CYSTIC FIBROSIS SOCIAL ASPECTS IN UKRAINE

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Abstract. Cystic fibrosis (CF) is a genetically determined pathology. It belongs to the orphan diseases group. CF is an important social problem not only in Ukraine but also all over the world. The main social problems of CF patients in Ukraine are insufficient and late diagnosis of the disease, lack of genetic passport of most patients, severe disease course with psychological problems in the family, lack of access to high-tech treatment algorithms (gene therapy, lung transplantation), short life expectancy and difficult financial position. In recent years, there have been the number of positive changes in the treatment and management of CF patients in Ukraine. Implementation of international standards of treatment and care is the only way to improve the life quality of CF patients.

Key words: cystic fibrosis, social problem, medical and psychological care.

Introduction. Cystic fibrosis (CF) is a genetically determined pathology and belongs to the orphan diseases group [1]. CF is an important social problem not only in Ukraine but also all over the world. CF was a post-mortem diagnosis even in the 19th century, and most patients died in the first year of life. However, the average life expectancy of CF patient is about 42-47 years in developed countries now [3, 4].

Lesions of the respiratory system are on the first place, and lesions of the gastrointestinal system are on second place among the death causes in patients with CF [5]. Modern algorithms of the basic therapy using demonstrates positive treatment results. Vital indicators are at the compensatory level for a very long time and, even the whole life of the patient with CF in the conditions of the full range of prescribed medications receiving [6, 7].

Everyone has the rights to a quality and long life. The modern medicine task is to ensure not only physical but also psychological and social well-being. Therefore, it’s

very important to have a favorable psychological and social state of health, along with high levels of physical being. This is a very important factor especially for a patient with CF.

Severe multiorgan disease, high medicines cost, misunderstandings in society cause the psychological disorders development in patients with CF and their families, including depressive and anxiety disorders [8]. This can reduce the positive therapeutic effect of quality drug treatment greatly. Therefore, patients with CF need not only quality medical care, but also psychological and social care too.

Purpose. To improve medical care for patients with CF.

Tasks:

1. To study the clinical and paraclinical features of children with CF.

2. To analyze the main social problems of a patient with CF.

Materials and methods. The research was conducted in the pulmonology department of the Kharkiv Regional Clinical Children's Hospital No 1 in 2015-2018. Clinical and paraclinical examinations of patient with CF were carried out according to the Order of Ministry of Healthcare of Ukraine of of July, 15 2016 No. 723 "On approval of the unified clinical protocol of primary, secondary (specialized) and tertiary (highly specialized) medical care “Cystic fibrosis”, Order of Ministry of Healthcare of Ukraine of January, 29 2013 No. 59 “On approval of unified clinical protocols of medical care for children with diseases of the digestive system”.

The study was conducted with respect to human rights in accordance with the legislation in force in Ukraine, in compliance with international ethical requirements and didn’t violate ethical norms in science and standards for conducting biomedical research.

The results were processed by variation statistics methods with IBM SPSS Statistics 23.

Results. The literature review and our own research revealed a number of social problems of patients with CF. The first problem is insufficient of CF patients identification. Yes, CF is a frequent autosomal recessive disease. Each 25th European is a carrier of the CF gene [1]. Every year 45-50 thousand children with CF are born in the world, and there are tens of millions of heterozygous carriers [1, 2]. The frequency of CF in populations is different. The prevalence of CF is 1:2500-3000 newborns among Caucasians on average in the world, in Ukraine – 1:2300 [8-11]. According to other data, the results of neonatal screening for CF in 2013-2014

established the average prevalence of CF in Ukraine 1:8400 [8]. The exact frequency of CF in Ukraine has not been established. According to the Ukrainian State Statistics Service, the population of Ukraine was 42,269,802 people on January 1, 2018 [12]. We should have more than 5 thousand CF patients as for CF prevalence on screening programs. At the beginning of 2018, 827 CF patients were registered in Ukraine, including 615 children for actual information [13]. There are 47 children with CF registered in the Kharkiv region, this index is a low number compared to other European cities.

And the insufficient number of patients at the dispensary examination means that patients either die at an early age, or do not receive therapy at all, or are treated for false illnesses.

The second social problem is the late CF diagnosis in Ukraine. It also has medical, scientific and economic aspects. The study is presented by 47 children with CF. The CF diagnosis was established on the basis of clinical and paraclinical signs and confirmed by the results of the pilocarpine test. It was found that for the Kharkiv region CF diagnosis median age was 8.0 (3.0; 24.0) months. But the diagnosis of CF was noted at 7, 9 and even 15 years old. The standard for CF diagnosis in the world is neonatal screening. But in Ukraine, screening reveals a small percentage of patients due to the difficult economic situation.

The following social problem is the high mortality of children with CF in Ukraine. There are no official statistics (the cause of death in official records indicates respiratory diseases), but some authors report 12-14 years average life expectancy of a patient with CF in Ukraine. Patients with this pathology can live up to 40-50 years and have the opportunity to have a high life quality due to modern medical technologies. Three fatal cases (at the age of 17 years, 4 years, 2 years old) were noted during the 2015-2018 period in the Kharkiv region. Only in 2015 in the Kharkiv region first child was transferred from the pediatric service to the therapeutic service of medical care upon reaching the age of 18 years old.

The next social problem of CF in Ukraine is the lack of a complete genetic study to identify gene mutations. The main factor in the CF pathogenesis is a mutation of the transmembrane regulator of CF gene (CFTR). The CFTR gene is located in the long arm of chromosome 7, contains 27 exons and consists of 250,000 nucleotide pairs [2]. The distribution and frequency of CFTR gene mutations vary widely across countries and ethnic groups. Although 2002 mutations have been described in

the CFTR. The most common mutation is the deletion of three nucleotides in the 10s exon, which leads to the loss of the phenylalanine residue at the 508 position of the protein molecule (F508del). This is almost 70% of all cases. But along with F508del mutation, there are other mutations that cause a different clinical picture (in the Mediterranean basin – G542X, N1303K, G551D; Northern and Central Europe – G551D, R117H; Middle East – N1303K, W1282X, 3120+1G>A; North America – 3120+1G>A; Canada – M1101K, Russia – CFTRdele2,3(21kb), 3849+10kbC-T, W1282X etc.). Only five other mutations (G542X, G551D, W1282X, N1303K, R553X) account for more than 1% of all CF cases. All other mutations are rare, and even exceptional, often found once in a single family [14].

There are 6 classes of CFTR mutations depending on the dysfunction of the transmembrane regulator:

1) violation of protein synthesis (G542A, W1282X, R553X, 621+1C>T, 2143delT, 1677delTA);

2) violation of protein maturation (F508del, N1303K, S549I);

3) violation of the chlorine channel regulation (G551D, G1244E, S1255P);

4) violation of the chlorine channel conductivity (R334W, R347P, R117H);

5) reducing the amount of functional protein (3849+10kbC>T, A455E, IVS8(5T), 1811+1,6kbA>G);

6) reducing the protein stability (S1455X) [14].

The world has developed gene therapy for some mutations. For example, on December 29, 2014, Vertex Pharmaceuticals Incorporated Company announced the approval of the Food and Drug Administration for the use of Kalideco (Ivacaftor) for the treatment of CF patients at the age of 6 years and older who have an R117H mutation in the CFTR gene. Until now, Kalideco has been approved for use in patients with G551D, G178R, S549N, S549R, G551S, G1244E, S1251N, S1255P, or G1349D CFTR gene mutations in the United States and Europe, and in Canada even with the G970R mutation. In Ukraine, it’s impossible to carry out a large number of CFTR gene mutations, therefore delF508 mutation is most often detected. The question of CFTR gene mutation determining is paid from family of CF patient budget and is quite expensive and unattainable. This problem is remained unresolved.

The most common CFTR gene mutation the in the Kharkiv region is delF508 (90.62 ± 5.36%) for children with CF, and in one case there are N1303K, S1196X, del21kb, 711 + 1G> A, Ratio132,721, Arg334Trp, W1282X mutations. The "genetic

passport" lack of a patient with CF doesn't allow them to enter the European register of CF patients, receive gene therapy, to be able to participate in international clinical trials of new drugs for the treatment of CF.

The following social problem of patients with CF in Ukraine is the severity of the disease. It causes great restrictions in the social life of the family. A cohort of children with CF in the Kharkiv region is characterized by a significant percentage of severe damage to the respiratory and gastrointestinal systems. This affects the psychological state of the patient and requires close attention, further development and improvement of measures of medical, psychological and social care for CF patients. CF manifestation was characterized by more frequent gastrointestinal signs (70.22 ± 7.78)%. The incidence of lung fibrosis was found in (76.59 ± 5.42)% of children (average age 5.85 ± 0.54 years), bronchiectasis – (40.42 ± 6.58)% (average age 7.61 ± 0.83 years), liver lesions – (85.11 ± 4.88)% (including cirrhotic changes – (17.02 ± 15.98)%, average age 5.82 ± 0.86 years), pancreatopathy – (91.48 ± 4.52)% (average age 4.36 ± 1.17 years), which are negative factors in the CF course.

Against the background of the development and improvement of medical care, the issues of psychological care are still open. The lack of help from a psychologist is a significant shortcoming and a necessary component for the CF patients life quality.

The other social problem in the treatment of CF patients is the lack of access to modern high-tech treatments. Big step has been made in patients supporting. The state provides these patients with basic drugs (oral and intravenous antibiotics, hepatoprotectors, enzyme replacement and mucolytic therapy). A basic therapy cost per month is about 80 thousand UAH, not including exacerbations episodes. But the issue of lung and liver transplantation for CF patients in Ukraine is still unclear, and any patient doesn't receive gene therapy. An important aspect of successful treatment and prevention of complications from the respiratory and gastrointestinal systems is the kinesitherapy exercises, which is currently not sufficiently developed in Ukraine.

The social problems of CF patients are exacerbated by the difficult financial situation of most families. A patient with CF needs constant supervision at home, so in most cases one of the parents (usually the mother) or grandmother doesn't work. The significant proportion of children with CF (38.3%) are brought up in single-parent families, where the mother must fully provide for a child with severe multiorgan disease that is constantly progressing. Patients in this category are

disabled in childhood. They receive social assistance payments of the second or third group, mostly in the amount of 1,710.0 UAH, which does not even cover the subsistence level (2018.0 UAH).

Each of these aspects affects the quality and life expectancy of a patient with CF and needs to be addressed.

Conclusions. The main social problems of CF patients in Ukraine are insufficient and late diagnosis of the disease, lack of genetic passport of most patients, severe disease course with psychological problems in the family, lack of access to high-tech treatment algorithms (gene therapy, lung transplantation), short life expectancy and difficult financial position.

In recent years, there have been the number of positive changes in the treatment and management of CF patients in Ukraine. Implementation of international standards of treatment and care is the only way to improve the life quality of CF patients.

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