REVIEW

Protein Metabolism in Critical Illness: Methodologies and Their Problems Underlying in Kinetic Studies Using Isotope Tracers *In Vivo*

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Abstract. The response to critical illness involves alterations in all aspects of metabolic control, favoring catabolism of body protein. In particular, as the result of the alteration of protein metabolism, body protein loss occurs, which has been reported to be inversely correlated with the survival of critically ill patients. Despite the availability of various therapeutic modalities aiming to prevent loss of body protein pool such as total parenteral nutrition, and enteral nutrition that has made to provide excessive calories as a form of energy substrate and protein itself, the loss of body protein could not be prevented. Loss of body protein store occurs as a consequence of the alteration of intermediate metabolism that works for the production of energy substrate. This alteration of substrate metabolism may link to the alteration of protein metabolism. However, no specific factors regulating protein metabolism have been identified. Thus, further investigations evaluating amino acid and protein metabolism are required to obtain a better understanding of the metabolic regulation in the body, which may lead to the development of novel and more effective therapeutic modalities for nutrition in the future. (Keio J Med 48 (2): 69–78, June 1999)

Key words: protein metabolism, nutritional support, stable isotope tracer, critical illness

Introduction

A rapid net catabolism of body protein, as well as a redistribution of the nitrogen pool and body composition within the body usually occurs in patients with major trauma,[1,2] thermal injury,[3,4] sepsis[5–7] and advanced cancer.[8,9] Persistent protein loss from the body pauses an important clinical problem, because the survival rate in patients with these conditions is inversely proportional to the loss of lean body mass.[10] Muscle protein breakdown is accelerated, whereas certain "acute-phase" proteins are produced at increased rates in the liver. Wound repair requires amino acids for protein synthesis, and increased immunological activity may also require accelerated protein synthesis. The magnitude of the net catabolism of muscle may be so pronounced that maintenance of lean body mass is an unreasonable goal in critically ill patients. Nonetheless, provision of dietary protein and/or amino acid is essential for minimizing net protein catabolism and/or net protein loss. Although it seems likely that a higher-than-normal intake of protein may be useful, simple provision of enough calories and/or protein failed to efficiently improve the net protein loss.[11] Even the mild stress of simple bed-rest increases the protein requirement to maintain nitrogen balance.[12]

This article reviews the alterations of amino acid and protein metabolism in critical illness and the response of nutritional support to amino acid and protein metabolism *in vivo*, and pathophysiological mechanisms by which amino acid and protein metabolism is altered in critical conditions are discussed. Underlying methodological issues involved in protein metabolism *in vivo* are also discussed.

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