SPIROMETRIC ASSESSMENT IN A LOT OF PATIENTS WITH CYSTIC FIBROSIS, FOLLOWING IMPLEMENTATION OF A PROGRAM FOR INCREASING OUTPATIENT USUAL PHYSICAL ACTIVITY LEVEL

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Abstract

Objectives. Cystic fibrosis (CF) is the most common autosomal recessive genetic disease of the caucasian race, with progressive and potentially fatal evolution. The objective of this study was to present the evolution of spirometry index in a group of patients with CF, a year after the implementation of a sustained program of outpatient physical activity. *Material and method.* The study design was prospective and included a group of 52 children, adolescents and young adults diagnosed with CF, found in the records of the 2nd Pediatric Clinic of Emergency Hospital from Craiova, Children's Emergency Hospital "Maria Sklodowska Curie" and the Institute for Maternal and Child, "Alfred Rusescu" (IOMC), both from Bucharest. Spirometry records (VC, FEV1, FEF25-75 and FEV1/VC) were performed at two different times: before and after implementation of sustained physical activity at home for one year. By age, patients were divided into two groups: 6-12 years and more than 13 years. For statistical processing we used the Student test. *Results.* Although all spirometric values increased after implementation of the physical activity program in both age groups, the difference was statistically significant only for FEV1, in the age group 6-12 years ($p = 0.016$). Also, the lower age group, we observed a decrease in the number of patients with altered lung volumes and flows. *Conclusions*. Increased level of the usual physical activity in patients with CF has led to slow decline in lung function and spirometry indices showed a slight improvement or remained stable throughout the study. Increase in mucociliary clearance, with significant decreases bronchial obstruction (assessed by the value of FEV1) in patients lower age suggest the need to implement such a program as early as possible to prevent or at least slow the progression of lung disease, for longer period of time, and reduce complications.

Key words: Cystic fibrosis, spirometry, physical activity

Introduction

Cystic fibrosis (CF) is the most common autosomal recessive genetic disease of the caucasian race, with progressive and potentially fatal evolution. It is characterized by generalized dysfunction of exocrine glands, mucous and serous (sweat glands in this case), primary anomaly being CF gene (5, 14, 27).

Although, clinical and evolutionary context is highly polymorphic, translated by numerous phenotypic aspects, a single gene is responsible for this disease.

Defective gene, described in 1989, is located in the long arm of *chromosome seventh* (2, 16). The consequence of genetic abnormality is blocking or malfunction of chloride channels at the cellular level, and thus the sodium chloride and water. As a result, the secretions from the majority of organs and systems will be content, poor water, viscous, adherent to canaliculelor excretory epithelia, difficult to eliminate outward. The accumulation of these causes in time impaired organs and their destruction (lung, pancreas, liver, gall bladder, gastro-intestinal tract, reproductive organs). Sweat secretion from the skin has a very high concentration of salt. As a result, the clinical picture is highly polymorphic but major clinical signs are suffering chronic respiratory (*chronic obstructive pneumopathy*), chronic diarrhea or steatorrhea, and stationary or weight loss despite a good appetite and adequate nutritional intake (1, 27).

Altough CF is a complex and multisystem disease, respiratory distress is the main element in terms of patient outcome; 85% of patients with CF die of the pulmonary disease (3, 14, 26).

The goal of therapy for respiratory distress is to limit the extension of the pulmonary lesions and to rarefy exacerbations (13). In the past, the main purpose of pulmonary rehabilitation therapy in CF was eliminating excessive secretions, and thus reduce symptoms. Modern rehabilitation treatment is used today with a more comprehensive purpose. It is a pro-active treatment to prevent or at least trying to slow the progression of the pulmonary disease (4, 9).

Exercise and physical activity are an essential part of treatment of respiratory distress for all patients with CF, along with aerosol therapy and airway clearance techniques (ACTs) (9, 13, 15).

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Increasing regular physical activity is accompanied by slowing the pulmonary function decline and constant participation in various physical activities may increase the compliance in the long term (12, 23). Short-term studies have shown an improvement in *lung function* and wellbeing of these children as a result of sustained physical activity programs in outpatient (20).

This study provides evidence for the earliest possible implementation of a sustained program of usual physical activity at home, as part of therapy in patients with CF. The study presents spirometry indices: *vital capacity* (VC), *forced expiratory volume in one second* (FEV1), *forced expiratory flow between 25 and 75% of forced vital capacity* (FEF25-75) and *airway permeability index* (FEV1/VC report), in a group of patients with CF, after implementing an outpatient program to increase the level of physical activity for one year.

Material and method

The study design was prospective, multicenter, and included a group of 52 children (older than 6 years), adolescents and young adults diagnosed with CF, which are found in the records of the 2nd Pediatric Clinic of Emergency Hospital from Craiova, Children's Emergency Hospital "Maria Sklodowska Curie" and the Institute for Maternal and Child, "Alfred Rusescu" (IOMC), both from Bucharest. We included patients with definite diagnosis of CF, based on characteristic anamnestic - clinical criteria and confirmed by two positive sweat tests and in some patients by the genetic test (1, 9, 13, 27), without acute respiratory failure, chronic pulmonary heart (CPC) or the coexistence of decompensated heart disease, independent of respiratory disease but exacerbated by it. Any patient in the study had no contraindications to perform airway clearance techniques (ACTs). Were included only patients who did regular treatment and were able to perform spirometry tests. General characteristics of patients, weight (W), size (S) and body mass index (BMI) were recorded in case report forms and those values (expressed in kg, m and kg / m²) were converted into number of standard deviations (SD) compared with mean values correlated with the age and gender (Z score).

Spirometry tests were conducted in laboratories functional exploration of the three medical units who studied for the treatment of CF. Has been recorded vital capacity (VC), forced expiratory volume in one second (FEV1) and forced expiratory flow between 25 and 75% of forced vital capacity (FEF25-75) and the report FEV1/VC (airway permeability index). During spirometry test was performed three forced expiration maneuvers were recorded the best results. All values were expressed in liters and percentage of predicted for age, height and sex. Spirometry records were analyzed in two different moments of time: before (the beginning of 2009) and one year after implementation of an outpatient program to increase physical activity level (end 2009). We considered the lower limit of normal the 80% of predicted for VC, FEV1 and FEF25-75 and 0.75 for the ratio FEV1/VC (6, 26).

All enrolled patients received a comprehensive treatment, according to management guidelines in CF (1, 9, 13, 27): dietary and hygiene measures, drug treatment (by systemic antibiotic, anti-inflammatory and antifungal therapy) and aerosol therapy (antibiotics , mucolytics, corticosteroids and bronchodilators), depending on the specifics of each case. In terms of respiratory physiotherapy, airway clearance techniques (ACTs) were given daily, two sessions per day, morning, before a meal and evening, two hours after eating, before going to bed, each session lasting 30 minutes. All patients performed *active cycle of breathing techniques* (ACBT): *controlled breathing* (CB), *thoracic expansion exercises* (TEE) and *forced expiratory technique* (FET), performed in different *postural drainage positions* (depending on the lobe or lung segment drained), which alternated with *percussion*, *vibration* and *assisted cough*. Number of postural drainage positions was limited to three for the each session. Once a patient with CF was placed in a *postural drainage positions*, the person assisting him performed chest wall percussion, for a period of 3-5 minutes for each position, followed by vibration on the same segment, for approximately 15 seconds (or during the five exhales). Then, the patient was encouraged *to cough* or perform *huff* for elimination of excess mucus. *Modified postural drainage positions* were indicated in patients with gastroesophageal reflux (GOR).

Since 2009, all the 52 patients have been included in an outpatient exercise program to increase the usual physical activity level. Although a correct prescription for such a program would have to start from the results of the *exercise testing* (17), this test could not be performed due to lack of adequate equipment, including blood gas analysis, lack of compliance for patients or carers in some cases, the absence of a full medical team to allow safe testing conditions.

According to the literature, practice has shown that the vast majority of patients with respiratory disease do not need an exercise testing to be prescribed them a program of physical activity (18, 19). Medical history of the different types (respectively degree) of physical effort that these patients are made daily in the normal activity, and on aspects of how the patient supports this efforts, provided us sufficient data to recommend complete safety an outpatient exercise program for patients from this study. Thus, depending of the intensity of exercise supported by the patient and of the patient age, we recommended the following types of physical activity, according to specialized studies (22, 28):

- moderate physical activities: walking briskly - about 3 ½ miles (5.6 km) per hour, hiking, gardening/yard work, dancing, golf (walking and carrying clubs), bicycling - less than 10 miles (16 km) per hour, weight training (general light workout);
- vigorous physical activities: running/jogging - 5 miles (8 km) per hour, bicycling - more than 10 miles (16 km) per hour, swimming (freestyle laps), aerobics, walking very fast - 4 ½ miles (7.2 km) per hour, heavy yard work, such as chopping wood (for teens and adults), weight lifting (vigorous effort), basketball (competitive).

Methodological indications that I gave patients were general. Patients have total freedom in choosing the methods of training and technique work itself, thus increase compliance, as recommended in the literature (18, 19). I insisted on the necessity of making physical activity at least 3 - 4 times a week, lasting at least 30 minutes, in conditions of unpolluted air, pleasant landscape, not excessive meteorological conditions. I explained to the patient and their family that walks slowly, like shopping and light housework are not useful for achieving goals. To prevent any adverse effects, patients and their families have been trained on **safety measures** to be taken into account during physical activity.

- **Additional therapy to exercise:** proper nutrition program, the use of bronchodilators (for patients with bronchospasm due to effort), additional oxygen intake (for patients who have hypoxia during exercise).
- **Adequate hydration** with liquids with a safe level of electrolytes, for best absorption of ions and fluid in the blood (similar to the fluids consumed by athletes of performance), when their physical activity in hot weather conditions or excessive moisture.
- **Appropriate clothing and footwear**: reflective vest (if the the exercise is executed at night, on the road), protective helmet (cycling), etc.
- **Stop the physical activity event**: the appearance or increase in dyspnea, a discomfort, appearance or increase in noisy breathing, the wheezing, tachypnea installation (over 30 breaths per minute), heart rate above 110-120 beats per minute or appearance of arrhythmias, the occurrence of constrictive chest pain or precordial pressure.

To analyze the results the 52 enrolled patients were divided into two age groups: **6 to 12 years** and **older than 12 years** (≥ 13 years).

Date collected in the two time points were recorded in a database made in **Microsoft Access**. Results were expressed as number of cases (percentage) and mean ± SD (standard deviation). For the statistical analysis we used the **Student test**. Statistical significance was set at $p < 0.05$ for significant difference and $p < 0.001$ for highly significant differences.

Results

The lot included 52 patients, 23 (44.23%) female and 29 (55.77%) male. The average age of patients was 12.2 ± 4.7 years (range 6-29 years). Of the 52 patients, 26 were diagnosed with CF before the age of 2 years (51.92%), 14 patients between 2 and 6 years (26.92%), to 8 patients (15.38%) diagnosis was established between 6 and 12 years and to 3 patients (5.76%), CF diagnosis was made during adolescence. The average age at established diagnosis of CF was 3.5 ± 4.3 years (**Table 1**).

Of the 23 female patients, 12 belonged to 6-12 years group and 11 patients ≥ 13 years group. Male patients were divided into two groups according to age, as follows: 16 in 6-12 years group and 13 in the group ≥ 13 years (**Figure 1**).

Table 1 – General characteristics of patients with cystic fibrosis.

Variable	n=52
Gender (female/male), n	23/29
Age (years), mean±SD	12.2±4.7 (range: 6 – 29)
Diagnostic age (years), mean±SD	3.5 ± 4.3 (range: one month – 16 years)
BMI (Z score), mean±SD	-1.8±1.4
Weight (Z score), mean±SD	-1.9±1.1
Height (Z score), mean±SD	-1.3±0.9

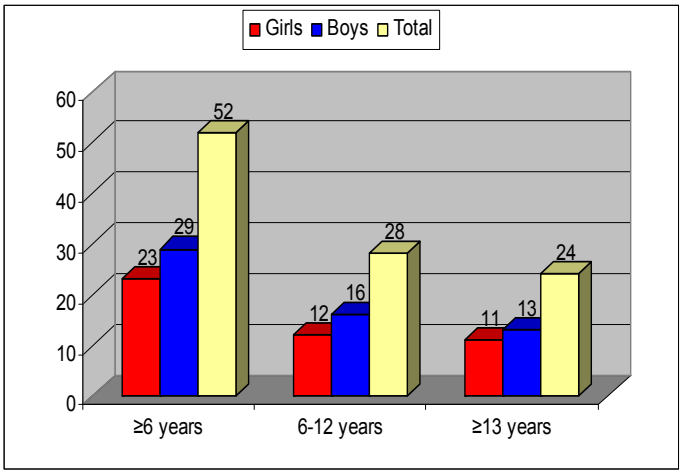

Figure 1. Distribution of the group depending on age and gender.

Table 2 shows the average of spirometry index (VC, FEV1, FEF25-75 and FEV1/VC) before and one year after the implementation of the physical activity program at home, in the age group 6-12 years. Although after one year of treatment was an average increase of all spirometry index, the increase was statistically significant only for FEV1 (p = 0.016) at this age.

I obtained similar results for girls group 6-12 years old: average spirometry indices increased to a year of treatment but the difference was significant only for FEV1 (p = 0.011) (**Table 3**).

For male patients of age group 6-12 years, we have achieved a significant increase in VC (p = 0.008) and highly significant for FEV1 (p = 0.00001), FEF25-75 (p = 0.0002) and airway permeability index (p = 0.0001), a year after the implementation of physical activity program at home (**Table 4**).

Table 2. Spirometry indices at one year after the implementation of sustained physical activity at home, for the age group 6-12 years.

Variable	Initial value (mean±SD)	Final value (mean±SD)	Student test p
VC (percent of predicted value)	69.84±19.33	76.21±18.02	0.2075
FEV1 (percent of predicted value)	55.60±23.74	70.36±20.55	**0.0160**
FEF25-75 (percent of predicted value)	50.31±30.04	59.91±25.59	0.2036
FEV1/VC	0.71±0.12	0.74±0.11	0.3393

Table 3. Spirometry indices at one year after the implementation of sustained physical activity at home for female patients of the age group 6-12 years.

Variable	Initial value (mean±SD)	Final value (mean±SD)	Student test p
VC (percent of predicted value)	68.22±20.13	70.68±19.67	0.06126
FEV1 (percent of predicted value)	49.41±23.26	60.45±19.54	**0.01116**
FEF25-75 (percent of predicted value)	42.52±27.50	48.90±22.00	0.14107
FEV1/VC	0.67±0.13	0.68±0.11	0.28361

Table 4. Spirometry indices at one year after the implementation of sustained physical activity at home, for male patients of the age group 6-12 years.

Variable	Initial value (mean±SD)	Final value (mean±SD)	Student test p
VC (percent of predicted value)	70.98±18.80	80.24±15.69	**0.00833**
FEV1 (percent of predicted value)	60.11±21.54	78.11±16.28	**0.00001**
FEF25-75 (percent of predicted value)	53.31±29.92	66.66±23.98	**0.00023**
FEV1/VC	0.73±0.10	0.77±0.09	**0.00011**

Regarding patients older than 12 years, the results are presented in **Table 5.** Although differences in flow and lung volumes values are not significant for two moments of time when records were made (p> 0.05), there is still a growth of averages spirometry indeces and airway permeability index (FEV1/VC) at one year after the start of outpatient physical activity program.

Table 5. Spirometry indices at one year after the implementation of sustained physical activity at home, for the age group ≥ 13 years

Variable	Initial value (mean±SD)	Final value (mean±SD)	Student test p
VC (percent of predicted value)	59.41±25.04	62.54±23.83	0.6595
FEV1 (percent of predicted value)	51.85±25.48	56.61±25.98	0.5249
FEF25-75 (percent of predicted value)	38.42±25.65	44.59±28.20	0.4319
FEV1/VC	0.65±0.14	0.66±0.14	0.9342

Analyzing the evolution of respiratory parameters by gender, in age group ≥ 13 years, to one year of treatment, there is no significant difference between the two moments of assessment, both for female patients and male patients ($p > 0.05$) (**Table 6 & Table 7).**

Regarding the number of patients with changes in pulmonary function tests for the group 6-12 years, we obtained a decrease in the number of patients with changes in VC, FEV1 and the FEV1/VC report. Number of patients with changes in FEF25-75 remained the same, to a year of treatment for this age group. For the age group ≥ 13 years, we have obtained only low numbers of patients with changes in FEF25-75, for other indices spirometry (VC, FEV1 and FEV1/VC) the number of patients with altered functional tests increased with a patient, to one year after starting the program (**Table 8**).

Table 6. Spirometery indices at one year after implementation of sustained physical activity at home, for female patients of the age group ≥ 13 years.

Variable	Initial value (mean±SD)	Final value (mean±SD)	Student test p
VC (percent of predicted value)	52.62±20.54	52.37±21.11	0.91510
FEV1 (percent of predicted value)	50.23±28.62	48.68±24.76	0.68367
FEF25-75 (percent of predicted value)	33.95±22.20	37.47±24.35	0.48410
FEV1/VC	0.64±0.17	0.62±0.15	0.42476

Table 7. Spirometry indices at one year after implementation of sustained physical activity at home, for male patients of the age group ≥ 13.

Variable	Initial value (mean±SD)	Final value (mean±SD)	Student test p
VC (percent of predicted value)	62.78±29.80	68.00±25.22	0.27856
FEV1 (percent of predicted value)	52.24±27.30	59.10±28.99	0.07738
FEF25-75 (percent of predicted value)	43.55±31.67	48.84±34.51	0.07725
VC/FEV1	0.66±0.14	0.68±0.15	0.18455

Table 8. Distribution of patients with impaired lung function, depending on age, in both times of assessment.

Variable	**The age group 6-12 years** -initially-	**The age group 6-12 years** -to one year of treatment-	**The age group ≥13 years** -initially-	**The age group ≥13 years** - to one year of treatment -
	n=28		**n=24**	
VC<80% of predicted value	13 (46.42)	11 (39.28)	18 (75.00)	19 (79.16)
FEV1<80% of predicted value	22 (78.57)	20 (71.42)	19 (79.16)	20 (83.33)
FEF25-75<80% of predicted value	13 (46.42)	13 (46.42)	22 (91.66)	21 (87.50)
FEV1/VC<0.75	19 (67.85)	18 (64.28)	18 (75.00)	19 (79.16)

Values are expressed as number of cases, n (%)

Discussions

There is many evidence of the benefits of daily physical activity, on the lung function. *Zach M et al* argue in this and adds that these benefits are lost very quickly when physical activity program is discontinued, it is not done regularly (25). Other studies show improvement in lung function after outpatient physical activity program. Thus, *Schneiderman-Walker J et al*, researchers randomized-controlled study on a group of 72 children and adolescents with CF, who have consistently performed an outpatient exercise program for three years, showed that this program, which increased to normal physical activity level was accompanied by a slower decline in VC and FEV1 and improved the wellbeing of these children (20). *Wilkes DL et al* they also get arguments in support of the recommendation to increase regular physical activity levels at patients with CF (23).

Although most patients of this study (52%) had early onset of symptoms and were diagnosed with CF in good time before the age of two years, and despite the small sample size, we chose to divide the group of 52 patients in two age groups because progression of the disease varies according by age. More, it is known that the health of these patients is less impaired in young ages, when are less extensive lung lesions (21).

In the group 6-12 years, the number of patients with changes in lung volumes and flows decreased and respectively remained the same for air flow indicates narrowing of small airways (FEF25-75). In addition, there was a significant increase in FEV1 after treatment applied,

while the average for other spirometry indices (VC, FEF25-75 and FEV1/VC) increased but not significant for female patients of this category age. Better results were obtained on lung function in male patients of this age castegorie. For them, the increase of usual physical activity level has led to significant improvement in VC and highly significant improvement for pulmonary flows recorded and airway permeability index. According with other studies (11), we showed that as a result of treatment applied correctly, lung function and lung development can be improved until the age of 12 years. Knowing that FEV1 is a prognostic and follow up analyting factor (8, 24), its significantly improvement, thanks to the increase in common physical activity level, will lead consequently to improved prognosis for both girls and boys of 6-12 years age group. Furthermore, this study shows that the benefic effects of the outpatient program of physical activity on lung function depend on gender, being more important for boys than girls. This is line with some studies which showed a better survival rate in males; the favorable causes are still speculative (7).

In the group ≥ 13 years, values of lung volumes and flows and airway permeability index presented not significant variations for both girls and boys. This suggests that program to improve of usual physical activity level although not leading to a significant improvement in lung function in patients ≥ 13, regardless of gender, however helped to preserve the lung function for the entire the study period.

The study has two important limitations.

- The sample size was small.
- Because of the small number of patients with CF are under monitoring (FC isn't a very common medical condition, on the one hand, and on the other hand it is still less diagnosed in our country, many patients dying with other diagnoses), I could form a control group to be excluded from the program to improve of regular physical activity level at home.

Conclusions

Increasing regular physical activity level had beneficial results on the lung function, whose value depends of age and gender. Male younger patients (6-12 years) had significant increases in all respiratory parameters studied, at one year of treatment.

Decreased number of patients with changes in lung volumes and flows, and significant improvement in FEV1 and consequently of prognosis, for all patients regardless of gender, observed in the group 6-12 years, suggests that any change is not permanent which is an additional incentive for continuous improvement therapeutic management of these patients.

In older patients, this program to increase outpatient usual physical activity level has helped to stability of the lung function.

This study provides evidence to recommend as early as possible exercise and physical activity as an educational measure of lifestyle for patients with CF, to prevent, improve or at least slow the progression of lung disease for a longer period of time, and thus reducing the complications.

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