INTRODUCTION

Cystic fibrosis (CF) is one of the most prevalent autosomal recessive genetic disease, with an increasing incidence in the European population of 1/2500 births (Sinaasappela et al., 2002). The disease is caused by mutations in the CFTR (CF transmembrane conductance regulator) gene on chromosome 7, which encodes the CFTR protein in epithelial cells membranes. The absence or reduction of CFTR functionality leads to decreased chlorine transport and implicitly of water out of the cells. The increase in sodium resorption due to the lack of negative feedback from the epithelia sodium channel CFTR results in viscous mucus secretion and desiccation of exocrine gland tubular structures (Tamas et al., 2007; Cohen-Cymberknoh et al., 2013). After decades of empirical histological studies and biophysical measurements, it is now generally accepted that CF is a multifactorial disorder characterized also by chronic pulmonary infection, as well as by gastrointestinal, nutritional and other abnormalities (Lyczak et al., 2002). As we also mentioned in our previous papers (Moraru et al., 2015), life expectancy and quality of life of CF patients have significantly improved in the last few years. One of the explanations for this is improved nutrition and
improved understanding of the cellular defects in this disorder (Lyczak et al., 2002). It is believed that nutritional management, together with infectious aspects, are two fundamental parameters to be followed in this field of research (Scaparrotta et al., 2012), as besides the complex genetic background, most cases with cystic fibrosis present increased susceptibility to infections and changes in nutritional status. There is an important interaction between these two factors. Although infections can be prevented by rigorous procedures, such as early aggressive antimicrobial chemotherapy, this measure is not completely effective, since nutrition represents an important aspect, with early identification of nutrition issues playing a vital role in pulmonary health (Goodin, 2005).

We have sought to establish, within a period of 3 years, the relevance of infectious and nutritional mechanisms and their interactions in this disorder, as well as their relevance in the management of CF.

MATERIALS AND METHODS

Patients

A retrospective observational study was carried out with a group of 56 children with a positive diagnosis of CF. Children were diagnosed and hospitalized in the clinic II Pediatrics of the ‘St. Maria’ Clinical Emergency Hospital, during the period 2010-2013.

Data analysis

The observation sheets from the patient were used. Statistical processing was carried out using Microsoft Office Excel 2007 data collection tables and Epi Info 3.4.1.

RESULTS

We observed a pulmonary condition in 21.28% of subjects, while 28.57% presented digestive deregulation. Moreover, 12.5% developed a combined condition, and 10.71% presented important hepatic problems. Regarding additional gastroenterological, metabolic and nutritional aspects, we also observed dyslipidemia in 19.64% of cases, gastroesophageal reflux in 7.14%, and biliary lithiasis in 3.57% of patients. We observed that the infectious status in cystic fibrosis was dominated by respiratory infections (71.42%). Analysis of hypopharyngeal aspirates revealed the presence of the following pathogens (before the administration of any antibiotherapy): S. pneumoniae, H. influenzae, M. catarrhalis, P. aeruginosa, B. cepacia, S. aureus and Aspergillus. Pneumococcus was identified in 32 patients from the 45 investigated at the time of diagnosis (71.11%), H. influenzae in 6 patients (13.33%), Aspergillus in 3 (6.66%), and 2 positive cultures were recorded for M. catarrhalis (4.44%). Upper respiratory tract infections were noted as well, as well as gastric, urinary tract and cutaneous infections, however, their distribution was approximately symmetrical to the control group.

DISCUSSION

Our data confirm that nutritional and infections monitoring are vital to the understanding of cystic fibrosis mechanisms and its management. The increased viscosity of respiratory tract secretions determines their stasis, creating an environment conducive to infection. Activation of the immune response leads to increased granulocyte elastase, myeloperoxidase, immunoglobulin G, so that macrophages activation is responsible for lung tissue degradation (Cohen-Cymberknoh et al., 2013).

Importantly, the colonization process in the respiratory tract involves a series of genetic and phenotypic adaptations, including switching to a mucoid phenotype, and, over time, the formation of a biofilm on the respiratory mucosa that prevents the action of specific anti-infectious local agents and decreases antibiotics efficiency. The appearance is mediated by the GM1 receptor, which exhibits high affinity for opportunistic infectious agents (van de Weert et al., 2011).

McCubbin et al. (1996) have identified an association between infection with piocyanic bacillus and bronchiectasis development in children with CF, while
Kerem et al. (1990) have demonstrated that the children with chronic infection exhibit a significant decline in the expiratory volume/s as compared to the uninfected individuals. However, despite the fact that lungs of cystic fibrosis patients are often colonized or infected in infancy with *Staphylococcus aureus* and *Haemophilus influenzae*, which destroy the epithelial surfaces, leading to increased attachment and eventual replacement by *P. aeruginosa*, Lyczak et al. (2002) observed that adequate clinical studies to determine the role of these organisms in the pathogenesis of lung disease in cystic fibrosis patients have never been performed. It is generally accepted that chronic infection with *P. aeruginosa* is the main threat for the lungs of cystic fibrosis patients, which results in ultimate mortality of CF patients, although some anti-inflammatory therapies have been shown to produce clinical improvements, as demonstrated for example by Konstan et al. (1995). However, we will insist later on the relevance of the inflammation and anti-inflammatory procedures in CF. This is very important, especially since some authors have also proposed the idea that inflammation and infection can begin at an early age, even before classical symptoms appear. Of course, this could be extremely relevant for the management of this disorder, which is limited for now to airway clearance and various chemotherapy approaches. Also, a major problem is “antibiotic resistance” (Kumarasamy et al., 2010), which influences the course of CF, as an increased percentage of patients will eventually die of chronic lung infection with multiresistant *P. aeruginosa* (Lyczak et al., 2002).

Nutritional aspects are very important in the management of CF, since malnutrition is an important characteristic of this disorder (Lai et al., 2008). There is also an important interaction between these processes, as patients with CF must consume energy in order to meet increased needs required for increased breathing and altered digestive absorption (Goodin et al., 2005). Thus, while pulmonary function is strongly linked with adequate nutrition and weight gain, monitoring weight and pulmonary function are fundamental aspects in understanding the mechanisms of CF; they are also very important parameters of improved management of this disorder. The early identification of nutrition and infectious risk factors is an important aspect of effective and timely management interventions that can have a positive impact on the outcome of the patients. In addition, nutritional aspects have previously been reported to be associated with abdominal pain (Littlewood et al., 2005). This could be important, considering that our group also previously reported the relevance of pain perception in CF management (Moraru et al., 2015).

The nutritional deficits from CF can result in serious metabolic dysfunction, including diabetes (Toarba et al., 2014; Serban et al., 2014), which is considered to be a separate clinical entity from diabetes types 1 and 2 diabetes, and it requires a slightly different management approach (Goodin et al., 2005).

Many authors have described an intense inflammatory response in CF, with increased levels of neutrophils, macrophages and inflammatory mediators, such as tumor necrosis factor-α and interleukins 1 and 8 (Yu et al., 2000; Hart et al., 2002). Considering the well-known correlation between decreased levels of antioxidants and increased inflammatory response (Kobrosly et al., 2010; Stefanescu et al., 2012), the oxidative stress status is important in the context of inflammation in CF. Galli et al. (2012) showed decreased levels of vitamin E, carotenoids, coenzyme Q-10, glutathione and polyunsaturated fatty acids in CF patients. Moreover, some oligoelements related to the oxidative stress status, such as Se, Cu and Zn (Guzman et al., 2010) were found to be affected in CF (Yankaskas et al., 2004). Kench et al. (2015) demonstrated a significant correlation between nutrition, exercise and CF, as our group also previously showed an important correlation between physical exercise and oxidative stress (Trofin et al., 2014).

REFERENCES


Moraru, E., Diaconu, R., Anton, E., Bozomitu, L., Anton, C., Cio-
Guzmán, D.C., García, E.H., Brizuela, N.O., Jiménez, F.T., Mejía,
and select oxidative stress markers in the presence of oligoelements
Hart, C. and C. Winstanley (2002). Persistent and aggressive bacte-
Kench, A. and H. Selvadurai (2015). Diet, food, nutrition, and
exercise in cystic fibrosis. Diet and Exercise in Cystic Fibro-
sis. 1, 317-332.
functions and clinical course in patients with cystic fibrosis
after pulmonary colonization with Pseudomonas aerugi-

Kobrosly, R. and E. van Wijngaarden (2010). Associations between
immunologic, inflammatory, and oxidative stress markers
with severity of depressive symptoms: an analysis of the
2005-2006 National Health and Nutrition Examination
Survey. Neurotoxicology. 31, 126-133.
of high-dose ibuprofen in patients with cystic fibrosis. N.
Kumarasamy, K.K., Toleman, M.A., Walsh, T.R., Bagaria, J., Butt,
F., Balakrishnan, R., et al. (2010). Emergence of a new anti-
biotic resistance mechanism in India, Pakistan, and the
UK: a molecular, biological, and epidemiological study.
Lai, H. and S. Shoff (2008). Classification of malnutrition in cys-
tic fibrosis: implications for evaluating and benchmarking
Med. 88, 9-17.
Lyczak, J.B., Cannon, C.L. and G Pier (2002). Lung infections
associated with cystic fibrosis. Clin. Microbiol. Rev. 15,
194-222.
(1996). Pseudomonas infection appears to precede the
development of bronchiectasis on chest CT scan in young
Moraru, E., Diaconu, R., Anton, E., Bozomitu, L., Anton, C., Cio-
ifica, A., et al. (2015). Understanding the relevance of pain,
depression and anxiety-like manifestations in the manage-
ment of cystic fibrosis. Arch. Biol. Sci. 2015, DOI: 10.2298/
ABS140228071M
Scaparrotta, A., Di Pillo, S., Attanasii, M., Consilvio, N.P.,
Cingolani, A. and D. Rapino (2012). Growth failure in
25, 393-405.
Serban, L., Toarba, C., Hogas, S., Covic, A., Ciobica, A., Chimita,
R., et al. (2014). The relevance of body mass index in the
cognitive status of diabetic patients with different alcohol
Sinaasappel, M., Sternb, M., Littlewoods, J., Wilceu, S., Stein-
kampd, G. and H. Heijermarnd (2002). Nutrition in pa-
Fibr. 1, 51-75.
Ste
descu, C. and A. Ciobica A. (2012). The relevance of oxida-
tive stress status in first episode and recurrent depression.
Tamas, L., Popa, I., Pop, L., Anghel, A., Zagorca, P. and C. Mar-
ian (2006). Genetic analysis of CFTR Mutations in cystic
Toarba, C., Serban, L., Covic, A., Padurariu M., Ciobica, A., Chi-
rita, R. et al. (2014). Establishing the connections between
alcohol intake, cognitive functions and type 2 diabetes,
Trofin, F., Chirazi, M., Hanceriu, C., Drosescu, P., Grădinariu, G.,
Vorniceanu, A., et al. (2014). Pre-administration of vita-
mn C reduces exercise-induced oxidative stress status in
Trofin, F., Ciobica A., Ceociparci, D., Chirazi, M., Hanceriu, C.,
Trofin, F. et al. (2014). Increased oxidative stress in rat after
9, 722-728.
van de Weert-van Leeuwen, P.B., Slieker, M.G. , Hulzebos, H.J.
and D. Rapino (2012). Chronic infection and inflammation affect exercise capacity
Yankaskas, J.R., Marshall, B.C. and B. Safian (2004). Cystic Fibro-
sis Adult Care consensus Conference Report. Chest. 125,
1-39.
compromised Pseudomonas aeruginosa clearance in the
malnourished mouse model of respiratory infections in

Gastroenterol. 1, 76-94.
Guzmán, D.C., García, E.H., Brizuela, N.O., Jiménez, F.T., Mejía,