Cystic Fibrosis: Symptoms And Ways Of Treatment

Cystic fibrosis (CF) is a genetic condition that affects more than 10,400 people in the UK alone. Cystic fibrosis cannot be caught later in life, people are born with it and 1 in 25 of us carries the faulty gene without us knowing. (Cystic Fibrosis trust, 2018)

Some of the effects cystic fibrosis can on people is the build-up of mucus in the lungs, digestive system and other organs like the pancreas, liver, kidneys and the digestive tract. The gene affecting CF controls the movement of salt and water in and out of cells.

The diagnosis of cystic fibrosis can be found during new-born screening. The heel prick test is carried out on all babies in the UK and this will then give the diagnosis. If the results come back positive it is then followed up by a swear test. A member of the family that may carry the gene has the option to have a carrier test to see if they are a carrier of the faulty gene.

There are tests that can be carried out during pregnancy although these tests come at a high risk. (Cystic Fibrosis trust, 2018)

Cystic fibrosis causes the body to produce a thick mucus which have a variety of effects. The thick mucus builds up in the lungs and can cause breathing problems which increases the risk of lung infection. Over time, the lungs may stop working properly.

Mucus clogs the pancreas, which prevents the enzymes reaching food in the gut and aiding in digestion. This results in people with CF are unable to absorb nutrients from food and need to consume more calories to avoid malnutrition.

Some of the symptoms of cystic fibrosis include, reoccurring chest infection, difficulty gaining weight, jaundice, wheezing, coughing, shortness of breath and damage to the airways, diarrhoea, constipation and new born babies may have meconium ileus (bowel obstruction).

There can also be a development of a number of related conditions, such as diabetes, weakened bones, liver problems and infertility in a male.

There is no cure, and over time it does tend to get worse and can be fatal. However, there are a range of treatments which help control the symptoms, prevent of reduce complication and makes this condition easier to live with.

It may be a case of taking a variety of medication to treat and prevent lung problems, clear the lungs of mucus, physical activity or other clearance techniques.

Body

Cystic fibrosis is caused by a mutation in a gene that encodes for the cystic fibrosis transmembrane conductance regulator (CFTR). CFTR is a protein that functions as a channel across the cell membrane that produces sweat, tears, saliva and digestive enzymes. The channel transports chloride ions in and out of the cells, this helps control the movement of water

in tissues. This is necessary to produce thin, free flowing mucus.

Mucus is a substance that lubricates and protects the lining of the airways, digestive system, reproduction system and other organs and tissues.

CFTR also transports sodium ions across cell membranes, this is essential for the normal functioning of organs, such as the lungs and pancreas.

The mutation F508del is the most common mutation in the gene. This is the deletion of phenylalanine at the 508th position of the CFTR protein. (NLM.gov, 2018) (Critical care nurse, 2018)

The disruption of sodium and chloride transport, with the abnormalities in water transport results in heinous secretions within the pancreas, GI tract, respiratory tract, sweat glands and other exocrine tissues. An increase in secretions makes them difficult to clear. People develop exocrine gland dysfunction of multiple organ systems. This then leads to chronic respiratory problems, pancreatic enzyme insufficiency, biliary abnormalities obstruction of the intestine, and due to the agenesis of the vas deference and delayed menarche in can also cause infertility in the male and females. (Acedamy, 2018)

The Respiratory System

Cystic fibrosis can cause respiratory failure. The respiratory functions in attaining oxygen in to the body and eradicating carbon dioxide. The respiratory system is divided into two tracts, the upper respiratory tract (URT) and the lower respiratory tract (ULT)

The URT consists of the nasal passages and sinuses. The ULT consists of the trachea, bronchi, bronchial tubes and alveoli. Lining the LRT is cilia, hair like structures that clean and clear the lungs, removes dust, germs and mucus from smaller passages to larger passages where can be coughed out.

In a person with severe case of cystic fibrosis, cilia cannot easily move the thick sticky mucus out of the smaller passages, the mucus then clogs the air passages causing chronic lung infections and coughing.

Obstruction to the airways can lead to alveoli expanding, where air trapping occurs and over time causes the barrel-shapes chest that is common in emphysema patients.

Damage of the pulmonary parenchyma leads to increased pulmonary arterial pressure that causes right sided heart failure or co-pulmonale.

Cystic fibrosis patients have a decreased level of interleukin-10, this is a cytokine that has anti-inflammatory properties in the lungs. The decreased levels result in severe lung inflammation after infection. Reoccurring lung infections can cause breathing problems, leading to deficiency of oxygen in the body or lung damage. (UW Health , 2018)

The Gastrointestinal Tract

The gastrointestinal tract (GI tract) consists of organs involved in digestion of food. Food is chewed, mixed with saliva, passed through the oesophagus into the stomach where it breaks down further. (UW Health , 2018)

The partially digested food enters the small intestines where enzymes (secreted by the pancreas and bile, made in the liver and stored in the gallbladder) finish the digestive process.

As the digested food passes through the small intestine, the nutrients are absorbed and taken to other parts of the body, the remaining food such as fibre passes through the large intestine. Undigested food and waste collect in the rectum and leaves the body as stool.

In a person with CF the volumes of pancreatic enzymes decrease, the pancreas secretes the thick and sticky mucus and blocks the pancreatic ducts preventing the enzymes from digesting the food in the small intestine. This causes poor growth and malnutrition because of the lack of nutrients absorbed. (UW Health , 2018)

Liver

The mucus blocks the bile duct causing liver disease (UW Health , 2018)

Sweat gland

CTFR controls the movement across a membrane. The chloride channel does not work; therefore, chloride cannot leave the membrane. Sodium ions have their own membrane which allows them to successfully go through. Due to the relationship these ions have, because the chloride ions cannot leave it affects the sodium ions in the membrane.

CFTR plays a large role in the sweat gland. When sweat is first secreted it has a lot of salt in it, along the gland there are channels that lead towards the skin. The channels are for the reabsorption of sodium and chloride ions. We do not want to secrete all the ions therefore some will be released back in to the body. The body likes a balance between sodium and chloride.

Within a sweat gland of a person with CF the channel structure is the same, however, the chlorine channels do not work and is affected by CTFR. The chlorine will not be reabsorbed back in to the body and will continue through the gland to be secreted out. Chlorine is a negative charged ion and sodium a positive charge which means they attract, because of this attraction and the body needing a balance, sodium ions do not get reabsorbed in to the body and along with the chloride ions goes to the surface of the skin to be secreted and results in saltier skin. (UW Health , 2018)

Reproductive system

Male and females who suffer with cystic fibrosis may have fertility issues. Within men the vas deferens may be blocked and although he may be able to experience an erection and ejaculation, the sperm may be immobile.

Women have a thick mucus blocking the cervix preventing the sperm from reaching the egg for fertilisation. (UW Health , 2018)

Haemoptysis

This is a mild case is CF. It can be a frightening complication, infection in a small area of the lung may irritate a small blood vessel causing it to bleed. Treatment of vitamin K is used and helps with coagulation. (UW Health , 2018)

Treatment

Years have been added on to peoples lives that deal with CF. The advancements in research and care has given todays CF sufferers a survival age close to 40 whereas in the 1950's a child with cystic fibrosis did not live long along to attend school.

There are a range of treatments that can help with controlling the symptoms, reducing or the prevention of complications.

Medication

Vaccinations should always be up to date. Medications for cystic fibrosis are either swallowed, inhaled or injected.

- Antibiotics are taken for chest infection
- Medication to make the mucus thinner and easier to cough up.
- Medication that reduces the amount of mucus in the body.
- Bronchodilators to widen the airways
- Steroid medicine to treat nasal polyps.

There are other remedies that can be used to help CF.

Exercise

Physical activity can help clear mucus from the lungs and improve physical strength.

Airway clearance techniques

Deep breathing, huffing, coughing and relaxed breathing or gentle controlled breathing can help with clearing or removing mucus.

There are devices that can be used that uses breathing techniques, vibration and air pressure to help remove the mucus from airways.

Nutrition

Maintaining a good diet is important. A person with cystic fibrosis needs to consume more calories because of the difficulty digesting food in the pancreas. These extra calories will avoid malnutrition. Vitamin and mineral supplements can be taken to help as well as digestive enzyme capsules with food to aid in digestion.

Lung transplant

In Severe cases, when all medical treatments have failed, and the lungs have now stopped working, the next step is lung transplant. This can improve the length and quality of life for a person with cystic fibrosis. (NHS, 2018)

Research

November 2017, two clinical trials were presented at the North America cystic fibrosis conference. The research was carried out at Royal Brompton hospital. Researchers revealed the impact of using a compound called tezacaftor in combination with invacaftor to treat various combinations of the CF gene. The research was led by Prof. Stuart Elborn, consultant in respiratory medicine. It involved two people with two copies of the F508del mutation.

The research found that the tezacaftor/ivacaftor combination produced similar benefits to the combination known as Orkambi (ivacaftor/lumafactor). There was a 4% lung improvement, but it caused patients to experience side effects.

Orkambi

Orkambi is an oral medication, developed to treat CF by Massachusetts based vertex pharmaceuticals. The Medication can be given to patients ages 2+.

Lumacaftor and ivacaftor target the non-functioning chloride channels. The lumacaftor compound increases the amount of this channel on cell surfaces, the ivacaftor compound helps the non-functioning chloride channels work better. The combination of these compounds maintains the balance of salt and water in the body to prevent mucus from clogging any organs or ducts.

Orkambi was approved by the FDA in 2015 for patients 12+. Traffic and transport trials were carried out that looked at 1,108 cystic fibrosis patients with two copies of the F508del gene.

The dosage consisted of 400mg or 600mg of lumacaftor plus 250mg of ivacaftor, this was taken at night for 6 months as a combination. The result was an improvement in lung function, fewer hospital admissions and a decrease in antibiotic usage.

There is a three-phase trial, these patients were invited to the progress trial which is the second phase. Some of the patients continued the same dosage assigned in traffic and transport. Patients were placed into a placebo group, these patients were put on 600mg of lumacaftor plus 250mg of ivacaftor every morning as a combination tablet, plus a ivacaftor at night. These patients were evaluated for two years.

Long term there was an improvement in lung function, a maintain in a healthier Body mass index (BMI) and was tolerated well and safe.

In 2016 the FDA approved for the expansion of the trials of Orkambi. These trials were expanded to include CF patients ages 6-11, 2,400 more children had the chance to access this medication.

These children were given 200mg of lumacaftor plus 250mg of ivacaftor every 12 hours for 6 months. The results were positive with improvement in lung function and tolerance to the medication.

As of August 2018, the trials were extended once more to toddlers as young as two years old though to five years old. They trialled lumacaftor at doses of 100mg and 150mg and ivacaftor at doses of 125mg and 188mg.

This trial was conducted with 60 children being treated for 12 hours a day every 6 months. The response was equal to the older children in the earlier trials. Although there were some side effects, a cough which effected 63% of these children.

Orkambi is now approved to treat children and adults with CF across Europe, Australia and Canada. This medication depends on a patient's weight, it should be taken every 12 hours with a fat containing food such as a dairy product, nuts or avocados, fat helps the body to absorb medication better.

Along with the side effects such as the couch that affected some of the children in the trials, there are other side effects that occur while taking this medication, this includes breathing problems, tightness of chest, nausea, diarrhoea, stomach discomfort, cold symptoms, rash, fatigue or for women an irregular menstrual cycle.

Children could experience other side effects, headaches, stuffy nose, stomach pain and increased level of phlegm. (Cystic fibrosis news today, 2018)

Conclusion

Treatment of cystic fibrosis has advanced to target the pathophysiological changes associated with the disease. Great strides are being made in the care of individuals with cystic fibrosis, but this condition remains incurable. There is no prevention as it is a genetic disorder passed down from parents. There is no saying which of the approaches of treatment will turn out to be the most promising, however it is likely that most of them will make some sort of different to someone's life making it easier to deal with.

Orkambi has shown considerable promise in clinical trials and has now been distributed to other countries to treat adults and children with cystic fibrosis.

Today, technology has advanced so that there are opportunities to undergo testing to see is people are carriers of the F508del gene, or there is pre-natal screening where parents can see if their child will be born with cystic fibrosis. This allows doctors and families to begin to strategize treatment plans ready.

Researchers will continue to look for further treatments for cystic fibrosis, as there is always room for improvement, but already with the treatments demonstrated, people who have CF are living into their forties or older. These medications have given people the lives they possibly never thought they would get and that is a great achievement for scientific research.