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Short Commentary

Essential Amino Acids as Immunonutrition in Critical Illness: Time for Trials?

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The derangement of both innate and adaptive immune responses of patients in the intensive care unit (ICU) led to the use of Immuno Nutrition Formula (INF) to reduce the risk of infection complications. While the observed findings might appear beneficial to high-risk surgical patients, they do not support the routine use of INF in medical ICU patients. In our opinion the inconsistent results from clinical trials might be due to the lack of Amino Acids (AA), in particular the Essential Amino Acids (EAAs), that patients receive either from a general nutrition support and from INF formula which does not contain EAAs.

To influence all aspects of leukocyte activities patients should be adequately supplied with all AAS [1,2]. However, most ICU patients receive an average of 0.7 g /Kg /d proteins, which is far lower than the recommended amount. This means that a patient weighing 70 Kg receives a maximum of only 16-20 gr EAAs/d, the amount approximatively contained in 240gr lean beef meat. The influences of AAs on the immune response have been documented in both *in vitro* and *in vivo* studies under physiological and clinical conditions (see Table). In extreme synthesis, adequate AA/EAA intake/provision is essential to leukocytes for the synthesis of cytotoxic proteins by T lymphocytes, antibodies by B lymphocytes and cytokines [3].

Griffith et al. [4] have shown that the intake of lysine reduces the transport of arginine into the virus of Herpes simplex thus leading to a depletion of polyamines, which are important for the growth of the virus. The EAA phenylalanine influences the immune response [5] both directly and indirectly; directly by regulating nitric oxide synthesis with leukocytes, and indirectly by its conversion to tyrosine. The latter leads to the formation of catecholamines, which stimulate the process of differentiation, proliferation of Th1 and B cells. Tyrosine, moreover, leads to the formation of dopamine which induces the production of anti-inflammatory mediators by leukocytes. The metabolism of the EAA methionine produces polyamines, which are important for the proliferation and differentiation of lymphocytes [6]. The EAA tryptophan is important for immunity in cancer, in which tryptophan plays a key role for an adequate cancer cell immune response. Indeed, tryptophan depletion suppresses the T cell response to cancer-specific antigens and causes tumour growth [7].

Given the huge influences on immune cell function of AAs and, in particular, of EAAs, we strongly believe that time has come to undertake appropriate trials targeting the effectiveness of adequate supplementation of EAAs with or without standard INF to enhance patient immune response and to reduce the risk for and shorten the duration of infection in critical patients. In addition, EAAs supplementation would increase the high-quality nitrogen provided to patients.

The following Table lists some human studies that report the immune response and beneficial clinical effects of administering BCAAs or EAAs mixture:

Setting	AA type	Effects
Cirrhosis [8]	BCAA	Enhanced function of myeloid dendritic cells
Postsurgery subjects [9]	BCAA	Blood lymphocyte counting higher than in controls
Postacute elderly patients [10,11]	EAA	30% reduction of nosocomial infections and reduced serum C-Reactive Protein
Postintensive severe brain injury patients [12]	EAA	23% reduction of nosocomial infections and reduced serum C-Reactive Protein (but not significant)
Elderly malnourished subjects [13]	EAA	Increase of mitochondrial bioenergetics in peripheral blood mononuclear cells

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