Heart failure and Gene therapy

Heart failure is becoming a huge issue in the UK affecting nearly 900,000 people. Heart failure is a condition caused by the heart failing to pump enough blood to meet the body's requirements. This means that the body tissues do not receive enough oxygen to respire aerobically, which is the process where the body acquires most of its energy. It usually occurs because the heart muscle has become too weak or stiff to work properly. It can be fatal. Each year there is around 27,000 new cases of Heart failure in the UK; highest number of heart failure cases has been seen in Northern Ireland. Many patients (30-40%) die due to heart failure in the UK within one year after diagnosis.

Simple tasks like getting up or even sitting down become a struggle for these patients. Heart failure is diagnosed by 2D echocardiography. The drugs that are used to treat heart failure (ACE inhibitors and beta-blockers) have many side effects such as: electrolyte imbalance, liver and kidney problems, under or overactive thyroid, stomach upset, gout, respiratory problems and in some cases cancer. Some people have side effects: for example some young children/babies have drugs injected into them at a young age it will help them with their heart failure symptoms, but after three or more years, these children may develop cancer. That's where gene therapy becomes very useful.

There are many reasons why people's chances of being diagnosed with heart failure can increase. The following are some of the reasons which increase the risk:
High blood pressure (which is medically known as hypertension and puts extra strain on the heart) can lead to heart failure; people who are overweight, people of African or Caribbean descent are more prone, increased intake of salt, unhealthy diet devoid of enough fruit and vegetables, drink too much caffeine based drinks and alcohol, People who have sedentary lifestyle, people aged over 65 are prone to get high blood pressure and heart failure, another condition is coronary heart disease where the arteries that supply blood to your body, get clogged up by cholesterol atheroma. This could lead to a heart attack, overactive thyroid gland is another condition where there are excess levels of thyroid hormones and can cause heart failure or people with family history of hypertension and heart disease
Many people may think that eating fatty foods alone increases your chance of getting heart disease. In a recent study, scientists have found that some people are also born with a genetic predisposition to heart failure. The latest study, published in the journal Nature where they scanned genes of 100,000 people and identified some genes associated with high levels of cholesterol in their blood. This research has helped doctors explore new ways of treating people with naturally high cholesterol. Gene therapy is an exciting new way to treat heart failure (reference: Independent.co.uk)

It is known that calcium is very important for the cardiac muscle, which is the heart muscle, to function. Calcium levels rise during contraction and fall during relaxation. This calcium is required for the heart to pump blood round the body. The gene RYR2
(ryanodine receptor 2), which is present on chromosome 1, gives instructions to make a protein called ryanodine receptor 2. This protein controls the calcium levels in the heart muscle. It is known that this protein is low in patients with heart failure and hence it affects the calcium levels and pumping capacity of the heart muscle. If the gene is defective, one is more likely to get heart failure. Gene therapy increases the levels of ryanodine receptor protein 2 and hence replaces the ability to use calcium more effectively in the heart muscle and in all the other muscles. This increases the output of blood from the heart and can keep you stable for a lot longer. This will help as the longer you are stable the easier it is to have other treatments to work.

Researchers have ‘hidden’ the gene inside a genetically modified virus, (inactivated adeno-associated virus) which has the ability to insert into heart muscle cells and is believed to be entirely harmless. The virus delivers extra DNA into the nucleus of the cell. Doctors inject this harmless virus that has been genetically modified to carry human DNA. This virus carries the DNA into the cardiac cells. There the DNA replaces the gene that has been switched off due to heart failure. This then helps the heart to pump blood more efficiently one again. Doctors believe this treatment can recover the heart muscle and prolong the patient’s life expectancy. The difference between this and other methods of treatment is that gene therapy is thought to be harmless but other methods have side effects mentioned above.

The first patient to get the treatment, gene therapy, was David Palmer from Norfolk and he is very optimistic. David’s left side of his heart is enlarged and he suffers from arrhythmias, irregular heart rhythms. He said: My heart is forever jumping out rhythm- I don’t pass out just feel faint and very weak. Once he fell into a fridge in Sainsbury’s. He wasn’t hurt but felt a bit embarrassed. For David, gene therapy is his last hope as he has had the condition for too long to get a heart transplant. For people like David it is their last chance for survival and he thinks it will stabilize his condition and in turn will allow him to live longer. He thinks it’s far from a cure but if it works, it would be a major advance for a huge number of patients suffering from heart failure. Lee Adams, a 37-year-old man from Herefordshire is one of the first of 24 patients, who have advanced heart failure, in the study to have Gene therapy. He was interviewed and said this about Gene therapy: “Of course the best thing that can happen would be for my heart function to show signs of improvement and for gene therapy to prove to be a miracle cure for myself and other patients. Another patient, Carol Gedda, said this “It could improve the heart muscle. I’m really pleased to be part of it.”

At Royal Brompton, the gene therapy is delivered at the NIHR biomedical research unit, via a coronary angiogram under local anaesthetic. It is only one of an only two hospitals being involved in the international study. A similar research is happening in the United States and the patients have been doing extremely well.

Mrs Gedda, from Essex, is among 200 patients who are being tested to see if introducing genetic material into damaged heart cells will improve the hearts function. Researchers found that the levels of protein SERCA2a are lower in patients who have heart failure. Before joining the trial Mrs Gedda had to have some baseline measurements that would determine her fitness. Doctors told her to walk 30m up
and down a hospital corridor for six minutes. The distance travelled was measured by one of the hospital researchers at the Royal Brampton hospital. Her heart function was also analysed.

Dr. Alexander Lyon, who is a consultant cardiologist at The Royal Brampton Hospital, is leading the Cupid 2 trial. The US biotechnology company, Cellado, is funding the Cupid 2 trial. Dr. Alexander Lyon, who is also a British Heart Foundation senior lecturer, believes that the treatment is far from being a cure, but says there is great excitement about the trial. He is an old Persean and came to talk about this exciting new breakthrough for Heart failure patients. The data that has been collected so far seems very exciting and I look forward to reading his final conclusions. This also interested me as I lost my favourite grandfather to heart failure recently.

Bibliography

1. https://www.youtube.com/watch?v=qR3fsluDKfw