Lay Language Protocol Summary

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Study/Protocol Title: **Triheptanoin Treatment of Long-Chain Fatty Acid Oxidation Disorders**

1. Purpose: Humans eat long-chain fat in their diet and use it for energy during exercise and during periods of fasting. Patients with long-chain fatty acid oxidation disorders cannot use dietary fat for energy. They sometimes develop muscle breakdown, and severe pain with exercise or illness. They can also have a heart that does not function properly. These patients are tired and expend less energy than people who do not have a long-chain fatty acid oxidation disorder. However, they can use a supplemental oil called medium chain triglyceride or MCT because it bypasses the block in long-chain fatty acid oxidation. MCT is available over the counter and can be purchased without a prescription. This study will determine if a new experimental oil called Triheptanoin can decrease the muscle pain, and increase the heart function and the amount of energy (calories) that patients with long-chain fatty acid oxidation disorders use.
2. Recruitment: Patients with a long-chain fatty acid oxidation disorder will be recruited through our clinic, past research participants, a patient support website, and recruitment letters mailed to physicians around the US. We will enroll 20 subjects at OHSU and 12 subjects at the University of Pittsburgh, age ≥7 years, with a disorder in fatty acid oxidation.
3. Procedures: Subjects will be admitted to the clinical research center for 4 days. They will collect all their urine for 24 hours. Heart function will be measured using ultrasound during an echocardiogram. For this test, the patient lies still on a bed and a probe is placed on their chest. A measurement of how fast a leg muscle makes energy during and after a short burst of exercise will be measured by magnetic resonance spectroscopy (MRS). For this test, the patient lies in the magnetic field of the magnetic resonance imaging (MRI) machine and does short bursts of leg kicking exercises in the Advanced Imaging Resource Center (AIRC) for about 1 hour. The amount of muscle and fat in the whole body and inside the liver and muscle will also be measured by MRS and by dual X-ray absorptiometry (DEXA). Subjects will walk on a treadmill for about 45 minutes. The amount of calories they use, their heart rate, and if they burn fat or carbohydrates will be measured. Blood samples will be collected before and after exercise. A meal test will be used to determine how much fat they burn.The subjects will drink a liquid breakfast with a stable isotope labeled fat added to food. Breath and blood samples will be collected before and after the meal, which will allow calculation of how much fat is burned for energy. The total amount of calories burned at rest will also be measured using indirect calorimetry, a method in which subjects lying on a bed will have a clear plastic bubble placed around their head to measure the oxygen and carbon dioxide levels in their breath. The amount of calories burned by subjects when they are doing their routine daily activities will be measured at home by doubly labeled water. All of these tests will be done at baseline. Then, subjects will be randomly assigned to consume MCT (current standard of care) or triheptanoin at 20% of their estimated calorie needs for 4 months. The subject and/or the parent will be taught how to use the supplement oil in their diet for cooking and baking. The subject will be sent home and the oil will be shipped to their home. The study coordinator will call the subject or subject's guardian each week to monitor the subject's diet, potential side effects and assist with diet planning. At the end of 4 months, all of the baseline tests will be repeated.
4. Survey Instruments: Subjects will record what they eat for three days. They will write down what foods they eat, how they were prepared and how much they ate on a form provided to them. Subjects will complete the 3-day diet record 3 times during the study.
5. Triheptanoin is an experimental oil. It is a clear, odorless oil that can be mixed with foods and used in cooking.
6. Data Analysis: The change in exercise ability, heart function, calories used and body fat after 4 months will be compared between subjects randomized to MCT versus triheptanoin.

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