Nutrition: A New Understanding

Muscle Metabolism in Spinal Muscular Atrophy and Other Muscle Disorders

Richard I. Kelley, M.D., Ph.D.

Atrophy or severe underdevelopment of muscle is common to SMA and many other neuromuscular diseases. Although the most obvious result of muscle atrophy is weakness, reduced muscle mass also has serious effects of nutrition, because muscle functions as an essential nutritional reserve, or "buffer," for protein, carbohydrate, and mineral metabolism.

The loss or reduction of this buffering capacity limits the ability of the body to adjust to simple nutritional changes, such as normal overnight fasting, or to more serious threats, such as diarrhea, vomiting, and fevers. For example, the limited ability of atrophied muscle to replace losses of potassium and water is one of the main reasons that an otherwise simple diarrhea illness can be lethal to a malnourished child or adult.

The role of muscle in the metabolism of fasting is especially important. Although the liver has a reserve of glucose in the form of "glycogen" that can sustain blood sugar levels for six to eight hours after a meal, muscle becomes the primary source of glucose for longer periods of fasting. Muscle does this by degrading its own protein into amino acids and then releasing the amino acids to the bloodstream. There the amino acids are picked up by the liver and turned into glucose. The glucose that is made in this manner is vital for brain and nerve function, and the body will sacrifice as much muscle protein as necessary to maintain blood glucose levels during fasting.

For the average child or adult, the amount of muscle protein that is degraded in one day of fasting may be only one percent of the total muscle mass. However, for a child with SMA who may have only 10% of normal muscle mass, a much greater proportion of muscle mass must be sacrificed to supply amino acids for glucose synthesis. Even the small

net loss of protein that occurs during normal overnight fasting may be a significant loss for a child with SMA who not only has limited muscle mass during the daytime.

Blood sugar and amino acid levels are the major signals for muscle protein metabolism: if they are high there is net muscle protein synthesis, and if they are low, as during fasting, there is net muscle protein breakdown. We have studied the adaptation to fasting of children with SMA for several years to learn more about muscle metabolism and nutrition in SMA.

We first confirmed that within only two or three hours of a normal meal or feeding, the blood amino acid levels of children with all forms of SMA decreased to levels that would not be reached until after at least eight hours of fasting in a normal child. We were also surprised to find that children with infantile or "acute" SMA could not efficiently metabolize fatty acids, which are a major source of energy during periods of fasting.

Rather, children with acute SMA had high levels of unused (and possibly toxic) fatty acid by-products in their urine and blood, sometimes after only overnight fasting. This abnormal fatty acid metabolism persisted in some children with SMA who were hospitalized for an illness and receiving glucose intravenously.

At this time we cannot explain all of the biochemical abnormalities that we see in SMA, nor can we prescribe a precise remedy for the problem. Nevertheless, following basic principles of normal muscle nutrition and metabolism may help preserve muscle mass in children with SMA.

The goals of such nutritional therapy should be to 1) limit fasting and the resulting low levels of blood glucose and amino acids that turn on muscle protein breakdown, and 2) assure adequate amounts of dietary protein to maintain normal blood amino acid levels and thereby enhance protein synthesis by muscle.

A suitable nutritional program to achieve these two simple goals would include 1) increased amounts of complex carbohydrates, 2) at least 2 grams of protein per kg per day, and 3) a feeding schedule that limits overnight fasting to 6 hours for a young infant and 10-12 hours for an older child. Of course, full caloric requirements for

each child's age and level of activity must also be met. Such a diet will necessarily have a lower percentage of fat, but is also important to assure that a child receives an adequate amount of essential fatty acids (a minimum of 5% of calories).

For older infants and children with SMA who sleep through the night, a late evening supplement of uncooked cornstarch (1 gm/kg) with a bottle or other food provides a good source of slowly absorbed complex carbohydrate. Uncooked cornstarch sustains blood glucose levels longer than other starches and, in effect, reduces the period of overnight fasting.

Finally, careful attention to nutrition must be given during illnesses, especially those that cause vomiting or otherwise limit caloric intake. If a child with SMA cannot eat or drink to supply the daily requirement of calories (typically 100Kcal/kg/day for an infant, 70-80 kcal/kg/day for an older child) then hospitalization for high caloric intravenous glucose (10% dextrose at 1.5 times "maintenance") may be necessary.

Although we recognize that nutritional "therapy" is not a definitive treatment for SMA or any other muscle disease, following these principles of muscle nutrition may help limit unnecessary losses of muscle mass. This approach might help maintain strength longer and enhance the important buffering function of muscle for many different aspects of body nutrition and metabolism.

We hope to explore these areas of muscle metabolism in SMA in more detail in the future. Perhaps then we and others who study SMA may be able to provide more detailed guidelines for nutrition for children with SMA.

Richard I. Kelley, M.D., Ph.D.
Kennedy Krieger Institute and the
Department of Pediatrics, John Hopkins University School of Medicine
Baltimore, MD 21205