Glutamine is an amino acid synthesized in skeletal muscle that is considered ‘conditionally’ essential in severe illness. It is the primary fuel source for enterocytes and has an essential role in lymphocyte and macrophage function. It is a precursor for nucleotide synthesis, and glutathione, a product of glutamine metabolism, has an important role as an antioxidant. Despite a significant release of glutamine, levels do not appear to increase in critical illness or injury; in fact, there is a decrease in plasma levels, by as much as 58%.

The immune-modulatory actions of glutamine depend on maintaining integrity of the mucosal barrier of the intestines. This is brought about by increase in DNA and protein synthesis, increase in villous height, and increase in mucosal proliferation leading to decrease in mucosal permeability. These actions reduce the possibility of bacterial translocation.

In humans, glutamine-supplemented formulas have resulted in greater preservation of skeletal muscle, improved nitrogen balance, and enhanced immune cell function. Fourteen randomized trials have evaluated the use of glutamine supplementation in surgical and critically ill patients. The aggregate results of these studies showed that glutamine supplementation was associated with a mortality risk ratio (RR) of 0.78 (95% CI 0.58, 1.04). It was also associated with a lower rate of infectious complications (RR 0.81; 0.64, 1.00) and shorter hospital stay. Parenteral glutamine in critical illness was associated with a non-significant reduction in mortality (RR 0.75; 0.52, 1.07). In patients who had undergone surgery and were given parenteral nutrition containing glutamine, there was a significant reduction in infection irrespective of whether they required parenteral nutrition or not (RR 0.45; 0.26, 0.78). Overall, for all patient groups there was a significant reduction in infection (RR 0.76; 0.64, 0.90).

The recent Canadian clinical practice guidelines for nutrition support in mechanically ventilated critically ill adult patients recommend that where parenteral nutrition is prescribed it should be supplemented with glutamine, and that enteral glutamine should be considered for patients with burns and trauma.

In this issue of the Journal, Kumar et al present their data on the effect of oral glutamine administration on oxidative stress, morbidity and mortality in critically ill surgical patients. The authors show no evidence of a physiological effect, or an effect on intermediate outcomes, or an effect on mortality. There is ambiguity about the scale of severity of illness in the patients studied, in the absence of any severity score. The authors affirm, “Our patients, though critically ill, did not usually require ICU care”. Moreover, they state that patients received oxygen by mask (5 L/min); no information is available on the numbers of patients needing mechanical ventilation. Also, some patients got their feeds orally. It appears therefore that the patient population was heterogeneous.

The dose of glutamine given was reasonable, at 45 g/day, but the markers of oxidative stress actually went up in the glutamine group, which is inconsistent with existing literature. There is no information regarding the type of product and the purity of the glutamine given. Was there a problem with its bioavailability or with compliance with the study protocol, because there is no evidence that the glutamine was absorbed or did anything for the patients? This study is also clearly underpowered to offer sound information on the endpoints portrayed.

The potential importance of nutritional manipulation to alter the outcome of critical illness has been tested in a number of trials. The heterogeneity of the patient population and the lack of adequate funding for statistically well-powered studies clearly seems to be the stumbling block in further research on the use of glutamine in the critically ill. At present there is fairly convincing evidence that glutamine deficiency is a significant problem in critical illness. There are no reports presently indicating harmful effects of glutamine.

In conclusion, it is necessary to emphasize the importance of good nutritional practice in the critically ill; glutamine may add usefulness to such therapy.

Pravin Amin
Bombay Hospital Institute of Medical Sciences, Mumbai
References


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