III. PEDIATRICS

IN FRONT OF THE GATES OF THE EU: A DIFFERENT PERSPPECTIVE FOR CYSTIC FIBROSIS

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Summary

Cystic fibosis (CF) is one of the most common recessive genetic disease in caucasian population. The improved knowledge about the pathophysiology of the disease and the spectacular advances in the delineation of the genetics of the defect have brought hope that a cure for CF may not be so far away. The paper present a background about perspectives of CF in the begining of a new milenium.

Key words: cistic fibrosis, genetic disease, caucasian population

First recognized as a clinical entity in the late 1930s, Cystic Fibrosis (CF) is one of the most common life limiting recessive genetic disease in caucasian population. It is characterized by chronic and obstructive lung disease, pancreatic insufficiency and high sweat electrolyte levels.

There are at least some explanations for the great interest in CF currently in the western world. Life expectancy has changed dramatically, more so, today life span for an infant diagnosed soon after birth is certainly very much longer than only a few decades ago when many children did not reach school age.

For those patients who attend specialized CF centers, life expectancy could reach 40 years, this being the result of improved traditionally treatment based on controlled airway infection, physiotherapy, reduction of inflammation and better nutrition.

The improved knowledge about the pathophysiology of the disease seems to provide new ways to attack pharmacological approaches.

In the same way, the spectacular advances in the delineation of the genetics of the defect have brought hope that a cure for CF may not be so far away.

Over time, the survival and quality of life for CF patients have improved markedly, due in large to regular periodic evaluation, monitoring of complications, aggressive intervention by physicians and other healthcare workers specifically trained in the management of CF.

Recorded median survival has risen from under 5 years of age in the 1950s to more than 30 years of age in 1995 (1,2).

Despite being a monogenic disease, CF appears to be very heterogeneous. First, since the cystic fibrosis transmembrane conductance regulator (CFTR) gene was cloned in 1989, more than 1,300 mutations have been described (3-5). And second – the distribution of these CFTR mutations vary widely between countries and/or ethnic groups.

The cloning of the CFTR gene and the ongoing identification of many mutations have promoted intensive research into the association between genotype and phenotype in attempt to find prognostic factors for the outcome.

Several studies have shown that some mutations (e.g. the delF508 as the most common mutation worldwide) are associated with severe disease presentation (6), while other mutations are associated with a milder phenotype (e.g. R553X and others).

There is, however, considerable heterogeneity in disease severity between different individuals, who share even an identical CFTR genotype.

It is widely recognized that the age at diagnosis and the type of severity of symptoms at the initial presentation reflect the clinical heterogeneity of CF.

In this respect it has been hypothesized that early diagnosis with an intensive therapeutic program may result in a better prognosis. It has also been shown that infants presenting with gastrointestinal symptoms are diagnosed earlier than those with pulmonary symptoms.

It seems that patients with pulmonary involvement at diagnosis exhibit the highest mortality. (7).

The hallmark of CF and the cause of death in more than 90% of patients is chronic progressive pulmonary disease. The bacterial endobronchial infection resulting in host inflammatory response appears to be the most important process occurring right after birth in CF patients.There are several other factors such as environmental, genetic, which seem to influence the colonization of the airways and further outcome of lung disease.

Meantime, further studies should determine whether early severe lung disease, associated with early death is related to CF genotype or if severe malnutrition at the time of diagnosis is related to poorer outcomes.

It will be a question if early detection in terms of early intervention and maybe environmental changes would improve outcomes.

It is important to underline the fact that early intensive treatment in CF will be beneficial for patients only in organized, staffed CF centers.

It has been shown that there are striking differences in the condition of people attending different CF centers, far more marked that can be accounted for by

climate, socio-economic circumstances, age of diagnosis or variation in prevalent gene mutations.

There has been recently published a European Consensus upon standards on care for patients with CF (8) defined as optimal service provision necessary to deliver the best outcomes possible.

The guidelines of the consensus are based on the belief that intensive treatment – both prophylactic and as a response to acute events decrease morbidity and increase survival and quality of life.

When speaking of early diagnosis and intervention as a necessary tool for improving outcome – it has to be done through developing programs for organizing care in Regional CF Centers, with trained physicians and nurses, with availability of diagnostic and treatment facilities.

What can we improve for our patients who are often severely malnourished when diagnosed with CF or who attend our clinics after years from diagnosis with severe lung disease?

We have to attempt the ultimate effort which is needed standing in front of the gates of the EU: to try to be organized and provide care at European standards, following protocols and guidelines in order to correct evaluate our patients. The way we treat, the way we'll see the results.

The emphasis on improving care is an important initiative in any disease; this should have a major favorable influence on the quality and duration of life of many people with CF.

The latest ECFS document that sets out the standards of care should be an aim for all people engaged in the management of CF.

We also dare to hope that along the transformation that has to happen when becoming an EU member, the approach to a life-limiting disease as CF will be different and will provide another perspective for the patients.

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