NETWORK STUDY OF SUPPLEMENTATION OF LINOLEIC ACID IN CYSTIC FIBROSIS

(NETLACF)

A DOUBLE-BLIND CONTROLLED RANDOMIZED STUDY OF SUPPLEMENTATION OF LINOLEIC ACID DURING ONE YEAR TO PATIENTS WITH CYSTIC FIBROSIS – Influence on clinical status and metabolism

Information to parents and informed consent

August 18th 2020

Which combination of fatty acids will best improve the clinics of patients with cystic fibrosis?

Background: We know since more than 50 years that most patients with cystic fibrosis (CF) have low concentrations of some important fatty acids, common in vegetable oils. Especially linoleic acid is important part of all membranes in the body and further are formed from this fatty acids longer fatty acids which give important products for metabolism and inflammation defense. Also one fatty acid, common in all fish and seafood products, DHA, is often low in some patients and its products are important to hamper long-term inflammation, which is a common feature in CF in many tissues, especially in the lungs and the intestine. Many decades of experience in Sweden to supply for linoleic acid, both intravenously and orally has indicated that it might have very good influence on the clinical status of both lungs and intestine and on weight gain. During the latest years it has been a trend world wide to only supply DHA but that has not given any conclusive beneficial results. Neither of the fatty acids has given any adverse reactions. Some studies have verified that supplementation of linoleic acid can improve weight gain and even has had some effect on lung function , but most studies have been performed during too short time to be conclusive.

We now want to ask you if you will let your child take part in a clinical research study with the aim to find an ideal combination of fatty acids to improve weight gain and reduce inflammation. The fatty acids are not drugs and have no side effects. The study will takeplace in more than one country but is monitored from Sweden, where the experience of supplementation is large.

Please read carefully the information we hereby provide before you make your decision. Don´t hesitate to ask questions if you wonder about something.

What happens if you decide to let your child participate?

If you accept to let your child take part in the study, he/she will be randomized to to one of two groups and neither your family or the doctor will know during the treatment period to which group your child will belong. This is a well known way to perform research studies to avoid any influence on the result. In one group the participants are given linoleic acid and DHA, and in the other group oleic acid and DHA. Oleic acid is the fatty acid in olive oil and considered the valuable one in the Mediterranean diet. This group is used as a control group to find out if just linoleic acid action is as specific as expected. Both supplements give the same amounts of calories. The supplement is provided in a small bottle (20 ml), which content can be mixed in the breakfast meal, like in two spoons of porridge, sour milk, yougurt or juice.

The study will run for one year and will not in any way interfere with the usual treatment for CF. We plan to start in connection with your yearly check up which means that we only need to take some extra blood and urine samples at the beginning and end of the one-year treatment. We would like to ask for an extra blood sample after half a year to check that the fatty acid status is improving.

In the year-check up of the start and end of treatment, the following will be included although it usually may not always be performed yearly but more seldom: - a 3 day dietary registration of what

your child eat including a simple questionnaire about which kind of food you usually use at home (it might be similar to what you always do at yearly controls), - a sugar test, which you might otherwise not do yearly, but probably has done at some times - a metabolic test, showing the metabolic rate important for burning energy and which does not include any sampling – and further some extra inflammatory markers in blood and urine, which will be sent(coded) to other European laboratories for more advanced analyses.

Is there any risk for your child to participate? There is no risk to participate because all the supplements are similar to what you can find in ordinary food. As a matter of fact some countries already have an exceptionally high amount of linoleic acid in their ordinary food s for the general population. In this study we want to compensate for a deficiency and that all participants get a similar amount related to their body weight.Many people, including CF consume extra omega-3 capsulae daily but these should not be taken during the study since it is included in order that all patients have a controlled consumption. Therefore but are compensated for-

Is there any benefit for your child to participate? There are earlier studies showing that extra calories without extra linoleic acid doesn´t improve weight in a similar way as a combination of calories and linoleic acid does. It is also publications that not so much calories are necessary for good weight when linoleic acid is supplied. In a Spanish study just a combination of fatty acids seemed superficial and that is therefore the structure we have chosen in this study. In one study from US those with high fatty acid concentration in the blood grow better and had better lung function than those with lower concentration and in another study patients with extra supply of linoleic acid didn´t need extra calories to grow normally. We therefore expect no risk and hopefully good benefit, which is the reason we want to the study.

If the study shows improvement as expected and more so in one group than the other, both consider to offer both groups another year with the best working supplement. If you decide to let your child participate and later he/she or you regret your decision you are free to stop the participation without given any special reason and it will not influence the ordinary treatment of your child in any way. If you have questions now or late , always feel free to ask.

Responsible doctor:

name

tel

email

Responsible dietician.

name

tel

email

Consent

We have been given information about the study and supplements verbally and in written and have had the possibility to ask questions and get enough time to think about our decision about our child

By signing the form we agree to the following:

We agree to let our child take part in the study

We are confident that the participation is voluntary and that we can end the participation of our child at any time and without special motivation. If we regret our decision we know that will not influence the further treatment and care at the center. We agree that blood samples are saved in biobank (see appendix)

We agree that data are collected, stored in a computer, with the identity of our child coded, and that results of the study - without any identification of participants - will be published in an international scientific journal after the study is ended. We also agree that an independent supervisor (monitor) may take part in the study, all according to general rules and agreements in the EU commission**.**

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Signing of patients´parents Date

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Parents´ names

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Informed doctor´s consent

I have explained the study and the aim of it and the role of the patient. He/she has had the possibility to ask questions and get explanations and responses. The patient is given a copy of the information as well.

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Signing of doctor date

……Doctor´s name