

Pulmonary Pseudomonas Colonization in Cystic Fibrosis

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ABSTRACT

Background: Respiratory tract mucus plugging and *Pseudomonas aeruginosa* (PA) colonization in cystic fibrosis patients can influence the health indices, morbidity and mortality.

Our aim was to evaluate the relation between pulmonary infection with PA and its effects on respiratory function test and some health-related parameters.

Materials and Methods: This study was a cross-sectional study. Thirty CF patients, who were admitted to GI department of Children Medical Center because of gastrointestinal and/or pulmonary disturbances, were enrolled in this study. Management began by taking a medical history, physical examination, sputum or pharyngeal swab for culture and antibiogram, spirometric assessment for cooperative children (over 6 years old) and filling out a questionnaire for the abovementioned items and some health related parameters (weight, mean hospital stay days, mean absent days from school, and mean ICU admission time during the last year).

Results: The mean (\pm SD) age was 6.39 (\pm 5.88) years (11 females, 19 males). *Pseudomonas aeruginosa* grew in sputum or pharyngeal swab of 13 cases (43.3%), did not grow in 12 cases (40 %) and other organisms grew in 5 cases (16.7 %). Mean of hospitalization period was higher in cases with positive culture (31.83 Vs 13.08 days, Paired sample t-test, $P= 0.005$). Mean (\pm SD) predicted FEV1 % was 34.6 (\pm 28.0), but this difference was not significant in age, age of diagnosis, days of ICU hospitalization, absent days from school, days of using respiratory assistance equipments, days of antibiotics administration during the last year, body weight, predicted FEV1 %, predicted FEV1/FVC% and predicted FEF 25-75 %.

Conclusion: Prevention and early treatment of PA colonization can reduce hospital stay and its cost. Further large controlled trials are required in this regard. (Tanaffos 2006; 5(2): 41-48)

Key words: Cystic Fibrosis, Pulmonary infection, *Pseudomonas aeruginosa*

INTRODUCTION

Mucus plugging and its structural abnormalities cause respiratory tract bacterial colonization. Bronchiolitis and bronchitis are the early pulmonary manifestation of this complication but over a period

of several months and years, bronchiolectasis and bronchiectasis occur due to the structural alterations in respiratory tracts. A finding not clarified in CF is the high prevalence of respiratory tract colonization of *staphylococcus aureus* and *pseudomonas aeruginosa* (PA); two organisms that rarely affect other peoples' respiratory tracts (1-4).

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Risk factors for colonization are aging, severity of the underlying disorder, and recent hospitalization. Persistent infection with this organism; specially, in patients with moderate to severe pulmonary disorder, may cause rapid unexpected deterioration. Malnutrition is a predisposing factor to pulmonary infection. Pulmonary disease development rate is the main determinant of morbidity and mortality. The aim of treatment is to achieve longer symptom-free periods (1, 2, 3, 4).

In general, two antibiotics must be used for the treatment of infection and sometimes a third one must be added to cover *S.aureus*.

The previous studies revealed that pulmonary infection with pseudomonas specially mucoid type in CF patients has poorer prognosis in pulmonary function particularly in FEV1. This deterioration influences other life aspects of children with CF, because pulmonary disease development rate is the main determinant of morbidity and mortality, as mentioned earlier (1, 2, 4, 5, 6).

Another significant point in CF is the difference in survival rate of males and females (7, 8, 9). In the present study, we evaluated the relationship between pulmonary infection with pseudomonas and its effect on pulmonary function indices and some health-related parameters and also the correlation of certain socio-economic and familial factors with P.A infection in CF patients. Since no similar study has been done in Iran, we can claim that this study is a unique one in this field and the results could be used in diagnosis and treatment of patients affected with CF. In addition, this study could be used as a basis for more extensive and accurate studies in this field (6, 10, 11).

In several studies the effects of PA on respiratory status and the deterioration of clinical signs were

proved; with this consideration it was supposed that PA results in worsening the quality of life in CF patients (12, 13, 14).

According to this study, it could be stated that PA infection may decrease the life quality through exacerbation of the disease, and increasing the hospitalization period (8, 15).

MATERIALS AND METHODS

This study was conducted in a Pediatrics Medical Center as a cross-sectional study of 30 known cases of respiratory CF. Patients were excluded if less than one year had been passed since they were diagnosed with CF.

At the admission time, a history was obtained from the patients and their accompanied persons (one parent or both parents in all cases) and recorded in their own checklists. Then the patient was examined clinically and the results were registered in the same checklist. To avoid measurement errors in patients' physical examination, all patients were examined by only one person. Then the spirometric assessments were performed and best predictable indices of FEV1, FEV1/FVC, FEF₂₅₋₇₅ were recorded.

After the spirometric assessment of pulmonary function, sputum sample was obtained after several coughs and deep breaths. If the patient was unable to do that, a swab was used (according to several studies, its accuracy is similar to sputum sampling).

Sputum or pharyngeal swab samples were cultured in agar medium for 48 hours at 37° C and the results were evaluated with gram stain, and antibiogram was done for every grown micro-organism.

The patients were categorized as PA+ and PA-, and the prevalence of other variables was evaluated in each group.

RESULTS

Thirty patients with respiratory CF (11 females and 19 males), with the mean(\pm SD) age of 6.39 ± 5.88 yrs. were enrolled in this study.

Mean age at the time of diagnosis was 12.73 months (range, 1 to 120 months). Twenty-two subjects (73%) were diagnosed at 6 months of age or younger. In the present study, mean values were compared and there was no significant difference between male and female groups. There was no significant difference between the age groups.

All cases were inhabitants of the urban areas. In 26 cases (86.7%) both parents and in 4 cases (13.3%) only mother, were caretakers of the child.

The average number of family members was 4.2 ± 1.270 , and a 4-member family was the most frequent one.

The family income was less than 2 million Rials in 19 cases (63.3%) and between 2 and 5 million Rials in 11 cases (36.7%). Father's educational background in 25 cases (83.3%) was high school diploma or lower and in all cases, the mother had at least high school diploma.

Mean hospitalization period was 24.33 ± 19.926 days. Four cases (13.3%) had never been hospitalized during the last year and in 19 cases (63.3%) the total hospitalization period was one month or less. Seven cases (23.3%) had been hospitalized for more than 1 month.

Mean number of days in which children over 7 years (10 cases) were absent from school during the last year was 54 days (range 0 to 180), 2 children had never been absent, 4 cases were absent for 1 month or less and 4 cases had been absent for 2 months or more.

Average number of days in which respiratory assistance equipments including oxygen therapy

were used during the last year was 186.3 ± 182.4 days (range, 0 to 365), 13 cases (43.3%) never used those equipments.

Mean number of days in which antibiotics were administered during the last year was 146.2 (range, 0 to 365).

Mean number of antibiotics administered was 1.7 ± 1.2 (range 0 to 4), 6 cases (20%) did not use antibiotic at all and 24 cases (80%) used 2 types of antibiotics or less.

Mean number of other medications in use was 3.7 ± 2.7 (range, 0 to 11). Five cases (16.7%) did not use any other medication at all and 2 cases (6.6%) were using 10 types of medications or more. Mean weight of patients was 17.3 ± 12.77 kg and no one was below the fifth percent of heights for weight and height for age curve.

Among children of 7 years and older (10 cases), 5 cases (50%) never needed help for taking a shower and one case (10%) often needed help.

Among children of 5 years, and older (12 cases), 10 subjects (83.3%) never needed help for getting dressed and 2 cases (16.7%) were in need, no one needed help for eating meals, and only one case (8.3%) sometimes needed help for going to restroom. Five cases (41.7%) never needed help for playing and 1 case (8.3%) often need help for playing. Ten cases (83.3%) never needed any help for going to bed and getting up or sitting on chairs appropriate for their height while 2 cases (16.7%) occasionally needed help. Among children of 2 years or older (25 cases) 19 cases (76%) sometimes did not need help for walking and 6 subjects (24%) were in need constantly.

In physical examination of all patients with respect to general appearance, 11 cases (36.7%) were

normal, 17 cases (56.7%) were ill and 2 cases (6.7%) were toxic.

In pharyngeal swab culture, in 12 cases (40%) no microorganism was grown, in 13 cases (43.3%) PA was grown, and in 5 cases (16.7%) other organisms including *staphylococcus* or *candida* were grown.

In cases with P growth, 5 subjects (34.41%) were non mucoid P, and 5 cases (38.4%) were mucoid P. In one case (7.6%) mucoid and non mucoid P were grown simultaneously and in 2 cases (15.3%) non M.P with other organisms were grown.

In cases with P growth (13 cases), resistance to tetracycline, chloramphenicol, kanamycine, cefalotine, co-trimoxazole, ampicillin, and amoxicillin was observed in all cases. Only 2 cases were sensitive to gentamicin in which pseudomonas was grown with other types of microorganisms. In one case, there was no sensitivity to antibiotics, and mucoid as well as non-mucoid P were grown simultaneously. All cases except two, were sensitive to ceftazidime (Table 1).

Table 1. Comparison of antibiogram in cases with pseudomonas.

	Sensitive	Intermediate	Resistant
Tetracycline	0	0	13
Carbenicillin	3	6	4
Chloramphenicol	0	0	13
Kanamycin	0	0	13
Cephalothin	0	0	13
Cotrimoxazole	0	0	13
Ampicillin	0	0	13
Gentamicin	1	1	11
Amikacin	6	3	4
Amoxicillin	0	0	13
Ceftazidim	11	1	1
Ciprofloxacin	4	4	5

Spirometric assessment of pulmonary function was performed in patients over 6 years old (9 cases) who were cooperative. Mean predictable FEV1% was 34.6 ± 28.10 (range, 14.1 to 108.2), mean predictable FEV1 / FVC % was 85.5 ± 11.4 (range, 68.8 to 103.1) and mean predictable FEF 25-75 % was 28.57 ± 35.39 .

Mean values were compared and there was no significant difference between the male and female groups.

In all cases, mean number of hospitalization days in culture positive group during the last year was significantly higher than culture negative group (31.83 days vs. 13.08 days) (Paired sample t- test $p=0.005$), but there was no significant difference between the mean values in culture positive and negative groups. (Paired sample t test, $p>0.05$ in all cases) (Table 2). Among culture positive patients, number of hospitalization days during the last year in patients with P growth in their culture medium was significantly higher in comparison with patients with the growth of microorganisms other than P in their culture medium (37.54 vs. 17 days, paired sample t test $p= 0.011$) but in other cases there were no significant difference between the two groups (paired sample t-test, $p >0.05$ in all cases) (Table 3).

The comparison between the physical examination and sputum culture results are shown in Table 3.

In this investigation, for measuring life quality, variables that influence the patients' improved feeling and daily activities, were scored in a table as the minimum score was given to the cases with maximum severity of symptoms, , and in case of complete recovery the maximum point was scored. The overall score of life quality was obtained by adding all these scores together (13).

Table 2. Comparison of the mean values in positive and negative culture groups

	P.Value	Standard deviation	Mean value	No.	Pharyngeal Swab culture
Age at the admission time	0.509	33.771 19.132	17.08 9.83	12 18	Negative positive
Age(year)	0.534	4.242 6.821	5.55 6.94	12 18	Negative Positive
Number of hospitalization days during last year	0.005	13.352 20.327	13.08 31.83	12 18	Negative positive
Number of ICU hospitalization days during last year	0.128	0.577 2.149	0.17 1.17	12 18	Negative Positive
Number of absent days from school	0.689	79.373 37.372	65.00 46.67	4 6	Negative Positive
Number of days in which respiratory assistance equipments were used during last year	0.919	189.751 183.000	182.00 189.17	12 18	Negative Positive
Number of days in which antibiotics were used during last year	0.067	122.165 143.818	90.25 183.56	12 18	Negative Positive
Weight(kg)	0.276	7.391 15.209	13.89 19.16	12 18	Negative Positive
Height(meter)	0.294	0.28650	0.9292	12 18	Negative Positive
FVC(L)%predicted	0.662	5.5717 31.4522	34.133 40.233	3 6	Negative Positive
FEV1(L)%predicted	0.530	0.5292 34.8927	28.200 37.817	3 6	Negative Positive
FEV1/FVC%predicted	0.684	14.7625 10.5806	82.400 86.683	3 6	Negative Positive
FEF 25-75(L/S)% Predicted	0.487	9.2731 43.5194	19.400 33.167	3 6	Negative Positive

Table 3. Comparison of mean values between pseudomonas positive and negative groups

	P.Value	Standard deviation	Mean value	No.	Gender
Age at the admission time	0.135	5.694 35.358	5.62 20.80	13 5	Mucoid pseudomonas
Age(year)	0.740	6.424 8.485	6.54 8.00	13 5	Mucoid pseudomonas
Number of hospitalization days during last year	0.011 *	20.699 9.460	37.54 17.00	13 5	Mucoid pseudomonas
Number of ICU hospitalization days during last year	0.632	2.323 1.789	1.31 0.80	13 5	Mucoid pseudomonas
Number of absent days from school	0.816	47.675 10.607	48.75 42.50	4 2	Mucoid pseudomonas
Number of days in which respiratory assistance equipments were used during last year	0.579	181.783 199.919	205.77 146.00	13 5	Mucoid pseudomonas
Number of days in which antibiotics were used during last year	0.690	128.957 191.424	194.38 155.40	13 5	Mucoid pseudomonas
Weight(kg)	0.863	13.649 20.525	19.65 17.86	13 5	Mucoid pseudomonas
Height(meter)	0.210	31.91989 0.50929	12.6908 0.9640	13 5	Mucoid pseudomonas
FVC(L)%predicted	0.649	34.1470	43.300 24.900	5 1	Mucoid pseudomonas
FEV1(L)%predicted	0.703	38.215	40.680 23.500	5 1	Mucoid pseudomonas
FEV1/FVC%predicted	0.619	11.4225	85.560 92.300	5 1	Mucoid pseudomonas
FEF 25-75(L/S)% Predicted	0.784	48.1430	35.740 20.300	5 1	Mucoid pseudomonas

The maximum score was 64 and the minimum was 14. In this study, patients categorized into two culture + and culture – groups. The culture + group was classified to P+ and P- groups and P+ group to mucoid P and nonmucoid P. In these statistical groups, the mean score of life quality was calculated and compared.

As it is shown in figure 1 there is a significant difference between the life quality of patients with negative pharyngeal swab culture or with other

organisms grown in their culture medium (40.88) and patients with pseudomonas growth in their swab culture.

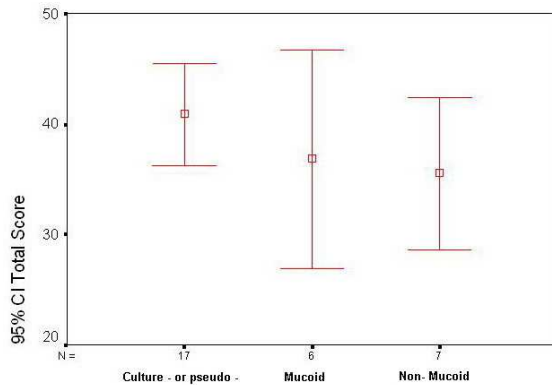


Figure 1. As it is shown, there is a significant difference between life quality of patients with negative pharyngeal swab culture or with other organisms grown in their culture medium (40.88) and patients which pseudomonas was grown in their swab culture.

DISCUSSION

In this study, we attempted to investigate the influence of CF disorder and its coexistence with PA pulmonary infection on patients' quality of life.

According to Jenney and Campbell definition, life quality is a unique image, representing patients' idea about his illness and his other life aspects (16).

A significant point in CF is the difference between female and male survival rates (7).

In a study by Demko et al. (7) the survival rate in females with mucoïd CF was stated to be 1.7 year less than males, but this difference was not detected in our study.

Another study by Gee et al. revealed that females' insight into their disease was relevant to their clinical condition in comparison with males, but we didn't observe such relevance, possibly because of the difference in method of data collecting and sample size (8).

On the other hand, according to Selvadurai et al. (17) study, gender differences in routine activities

only appear after puberty. The difference perhaps lies in genetic, hormonal and social factors requiring an extensive longitudinal study (18).

In the present study mean values were compared and there was no significant difference between male and female groups. There was no significant difference between the age groups.

A 10-year study on this subject, showed that patients affected with mucoïd type of PA, had lower survival rate, worse chest x-ray grading and pulmonary function test in comparison with those not affected with PA or had nonmucoïd type of PA. However, pulmonary test result deviations from normal in affected males and females were similar. Besides, in patients affected only by mucoïd or non mucoïd type, males had better FEV1 and survival rate. Therefore, there may be factors other than early infection with mucoïd type PA that results in lower survival rate in females (7).

Previous studies revealed that pulmonary infection with pseudomonas specially mucoïd type in C.F patients had poorer prognosis in pulmonary function particularly in FEV1 and this deterioration influenced other life aspects of children with CF, because pulmonary disease development rate was the main determinant of morbidity and mortality, as mentioned earlier (1, 10, 19).

In several studies, the effects of PA on respiratory status and deterioration of clinical signs have been proved.

In our study, in all cases mean number of hospitalization days in culture positive group during the last year was significantly higher as compared to culture negative group (31.83 days vs. 13.08 days), but there was no significant difference between the mean values in culture positive and negative groups. Among culture positive patients, number of hospitalization days during the last year in patients with P grown in their culture medium was significantly higher in comparison with patients with

the growth of microorganisms other than P in their culture medium but in other cases there were no significant differences between the two groups.

Therefore, we decided to evaluate the quality of health with respect to clinical symptoms, individual abilities, and spirometric assessment and we assumed that the lower the individual abilities with respect to the age group, more severe clinical signs, greater necessity of hospitalization or use of medications, the lower will be the life quality.

CONCLUSION

In respect to former results we can declare that pseudomonas has negative effects on CF patients' life quality. Therefore, we recommend the below mentioned measures to improve the life quality of CF patients:

- Avoid unnecessary hospitalization to prevent pseudomonas colonization, if possible.
- Avoid hospitalizing of CF patients together in one room
- Avoid using air-conditioner in houses and cars
- Avoid living in damp places
- Isolate personal belongings such as toothbrush and dishes.
- Use pharyngeal swab culture and antibiogram for diagnosis
- Perform pharyngeal swab cultures periodically (e.g. every 3 months) for early diagnosis of pseudomonas colonization.

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