

Therapeutic guidelines for the treatment of cystic fibrosis

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Abstract

Cystic fibrosis (CF) is a complex, systemic autosomal recessive disease that affects the functions of the respiratory system, the digestive tract and all exocrine glands. The frequency for Europe averages 1: 2500 to 1: 3500 live births. The total number of patients with cystic fibrosis in Bulgaria is about 180. About 10% of the patients are diagnosed at birth. About 60–70% of patients are diagnosed before they reach one year of age. Respiratory symptoms predominate in the clinical picture in patients with cystic fibrosis and determine the prognosis in more than 90% of the patients. The treatment of patients with cystic fibrosis is strictly individualized, pharmacological and non-pharmacological and requires a comprehensive therapeutic approach. The complex therapy also includes bronchodilators, NSAIDs, corticosteroids, respiratory rehabilitation in combination with general body massage. Continued courses of broad-spectrum antibiotics are required to suppress chronic infection. With the progression of the disease, complications such as atelectasis, pneumothorax and pulmonary hemorrhages are observed. The establishment of specialized centers with trained and experienced professionals is essential in order to provide optimal patient care. These include frequent clinical evaluations, follow-up of complications, and early interventions for the treatment of patients with cystic fibrosis.

The aim of the article is to familiarize the audience with the therapeutic measures applied in the treatment of patients with cystic fibrosis.

Keywords

Complications, cystic fibrosis, treatment

Introduction

Cystic fibrosis (CF) is a complex, systemic autosomal recessive disease that affects the functions of the respiratory system, digestive tract and all exocrine glands (O’Sullivan et al. 2009). The disease is due to a mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene for the transmembrane transport regulator. The frequency for Europe averages 1: 2500 to 1: 3500 live births. It is most commonly found in Caucasian representatives

in Europe, North America, Australia. The frequency of the disease is variable depending on ethnicity and geography (Mihov et al. 1997)

The total number of patients with cystic fibrosis in Bulgaria is about 180. About 10% of the patients are diagnosed at birth. About 60–70% of the patients are diagnosed before one year of age. Late diagnosis is associated with insufficient expression and poor progression of clinical symptoms. Such patients are usually not seriously ill and have a relatively good quality of life (Nedkova 2010).

Clinical symptoms

Respiratory symptoms predominate in the clinical picture in patients with cystic fibrosis and determine the prognosis in more than 90% of patients. The first respiratory symptoms of cystic fibrosis in 60% of the children manifest themselves by the age of 6 months, by the end of the first year – in 80%, and by the second year – in 91% of the patients. In 2% of the children, the disease can occur after 2 years of age (Kondratieva et al. 2013).

Respiratory symptoms and manifestations most commonly include the upper respiratory tract – chronic rhinitis / rhinorrhea (> 90% at > 8 months), nasal polyposis – 10–32%, sinusitis and involvement of the lower respiratory tract, with the early symptom being chronic cough (excruciating), whooping cough, nocturnal, wet rales, obstructive pulmonary disease (wheezing, tachydispnea) with bronchial hyperreactivity in 50% of cases and a positive bronchodilator test in some patients. Late respiratory symptoms include respiratory failure, exacerbation of respiratory distress, hypercapnia, pulmonary hypertension, cor pulmonale (Kapranov et al. 2011).

Children appearance with cystic fibrosis is characteristic – retardation in physical development, dystrophic changes of skin and hair, enlarged, often deformed chest, large abdomen (sometimes the occurrence of umbilical hernia), thin limbs with deformed extremities of the fingers with “drum sticks” and nails like “clock glass”. With severe disease, the processes in the lungs are constantly progressing, exacerbations occur more often, phlegm is purulent, with a rotten odor. Bronchial obstructive syndrome is severe and is associated with a narrowed lumen of the bronchi as a result of inflammatory changes in the bronchial wall and the accumulation of viscous secretions. In the evolution of the disease, the symptoms of hypoxia gradually increase – shortness of breath, cyanosis, tachycardia, the cor pulmonale clinic, respiratory and heart failure develops (Boykinov et al. 2003).

Pulmonary function tests

The pulmonary function is an important measure of disease severity and prognosis in cystic fibrosis patients. Spirometry was performed including measurement of FVC (forced life capacity), FEV1 (forced expiratory volume for 1 sec), FEF25-27 (forced expiratory flow between 25% and 75% of vital capacity) (Debray et al. 2006). FEV1 is the most proven clinical means of lethal prognosis and is the primary means of measuring the outcome in many clinical trials (Krasovsky et al. 2013). Other pulmonary function measurements should be performed when clinically indicated. Pulmonary function variables are usually expressed as a percentage of the predicted value calculated by regression equations obtained from a reference population (Kapranov et al. 2006). The role of lung function tests during infancy and early childhood remains unclear. Cross-infection with laboratory equipment for pulmonary

function has been a problem for a long time. When a patient exerts forced exhalation, droplets of oropharyngeal secretions that may contain bacteria or viruses are aerated (Petrova et al. 2011). It is recommended that lung function studies be performed in large, well-ventilated rooms with internal filters, using methods to reduce cross-infection and exclude patients according to their microbial status (Petrova 2008a).

Therapies applied

Treatment of cystic fibrosis patients is a difficult, not yet fully resolved, task. It is strictly individualized, pharmacological and non-pharmacological, requiring a complex therapeutic approach (Kerem et al. 2005). Complex therapy includes bronchodilators, NSAIDs, corticosteroids (Kapranov et al. 2008) respiratory rehabilitation in combination with general body massage.

The purpose of therapy is to control lung infections and improve nutritional status, early adequate behavior and delay definitive changes (Marinova et al. 2009). Evacuation of the bronchial secretion is achieved by oral mucolytic agents – N-acetylcysteine, Ambroxol and others. (Smyth 2006). Inhalation therapy with mucolytics is also used. Pulmozyme (dornase- α) is also included in the treatment of all patients with cystic fibrosis after the age of 5, modifying the abnormal viscosity and elasticity of the phlegm, improving the clearance of lung secretions (Kapranov et al. 2009). In patients with frequent haemoptysis, it is appropriate to discontinue dornase- α for at least the period of active bleeding and may be stopped as indicated (Rowe et al. 2005). In the absence of effect and increase in bronchial obstruction, a therapeutic bronchoscopy is performed. The choice of antibiotic for the treatment of respiratory symptoms is determined by the microorganisms isolated from the bronchial secretion of the patients (Kerem et al. 2005).

A small number of pathogens, initially *S. aureus* and *H. influenzae*, are found in the lungs of patients with CF, followed by chronic colonization with *P. aeruginosa*. Antibiotic courses are used for treatment. Even oral courses (but lasting 2–4 weeks) are sometimes sufficient. For more severe infections, intravenous administration is required (Strateva et al. 2009). Chronic *P. aeruginosa* infection is associated with faster progression and impaired pulmonary function. Therefore, at first colonization with *P. aeruginosa*, the behavior should be extremely aggressive for eradication – for example, 3 months oral administration of ciprofloxacin in combination with colistin inhalation (Saiman et al. 2002). In patients suffering from chronic *P. aeruginosa* infection, the growth pattern in the form of a biofilm means that the bacterium is never completely destroyed. Therefore, the therapeutic goal is chronic bacterial suppression, a strategy not commonly used in other patient groups (Gibson et al. 2003). However, intensive and early antibiotic therapy is used in many countries, which is effective in eradicating the first or intermediate

colonies of *P. aeruginosa* in all age groups. Certain bacterial species can cause cross-contamination among patients at CF centers or during social activities (Elborn 2006).

Sputum microbiological examination in patients with cystic fibrosis should be performed at least once every 3 months.

Kinesitherapy

One of the important components of treatment is kinesitherapy. Depending on their health status, patients with cystic fibrosis may perform locomotor activity in hospital under the guidance of paramedics (respiratory rehabilitation), at home (adapted physical activity), at school or in sports (Sugny et al. 2018). Its main purpose is to clear the bronchial tree from the viscous secretion. The tasks of kinesitherapy are to relax the respiratory muscles and the diaphragm, reduce the frequency of breathing and control the exhalation, facilitate the removal of the bronchial secretion and its evacuation by increasing the volume of bronchial oscillations and the speed of air flow, improving exercise mobility. In coughing and expectoration and training in compensatory diaphragmatic breathing (Becheva 2019).

Kinesitherapy is performed against the background of inhalation treatment (Kashirskaya et al. 2010). After inhalation, the child is placed in a drainage position, and by tapping on the chest and vibrating massage the nourishment of the diluted secretions is helped. Older children successfully use respiratory gymnastics. Aeration, inhalations (Kashirskaya et al. 2009), breathing postures, drainage (Boyer et al. 2018) are applied, accompanied by vibrations and tapping, chest shaking, relaxation massage, localized breathing, four-stroke breathing, diaphragmatic breathing, jumping trampoline, coughing and expectoration exercises, lower limb exercises, upper limb exercises, shoulder girdle, gluteal muscular exercises, abdominal and paravertebral muscles exercises, chest and abdominal exercises, chest mobilization, exercises proper body posture and walking (Bradley et al. 2006), balance exercises and coordination (Kashirsky et al. 2009). Continued courses of broad-spectrum antibiotics are required

to suppress chronic infection (Döring et al. 2000). Blood and plasma are poured as needed. Children are subject to dispensary supervision.

Complications

As the disease progresses, complications and conditions are observed that require immediate intervention. These include atelectasis, pneumothorax, pulmonary hemorrhage. In asymptomatic, limited pneumothorax detected by chance, the patient is actively observed for 24 hours (Elborn 2006; Smyth 2006).

If clinical symptoms do not appear and the changes do not progress radiologically, regular follow-up behavior may be initiated. In all other cases, drainage, possibly surgery (Petrova et al. 2009), pleurodesis, locally sclerosing agents, pleural abrasion (Hodson et al. 2007).

Conclusion

Cystic fibrosis is a complex disease that requires a holistic treatment approach. In recent years, medicine has progressed significantly with CF with a dramatic improvement in life expectancy (Papanov et al. 2015; Petkova et al. 2017). Nowadays, the expectation of children suffering from cystic fibrosis to survive more than 60 years comes with the cost of heavy, intensive daily treatment, which should not be interrupted (Petrova 2008b). Adequate day-to-day treatment is expensive and very time-consuming, with frequent hospital visits also making a negative impression (Tsvetkova et al. 2017). On the other hand, in connection with the prolonged life expectancy, there are more and more “unusual” manifestations of cystic fibrosis, which is a challenge for both the physician team and the patient (Mahadeva et al. 1998).

The establishment of specialized centers with trained and experienced professionals is essential in order to provide optimal patient care. These include frequent clinical evaluations, follow-up of complications, and early interventions for the treatment of patients with cystic fibrosis (Tsvetkova et al. 2015; Tsvetkova et al. 2016).

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