Microbial Evaluation of Sputum of Cystic Fibrosis Patients

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Abstract

Background: Cystic fibrosis disease is a common hereditary autosomal recessive disorder in which loss of lung function caused by infectious factors is the most common cause of the patient’s death. In this study, the microbes in sputum of the cystic fibrosis patients have been studied during relapses of the disease.

Materials and Methods: In this cross-sectional study, 129 sputum cultures of the patients with cystic fibrosis, who were hospitalized in Mofid Children’s Hospital in Tehran during 2004-2009 with relapse of disease, were studied. The data were collected through census method and based on the information concerning (gender, age, type of germ and the appropriate antibiotics).

Results: The most common germs in the sputum of these patients are Pseudomonas aeruginosa (approximately 36%) and then respectively klebsiella (13%), Staphylococcus aureus (9.3%) and Streptococcus pneumoniae (5.4%). Examination of antibiogram showed that these germs give an appropriate response to antibiotics such as Ceftazidine, vancomycin, imipenem, ciprofloxacin, azithromycin, rifampin and largely to aminoglycosides.

Conclusion: Considering the more prevalence of Pseudomonas aeruginosa, combined therapy with ceftazidime or imipenem along with aminoglycoside and further treatment with oral azithromycin are recommended. More studies in this area are necessary.

Introduction

Cystic fibrosis is an inherited disease that affects several organs including the digestive system, sweat glands and the reproductive system and causes a progressive disease in respiratory system that eventually will be one of the main causes of death in these patients. The hereditary pattern of this disease is autosomal recessive and its prevalence is different in various races from about 1 in 2500 to 1 in 32000 live births and carrier’s frequency has been reported to be about 1 in 25 patients (4%). Cystic fibrosis disease occurs due to mutations in the large single gene on chromosome seven that encodes the CFTR protein. Most mutations are related to exon 10 of this gene. In patients with cystic fibrosis (CF), any disorder in chloride sodium transport through respiratory epithelium causes thick and sticky secretions in the airways and it leads to chronic infection of the respiratory system and ultimately, will create progressive respiratory failure. Loss of lung function in cystic fibrosis patients is the most common cause of their death [1,2].

The prevalence of airway colonization with Staphylococcus aureus, Pseudomonas aeruginosa and Burkholderia cepacia is common in children with CF [1]. Essentially, the immune system of CF patients is normal. Nutritional disorders such as fatty acid deficiency increase the susceptibility to respiratory infection [1,3]. Patients with CF usually have no problems with appetite, but there is difficulty in absorption. Finding of S. aureus and Pseudomonas aeruginosa in culture of the secretions obtained from the lower parts of the airways (e.g., sputum), strongly suggests the diagnosis of CF [2]. Finding of Burkholderia cepacia should also suggest the diagnosis of CF [4]. The other organisms which are obtained especially in advanced pulmonary disease include a variety of gram negative rods, fungi and non-tuberculosis mycobacterium species [5,6]. Failure to improve respiratory symptoms with regular antibiotics necessitates the test for mycoplasma and viruses [1,5]. These patients should be treated completely and comprehensively. Due to the frequent relapse of infections, it is very important to take quick hospital actions and care for proper nutrition in these children, because it reduces the severity of lung damage. Antibiotic are the basis of treatment to control the advancement of lung infections and eventually lung damage. The goal of treatment is to reduce the severity of bronchial infection and delay the progression of lung damage. Antibacterial prophylaxis is effective in prevention of Staphylococcus aureus infection [1,2]. Using nebulizer aminoglycoside, especially tobramycin, helps to prevent and reduce infection. Gentamicin can also be used as the helper aminoglycoside [7,8].

It is hard to take drugs and medical interventions for long, but it can keep the child asymptomatic and give an almost normal life to the patient. There are simple measures to reduce the risk of expansion of the germs...
causing infection in CF patients. Medications should be
taken constantly. Given that the most common cause of
mortality in CF patients is pneumonia [2,9], and
considering the short lifespan of these patients if the
infections are not treated appropriately and on the other
hand, significant improvement in quality and quantity of
life of these patients with treatment, this study was
designed and implemented to examine the type of
microbes in the sputum of cystic fibrosis patients after
relapses, the patients who referred to Mofid hospital in

Materials and Methods

In this descriptive-analytical study, the study population
included files of all children with cystic fibrosis, who
were hospitalized at Mofid hospital during 2004-2009
after relapses of the disease. The patients referring to
children pulmonary ultra-specialized clinic who were
-treated as outpatients were excluded from this study. First,
the files of CF patients admitted during 2004-2009 were
specified and reviewed. Then, according to the results of
cultures and other required data, the respective data form
was completed. The sputum samples sent to culture and
smear were taken after physical therapy and their culture
results were presented in their file. The method is disk
diffusion antibiogram and the medium was McFarland
and Molar and Molar Khondar. Data was collected using
data from including the questions such as age, gender,
type of microorganisms, duration of therapy, the most
appropriate antibiotic, diagnosis age and referral age. In
addition, sputum culture and smear of the secretions of
sputum and throat the results were conducted for these
patients, whose results were also evaluated. The data
obtained from the questionnaires were analyzed using
SPSS-15 software. When entering the data into the
software, since a patient might have been tested several
times, each time was considered as a separate record.
Frequency of the obtained Microorganisms was calculated
as the relative frequency and frequency of the operating
microorganisms in different classes of variables were
calculated by $\chi^2$ test. Variable of duration was measured
as the mean. The relationship between various
independent variables and dependent variables were
examined by regression analysis. The necessary permits
were obtained from the Ethics Committee to use patient’s
files.

Results

According to the variables assessed in this study, the
average age of CF diagnosis in these patients was 4.9
months, the average age of onset of pulmonary symptoms
was 9.3 months, the age of admission of patients in the
lung unit was 75.6 months, and the average duration of
therapy based on culture results and clinical symptoms
improvement was 12.9 days in the hospital. Among the
samples who had the inclusion criteria, 60% were male
and 40% were female. Given the expansion of the study
and to simplify large volumes of data, the subjects were
divided into two age groups of less than 24 months and
more than 24 months. Percentage frequency distribution
of the geographic location of patients was considered in
three categories of Tehran and suburbs, rural areas and
other cities. The results showed a higher frequency of
Pseudomonas aeruginosa bacteria (46 cases) (Fig. 1).

![Figure 1. Frequency distribution of the microorganisms reported in culture of the studied patients](image1)

Examination of the frequency of the microorganisms
obtained from cultures in two age groups (less and more
than 24 months) shows that Klebsiella was more prevalent
in patients less than 24 months and Pseudomonas
aeruginosa was more prevalent in patients more than 24
months (Fig. 2).

![Figure 2. Frequency distribution of the microorganisms reported in culture of the studied patients separated by age group](image2)

The examination of reaction of aeruginosa bacteria
based on antibiogram revealed that this bacterium was
most sensitive to the antibiotics of ciprofloxacin,
imipenem and ceftazidine and most resistant to
antibiotics of ampicillin, oxacillin, penicillin, cephaptolin,
cefixime, ceftriaxone and cotrimoxazole (Fig. 3).

![Figure 3. Frequency distribution of P. Aeruginosa resistance to the antibiotics studied in cystic fibrosis patients](image3)
The examination of reaction of Klebsiella based on antibiogram revealed that it was most sensitive to the antibiotics vancomycin, rifampin, imipenem, azithromycin, ceftazidime, clarithromycin, ofloxacin and was most resistant to cefixime, ampicillin, cephalotin and  pipracillin. Staphylococcus was most sensitive to the antibiotics vancomycin, tobramycin, imipenem, ceftazidime, amikacin and most resistant to ampicillin, co-amoxiclav, penicillin and ceftriaxone. Streptococci was most sensitive to the antibiotics vancomycin, rifampin, imipenem, ciprofloxacin and ofloxacin, and most resistant to ampicillin, cefixime, penicillin and ceftriaxone and finally E.coli was most sensitive to the antibiotics vancomycin, ofloxacin, cefotaxim, azithromycin, ceftazidime, ciprofloxacin, imipenem and amikacin and most resistant to antibiotics such as ampicillin, piperacillin, oxacillin, penicillin, carbencillin and cefoxitin. There was no evaluable antibiogram regarding other microorganisms.

Discussion

The results showed that the average CF diagnosis age of patients, 4.9 months, the average age of onset of pulmonary symptoms was 9.3 months, the age of admission of patients in the lung unit was 75.6 months, and the average duration of therapy based on culture results and clinical symptoms improvement was 12.9 days in the hospital and 60% were male and 40% were female. The studies conducted so far have shown that Pseudomonas aeruginosa is the most common germ affecting pulmonary system of cystic fibrosis patients [7,9,10].

In this study, Pseudomonas aeruginosa was also the most common germ affecting pulmonary system. Other important microorganisms which are isolated from the sputum of these patients in the relapse stage are respectively Klebsiella, Staphylococcus aureus, Streptococcus pneumoniae, Burkholderia cepacia and other gram-negatives. The results showed that the incidence of microorganisms with greater sensitivity to antibiotics is more in the first two years of life and by increase of age in CF patients; the microorganisms resistant to different antibiotics such as Pseudomonas aeruginosa will become more prevalent.

The results of the studies of Alibakhshi [11,12] are consistent with the results of this study. In addition, the results obtained from the antibiogram of these cultures showed that totally there was more sensitivity to antibiotics such as ceftazidime, vancomycin, imipenem, ciprofloxacin, azithromycin, rifampin, and somewhat aminoglycosides to empirically treat more sensitive patients and there was more resistance to the antibiotics such as cefixime, penicillin, cotrimoxazole, ampicillin, ceftriaxone, cephalotin, piperacillin and oxacillin.

Other studies showed that the therapies combined with meropenem or imipenem and inhaled or intravenous tobramycin and inhaled or intravenous ceftazidime and aminoglycoside (with more inhaled effect) are most effective in improving the symptoms of CF patients [13,14]. The results showed that the most common germ extracted from the sputum culture of CF patients was Pseudomonas aeruginosa whose incidence increases with age increase, and drug resistance will be increased the same.

This study also showed that the patients admitted for pulmonary symptoms treatment are over 2 years old. This suggests poor diagnosis and referral system and that these patients who have given less medical care, have more severe disabilities. Trudy has claimed that the patients who enjoy appropriate medical services, education and occupation, will have higher FEV1, fewer hospitalizations, less Pseudomonas aeruginosa contamination, higher caloric intake, better performance and more favorable social conditions. Totally, the antibiotics such as ceftazidime, vancomycin, imipenem, ciprofloxacin, azithromycin, rifampin, and somewhat aminoglycosides showed a higher sensitivity for empirical treatment of patients.

According to the results of this study, it is suggested that longevity of CF patients, social, educational and occupational conditions of CF patients, bone densitometry of the CF patients over 8 years, different strains of Pseudomonas aeruginosa in CF patients (mucoid or non-mucoid), FEV1 measurement before and after antibiotic treatment, viral and fungal factors, and non-tuberculosis mycobacterium species (NTM) should be studied in CF patients.

CF patients should have two sputum samples during the admission (at first and during treatment) and they should have sputum samples for culture and antibiogram during their outpatient visits every 3 months and homogenizing should also be done in the culture and antibiogram results for further comparative studies. Since the number of these patients is not low in Iran and on the one hand, early diagnosis and appropriate treatment can improve the quantity and quality of their life and on the other hand, lack of treatment leads to early death, the studies in this field can be very valuable. It is important to have adequate monitoring of proper treatment based on antibiogram, that all these will be possible through the establishment of CF Association.

Acknowledgements

This study has been conducted as a research project (thesis of Dr. Akbarizadeh registration No. 15) and financially supported by Research Deputy of Shahid Beheshti University and Department of Infectious Disease Research Center of Mofid Children Hospital.
References