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Short Critical Assay on Cystic Fibrosis

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Abstract. Cystic fibrosis (CF), a monogenic disease, is the most common autosomal recessive, life-shortening disease affecting people of Northern European descent. According to the American Cystic Fibrosis Foundation patient registry, there are currently more than 30,000 CF patients in the United States and more than 70,000 CF patients worldwide. This disease is caused by dysfunctional transport of chloride and/or other ions (such as sodium and bicarbonate) leading to the generation of thick, viscous secretions (e.g., mucus) in the lungs, pancreas, liver, intestine and reproductive tract and increased salt content in sweat gland secretions. Ultimately, progressive lung disease is the main cause of CF complications and patient mortality. This disease manifests in many organs, but mostly in the upper and lower respiratory tract, pancreas, intestines and reproductive system. For most patients, lung disease is the most important problem in terms of symptoms and the treatment required and the fact that it is the most likely cause of death the optimal diagnostic test for cystic fibrosis is the measurement of electrolyte levels in sweat. Patients with the disease have elevated sodium and chloride concentrations (>60 mmol/l, diagnostic; 40-60 mmol/l, intermediate (but more likely to be diagnostic in infants); <40 mmol/l, normal). However, undoubted cases of cystic fibrosis have been described with normal sweat electrolytes. Newer techniques have reduced the amount of sweat needed, although cystic fibrosis is currently incurable and greatly reduces life expectancy, the average age of survival of CF has increased significantly over the past 50 years and now exceeds 40 years. Therefore, CF is no longer considered solely as a childhood disease, but is now recognized as a disease of children and adults. Currently, more than half of CF patients are adults up to 60 years of age, indicating that active treatment can improve prognosis, increase quality of life and prolong life expectancy.

KEYWORDS: CFTR, cystic fibrosis, mutation.

Cystic fibrosis

Cystic fibrosis (CF), a monogenic disease, is the most common autosomal recessive, life-shortening disease affecting people of Northern European descent. According to the American Cystic Fibrosis Foundation patient registry, there are currently more than 30 000 CF patients in the United States and more than 70 000 CF patients worldwide (Shteinberg et al.,2021). Worldwide, about 1000 new cases of CF are diagnosed each year, with more than 75% of CF patients diagnosed at 2 years of age and an average age at diagnosis of about 3 years. Numerous animal models of CF have been established based on specific types of human CFTR mutations, but the models differ in their effectiveness in reflecting the specific disease characteristics of human CF. For example, the mouse CF model differs markedly from human CF at the pathological level, while at the molecular level the pig and human CFTR genes are highly homologous, but their corresponding CFTR protein structures and functions are very different. At present, ferret and rabbit CF models are promising as human CF models, but additional models based on other species should also be evaluated. Meanwhile, the introduction of human CFTR Genes harboring CFTR mutations into animal genomes are promising as a strategy to create better animal models for human CF. However, each of the current animal models has its own unique characteristics that are useful for studying particular aspects of human CF disease (Shen et al.,2021)

Cause of cystic fibrosis

cystic fibrosis is caused by dysfunctional transport of chloride and/or other ions (such as sodium and bicarbonate) leading to the generation of thick, viscous secretions (e.g., mucus) in the lungs, pancreas, liver, intestine, and reproductive tract and increased salt content. in sweat gland secretions. Ultimately, progressive lung disease is the major cause of CF complications and patient mortality. 8 The course of the disease varies widely and can begin from a few months after birth to decades after birth, and many patients present with mild or atypical symptoms. Therefore, clinicians should avoid excluding CF as a possible diagnosis in cases where patients present with only a few typical signs and symptoms of CF. (Shteinberg et al.,2021).

Clinical features

The disease manifests in many organs, but mostly in the upper and lower respiratory tract, pancreas, intestines and reproductive system. For most patients, lung disease is the most important problem in terms of symptoms and the treatment required and the fact that it is the most likely cause of death. (Davies et al.,2007)

Diagnosing cystic fibrosis

The optimal diagnostic test for cystic fibrosis is the measurement of electrolyte levels in sweat. Patients with the disease have elevated sodium and chloride concentrations (>60 mmol/l, diagnostic; 40-60 mmol/l, intermediate (but more likely to be diagnostic in infants); <40 mmol/l, normal). However, undoubted cases of cystic fibrosis have been described with normal sweat electrolytes. Newer techniques have reduced the amount of sweat needed. The test should be performed by someone trained and experienced. For this reason, the diagnosis will usually be made at second and third level centers, although primary care professionals play a key role in identifying patients who need investigation. In the rare cases where the diagnosis remains in doubt, other diagnostic tests are available; for example, nasal potential difference measurement to assess salt transport disturbance is available in some specialist centers e.g. in the UK (Davies et al.,2007).

Prognosis of cystic fibrosis

Although cystic fibrosis is currently incurable and greatly reduces life expectancy, the median age of survival for CF has increased significantly over the past 50 years and now exceeds 40 years. Therefore, CF is no longer considered solely a childhood disease, but is now recognized as a disease of children and adults (Michal et al.,2021). The fight against CF disease is of national interest, and includes research into its causes, prevention, care and rehabilitation, with the aim of achieving social, economic and cultural development and inclusion. In recent years, much progress has been made in the knowledge and treatment of the disease, but, despite this, it is still a pathology without a cure, which is why access to the latest treatments, such as the new CFTR protein modulators, is very important.

In the use of treatment with Kaftrio, modulators patients have been able to verify in real life what had been observed in clinical trials: this new drug changes their lives, it opens up a future where there was none. However, as it is a congenital disease, this treatment covers about 70% of the almost 4,000 people with cystic fibrosis in Spain, therefore it is necessary to advance in terms of policies since, for example, although this drug is already included in the National Health System (SNS) per year, these treatments cost 200,000 euros per year per patient, therefore not everyone can have access to them (Purkayastha et al.,2023; Davies et al.,2007; Shteinberg et al.,2021)

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