

Fatty Acid Oxidation Disorders in Adults: A potentially treatable cause of muscle disease

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Background: The metabolic myopathies are a heterogeneous group of muscle diseases that occur as a result of defects in glycogen, lipid, mitochondrial, and adenine nucleotide metabolism. The 3 primary categories of disease include the mitochondrial myopathies, glycogen storage diseases (GSD), and fatty acid oxidation (FAO) defects. Mitochondrial FAO defects can be difficult to identify because clinical and biological manifestations may be transient. They comprise at least 12 diseases caused by a number of distinct enzyme or transporter deficiencies. Most present in childhood with cardiac or liver involvement, but exercise intolerance, myalgia, proximal muscle weakness, and attacks of rhabdomyolysis have been reported in later life. So, it is important that FAO defects are not overlooked as a potential cause of these symptoms in adults.

Aim: To report the clinical, biochemical and molecular studies in adult patients with FAO defects and identify the degree of muscle involvement in this group of disorders.

Methods: Patients with confirmed FAO defects under the care of the adult metabolic and neuromuscular teams at the National Hospital for Neurology and Neurosurgery were included in the study. The clinical, biochemical, and molecular details of each patient were collected and management was recorded.

Results: Fifteen patients were found to have FAO defects; 3 patients with Carnitine Palmitoyl Transferase (CPT) II deficiency; 4 with Medium-Chain Acyl-Coenzyme A Dehydrogenase (MCAD) deficiency; 2 with Long-Chain 3-Hydroxyacyl-Coenzyme A Dehydrogenase (LCHAD) deficiency; 3 with Very Long-Chain Acyl-Coenzyme A Dehydrogenase (VLCAD) deficiency; and 1 patient with each of CPT I, Primary Carnitine Deficiency (PCD) and Glutaric Acidemia (GA) II respectively. Four patients suffered attacks of rhabdomyolysis; 2 with CPT II deficiency; 1 with VLCAD; and 1 with LCHAD. 3 patients had myalgia or proximal muscle weakness; 1 with GA II deficiency and 2 with VLCAD. All but 1 of the patients with muscle symptoms were on modified diets supervised by a dedicated metabolic dietician.

Discussion: It is important to consider FAO defects when patients present with exercise intolerance, myalgia or attacks of rhabdomyolysis, particularly when there is an early age of symptom onset. Diagnosis may be achieved by simple measurement of fasting plasma Acylcarnitine profile and confirmed with assay of cultured skin fibroblasts, avoiding the need for muscle biopsy. We report that amongst the many FAO defects, CPT II and VLCAD are the most likely causes of muscle symptoms. We must attempt to identify these patients in our practice so that they may benefit from dietary intervention to alleviate symptoms and improve morbidity.