

Wetenschap voor Patiënten (Science to patients)

It is permitted to disseminate all transcripts within the project Wetenschap voor Patiënten (Science to Patients), under the explicit condition that the source ME/cvs Vereniging, <http://www.me-cvsvereniging.nl/> is clearly mentioned.

Webinar 45: ME and the bloodflow

Prof. Julia Newton. Broadcast June 17th 2014

What causes orthostatic intolerance?

Orthostatic intolerance is a very common complaint by patients with ME. It is a symptom of lightheadiness or dizziness when assuming the upright position. And about 90 % of patients with ME will describe this symptom. It is very easy to quantify using validated tools in the clinic. Things like the orthostatic grading scale will allow you to quantify this and as a result decide whether or not orthostatic intolerance is present. So a score on the OGS of 4 or above would be consistent with orthostatic intolerance.

How can orthostatic intolerance be managed?

Managing orthostatic intolerance is fairly routine in our clinic here in New Castle. The first thing we do is recommend to people that they need to increase their fluid intake to make sure that their vascular volume is high as it can possibly be. So we encourage people to drink at least two and a half litres of water a day, to reduce how much caffeine they drink to no more than 5 cups of caffeine a day. And in people where they have a normal blood pressure when they are sitting we recommend that they increase their salt intake. We call all of that together conservative advice. We then also recommend that people wear support stockings or tights of a type called Duomed grade 2 which prevents blood from pooling in their legs when they stand up. In addition to that there is some evidence in patients with orthostatic intolerance and in ME that a process called 'tilt training' can be of benefit. Tilt training works by helping the autonomic nervous system reset itself so that your body is able to detect the drops in blood pressure more ably when you stand up. Tilt training is very safe and involves individuals standing tilted against a wall twice a day for up to half an hour each time.

In addition to those conservative measures and tilt training in some people where we detect drops in their blood pressure we will try medication. This medication is generally aimed at increasing the blood pressure. So we use medicine such as fludrocortison which is a mineralocorticoid that helps your body retain salt and pushes your blood pressure up by that mechanism. And another medication that we use is a tablet called Midodrine and this is something called an alpha agonist and this vasoconstricts your peripheral blood vessels and pushes your blood pressure up by that mechanism.

What causes POTS?

POTS is a very interesting condition. POTS stands for Positional Tachycardia Syndrome. And our studies have shown that up to a third of patients with the diagnosis of ME actually when

they have formal autonomic testing will have a diagnosis of positional tachycardia syndrome. We diagnose this on the basis of your heart rate when you stand up. If it increases when you stand to above 120 beats per minute or by 30 beats per minute than this would be consistent with the diagnosis of POTS. POTS is known to be a form of dysautonomia. So it is an inappropriate tachycardia in response to the stress of standing. Usually it arises after a viral illness or after a pregnancy. So a similar presentation to that of ME.

How can POTS be managed?

The management of POTS is very similar to that for ME. So at the moment in New Castle, when we diagnose POTS we give people conservative advice. So we encourage them to drink two and a half litres of water a day, reduce the amount of caffeine that they are drinking and help them avoid blood pooling in their legs using stockings or getting them to squeeze their muscles regularly to get the blood out of their legs or the big muscles. We also try tilt training with them so we encourage them to become tilted against the wall for up to twice a day for six weeks. And then if that does not work then we will usually consider medication in people. So we might try the same kind of medicines as we try for orthostatic intolerance such as fludrocortisone and Midodrine. We also try using rate reducing drugs such as beta blockers and calcium antagonists. All aimed at trying to slow the heart rate down to allow people to feel better and as a consequence do more.

What is oxidative stress? What causes it?

Oxidative stress is something that happens inside cells usually in response to actions like exercise for example. So in your cells there is a whole range of biochemical processes that go on to create energy, to allow the cells to function. And if there is a problem with this, then sometimes the cells will create molecules that can be damaging to the cell. And this is called oxidative stress. There is some evidence that in patients with ME they are more likely to have oxidative stress and suffer more significantly from the consequences of oxidative stress. In terms of what we understand causes oxidative stress is still not really fully understood. What may happen is that there are deficiencies in those enzymes or molecules that form part of the chemical pathways that produce energy in the cells. In terms of studies that we are doing here in New Castle with our muscle cell experiments we are beginning to look at how oxygen free radicals are generated and how acid is generated within the cells to begin to explore how much oxidative stress there is and what the mechanisms might be that lead to the higher levels that are seen in patients with ME.

Are there other effects of blood flow disturbances (like pain)?

So the autonomic nervous system controls your blood pressure. And your blood pressure is the head of steam that gets the blood around your body. When we stand up 700 ml of blood will drop into our legs and as a consequence your autonomic nervous system has a microsecond response. It tries very hard to keep your blood pressure perfusing your brain and it does that by making your heart go a little bit faster and your peripheral blood vessels constrict. All aimed at maintaining this head of steam your blood pressure circulating the blood around your body. If not enough blood is getting around your body, then you might not get enough blood to those bits of your brain that keep you awake and you may black out, or you may be a bit dizzy or lightheaded if you are not getting enough blood to your brain. If you are not getting enough blood to your muscles or your heart then that's what I believe manifests as the symptom of fatigue.

We know in patients with autonomic nervous system problems that one of the symptoms they frequently describe is pain in their muscles. Particularly the big muscles across their shoulders or across their pelvis, the girdle muscles. And what we recognize this as, is something called coat hanger pain. A sensation of a coat hanger across the shoulders and up into the back of the neck. And this pain can be very debilitating for patients with autonomic nervous system problems. And actually when you ask patients with ME they frequently experience a similar type of pain. So as a result we believe that some of the pain that patients with ME experience is because of problems with blood flow to the large muscles. Sometimes people also describe pain in the extremities, in their fingers and their hands. And some of that might relate to low blood pressure. So if the blood isn't getting to the peripheries as well as it ought then the muscles aren't getting an adequate supply of blood and as a consequence they're accumulating acid and waste products within the muscles which causes malaise and symptoms of pain as a consequence.

How can these effects be coped with?

Coping with some of the problems of pain can be very difficult for patients. And often when I see people in clinic their biggest problem is pain as well as fatigue. We'll often use tablets just as Gabapentin to help with the pain and recommend sometimes for people to take regular pain killers to try and ease the pain. At the moment we are doing experiments in the lab to look at how acid accumulates in the muscles to see whether or not we can modify this and help people manage the pain that might arise because of the accumulation of acid in the muscles. At the moment we are excited about the results because it looks like the acid accumulation is reversible. And we are now doing further experiments funded by 'Action for ME' to look at teasing out the exact pathways so that we can identify medications that we may be able to use in clinical trials.

How might autonomic dysfunctions lead to gastrointestinal problems?

In terms of how autonomic dysfunction may lead to gastrointestinal problems there is a range of different ways that this could happen. We know in people who have problems of their autonomic nervous system, such as those with vasovagal syncope, that one of the frequent things they describe as they drop their blood pressure is nausea and a sensation of abdominal pain. So if patients with ME are experiencing drops in their blood pressure it is not unreasonable that symptoms like nausea and abdominal pain might occur at the same time. The other thing we know is that patients often will divert blood to their guts in response to taking their meal. Particularly a high carbohydrate meal. And as a result this can make people feel very dizzy and lightheaded because the blood is pooling in their gut just like it might pool in their legs when they stand up. And as a consequence we often recommend to people that they should not take high carbohydrate meals and take smaller meals with less carbohydrates.

Other things that people with ME frequently tell us is that they have symptoms consistent with irritable bowel syndrome. Now that is very interesting to me as somebody who is interested in the autonomic nervous system because there is quite an extensive scientific literature confirming a relationship between IBS and abnormalities of the autonomic nervous system. So again I would suggest that abnormalities of the autonomic nervous system are the underpinning phenomena that explains most if not all of the symptoms that people with ME experience.