

TREATMENT

The Role of Nutrition in Mitochondrial and Metabolic Diseases

Jennifer Gwynne, RD, CNSD

Nutrition plays a vital role in the multidisciplinary management of mitochondrial and metabolic diseases. Depending on the pathophysiology and biochemistry of the disease, nutritional therapy can encompass single nutrient manipulations, vitamin supplementation and/or alternative routes of feeding. Registered dietitians who have specialized knowledge in metabolic processes and disorders are an integral part of the nutritional management for these diseases.

The goal of all nutritional therapy is to promote normal growth and development by meeting the child's nutrient needs for energy, protein, fluids, vitamins, and minerals. Nutrition's role in promoting immune function is also well recognized. An optimally functioning immune system is vital for children with a mitochondrial or metabolic disease as infection can be life-threatening for them.

Symptoms such as progressive muscle weakness, gastroesophageal dysmotility, ataxia, and dementia, all common in mitochondrial diseases, can interfere with nutritional intake. Children who are able to eat orally often require nutrient-dense foods in order to maintain an adequate intake of calories. Dietitians teach parents how to add calories to their child's favorite foods and how to use foods with different textures, such as soft foods or thickened liquids, especially if swallowing difficulties are present. If feeding ability deteriorates, causing failure to thrive, tube feedings offer an alternate route for supplementary or complete nutrition. Standard formulas may be appropriate; if not, home-blended formulas may be designed to meet a child's individual needs. In some cases, modular formulas (formulas which allow the independent manipulation of macronutrients—carbohydrates, proteins, and fats) may be necessary.

Disorders of fatty acid oxidation, such as medium-chain acyl-CoA dehydrogenase deficiency (MCAD)* and very-long-chain

acyl-CoA dehydrogenase deficiency (VLCAD)*, require macronutrient changes. In VLCAD, long-chain fats are limited to no more than 10 percent of caloric intake and are replaced with medium chain triglyceride (MCT) oil*. In MCAD, medium-chain fats are eliminated and long-chain fats are restricted to 20% to 30% of caloric intake. Fasting must be avoided to prevent hypoglycemia. Frequent meals and

snacks with high-complex carbohydrates are encouraged. Cornstarch is often added to meals or snacks, especially at bedtime to prevent nocturnal hypoglycemia. L-carnitine supplementation is often used in the management of MCAD, as well as in a number of organic acidemias.

Some children with lactic acidemia have demonstrated carbohydrate sensitivity. They may respond to a higher fat,

The Use of Dichloroacetate in the Treatment of Mitochondrial Disease

Richard Haas, MD

Effective and specific treatments for mitochondrial disease are not yet available. Treatment approaches such as dietary changes, vitamin and cofactor supplementation, and drug treatments appear to be helpful for some patients, but are unsuccessful for others.

Dichloroacetate (DCA) is currently the only available drug treatment for mitochondrial disease, and it is still experimental. DCA was pioneered by Peter Stacpoole, MD, PhD, of the University of Florida. It is being tested Dr. Stacpoole at the University of Florida (placebo-controlled study) and by our group at the MMDC at the University of California, San Diego (unblinded study).

DCA stimulates pyruvate dehydrogenase (PDH), resulting in lower lactic acid levels in almost all patients treated. Its use is presently restricted to children and adults with high levels of lactic acid in the blood or cerebrospinal fluid. Lactic acid itself is not toxic at low levels but elevated levels may be damaging. DCA treatment is appropriate only in cases of primary lactic acidosis. All patients are required to undergo a comprehensive evaluation in a metabolic unit before initiation of treatment to rule out cases of secondary lactic acidosis (e.g., organic acidemias, glycogen storage disorders, gluconeogenesis defects, and fatty acid oxidation defects). Patients who have high lactate levels only under stress (e.g., during a fever or illness) are not candidates for DCA therapy.

The goal of the clinical trials is to determine the safety of effects of and indications for treatment with DCA. To date, we have treated 30 patients with DCA at the University of California, San Diego. Some types of mitochondrial disease seem to be particularly responsive to this new treatment, most especially MELAS (mitochondrial encephalopathy with lactic acidosis and stroke-like episodes)*. Unfortunately, it has significant side effects, including peripheral nerve damage, which require careful monitoring. In some patients, these side effects limit the usefulness of this treatment. At this time, DCA should be used only in the context of a formal study. For more information on the clinical trials of DCA in primary lactic acidosis, visit <http://biochemgen.ucsd.edu/umdf/Information.htm>.

MITOCHONDRIAL and METABOLIC DISORDERS

lower carbohydrate and/or fructose-restricted diet. **As with all special diets, this should never be initiated without the careful monitoring available at a special center.**

In urea cycle disorders and organic acidemias, protein is limited. Strict biochemical and clinical monitoring with frequent dietary adjustment is essential to ensure an adequate intake of the essential amino acids and calories necessary for growth.

Diets that have been manipulated are

especially prone to nutrient imbalances. Evaluation of diets for nutritional adequacy and recommendations for appropriate supplementation are essential. Dietitians frequently use computer nutrient-analysis programs. Complete vitamin and mineral supplements are often prescribed to address deficiencies in the diet. Individual nutrients such as thiamin, riboflavin, biotin, ascorbic acid, and coenzyme Q10 may be prescribed in pharmacologic quantities as well.

The Consumer Nutrition Hotline of the American Dietetic Association's National Center for Nutrition and Dietetics, (800) 366-1655, can refer you to local dietitians who specialize in the area of pediatrics or mitochondrial and metabolic disease.

Ms. Gwynne is a registered dietitian who specializes in nutrition in pediatric metabolic disease. She works at the Children's Hospital and Health Center in San Diego, CA.

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