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Exercise Testing in Children with Cystic Fibrosis

Kistik Fibrozisli Çocuklarda Egzersiz Testleri

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ABSTRACT Cystic fibrosis is a genetic disease in children. The respiratory system is affected due to thickening of secretions. Therefore, pulmonary functions are deteriorated and dyspnea may occur during exercise. Children with cystic fibrosis may not tolerate exercise. Exercise testing is important to determine exercise-related complications and to plan exercise. Exercise tests are necessary applications for all individuals engaged in exercise. Exercise tests are used to determine the prognosis of the disease, exercise tolerance, mortality, efficacy of the treatment and exercise prescription. In this review, the studies using exercise test with children with cystic fibrosis aged between 4 and 18 years were examined. The subjects related to exercise and exercise test are briefly mentioned. The studies have been published between 1986 and 2018 years. The purpose of this review is to emphasize the importance of exercise tests in children with cystic fibrosis and to examine the various exercise tests used in previous studies. In this study, laboratory and field tests were used. Laboratory tests were performed using bicycle ergometers and treadmill. Wingate, Godfrey, CPET-SRT and Bruce protocol were used in laboratory tests. In the field tests, generally 6 minutes walk test, 2 minutes walk test, 3 minutes step test, Munich fitness test and shuttle test were used. These protocols were selected according to the age, height and weight of the child. These tests were modified for children.

Keywords: Children; cystic fibrosis; exercise test

ÖZET Kistik fibrozis çocuklarda görülen genetik bir hastalıktır. Sekresyonların kalınlaşmasından dolayı solunum sistemi etkilenir. Bu nedenle, pulmoner fonksiyonlar bozulur ve egzersiz sırasında dispne meydana gelebilir. Kistik fibrozisli çocuklar egzersizi tolere edemeyebilir. Egzersize bağlı komplikasyonları belirlemek ve egzersiz planlaması yapabilmek için egzersiz testi önemlidir. Egzersiz testleri egzersiz yapan tüm bireyler için gerekli bir uygulamadır. Egzersiz testleri hastalığın prognozunu, egzersiz toleransını, mortaliteyi, tedavinin etkinliğini ve egzersiz reçetesini belirlemede kullanılır. Bu derleme çalışmasında, 4-18 yaş arası kistik fibrozisli çocuklarla yapılan egzersiz testi kullanılan çalışmalar incelenmiştir. Egzersiz ve egzersiz testi ile ilgili konulara kısaca değinilmiştir. İncelenen çalışmalar 1986 ile 2018 yılları arasında yayınlanmıştır. Derlemenin amacı kistik fibrozisli çocuklarda egzersiz testinin önemini vurgulamak ve daha önceki çalışmalarda kullanılan çeşitli egzersiz testlerini incelemektir. Bu çalışmada laboratuvar ve alan testleri kullanılmıştır. Laboratuvar testleri bisiklet ergometresi ve koşu bandı kullanılarak uygulanmıştır. Laboratuvar testlerinde Wingate, Godfrey, CPET-SRT ve Bruce protokolü kullanılmıştır. Alan testlerinde ise genellikle 6 dakika yürüme testi, 2 dakika yürüme testi, 3 dakika step testi, Münih fitnes testi ve mekik testi kullanılmıştır. Bu protokoller çocuğun yaşına, boyuna ve kilosuna göre seçilmiştir. Testler çocuklar için modifiye edilmiştir.

Anahtar Kelimeler: Çocuk; kistik fibrozis; egzersiz testi

Cystic fibrosis (CF) is a complex metabolic disease involving the mucous glands in the pancreas, sweat glands, respiratory tract, GIS and reproductive system. It is inherited in an autosomal recessive pattern. The probability of occurrence in Caucasian race is between 1/2000-2500 in live newborn infants. It is caused by a mutation of the cystic fibrosis transmembrane conductance regulator (CFTR) gene which is located on the

7th chromosome. It creates a protein that is 1480 aminoacids long and serves as a chloride ion channel on the apical surface of the epithelial cells. The result of the genetic defect is the osmotic gradient resulting from the active transport of sodium and chloride, the passage of chloride and sodium in the cell membranes and the corresponding water in them. This causes loss of function in exocrine glands due to increased viscosity of secretions and blockage of these glands.[1]

Cystic fibrosis is a life-threatening disease usually seen in the Caucasian population.[2] Due to the deterioration of the chloride channels in the cell membrane, thickening of the secretion is observed. Due to this thickening, the lungs, pancreas and sweat glands are affected. As a result, the lungs are damaged due to excessive mucus production, inflammation in the airways, endobronchial infection and airway obstruction in these patients.[3] The degree of exercise capacity of cystic fibrosis patients is related to the severity of the disease. The factors limiting exercise are malnutrition and respiratory system's status.[2] Exercise is important in order to maintain the physical fitness levels of patients because myopathy and osteopenia develop due to the steroids used in cystic fibrosis. Exercise is limited initially due to respiratory problems, but quality of life increases after regular exercise.[4]

Exercise testing should be performed in order to create a safe exercise plan suitable for patients. In a UK survey of patients with cystic fibrosis, the number of patients undergoing exercise testing was found to be less than 40%.[5] The purpose of this review is to emphasize the importance of exercise tests in children with cystic fibrosis and to examine the various exercises used in previous studies. In this review, the studies with children aged 4-18 years were examined. The studies examined in the review were published between 1986 and 2018 (31 April). The articles we included in our review are shown in Table 1. In the studies used in the review, the most important criteria were the diagnosis of cystic fibrosis and the performing of any exercise tests to determine exercise tolerance.

TABLE 1: Researchs in which exercise test is used.

Researchers	Date	n	Age	Exercise test	Protocol	Country
Edlund et al.	1986	23	7-14	Treadmill		Utah, Salt Lake City
Upton et al.	1988	139	5-16	2-min walk test		Nottingham, UK
Ian M. Balfour-Lynn	1997	31	6-17	3-min step test 6 min walk test	-	United Kingdom
Narang et al.	2003	19	10.1-16	3-min step test	-	London
Peter et al.	2003	65	4-18	12-18: Cycle ergometer	4-11 year: Bruce protocol	
Cunha et al.	2006	16	8-16	6-min walk test	-	Brazil
Cox et al.	2006	28	7.6-17.6	MST	Bradley	Weastmead, Australia
Kent et al.	2012	18	6-11	Cycle ergometer	Godfrey	Northern, Ireland
Kreemler et al.	2013	57	12+		-	Germany-Swetzerland
Kent et al.	2012	18	6-11	Cycle ergometer	Godfrey	Northern Ireland
Werkman et al.	2013	363	12-18	Godfrey	Godfrey	Netherlands, Utrecht
Lima et al.	2014	13	7-16	6-min walk test	-	Brazil
Saynor et al	2014	14	7-18	Cycle ergometer	Ramp prt. Smax	Devon, UK
Bart et al.	2015	40	11-18	CPET-SRT, SRT-CPET	-	USA
Arıkan et al.	2015	27	7-25	6MWT, MFT	-	Ankara, Turkey
Bounger et al	2015	40	11-18	Cycle ergometer	Godfrey- SRT	Netherlands, Utrecht
Weir et al.	2017	38	7-14	CPET	Godfrey	UK

6MWT: 6-min walk test; CPET: cardiopulmonary exercise test; SRT: steep ramp test; MFT: Munich fitness test; MST: modified shuttle test.

EXERCISE

Exercises are divided into two groups by the source of energy used and whether oxygen is used or not during them. To summarize the energy systems briefly; 1-Phosphogen system: Stored ATP (adenosine triphosphate) and phosphocreatine is used for energy (sprint, barbell). This energy system is used while performing high intensity activities that last 15-30 seconds. 2-Glycolytic energy system: Phosphorylation of adenosine diphosphate (ADP) is done by anaerobic glycolysis, which causes glycogen in muscle tissue to subside from pyruvic acid to lactic acid. (100 mt fast swimming, 2.5-3 minutes fast-intensive exercises). 3-Aerobic energy system: Entering of pyruvic acid directly into the crebs cycle, β-oxidation of fats and production of ATP by the introduction of mitochondrial oxygen transfer systems. Provides ATP for exercises lasting longer than 3 minutes.

Especially VO_{2max}, VO_{2peak}, FEV_1, physical work capacity and peak power output is measured with exercise testing. VO_{2max} is the value at the point where the oxygen consumption value is plateaued during exercise. VO_{2peak} is the VO_2 value at the time the athlete cannot stand the exercise. Less than 80% of the predicted VO_{2peak} value was interpreted as low exercise capacity.[6]

Exercise is limited for many reasons. In cystic fibrosis disease, respiratory factors and cachexia are the most important causes of exercise limitation. Almajed et al. analyzed the factors that determine exercise capacity and limit exercise in their review. This review classified the factors that influence exercise performance as respiratory, cardiac, musculoskeletal and physical activity. The most important cardiac factors were right and left ventricule dysfunction, low stroke volume and pulmonary hypertension. Respiratory factors were expiratory problems, weakness of respiratory muscles, increased work of breathing and hypoxemia. Musculoskeletal factors were low muscle mass, neural conduction problems and andropause. Decrease of physical activity causes FEV1 (forced expired volume in one second) to decrease as well, affecting exercise capacity negatively.[7]

EXERCISE TESTING

Exercise testing is a necessary application for all individuals engaged in exercise. It is recommended to perform these tests annually. History related to health and exercise should be taken in the exercise testing. Patient history should especially include questions about past exercise tests and whether the patient had any adverse reactions with those tests. Anthropometric measurements should be taken. Anthropometric evaluation is an essential feature of children exercise evaluation for determining malnutrition, cachexy, muscular mass loss, fat mass gain and adipose tissue redistribution. Anthropometric indicators are used to evaluate the prognosis of chronic and acute diseases.

Exercise testing is performed to determine the prognosis of the disease, exercise tolerance, mortality, effectiveness of treatment and exercise prescription.[8,9]

Exercise tests are divided into seven main groups. These groups are anaerobic tests, aerobic tests, endurance tests, force tests, flexibility tests, neuromuscular tests, functional tests specific to daily living activities.[10] Commonly used exercise tests are incremental, submaximal, maximal exercise tests or ramp test protocols, submaximal steady state constant load tests and timed distance walk tests.[2]

In order to detect the basic performance capacity, submaximal exercise tests are performed to determine the incremental exercise tests, anaerobic ventilator threshold or lactate threshold. When the disease is severe, a maximal exercise test is performed to determine the safe exercise interval. The maximal exercise test is done with the treadmill and the electronic mechanical bicycle ergometer.[2]

Children have short explosive and high intensity activities in daily life. The exercise capacity of children should therefore be determined by anaerobic tests where the force is measured.[11]

Aerobic capacity measurement tests are; bicycle ergometer tests (Astrand Test, YMCA Test, Fox Test), Treadmill Tests (Balke Test, Bruce Method, Submaximal Treadmill tests), Step Tests (Astrand

Step test, Harward Step test, YMCA Step tests), Field Tests (Balke Test, 20 meter shuttle running test, 10 meter shuttle running test). Anaerobic power tests are; Bicycle ergometer tests (Wingate Test), Treadmill tests (Conconi Treadmill Test, Morrin Sherrott-Taylor Treadmill Test), Field tests (Basco Test, Conconi Test, Margaria Kalaman Power Test).[12] The exercise tests and the parameters measured in exercise tests are shown in Table 2.

CONTRAINDICATIONS FOR THE EXERCISE TESTING

The contraindications for the tests are; history of unstable angina or myocardial infarction in the last month, persistant tachycardia despite 10 minutes of rest, hypertension (systolic BP over 200 mmHg, diastolic BP over 100 mmHg), desaturation (SaO_2 lower than %88) or physical disabilities preventing regular exercise.[15]

The test must be terminated if any of the following are reported; angina pectoris, signs of poor perfusion (ataxia, central cyanosis, cold clammy skin, dizziness, pallor, confusion, sweating), loss of consciousness, leg cramps, dyspnea, fatigue, tachycardia (heart rate over 210/min), desaturation (SpO_2 below %85), lack of cardiac response to exercise.

In addition, if the child indicates that he / she cannot continue the test and the rate of fatigue decreases to a certain level (eg falls below 60 rpm), then the exercise test must be terminated.

LABORATORY TESTS

1- WINGATE TEST (WAnT)

With this test, anaerobic exercise capacity and explosive power are measured. This test was developed in 1970 at the Wingate Institute in Israel. It is stated that the test consists of 4 circuits in some sources, 5 in some sources and 3 in others. These circuits are composed of warm-up, recovery, acceleration, wingate test and cool down stages.

In this test, the number of pedal revolutions in 30 seconds and resistance is evaluated. The resistance of the ergometer is set in the 2nd and 3rd seconds of the test. For the legs, Fleisc ergometer is

TABLE 2: Exercise tests and parameters.

Exercise tests	Equipment	Measured paremeters
Field tests		
6-min walk test	25 m floor, stethoscope, blood pressure monitor, pulse oksimeter, stopwatch, dispne scale, oxygen, chair	SaO_2, HR, Walking distance
2- min walk test	Stopwatch	SaO_2, HR
3-min step test	Stopwatch	SaO_2, HR,
Shuttle test	Stopwatch, 10 mt floor	
Laboratory tests		
Wingate test	Cycle ergometer	Peak power output
Modified Münich Fitness test		Speed, coordination, power, flexibility, balance, endurance, strength[13]
CPET	Pulse oksimeter, treadmill or cycle ergometer	Predicted MVV, VE_{peak}, HR, VO_{2peak}, VO_{2max}
Bruce Protocol	Treadmill	VO_{2max}, VO_{2peak}, SaO_2, spirometry, HR, BP, ECG, physical work capacity, Respired gas analysis, VE_{peak}/MVV[14]
Godfrey Protocol	Cycle ergometer	Pred.VO_{2peak},
Steep ramp test (SRT)	Cycle ergometer	peak work rate (WR_{peak}), VO_{2peak}, HR, SaO_2, VE, RER, VCO_2, VO_2

CPET: Cardiopulmonary exercise test, HR: Heart rate, MVV: Maximal voluntary ventilation, BP: Blood pressure; VO_2:Oxygen uptake, VCO_2: carbon dioxide production, VE: minute ventilation, RER: respiratory exchange rate, SaO_2: oxygen saturation, ECG: Electrocardiography, VO_{2peak} = peak oxygen uptake.

used at 45 gr/weight (kg) and Monark ergometer is used at 75 gr/weight (kg). 35 gr/weight (kg) is applied for children under 15 years old. For the arms, 30 gr/weight (kg) in Fleisc ergometer and 50 gr/weight (kg) in Monark ergometer are used.

Selvadurai et al. published a study that examined the relationship between exercise capacity of 97 children with cystic fibrosis who were aged between 8-17 and genetics. In order to determine the anaerobic capacity in the study, they used the Wingate test and the Bruce protocol to determine peak aerobic capacity.[16] Klijn and colleagues used the Wingate test in their study with 39 children with cystic fibrosis with a mean age of 13 years. The correlation between FEV1 and Wingate test was examined. At the end of the study, pulmonary functions and lean body weight were found to be important determinants of anaerobic capacity.[17]

2- CPET-CARDIOPULMONARY EXERCISE TEST

Exercise intolerance cannot be determined with pulmonary function tests performed at rest. Therefore, the CPET test is very important to determine exercise intolerance. The purpose of this test is to put pressure on the organs involved in exercise. For this reason, lower extremities with large muscle groups are preferred.

There are two types of applications. In the first one, the increasing test protocol, a constant pedal speed of 60 rpm is used. The test is terminated when the pedal speed falls below 40 rpm. The initial load and increases are determined by the characteristics of the patient so that the exercise can be maintained for 10-12 minutes. The second type is the constant load protocol, in which a fixed load is applied, the patient is asked to exercise as much as he can and the time is recorded.

The difference between exercise times before and after treatment is taken into account. Protocol selection is based on the patient's functional capacity and the purpose of the test. A treadmill or bicycle ergometer can be used for this purpose. The advantage of the treadmill is that the walking / running model is well known and operates more muscle groups than the bicycle ergometer. The European Cystic Fibrosis Study Group routinely uses CPET exercise test in children aged ≥10 years The UK uses walking tests more frequently.[4,18]

Weir et al. performed the CPET exercise test using the modified Godfrey protocol on 38 children with cystic fibrosis aged between 7-14. The test was modified by minimizing the large changes in power output. Ramp range is determined as 6.5-25 W/min. Ramp increase was made in 10 sec intervals. The optimal test time is 8-12 minutes. Rpm was kept above 60. The power output is determined by the height of the children. Estimated value is calculated by dividing the ramp increase by 10. The parameters were taken from the measurements in the last 30 seconds of the test. In this study, the correlation between VO_{2max} and FEV_1 with disease stage was investigated. 95% of children completed the test successfully. As a result of the study, no correlation between VO_{2max}, VO_{2peak}, FEV_1, BMI (Body mass index) and disease severity was found.[19]

3- BICYCLE ERGOMETER

Godfrey protocol: This protocol is used with bicycle ergometry. The load is increased with 1 minute intervals until the patient is fatigued. The goal is to complete the test in 8-12 minutes. Heart rate measurements and gas analyses are performed in the last 15 seconds of each increment cycle. The test is terminated when the patient can not continue with the test (the pedal speed falls below 60 rpm) or when the oxygen saturation falls below 80%.

Kent et al. used the bicycle ergometer for a study they performed with children diagnosed with cystic fibrosis.[20] Cerny et al. used the bicycle ergometer to evaluate exercise tolerance and the improvement of pulmonary function during hospitalization.[21] Klijn et al. investigated the relationship between aerobic performance, pulmonary function and body composition in their studies with children with cystic fibrosis. The study included 79 children aged 4-18 years. In this study, treadmil test was performed according to Bruce protocol in children under 12 years of age, and tests were performed with electronic mechanical bicycle ergometer in children aged 12 and over. The load was increased by 15 W per minute and the pedal speed was desired to be 60 rpm. Throughout

the test, children have been encouraged by verbal stimulation to ensure the best performance.[22] Respiratory gas analyses were performed during the test and lung volumes were measured. The measurement was performed by applying a V valve mask with a breath by breath method. Oxygen uptake (VO_2), carbon dioxide production (VCO_2), minute ventilation (VE), respiratory exchange rate (RER), pulse rate (HR) and SaO_2 (oxygen saturation) were measured. The highest VO_2 VO_{2peak} in the last 30 seconds of the test was measured.

A 9% increase in lean body weight change can be explained by the change in VO_{2peak}. Nutritional status is an important parameter affecting aerobic performance. This study showed that longitudinal changes in lung function are related to aerobic capacity. VO_{2peak} decreased as the lean body weight increased.

Werkman et al. used the Godfrey exercise protocol to estimate the VO_{2max} values in their studies with 363 cystic fibrosis patients with an average age of 14 years and 60 healthy controls. The workload was determined according to the height of the children (10W for children less than 120 cm in heigth, 15W for 120-150 cm and 20W for those taller than 150 cm). The workload is increased according to the compliance of the children at 1 minute intervals. In the study, the measured values were taken 30 seconds before the test was completed. At the end of the study, it is concluded that if the VO_{2peak} can not be measured directly, the estimated value of VO_{2peak} can be obtained only by bicycle ergometer.[23]

Saynor et al. measured aerobic fitness (VO_{2max}) in 14 children with cystic fibrosis aged 7-18, using the ramp protocol in maximal CPET. In the study, 14 children completed the exhausting ramp test to determine VO_{2max}. After 15 minutes recovery time, supramaximal (S_{max}) (applied with 110% of peak power output measured in ramp test) test was performed. At the end of the study, they found that supramaximal testing following CPET was a suitable method for measuring the VO_{2max} values of children with cystic fibrosis. In the ramp test, VO_{2max} was (1.83±0.78 L min^{-1}) while in the supramaximal test it was (1.82±0.67 L min^{-1}), but the difference was not statistically significant (p=0.88).[24]

Keochkerian et al. performed a study with 18 children aged 10-14, 9 of who had cystic fibrosis. The aim of the study was to determine the respiratory strategies during exercise and to look at the correlation between these strategies and pulmonary function. Progressive testing was performed with ergocycle (ER 900, Jaeger, Germany). In this test, symptom-limited maximum ramp protocol was used by using electronic mechanical brake bicycle ergometer. Increases in load was determined according to the clinical status of each individual. Exercise test completed within 8-10 minutes. After 2 minutes of warm-up exercise, the test was started while the children were breathing stable. In the test, the burden of children with cystic fibrosis was increased to 10-15 W in every 90 seconds, and the load of healthy children was increased to 15-20 W. The increase was continued until the burnout level. P(0.1) was measured in the last 45 sec after each loading.[25]

Steep ramp test: Bongers et al. used the step ramp test in their study with 40 children with cystic fibrosis aged 11-18 years. Twenty-five minutes after using salbutamol (800 μg), children underwent respiratory function test followed by an electrostatic ergometer with CPET and SRT tests. Between the two tests, a 15 min recovery time was left. The CPET exercise test was performed according to the Godfrey protocol. The maximal level was determined as the heart rate above 180 or the RER value above 1.0 value. Burnout level was measured using "OMNI Scale of Perceived Exertion".[26] This scale included 10 levels.

The SRT test was started with a 25W resistance for 3 minutes and SRT was started with an increase of 2, 3, 4 W with 2 second intervals. The total increase in 10 sec was determined as 10 W for children shorter than 120 cm, 15 W for children between 120-150 cm, and 20 W for children taller than 150 cm. The pedal speed was kept between 60-80 rpm. Despite the warning, the point where it fell below 60 rpm was determined as peak exercise.

4- TREADMILL TESTS

Starts after 5-10 minutes of warm-up. A monitor is needed to determine the patient's heart rate every

5 seconds. The test is terminated when the subject reaches the maximal heart rate. Then a 10-minute cool down program is carried out.[12]

Bruce protocol: This test is a treadmill protocol. It was developed by Dr. Robert A. Bruce in 1963. The test is used to measure maximal O_2 consumption, lean body mass, and respiratory function. ECG monitoring is performed during the test. The initial speed is set at 2.74 km / hr (1.7 mph) and the slope is set at 10%. In sedantary individuals, the initial speed is set at 1.7 mph but the slope is kept at 0%. The speed and slope are increased by 2% with 3 minute intervals. Oxygen consumption is calculated using a formula that comprises of testing time and gas analysis.

Edlund et al. used the Bruce protocol to investigate the effects of the swimming program on pediatric patients with cystic fibrosis. The study included 14 male and 9 female patients with cystic fibrosis aged 7-14 years. 12 participants were included in the study and 11 were included in the control group. All patients in the experimental and control groups participated in the treadmil test. 12-lead ECG measurements and maximum oxygen uptake (VO_{2max}) were measured in the test.[27]

FIELD TESTS

1- 6 minute (6MUT) walk test: Modified from 12 minutes running test. It is one of the field tests which measures the aerobic endurance of the patients. According to the test results, the intensity of walking exercises of children with cystic fibrosis is determined. The 6MWT test should be applied 2 times and the best walking distance should be recorded. Tests should be performed for at least 30 minutes between the tests. Dyspnea is evaluated by BORG scale.

Lima et al. performed the 6 minute walking test on a treadmill, after applying non-invasive ventilation for 30 minutes using BILEVEL mode (EPAP: 6cm H_2O, IPAP:12cm H_2O) on 13 children with cystic fibrosis, who were aged 7-17.[28] Initially, the speed of treadmill was started at 2.5 km/h. According to the participant's capacity, the speed was increased in 30 sec intervals not to exceed the speed limit of 7 km /h. As a result of the study, the walking distance after the use of noninvasive ventilator was 415.38±77.2 m and the walking distance of the test without using noninvasive ventilator was 386.92±84.89 m. In this study, Borg scale was used to evaluate dyspnea (Table 3).

2- Shuttle walking test (SWT): It is a test type used to measure aerobic capacity. It was first applied in 1982 at the University of Montreal in Canada. It is a corridor test in which progressive walking speed is increased and there are two types.

I- Walking speed increasing incrementally: It is based on increasing the speed of walking at every minute with sound stimulus and is a test for determining the peak oxygen consumption. The test is made as a round trip between two points at a distance of 10 meters. In these shuttle tours, the results of the last round are as follows: meters or rounds. The walking speed starts with 0.5 m/s and the speed increases by 0.17 m per second. There are twelve levels. The test criterion is to monitor fatigue or symptoms. During the test, cardiac side effects cannot be monitored.

II- Endurance shuttle walking test where the speed is constant. After a two-minute warm-up period, patients are asked to walk a distance of 10 meters. The constant speed is adjusted according to

TABLE 3: Borg scale.

Borg Scale	
15 Points Scale	10 Points Scale
6 No exertion at all	0 Nothing at all
7 Extremely light	0,5 Very very light
8	
9 Very light	1 Very light
10	
11 Light	2 Light
12	3 Moderate
13 Somewhat hard	4 Somewhat hard
14	5 Hard
15 Hard	6
16	7 Very hard
17 Very hard	8
18:	9 Very very hard
19 Extremely hard	10 Exremely hard
20 Maximal exertion	

85% of the VO_{2max} determined in the shuttle test where the walking speed is gradually increasing. Total walking time is recorded. It is a more useful test for evaluation after pulmonary rehabilitation programs.

Cox et al. used a modified shuttle test to determine exercise tolerance in a study of 28 children with cystic fibrosis who were hospitalized and treated with antibiotics. The ages of the children were 7.6-17.6 (mean 12.7 years). In the study, children used fatigue scale.[29]

As a result of the study, it was seen that shuttle walking test was a good choice in determining the effect of hospitalization and antibiotic treatment. There was a significant increase in walking distance. In the protocol used by Bradley et al. 10 m distance was determined and markings were made. Beep sound started the test. It contains 15 stages and allowed to run if the child wants. Each level consists of 1 min. Speed increased by 0.61 km per minute. The test was terminated when the individual could not continue or when 15 sets were completed. HR and SPO_2 measurements were performed before and after the test.

3- 2-minute walk test (2MWT): Upton et al. used the 2-minute walk test to determine exercise tolerance of 155 patients, 89 of who were healthy, 66 had cystic fibrosis and of those, 16 who had pneumonia. They used this test because they thought the 12-minute walk test and 6-minute walk test were more tolerable for children with adult airway disease.[30] Butland et al. claimed that 2 minute and 6 minute walk tests were well correlated with the longer tests. As a result of the test, there was a positive correlation between walking distance and height of the children. The test was carried out in a 35 meter flat hospital corridor, each 5 meters marked in the closed area. Children were asked not to run and were encouraged verbally every 5 minutes. After resting for 5-10 minutes, the test was repeated and if the distance was over, the result of the test was accepted as valid.[31]

4- 3-minute step test: It is a test type that evaluates the aerobic fitness level. 3-minute step test have advantages and disadvantages. Advantages: Minimal tool and money requirement, little time is required and you can apply it alone. Disadvantages: Biomechanical properties vary according to individuals (eg, tall people have advantage, those who are short and overweight have disadvantage).

In the study, Narang et al. evaluated the exercise capacity of 19 children with cystic fibrosis between the ages of 10 and 18 in a 3-minute step test. Dyspnea was evaluated by visual analog scale.[32] In the study, children were divided into groups of 13 and 6. First 13 children applied the bicycle ergometer. 6 children performed a 3-minute step test. Afterwards, 6 children who applied bicycle ergometry and 13 children applied 3 min step test. Heart rate and VAS (Visual Analogue Scale) values were compared during the application of children's step test and bicycle ergometer. The average heart rate change was 78 in the children's bicycle ergometer and 46 in the 3-minute step test. The VAS value was 42 mm after 3 minutes of step test, and 51 mm after the bicycle ergometer. The change in SO_2 value during the step test and the bicycle ergometer was not statistically significant. Subjects stepped up and down a commercially available single-step test as in previous studies, 8 set at a height of 15 cm (6 inches). The stepping procedure was demonstrated to the subject prior to the onset of exercise. The stepping rate was 30 per minute for 3 min, and this was controlled by a metronome. Subjects could stop if they felt tired or if the SaO_2 fell below 75%, in which case the total number of steps taken was recorded. The subjects were shown how to change the leading leg to reduce localized muscle fatigue, and standardized encouragement was given.

Cunha et al. evaluated the exercise tolerance of 16 children with cystic fibrosis using the 6 minute walk test.[33] The test was carried out in a 28-meter straight corridor. At the end of the study, it was observed that the walking distance was not affected by age but was affected by height. However, studies with children with cystic fibrosis showed a significant correlation between age and walking distance.[34,35]

5- Modified Munich Fitness Test (mMFT): This is a test applied to 6-18 years old students. The test was developed in Germany. This test was

TABLE 4: Modified munich fitness test.

Test-task	Evaluated parameter	Administration	Score
Balancing and bouncing	Speed and coordination	Standing on a step and bouncing a ball with both hands as fast as possible	The total number of correctly performed bounces in 30 s
Accurate throw	**Speed and coordination**	**Throwing a bean bag (500 g) to 5 target fields**	**Each of them has a number 1-2-3-2-1. Counting the numbers of 5 consecutive correctly performed attempts after 3 trial throws**
Trunk flexibility	Flexibility	Stand and reach test, reaching forward as far as possible from a standing position with knees straight	The better of two attempts in centimeters
Standing vertical	**Power**	**Jumping as high as possible at the side of walls**	**The better of two attempts in centimeters as the difference between standing reach high and jump-and-reach-high**

adapted from the Munich Fitness Test. This test evaluates the 4 major abilities of children aged 6-18 years.[36] These abilities are: Balancing and bouncing, 2- Throwing, 3 - Body flexibility, 4 - Standing vertical jump. The parameters evaluated in the test are shown in Table 4.

Arikan and his colleagues used the Munich Fitness Test without modification. In the study conducted with 20 healthy participants with 19 cystic fibrosis aged between 7 and 25 years, they used the MFT test to evaluate the motor performance of the participants.[13] The original effort scale (normal heart rate 60-200), defined by the Borg, consisting of a 6-20 scale, is used to measure all effort during physical activity. It was modified in 10 points scale.[37]

Urguhart et al. conducted a review of cardiopulmonary exercise in children with cystic fibrosis.[38] In the study, it was concluded that pulmonary functions are not the only factors effective in determining exercise capacity but cardiovascular and musculoskeletal systems also play an important role. In their study, Rogers et al. examined the exercise test in children with cystic fibrosis.[39]

CONCLUSIONS

In studies that we examined, exercise test was performed to evaluate the effect of exercise, prognosis of disease, effect of treatment and quality of life in children with CF. Field and laboratory tests were applied to measure aerobic and anaerobic capacity. Preferred field tests were 6-MWT, 2MWT, mMFT, MST, 3 minute step tests. Laboratory tests were performed using treadmill and bicycle ergometer. Bruce, Godfrey and Wingate protocols were used in laboratory tests. These test types and the duration of the tests were selected according to the anthropometric characteristics of children and the prognosis of the disease. These studies used parameters that, directly or indirectly showed cardiorespiratory function, such as VE, VO_{2max}, VO_2, heart rate and FEV_1. In the last years, 1 min sit-to-stand test and mMFT test were applied. However the studies that focus on those are few in number. Our recommendation is to emphasize on studies that has tests which evaluate the peripheral muscle strength of children . As the adaptation to exercise will develop over time, children may benefit from exercise during the execarbation period of the disease. The studies we have examined stated that exercise testings are generally not performed regularly and they have recommended exercise testing at least once a year. Our recommendation is to perform these tests before winter since respiratory infections exacerbate CF and their exercise prescription should be prepared.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Selma Civar Yavuz;* ***Design:*** *Azime Acar Hisarkaya;* ***Control/Supervision:*** *Selma Civar Yavuz;* ***Data Collection and/or Processing:*** *Azime Acar Hisarkaya,* ***Analysis and/or Interpretation:*** *Alkım Bayhan;* ***Literature Review:*** *Azime Acar Hisarkaya;* ***Writing the Article:*** *Azime Acar Hisarkaya;* ***Critical Review:*** *Alkım Bayhan.*

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