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Research Article

Cystic Fibrosis in Female Gender

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Abstract

Introduction: Cystic fibrosis (CF) is a lethal autosomal recessive disease. It has been reported that females are diagnosed later than males (2) and have a significantly decreased survival.

Methods: Clinical trials were identified by PubMed until June 30 2020. The search keywords were "sex, gender differences, cystic fibrosis".

Result: It has been suggested, that cystic fibrosis is diagnosed later in female children, because underdiagnosed. Unfortunately, cystic fibrosis determines airway inflammation and chronic respiratory infection, such as *Pseudomonas aeruginosa.* Different factors are related to these inflammations. However, mortality and cystic fibrosis–related diabetes (CFRD) prevalence were higher, in female subjects than males.

Conclusion: Female subjects have significantly higher mortality than males, with about 4-year difference in median survival. However, adolescent girls with CF have a greater emotional impact compared to boy.

Keywords: Sex; Gender Differences; Cystic Fibrosis

Introduction

Cystic fibrosis (CF) is a lethal autosomal recessive disease, affecting 1 in 3.200 births [1]. Gender differences are a crucial factor on the diagnosis and progression of CF. In fact, it has been reported that cystic fibrosis is diagnosed later in female children than males [2]. However, female with age between 1 to 20 years [3] have a significantly decreased survival. To this regard, it has been described that female subjects are less adherent to therapy [4] and they have a life span shorter (about 3 to 5 years) than that of males [3]. We report a minireview on the cystic fibrosis in female subjects.

Methods

Clinical trials were identified by PubMed until June 30 2020. The search keywords were "sex, gender differences, cystic fibrosis". The studies were selected and their references were reviewed for potential inclusion. Studies written in languages other than English were excluded. Two authors (O.P. and T.C.) reviewed all study abstracts. Studies were included if analyzed and reported gender differences in cystic fibrosis. All selected studies are qualitatively analyzed.

Results and Discussion

Cause of the gender gap in cystic fibrosis

The underlying cause of the gender gap in cystic fibrosis can be reported [5]:

- Genetic modifications
- Socio-environmental effects of gender

It has been reported that cystic fibrosis is diagnosed later in female children than males probably for reduced recognition of respiratory symptoms in female infants. Unfortunately, the prevalence of the adult CF diagnosis is significantly greater in females [6]. Moreover, the rate of FEV_1 is similar by gender, but female subjects have a survival advantage of about 9-13 years [7]. In fact, cystic fibrosis induces an airway inflammation and chronic respiratory infection, such as *Pseudomonas aeruginosa*. To this regard, it has been reported that, females with CF, acquired chronic Pseudomonas aeruginosa infection at an earlier age. In particular, female subjects express a quickly decline in lung function after P. aeruginosa colonization [8].

Estrogen and cystic fibrosis

Sex hormones induce alterations on the components of the muco-ciliary apparatus, in airway epithelial cell apical sodium and chloride transport [9], alter airway surface liquid (ASL) volume [10] and change cilia beat frequency in the airways [11]. The role of estrogen in female subjects in cystic fibrosis is reported in table 1. These factors can determine, in females with cystic fibrosis, a major disadvantage than males. In fact, these characteristics can induce an increase on the mucus viscosity [12]. To this regard, it has been reported that estrogens determine conversion of P. aeruginosa, from a non-mucoid to mucoid form. Unfortunately, this form is the more drug resistant [13]. Moreover, female subjects acquire infection by *P. aeruginosa*, *H. influenzae*, *A. xylosoxidans*, *B. cepacian*, *Aspergillus* species and methicillin resistant Staphylococcus aureus (MRSA), at an earlier age [14]. Another role of estrogen in cystic fibrosis was related to immune system. In particular, it has been reported, that estrogen induce inhibition of interleukin-8 production in CF bronchial epithelial cells in vitro and it would inhibit neutrophil recruitment and inflammatory responses in female subjects [15].

Air surface liquid	Decrease
Mucus viscosity	Enhanced
Conversion of *P. aeruginosa* from a nonmucoid to mucoid form	Increased
Drug resistant and pathogenic form	Increased
P. aeruginosa and other infection	An earlier age
Interleukin-8 production	Inhibited

Table 1: Estrogen role.

Other factors and gender

It has been reported that there was also a sex difference in adults' diabetes with severe CF. In particular, mortality and prevalence on the cystic fibrosis were higher, in female diabetic than males. To this regard, it has been observed that insulin clearance increases with age. This increment was described especially in females, and it contribute to the deterioration in glucose tolerance [16].

However, disease severity has an impact on the quality of life (HRQoL). To this regard, females generally have poorer HRQoL. In fact, female subjects have a more accurate perception of clinical health status [17]. This perception has a greater emotional impact on adolescent girls compared to boys.

Conclusion

Females with cystic fibrosis have significantly higher mortality than males. In fact, it has been reported about four-year difference in median survival by gender. However, cystic fibrosis induces a major emotional impact on adolescent girls compared to boys. The adolescent girls are less adherent to therapy. Therefore, these gender differences may outline the reduced pulmonary function observed in girls with cystic fibrosis [18]. Future studies are need to evaluate the different outcome by gender in CF patients.

Conflict of Interest

The authors declare that haven't conflict of interest.

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