction and changes in saliva composition are frequent complications of CF.[1,2]

The increased use of aerosols with mucolytic and expectorant properties, the increased use of specific antibiotics and correct usage of dietary supplements and pancreas enzymes have made it possible for CF patients to survive into their 20s and 30s and some even longer. Unfortunately, the effect of aerosols on teeth is discussed and considered as a potential high caries risk factor.[1,3-5] The acidity of the aerosols in combination with the carrier (lactose or another sugar) could play an important role in the development of caries.

On the other hand, it should be emphasized that, when the resistance to oral cariogenic microorganisms would develop, antibiotics would have an opposite effect and caries would still develop. It is clear that no straight answers can be provided, as few studies are available on oral cariogenic microflora being affected by oral systemic antibiotic taken on a long-term basis. Studies on patients with CF have reported variable caries prevalence.[1,2,6-9]

Thromboplastin, also known as tissue factor or factor III, is an important coagulation factor, which initiates the extrinsic blood coagulation with factor VII. It is not actively found in the blood, but as a component of the cell membranes.[10,11] It has been shown that some body tissues and fluids have thromboplastic activities. This parameter can be presented as a marker of wound healing and bleeding tendency of oral cavity when measured in saliva.[10,12-16] There is no study related to CF and salivary thromboplastic activity in the literature. The aim of this study was to evaluate and to compare caries experience, dental erosion and salivary pH, flow rate and salivary thromboplastic activity as well as the oral hygiene in children with CF and healthy controls.

Materials and Methods

Patients

In this cohort study, a group of 35 children with CF aged between 3 and 12 years (23 girls and 12 boys) were selected and their data were compared to healthy children (6 girls and 6 boys) who are at the same age. Control subjects were chosen from the same street, school or siblings. In this way, socioeconomic and demographic factors were matched. The study protocol was reviewed and approved by the Research Ethics Committee and the parents of the children gave informed consent to participate in this study.

Questionnaire

A questionnaire was used to obtain information about home oral care and other dental aspects of each child's care that may influence their oral health [Table 1].

Clinical procedure

All children were examined clinically under standard illumination by one pediatric dentist. Teeth were scored using type E-probe and a dental mirror. Caries experience was expressed as decayed, missing and filled-teeth (DMF-T). The state of oral hygiene was determined using Silness-Löe plaque index.[17] The surfaces of the teeth (buccal, lingual, mesial, and distal) were given a score from 0 to 3. A modification of the Smith and Knight Tooth Wear Index was used in the assessment of dental erosion.[18]

Saliva collection, salivary pH, salivary flow rate

Unstimulated mixed saliva samples were collected at 08:00–10:00 a.m. after the mouth had been rinsed with distilled water, by spitting into a funnel. Saliva volume and collection time were recorded to calculate salivary flow rate. Saliva samples were analyzed for pH by using a pH paper (pH-Indikatorpapier, Neutralit 5.5-9.0, Merck KGaA, Darmstadt, Germany).

Salivary thromboplastic activity and salivary total protein level

Thromboplastic activities of saliva samples were evaluated according to Quick's one stage method using normal plasma.[19] This was performed by mixing 0.1 ml saliva with 0.1 ml of plasma, with the clotting reaction being started on addition of 0.1 ml of 0.02 M $CaCl_2$. All reagents were brought to the reaction temperature (37°C) before admixture.[19] Total protein content of the saliva samples was determined by the method of Lowry.[20] In alkali medium, proteins are reacted with cupper ions than reduced by pholine reactive (phosphomolibydic-phosphotungstic acid). The absorbance of the blue colored product at 500 nm was evaluated. Bovine serum albumin was used as a standard. Total protein levels were expressed as % mg of saliva.

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) 16 software program (SPSS Inc., Chicago, IL). Results were expressed as mean ± standard deviation. Differences between the groups were evaluated using Chi-square test. $P < 0.05$ was considered as statistically significant.

Results

The mean age of 35 children with CF (23 girls and 12 boys) was 9.09 ± 2.82 years whereas the mean age of 12 healthy controls (6 girls and 6 boys) was 7.45 ± 1.86 years.

Table 1: Questionnaire

Parameters evaluated in the questionnaire	Healthy (n=12), %	CF (n=35), %
Age (year)	7.45±1.86	9.09±2.82
Tooth brushing frequency (twice a day)	45	43
Fluoride tablet usage	36	43
Dental erosion	40	62
Dry mouth sensation	8	10
Burning mouth sensation	2	12
Taste alteration	5	14
Bleeding during brushing	21	23
Difficulty in opening/closing jaw	5	7
Unpleasant taste/bad breath	15	22
Orthodontic need	22	24
Sensitive to hot, cold, sweets	14	16
Sensitive to biting	12	17
Food impaction	13	12
Swelling/lumps in mouth	3	4
Frequent blister, lips, mouth	4	5
Date of last dental visit	19 months	15 months
Do you want to get any education about oral health? (yes)	90	94

Values are given as mean±SD for age and as percent for other parameters. SD=Standard deviation; CF=Cystic fibrosis

Socioeconomic and demographic factors of the groups were matched. No significant differences were found in ages, tooth brushing frequency and the use of fluoride tablets for children with CF and healthy controls ($P > 0.05$). About 43% of the CF and 45% of the healthy controls brushed their teeth twice a day. 43% of the children with CF and 36% of the healthy controls used fluoride tablets. Sixty-two percent of the children with CF ($n = 21$) had dental erosion versus 40% for controls ($n = 12$). Smith and Knight Tooth Wear Index was 0.63 ± 0.49 for children with CF and 0.70 ± 0.47 for healthy controls. Silness-Löe plaque index was 1.43 ± 0.22 for children with CF and 1.44 ± 0.22 for healthy controls. Dental erosion and oral hygiene values were not statistically significant for children CF and healthy controls ($P > 0.05$). DMF-T value was 1.93 ± 2.45 for children with CF and 1.90 ± 1.68 for healthy controls. There were no significant differences in caries experience between children with CF and healthy controls ($P > 0.05$).

Salivary pH was significantly lower in CF group when compared to healthy control group ($P < 0.05$). Total protein level did not significantly change in CF group when compared to control group ($P > 0.05$). Salivary flow rate was decreased in CF group but this was not statistically significant when compared to control group ($P > 0.05$) [Table 2]. As salivary thromboplastic activity has been measured by prothrombin time test, prolonged clot formation time shows decreased thromboplastic activity. Thromboplastic activity of CF group was significantly decreased when compared to the control group ($P < 0.01$) [Table 2].

Table 2: Salivary pH, flow rate, total protein, and thromboplastic activity for children with CF and healthy controls

Salivary parameters	Mean±SD	
	Healthy control (n=12)	CF (n=35)
Saliva pH	7.55±0.61	7.06±0.55*
Saliva total protein (mg)	389.64±164.47	364.19±187.03
Salivary flow rate (ml/min)	0.64±0.39	0.53±0.30
Salivary thromboplastic activity (s)	75.73±36.99	105.25±27.74†

Values are given as mean±SD. *P<0.05. Significantly different from healthy controls; †P<0.01. Significantly different from healthy controls. CF=Cystic fibrosis; SD=Standard deviation

Discussion

Saliva plays an important role in the protection of oral cavity and alterations in either salivary flow rate or protein composition may have dramatic effects on oral health.[21] In this study, caries experience, oral hygiene, salivary flow rate, salivary pH, total protein, and thromboplastic activities of CF patients and healthy individuals were examined.

Aps and Martens[9] have revealed that CF homozygotes had a significantly higher total salivary protein concentration than CF heterozygotes and healthy controls. In the present study, Table 2 shows that total protein level was lower in children with CF (364.19 ± 187.03) than in healthy controls (389.64 ± 164.47), but this was not significantly different. The impression that CF homozygotes and heterozygotes seem to possess an intrinsic salivary compensatory mechanism should be further investigated.

Studies in the 1980s and the beginning of the 1990s claimed that CF patients with the age 7 years had significantly less caries experience than healthy controls. This was attributed to their higher salivary buffering capacity, higher salivary calcium and their frequent use of antibiotics.[4,5,22,23]

A more recent age matched control study (15.3 years) reported no significant differences in caries experience between CF homozygotes and healthy controls.[24] In this study, caries experience results were consistent with the previous studies. Narang *et al.*[8] have suggested that long-term antibiotic and pancreatic enzyme therapy may confer some protection against the development and progression of dental caries and may be major cause of the lower levels of dental caries observed in patients with CF. In the present study, CF group have lower caries prevalence when compared to the healthy group, but the difference was not statistically significant. The reason of this finding can be attributed to the good oral hygiene although the children consumed sugar-rich food, drugs, etc.

Peker *et al.*[25] also found lower DMF-T scores compared with control group (4.6 ± 4.0 in CF and 7.7 ± 2.7 in control).

They have revealed no significant differences in the caries experience. Salivary flow rate was decreased in CF group but this was not statistically significant when compared to control group. Peker *et al*.[25] also found no significant differences in salivary flow rate between children with asthma and controls.

Blomfield *et al*.[26] demonstrated that CF had no influence on the salivary flow of the patients. Marmar *et al*.[27] found that the volume of saliva was higher in CF patients at all times after salivary stimulation.

Gonçalves *et al*.[28] found that the salivary flow is decreased in the CF group, consistent with the findings of other studies cited herein. Kollberg *et al*.[29] observed reduced salivary flow in CF patients.

Ceder *et al*.[30] observed a reduction in the salivary flow of CF patients when compared with the control group. In these studies, the authors concluded that the results suggest a primary defect related to the disease or a secondary defect due to the destruction of the glandular parenchyma. Previous studies showed conflicting results regarding the changes in salivary flow in CF, but in these studies the number of subjects was too small to draw decisive conclusions on the subject, while the results reported herein suggest a more consistent finding of hyposalivation.

In this study, the mean pH of the saliva of the CF patients was lower than that of the healthy control group. Gonçalves *et al*.[28] also showed that pH of the saliva was lower than in the case of healthy subjects.

Dental erosion was not statistically significant for children with CF and healthy controls. In this regard, we could not find another study considering the erosion in the children with CF in the literature. Al-Dlaigan *et al*.[31] found significantly higher levels of dental erosion in the children with asthma compared with controls.

A higher incidence of erosion was found in asthmatic children.[32] The clinical significance is that asthmatics are at risk of dental erosion from extrinsic acid due to inhaler and nebulized drug usage, but gastro-esophageal reflux does not appear to contribute in a site-specific manner. In the present study, dental erosion was not significantly different in CF group when compared to control group.

The difference may be attributed to geographical and socioeconomic factors. Further investigation is required into the factors affecting the increased prevalence of erosion in CF children.

It has been shown that some body tissues and fluids have thromboplastic activities.[10,12-16,33] As stated by several authors, coagulative function of the saliva is derived from the thromboplastin found in saliva. Approximately 78% of salivary thromboplastic activity is attributable to the presence of cells in saliva and the remainder to particulate cell debris.[16] Physiopathology of human saliva thromboplastin has not yet been well demonstrated. It has been shown that oral cavity is affected from the disturbances of the hemostatic systems. Salivary thromboplastic activity is important in representing the oral hemostatic parameter. Salivary thromboplastin may establish the hemostasis after oral traumas and bleeding peptic ulcer or diminish bleeding, as in tonsillectomies.[16,34] There is no study related to CF and salivary thromboplastic activity in the literature. In the present study, unchanged salivary flow rate and decreased thromboplastic activity implied that local salivary hemostasis function can be affected from CF and/or its medication. This may result in increased bleeding tendency in periodontal problems and late wound healing process in the oral cavity. Larger population studies are needed to establish the etiopathologic role of saliva thromboplastin in children with CF.

Conclusion

As there is no study related to CF and salivary thromboplastic activity in the literature, our findings related to the decreased salivary thromboplastic activity should be taken into account in CF patients. However, as the etiology of dental caries is multifactorial, other aspects need to be taken into consideration. Consequently, there is a need for a thorough investigation on this issue for the oral health management of children with CF.

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