Malic Acid, Energy, & Fibromyalgia

Primary fibromyalgia (FM) is a condition affecting principally middle-aged women, characterized by a syndrome of generalized musculoskeletal pain, aches, stiffness, and tenderness at specific anatomical sites. This condition is considered primary when there are no obvious causes. Since it was first described, FM has become recognized as a fairly common rheumatic complaint with a clinical prevalence of 6 to 20 percent. Additionally, FM has been associated with irritable bowel syndrome, tension headache, mitral valve prolapse, and chronic fatigue syndrome. Numerous treatment modalities have been attempted to treat patients with FM, but unfortunately the results have usually been poor. The primary reason for this lack of success was undoubtedly due to our lack of understanding FMs etiology.

In recent years, evidence has accumulated to suggest that FM is the result of local hypoxia in the muscles. For instance, patients with FM have low muscle-tissue oxygen pressure in affected muscles, and to a lesser degree the same was found in other tissues. Muscle biopsies from affected areas showed muscle tissue breakdown and mitochondrial damage. Additionally, low levels of the high energy phosphates ATP, ADP, and phosphocreatine were found. It has been hypothesized that in hypoxic muscle tissues glycolysis is inhibited, reducing ATP synthesis. This stimulates the process of gluconeogenesis, which results in the breakdown of muscle proteins to amino acids that can be utilized as substrates for ATP synthesis. This muscle tissue breakdown, which has been observed in muscle biopsies taken from FM patients, is hypothesized to result in the muscle pain characteristic of FM.

Malic acid is both derived from food sources and synthesized in the body through the citric acid (Krebs) cycle. Its importance to the production of energy in the body during both aerobic and anaerobic conditions is well established. Under aerobic conditions, the oxidation of malate to oxaloacetate provides reducing equivalents to the mitochondria through the malate-aspartate redox shuttle. During anaerobic conditions, where a buildup of excess of reducing equivalents inhibits glycolysis, malic acids simultaneous reduction to succinate and oxidation to oxaloacetate is capable of removing the accumulating reducing equivalents. This allows malic acid to reverse hypoxias inhibition of glycolysis and energy production. This may allow malic acid to improve energy production in FM, reversing the negative effect of the relative hypoxia that has been found in these patients.

Because of its obvious relationship to energy depletion during exercise, malic acid may be of benefit to healthy individuals interested in maximizing their energy production, as well as those with FM. In the rat it has been found that only tissue malate is depleted following exhaustive physical activity. Other key metabolites from the citric acid cycle needed for energy production were found to be unchanged. Because of this, a deficiency of malic acid has been hypothesized to be a major cause of physical exhaustion. The administration of malic acid to rats has been shown to elevate mitochondrial malate and increase mitochondrial respiration and energy production. Surprisingly, relatively small amounts of exogenous malic acid were required to increase mitochondrial energy production and ATP formation. Under hypoxic conditions there is an increased demand and utilization of malic acid, and this demand is normally met by increasing the synthesis of malic acid through gluconeogenesis and muscle protein breakdown. This ultimately results in muscle breakdown and damage.

In a study on the effect of the oral administration of malic acid to rats, a significant increase in anaerobic endurance was found. Interestingly, the improvement in endurance was not accompanied

by an increase in
carbohydrate and oxygen utilization, suggesting that malic acid has carbohydrate and oxygen-sparing effects. In addition, malic acid is the only metabolite of the citric acid cycle positively correlated with physical activity. It has also been demonstrated that exercise-induced mitochondrial respiration is associated with an accumulation of malic acid. In humans, endurance training is associated with a significant increase in the enzymes involved with malic acid metabolism.

Because of the compelling evidence that malic acid plays a central role in energy production, especially during hypoxic conditions, malic acid supplements have been examined for their effects on FM. Subjective improvement in pain was observed within 48 hours of supplementation with 1200 - 2400 milligrams of malic acid, and this improvement was lost following the discontinuation of malic acid for 48 hours. While these studies also used magnesium supplements, due to the fact that magnesium is often low in FM patients, the rapid improvement following malic acid, as well as the rapid deterioration after discontinuation, suggests that malic acid is the most important component. This interesting theory of localized hypoxia in FM, and the ability of malic acid to overcome the block in energy production that this causes, should provide hope for those afflicted with FM. The potential for malic acid supplements, however, reaches much farther than FM. In light of malic acids ability to improve animal exercise performance, its potential for human athletes is particularly exciting.

Additionally, many hypoxia related conditions, such as respiratory and circulatory insufficiency, are associated with deficient energy production. Therefore, malic acid supplements may be of benefit in these conditions. Chronic Fatigue Syndrome has also been found to be associated with FM, and malic acid supplementation may be of use in improving energy production in this condition as well. Lastly, malic acid may be of use as a general supplement aimed at ensuring an optimal level of malic acid within the cells, and thus, maintaining an optimal level of
energy production.