Int J Pharma Res Health Sci. 2017; 5 (5): 1831-37
DOI:10.21276/ijprhs.2017.05.02
Pankaj R *et al*
CODEN (USA)-IJPRUR, e-ISSN: 2348-6465

PHS Scientific House
PHARMAHEALTHSCIENCES

International Journal of Pharma Research and Health Sciences

Available online at www.pharmahealthsciences.net

Review Article

Cystic Fibrosis: A Review

Pankaj R Khuspe*, Kishori Kokate, Trushali Mandhare
Navsahyadri Institute of Pharmacy, Naigoan, Pune-412213, India

ARTICLE INFO

Received: 10 Oct 2017
Accepted: 24 Oct 2017

ABSTRACT

Inherited disease of secretary glands is known as Cystic fibrosis (CF). Cystic fibrosis mostly affects the pancreas, lungs, liver, intestines and sex organs. Like it affects other vital organs it doesn't affect the brain. The main causes of cystic fibrosis are defect in the CFTR gene. The CFTR gene makes a protein that controls the movement of salt and water in and out of body's cells. Every person inherits two CFTR genes one from each parent. Persons who receive or inherit a faulty gene from each parent will have cystic fibrosis. Diagnosis of cystic fibrosis is based on the results from various tests sweat test, newborn screening, cystic fibrosis carrier testing, prenatal screening and other tests. In treatment of cystic fibrosis exercise therapy, chest physical therapy and medicines are used. In medicinal therapy mostly antibiotics, anti-inflammatives, mucolytics, antihistamines, vitamins, drugs acting on GI track, stool softeners, bronchodilators, and pancreatic enzymes are used. Oxygen therapy and lung transplant are the advance treatments for lung diseases. As new treatments are developed for patients with cystic fibrosis, efforts should be made to balance treatment burden with quality of life. This review highlights emerging treatments, obstacles to optimizing outcomes, and key future direction for research on cystic fibrosis and its treatment.

Key words: Cystic fibrosis, CFTR, Sweat Test, Chest Physical Therapy.

1. INTRODUCTION

Cystic fibrosis is an inherited disease of secretory glands, including the glands that make mucus and sweat. "Inherited" means that the disease is passed through the genes from parents to children[1, 2]. People who have cystic fibrosis inherit two faulty cystic fibrosis genes one from each parent. The parents likely don't have the disease themselves. Cystic fibrosis mostly affects the lungs, pancreas, liver, intestines, sinuses, and sex organs. Mucus is a substance made by the lining of some body tissues. Normally, mucus is a slippery,

Corresponding author *
Pankaj R Khuspe
Navsahyadri Institute of Pharmacy, Naigoan, India
Email ID: khuspepankaj@gmail.com

watery substance[3, 4]. It keeps the linings of certain organs moist and prevents them from drying out or getting infected. However, if have cystic fibrosis, mucus becomes thick and sticky. The mucus builds up in lungs and blocks airways, the tubes that carry air in and out of lungs. The buildup of mucus makes it easy for bacteria to grow. This leads to repeated, serious lung infections. Over time, these infections can severely damage lungs. The thick, sticky mucus also can block tubes, or ducts, in pancreas. As a result, the digestive enzymes that pancreas makes can't reach small intestine these enzymes help break down the foods that eat. Without them, intestines can't fully absorb fats and proteins. This can cause vitamin deficiency and malnutrition because nutrients leave body unused[5]. It also can cause bulky stools, intestinal gas, a swollen belly from severe constipation, and pain or discomfort. Cystic fibrosis also causes sweat to become very salty. As a result, body loses large amounts of salt when sweat. This can upset the balance of minerals in blood and cause a number of health problems. Examples include dehydration, increased heart rate, tiredness, weakness, decreased blood pressure, heat stroke and rarely death. The cystic fibrosis also increases risk for diabetes or a bone-thinning condition called osteoporosis. Cystic fibrosis also causes infertility in men, and it can make, harder for women to get pregnant. The other names for cystic fibrosis are CF, cystic fibrosis of the pancrea, fibrocystic disease of the pancreas, mucoviscidosis of the pancreas, pancreas fibrocystic disease and pancreatic cystic fibrosis.

CAUSES OF CYSTIC FIBROSIS

A defect in the CFTR (cystic fibrosis transmembrane conductance regulator gene) gene causes cystic fibrosis (CF). This gene makes a protein that controls the movement of salt and water in and out of body's cells. In people who have cystic fibrosis, the gene makes a protein that doesn't work right. This causes thick, sticky mucus and very salty sweat. Research suggests that the CFTR protein also affects the body in other ways. This may help explain other symptoms and complications of cystic fibrosis. More than a thousand known defects can affect the CFTR gene. What type of defect adult or child has may influence how severe cystic fibrosis is.

INHERITANCES OF CYSTIC FIBROSIS

Every person inherits two CFTR genes, one from each parent. Children who inherit a faulty CFTR gene from each parent will have cystic fibrosis. Children who inherit a faulty CFTR gene from one parent and a normal CFTR gene from the other parent will be "CF carriers". Cystic fibrosis carriers usually have no symptoms of cystic fibrosis and live normal lives. However, carriers can pass the faulty CFTR gene on to their children. The following image shows how two parents who are both cystic fibrosis carriers can pass the faulty CFTR gene to their children.

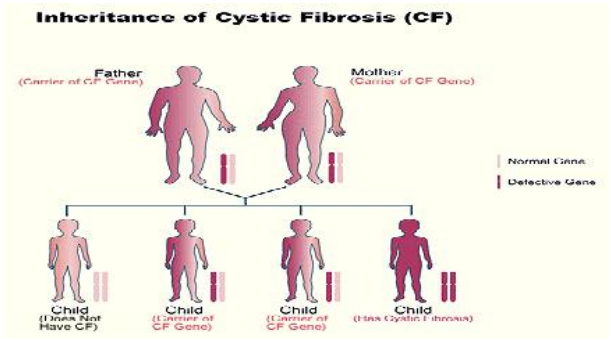

Fig 1: Inheritances of Cystic Fibrosis.

The image shows how CFTR genes are inherited. A person inherits two copies of the CFTR gene, one from each parent. If each parent has a normal CFTR gene and a faulty CFTR gene, each child has a 25 percent chance of inheriting two normal genes; a 50 percent chance of inheriting one normal gene and one faulty gene; and a 25 percent chance of inheriting two faulty genes.

SIGNS AND SYMPTOMS OF CYSTIC FIBROSIS

The symptoms of cystic fibrosis vary from person to person and sometimes will have few symptoms. Other times, symptoms may become more severe. One of the first signs of cystic fibrosis (CF) that parents may notice is that their baby's skin tastes salty when kissed or the baby doesn't pass stool when first born. Most of the other signs and symptoms of cystic fibrosis develop later. They are related to how cystic fibrosis affects the respiratory, digestive, or reproductive systems of the body.

Respiratory System Signs and Symptoms[9]

People who have cystic fibrosis have thick and sticky mucus that builds up in their airways. This buildup of mucus makes it easier for bacteria to grow and cause infections. Infections can block the airways and cause frequent coughing that brings up thick sputum (spit) or mucus that's sometimes bloody. People who have cystic fibrosis tend to have lung infections caused by unusual germs that don't respond to standard antibiotics. For example, lung infections due to bacteria called mucoid pseudomonas are much more common in people who have cystic fibrosis[9]. An infection caused by these bacteria may be a sign of cystic fibrosis. People who have cystic fibrosis have frequent bouts of sinusitis, an infection of the air-filled spaces behind eyes, nose, and forehead[4]. Frequent bouts of bronchitis and pneumonia also occur. These infections can cause long-term lung damage. As cystic fibrosis gets worse, may develop more serious complications, such as pneumothorax, or collapsed lung; or bronchiectasis. Some people who have cystic fibrosis also develop nasal polyps (growths in the nose) that may require surgery [31].

Digestive System Signs and Symptoms

Mucus that blocks tubes, or ducts, in pancreas and prevents enzymes from reaching intestines causes most digestive system signs and symptoms. Without these enzymes,

intestines can't fully absorb fats and proteins. This can cause ongoing diarrhea or bulky, foul-smelling, greasy stools. Intestinal blockage also may occur, especially in newborns. Too much gas or severe constipation in the intestines may cause stomach pain and discomfort. A hallmark of cystic fibrosis in children is poor weight gain and growth. These childrens are unable to get enough nutrients from their food due to the lack of enzymes to help absorb fats and proteins[32]. As cystic fibrosis gets worse, other complications may occur, such as pancreatitis, rectal prolapsed, liver disease due to inflamed or blocked bile ducts, diabetes and gallstones.

Reproductive System Signs and Symptoms

Men who have cystic fibrosis are infertile because they are born without a vas deferens. This is the tube that delivers sperm from the testicle to the penis. A woman who has cystic fibrosis may have a hard time getting pregnant because of mucus blocking her cervix or other cystic fibrosis complications.

OTHER SIGNS, SYMPTOMS, AND COMPLICATIONS

Other signs and symptoms of cystic fibrosis are related to an upset of the balance of minerals in blood. Cystic fibrosis causes sweat to become very salty. As a result, body loses large amounts of salt when sweat. This can cause dehydration, increased heart rate, tiredness, weakness, decreased blood pressure, heat stroke and rarely death. Cystic fibrosis also can cause clubbing and low bone density. Clubbing is the widening and rounding of the tips of fingers and toes. It develops late in cystic fibrosis because lungs aren't moving enough oxygen into bloodstream. Low bone density also tends to occur late in cystic fibrosis. It can lead to a bone-thinning disorder called osteoporosis.

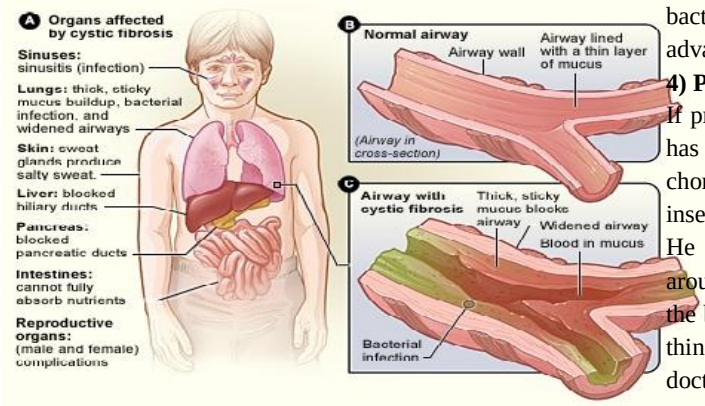

Figure2 a: Shows the organs that cystic fibrosis can affect; **Figure 2b:** Shows a cross-section of a normal airway; **Figure2c:** Shows an airway affected by cystic fibrosis. The widened airway is blocked by thick, sticky mucus containing blood and bacteria.

2. DIAGNOSIS OF CYSTIC FIBROSIS (CF)

Following are the various test used widely for the diagnosis of cystic fibrosis.

1) Newborn Screening

Most newborns should be screened for cystic fibrosis using a genetic test or a blood test. The genetic test shows whether a newborn has faulty CFTR genes or not. The blood test shows whether a newborn's pancreas is working normally or not.

2) Sweat Test

If a genetic test or blood test suggests cystic fibrosis, a doctor will confirm a diagnosis using a sweat test. This test is the most useful test for diagnosing cystic fibrosis. It measures the amount of salt in sweat. For this test, doctors trigger sweating on a small patch of skin on an arm or leg. They rub the skin with a sweat-producing chemical and then use an electrode to provide a mild electrical current. This may cause a tingling or warm feeling. Sweat is collected on a pad or paper and then analyzed. The sweat test usually is done twice. High salt levels confirm a diagnosis of cystic fibrosis[25].

3) Other Tests

If a child has cystic fibrosis, doctor may recommend other tests, such as: Genetic tests to find out what type of CFTR defect is causing cystic fibrosis.

A chest x ray: This painless test creates pictures of the structures in chest, such as heart and lungs. A chest x ray can show whether lungs are inflamed or scarred or whether they trap air.

A sinus x ray: This test may show signs of sinusitis, a complication of cystic fibrosis.

Lung function tests: These tests measure the size of lungs, how much air can breathe in and out, how fast can breathe air out, and how well lungs deliver oxygen to blood.

A sputum culture: For this test, doctor will take a sample of sputum (spit) to see what bacteria are growing in it. If have bacteria called mucoid pseudomonas, may have more advanced cystic fibrosis that needs aggressive treatment[26].

4) Prenatal Screening

If pregnant, prenatal genetic tests can find out whether fetus has cystic fibrosis. These tests include amniocentesis and chorionic villus sampling (CVS). In amniocentesis, doctor inserts a hollow needle through abdominal wall into uterus. He or she removes a small amount of fluid from the sac around the baby. The fluid is tested to see whether both of the baby's CFTR genes are normal. In CVS, doctor threads a thin tube through the vagina and cervix to the placenta. The doctor removes a tissue sample from the placenta using gentle suction. The sample is tested to see whether the baby has cystic fibrosis.

5) Cystic Fibrosis Carrier Testing

People who have one normal CFTR gene and one faulty CFTR gene are cystic fibrosis carriers. Cystic fibrosis carriers usually have no symptoms of cystic fibrosis and live normal lives. However, carriers can pass faulty CFTR genes on to their children[13]. If has a family history of cystic fibrosis or a partner who has cystic fibrosis (or a family history of it) and are planning a pregnancy, may want to find

out whether are cystic fibrosis carrier. A genetic counselor can test a blood or saliva sample to see whether have a faulty cystic fibrosis gene. This type of testing can detect faulty cystic fibrosis genes in 9 out of 10 cases.

3. TREATMENT

Cystic fibrosis (CF) has no cure. However, treatments have greatly improved in recent years. The goals of cystic fibrosis treatment are to prevent and control lung infections, loosen and remove thick and sticky mucus from the lungs, prevent or treat blockages in the intestines, provide enough nutrition and prevent dehydration[4, 6]. Depending on how severe the disease is, or child may be treated in a hospital. For loosen and remove thick and sticky mucus from the lungs, normally Chest Physical Therapy (CPT) is prescribed. CPT also is called chest clapping or percussion. It involves pounding chest and back over and over with hands or a device to loosen the mucus from lungs so that can cough it up. Might sit down or lie on stomach with head down while do CPT. Gravity and force help drain the mucus from lungs. Some people find CPT hard or uncomfortable to do. Several devices have been developed that may help with CPT, such as electric chest clapper, known as a mechanical percussor, an inflatable therapy vest that uses high-frequency airwaves to force the mucus that's deep in lungs toward upper airways so can cough it up, a small handheld device that breathe out through. It causes vibrations that dislodge the mucus and mask that creates vibrations that help break the mucus loose from airway walls. Breathing techniques also may help dislodge mucus so can cough it up. These techniques include forcing out a couple of short breaths or deeper breaths and then doing relaxed breathing. This may help loosen the mucus in lungs and open airways[30]. Aerobic exercise that makes breathe harder helps loosen the mucus in air ways so can cough it up. Exercise also helps improve overall physical condition [7, 31]. However, cystic fibrosis causes sweat to become very salty. As a result, body loses large amounts of salt when sweat. Thus, doctor may recommend a high-salt diet or salt supplements to maintain the balance of minerals in blood. If exercise regularly, may be able to cut back on CPT[14]. However, should check with doctor before doing this. For prevent and control lung infections, reduce swelling, open up the airways, and thin mucus. Antibiotics are the main treatment to prevent or treat lung infections. Many environmental bacteria are found in Cystic fibrosis airway infections, including *S. aureus, P. aeruginosa, Stenotrophomonas maltophilia, B.cepacia* complex, fungi, atypical mycobacteria, whereas *Streptococcus pneumoniae, H. influenzae or Moraxella catarrhalis* and bacteria of theendogenous flora, *S. aureus , P. aeruginosa.* Oral antibiotics often are used to treat mild lung infections. Inhaled antibiotics may be used to prevent or control infections caused by the bacteria mucoid Pseudomonas. For severe or hard-to-treat infections, may be given antibiotics through a tube inserted into a vein[24] Following table show the antibiotics which are prescribed in cystic fibrosis.

Table 1: Antibiotics drugs

Names	How Taken	Brand names for the same drug
Ciprofloxacin	Oral	Cipro
Cotrimoxazole	Oral	Septra, Bactrim
Tobramycin	Aerosol, IV	Tobi, Nebcin
Cephalexin	Oral	Keflex
Colistin	Aerosol	Colymycin
Dicloxacillin	Oral	Diclox
Azithromycin	Oral	Zithromax
Azithromycin lysine	Inhalation	
Levofloxacin	Inhalation	
Colistin	Inhalation	
Vancomycin	IV	
Teicoplanin	IV	
Moxifloxacin	Oral, IV	
Clarithromycin	Oral	
Pivampicillin	Oral	

Anti-inflammatory medicines can help reduce swelling in airways that's caused by ongoing infections. These medicines may be inhaled or orally administered [25]. Following table show the anti-inflammatory drugs which are prescribed in cystic fibrosis.

Table 2: Anti-inflammatives drugs

Names	How Taken	Brand names for the same drug
Triamcinolone	MDI	Azmacort
Flunisolide	MDI	Aerobid
Fluticasone	MDI, Aerosol	Flovent
Beclomethasone	MDI	Vanceril, Beclovent
Prednisone	Oral, IV	--
Methylprednisone	Oral, IV	Medrol
Ibuprofen	Oral	Advil, Motrin
Montelukast	Oral	Singulair
Cromolyn	MDI, Aerosol	Intal

Bronchodilator medicines help open the airways by relaxing the muscles around them [2]. These medicines are inhaled and often are taken just before CPT to help clear out mucus. Also may take bronchodilators before inhaling other medicines into lungs[10]. Following table show the Bronchodilator medicines which are prescribed in cystic fibrosis.

Table 3: Bronchodilators drugs

Names	How Taken	Brand names for the same drug
Albuterol	MDI	Proventil,Ventolin
Theophylline	Oral	Theodur,Slobid,Uniphyl

Ipratropium	Aerosol, MDI	Atrovent

If have advanced lung disease and the level of oxygen in blood is low, may need oxygen therapy. Oxygen usually is given through nasal prongs or a mask. If other treatments haven't worked, lung transplant may be an option if have severe lung disease. A lung transplant is surgery to remove a person's diseased lung and replace it with a healthy lung from a deceased donor.

For prevent or treat blockages in the intestines, following table show the bronchodilators drugs which are prescribed in cystic fibrosis.

Table 4: Pancreatic Enzymes

Names	How Taken	Brand names for the same drug
Pancrelipase	Oral	Creon, Pancrecarb, Pancrease, Ultrase

Nutritional therapy can improve strength and ability to stay active. It also can improve growth and development in children. Nutritional therapy also may make strong enough to resist some lung infections. A nutritionist can help create a nutritional plan that meets needs. In addition to having a well-balanced diet that's rich in calories, fat, and protein, nutritional therapy may include oral pancreatic enzymes to help digest fats and proteins and absorb more vitamins. Supplements of vitamins A, D, E, and K to replace the fat-soluble vitamins that intestines can't absorb. High-calorie shakes to provide with additional nutrients. High-salt diet or salt supplements that take before doing vigorous exercise. Feeding tube to give more calories at night while sleeping. The tube may be threaded through nose and throat and into stomach. Or, it may be placed directly in to stomach through a surgically made hole. Before go to bed each night, will attach a bag with a nutritional solution to the entrance of the tube. It will feed while sleep [5]. Following table show the vitamins which are prescribed in cystic fibrosis.

Table 5: Vitamins

Names	How Taken	Brand names for the same drug
ADEK Fer-in-Sol Polyviflor drops Aquasol-A Drisdol Aquasol-E	All taken orally	no specific brand names

Some GI medicines to reduce stomach acid and help oral pancreatic enzymes work better and also use for relief of gastroesophageal reflu. Following table show GI medicines which are prescribed in cystic fibrosis.

Table 6: GI drugs

Names	How Taken	Brand names for the same drug
Omeprazole	Oral	Prilosec
Ranitidine	Oral	Zantac

Cystic fibrosis can cause a number of digestive problems, including poor growth and development, bulky stools, intestinal gas, a swollen belly, severe constipation, and pain or discomfort. Then stool softeners medicines are used. Following table show stool softeners medicines which are prescribed in cystic fibrosis.

Table 7: Stool softeners drugs

Names	How Taken	Brand names for the same drug
Docusate	Oral	Colace
Casanthranol & Docusate	Oral	Pericolace

If any allergic condition or symptoms arises in cystic fibrosis following medicines are prescribed

Table 8: Antihistamines drugs

Names	How Taken	Brand names for the same drug
Loratadine	Oral	Claritin
Cetirizine	Oral	Zyrtec
Fexofenadine	Oral	Allegra

For rhinitis or sinusitis problem in cystic fibrosis Vancenase/Vanc AQ, Rhinocort, Nasocort/NasocortAQ, Beconase/BecAQ, Nasel medicines are prescribed.

4. CONCLUSION

Cystic fibrosis remains a life-shortening condition associated with significant morbidity, recent advances and new treatments offer great hope and promise. Expanded newborn screening programs and improvements in early disease management may delay disease progression in future cohorts, an increasing number of adults with CF are living with more mild disease and are engaged in normal work and family roles. Treatment of cystic fibrosis will likely improve with new antimicrobials, better delivery mechanisms for existing antibiotics, and better microbial detection, supplement of vitamins. Patient-reported outcome measures provide data on the effects of new medications, as well as an increased understanding of how CF affects daily functioning. Quality improvements are expanding to improve outcomes with currently available treatments. Continued research is needed to identify optimal outcome measures for clinical trials.

5. REFERENCES

1. Cystic Fibrosis Mutation Database (CFMDB). 2010. Available at http://www.genet.sickkids.on.ca/cftr/StatisticsPage.html . Accessed April 01,2010.
2. Quittner AL, Barker DH, Marciel KK, Grimley ME: Cystic fibrosis: amodel for drug discovery and patient care. In: Roberts M, editor. Handbook of pediatric psychology. Fourth edition 2009.
3. Sawicki GS, Sellers DE, Robinson WM: High treatment burden in adults with cystic fibrosis: challenges to disease self-management. J Cyst Fibros 2009;8:91–6.
4. Borowitz D, Robinson KA, Rosenfeld M, Davis SD, Sabadosa KA: Cystic Fibrosis Foundation evidence-based guidelines for management of infants with cystic fibrosis. J Pediatr2009;155:S73–93.
5. McPhail GL, Acton JD, Fenchel MC, Amin RS, Seid M: Improvements in lung function outcomes in children

with cystic fibrosis are associated with better nutrition, fewer chronic Pseudomonas aeruginosa infections,and dornase alfa use. J Pediatr 2008;153(6):752–7.
6. Quinton PM: Too much salt, too little soda: cystic fibrosis. 2007;59(4):397– 41
7. Donaldson SH, Boucher RC: Sodium channels and cystic fibrosis. Chest 2007; 132(5):1631–6.
8. Mayer-Hamblett N, Ramsey BW, Kronmal RA: Advancing outcome measures for the new era of drug development in cystic fibrosis. Proc Am Thorac Soc 2007; 4(4):370–7.
9. Corey M: Power considerations for studies of lung function in cystic fibrosis. Proc Am Thorac Soc 2007; 4(4):334–7.
10. Bush, A, Davies, J: Non! to non-steroidal anti-inflammatory therapy for inflammatory lung disease in cystic fibrosis (at least at the moment). J. Pediatr., 2007; 151, 228–230.
11. Sibley CD, Rabin H, Surette MG: Cystic fibrosis: a polymicrobial infectious disease. Future Microbiol 2006; 1:53–61.
12. Smyth AR, Tan KH: Once-daily versus multiple-daily dosing with intravenous aminoglycosides for cystic fibrosis. Cochrane Database SystRev 2006;3:CD002009.
13. Adler, KB, Shapiro, SD., Gallup M, Wu, R., Randell, SH., Holtzman, MJ: Airway epithelium, inflammation, and mechanisms of disease: A tribute to Carol B. Basbaum. Am. J. Respir. Cell Mol. Biol.,2006; 34: 523–526.
14. Astudillo P, Mancilla P: Collaborative Chilean National Cystic Fibrosis Program. Cystic Fibrosis National Program: A Chilean Experience. Pediatric Respiratory Reviews. (Proceedings of The VII InternationalCongress in Paediatric Pulmonology) 2006;7:s303.
15. Terheggen-Lagro SW, Rijkers GT, van der Ent CK: The role of airway epithelium and blood neutrophils in the inflammatory response in cystic fibrosis. J Cyst Fibros 2005;4(Suppl 2):15–23.
16. Kerem E: Pharmacological induction of CFTR functions in patients with cystic fibrosis: mutation-specific therapy. Pediatr Pulmonol 2005; 40(3):183–96.
17. Li Z, Kosorok MR, Farrell PM, Laxova A, West SE, Green CG: Longitudinal development of mucoid Pseudomonas aeruginosa infection and lung disease progression in children with cystic fibrosis. JAMA 2005; 293(5):581–8.
18. Quittner AL, Buu A, MesserMA, Modi AC, Watrous M: Development and validation of The Cystic Fibrosis Questionnaire in the United States: a health-related quality-of-life measure for cystic fibrosis. Chest 2005; 128(4):2347–54.
19. DeLambo KE, Ievers-Landis CE, Drotar D, Quittner AL: Association of observed family relationship quality and problem-solving skills with treatment adherence in older children and adolescents with cystic fibrosis.J Pediatr Psychol 2004;29(5):343–53.
20. Gibson RL, Burns JL, Ramsey BW: Pathophysiology and management of pulmonary infections in cystic fibrosis. Am J Respir Crit Care Med 2003; 168(8):918–51.
21. Cantin AM, White TB, Cross CE, Forman HJ, Sokol RJ, Borowitz D: Antioxidants in cystic fibrosis. Conclusions from the CF antioxidant workshop, Bethesda, Maryland, November 11–12, 2003. Free Radic. Biol. Med., 2007; 42: 15–31.
22. Puchelle E, Bajolet O, Abely M: Airway mucus in cystic fibrosis. Paediatr Respir Rev 2002;3(2):115–9.
23. Emerson J, Rosenfeld M, McNamara S, Ramsey B, Gibson RL: Pseudomonas aeruginosa and other predictors of mortality and morbidity in young children with cystic fibrosis. Pediatr Pulmonol 2002; 34(2):91–100.
24. Zemel BS, Jawad AF, FitzSimmons S, Stallings VA: Longitudinal relationship among growth, nutritional status, and pulmonary function in children with cystic fibrosis: analysis of the Cystic Fibrosis Foundation National CF Patient Registry. J Pediatr 2000;137(3):374–80.
25. Quittner AL, Drotar D, Levers-Landis C, Seidner D, Slocum N, Jacobsen J.In: Drotar D: Adherence to medical treatments in adolescents with cystic fibrosis: the development and evaluation of family-based interventions Mahwah, NJ: Lawrence Erlbaum Associates; 2000. p. 383–407.
26. Bernstein PS, Khachik F, Carvalho LS, Muir GJ, Zhao DY, Katz NB: Identification and quantitation of carotenoids and their metabolites in the tissues of the human eye. Experimental Eye Research, 2001; 72: 215–223.
27. Gee L, Abbott J, Conway SP, Etherington C, Webb AK: Development of a disease specific health related quality of life measure for adults and adolescents with cystic fibrosis. Thorax 2000; 55(11):946–54.
28. Murphy MK, Black NA, Lamping DL, McKee CM, Sanderson CF, Askham J, Consensus development methods, and their use in clinical guideline development. Health Technol Assess (Winchester, England).1998;2(3):i–iv, 1–88.
29. Davis PB, Drumm M, Konstan MW. Cystic fibrosis. Am J Respir Crit Care Med 1996; 154(5):1229–56.
30. Konstan MW, Byard PJ, Hoppel CL, Davis PB: Effect of high dose ibuprofen in patients with cystic fibrosis. N Engl J Med 1995; 331:848– 54.
31. Holzer FJ, Schnall R, Landau LI: The effect of a home exercise programme in children with cystic fibrosis and asthma. Aust Paediat J 1984; 20(4):297–301.

32. Park RW, Grand RJ: Gastrointestinal manifestations of cystic fibrosis: A review. Gastroenterology 1981; 81: 143-61.

Conflict of Interest: None

Source of Funding: Nil