Immunocompetence assessment: A useful tool to evaluate nutritional status in eating disorders and in athletes

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IMMUNOCOMPETENCE ASSESSMENT

The assessment of the nutritional status compiles the study of dietary intake, anthropometry and biological markers involving haematology, biochemistry, and especially, immunology. Thus, the evaluation of the immunocompetence has been defined as a useful tool to assess situations of malnutrition even at a subclinical level.

In fact, the complexity of the interactions between nutrition, immunity and infection has widely well recognised. The immune function depends on the nutrient supply to carry out cell growth and proliferation together with the synthesis of effector compounds as needed to mount an immune response as well as to recover immune homeostasis after an immune response has been triggered.

Moreover, it is important to take into account that malnutrition and infection have mutually aggravating effects. In protein energy malnutrition there is a significant impairment of several aspects of immunity, including cell-mediated immune responses, production of secretory immunoglobulin A, phagocyte function, complement system and cytokine production. And besides, infectious processes cause anorexia leading to a more compromised situation of malnutrition.

EATING DISORDERS

The malnutrition status of patients with eating disorders is very particular. These patients usually do not show the same symptoms as in typical protein-energy malnutrition. However, this particular situation of malnutrition has been defined as relative protein-energy malnutrition.

Our research group has found a trend to show leukopenia with relative lymphocytosis, depletion of T lymphocytes and a decrease of the CD4/CD8 ratio in advanced stages of their illness, in patients without an early and adequate diagnosis, while the B lymphocyte subset is usually not affected. Actually, cell-mediated immunity is generally admitted to be more affected than humoral immunity in these patients.

However, despite the impairment observed in cell-mediated immune function, there is evidence that patients with eating disorders are free from infections, although they stay in hospital for long periods of time.
That is the reason why professionals involved in this filed still wonder:
Why do AN patients seem to be protected against infection?

The answers might come from the following facts:

- The primary nutrient inadequacy affects carbohydrates and fat intake while protein intake seems to be quite preserved.
- Due to the quality of the food choices of the patients, micronutrient deficiencies are not so common as expected, at least until the illness is far advanced.
- Patients with eating disorders are very heterogeneous and can present variable degrees of malnutrition.
- They also show different ways of developing adaptive mechanisms to the restricted intakes, and different levels of neuroendocrine and psychopathological alterations, which in turn, may compromise the immune function.

These premises could explain the controversial findings in these patients regarding immune function and their apparent resistance to infection.

To try to answer this question we should start by remembering the complex interactions between the immune system, the endocrine system and the central nervous system. Malnutrition may have an impact on these interactions and may impair the communication between these systems. The neurochemical disorders in these patients may perpetuate pathological eating behaviour and might be responsible for several associated psychiatric symptoms including stress, anxiety and depression, all of them are related to an altered immune system.

Furthermore, cytokines could be involved in some mechanisms, since they can be secreted at different levels within these systems. Thus, when the nutrient supply is insufficient, proinflammatory cytokines may be highly secreted, leading to weight loss, cachexia, osteoporosis, which are typical features in eating disorders. There is a feed-back mechanism through corticoids in order to restore cytokine levels.

On the other hand, infection is characterized by an acute phase reaction, including fever, loss of appetite, loss of food intake, cellular hypermetabolism and altered endocrine and enzyme responses. However, it is important to highlight that fever does not appear frequently in these patients.

Different results can be found in proinflammatory cytokines from patients with eating disorder, depending on whether they have been determined from:

1. plasma
2. the spontaneous production by peripheral blood mononuclear cells, or
3. the "in vitro" phytohemaglutinin-stimulated production by PBMCs

However, the endocrine system might be involved in the attainment of this particular outcome. In summary, in a basal situation, patients with eating disorders typically show a decreased plasma leptin concentration and an increased cortisol concentration. Proinflammatory cytokines (IL-1, TNF-α, IL-6) seem to be maintained at high levels in these patients, which might indicate that the negative feed-back mechanism mediated by cortisol is not working. However, when an infection occurs, high plasma cortisol levels could regulate IL-1β production through a cortisol receptor in monocytes, preventing the normal increased IL-1β secretion in response to an infection. Also during infection episodes, leptin levels are normally increased in plasma, which in turn seem to activate pro-inflammatory cytokine production by macrophages. In fact, leptin is produced during acute-phase response and represents and early reactant together with C reactive protein and IL-1 during systemic inflammation and fever. However, an incapacity to increase leptin could be hypothesized due to neuroendocrine and BMI alterations would result in a suppression of the expected increase of these cytokines and consequently to the surprising lack of infection symptoms described in AN patients, such as fever.

ATHLETICS

In aesthetic sports such as gymnastics, distance running, diving, figure skating and classical ballet, one of the main objectives for athletes is to maintain low body weights. These athletes are under restricted diets with obsessive weight control behaviour, which

frequently last a short time in which they are without appropriate guidance, and obviously they could be at risk of compromised nutritional status.

This situation of disordered eating, menstrual dysfunction and subsequent osteoporosis is well known as the female athlete triad.

Regarding the immune system, many immune functions are stimulated by moderate physical activity and long-term regular training; however, more vigorous effort and periods of heavy training can suppress various immune response parameters, particularly if the physical activity is accompanied by a situation of malnutrition, and environmental or competitive stress.

Our research group carried out a study in order to compare the situation of malnutrition between patients with anorexia nervosa, gymnasts, and young control females, all of them matched by sex, age (13 to 17 years) and socio-cultural level.

The energy intake was very low in the gymnasts in comparison with controls and the anorexia nervosa patients during their stay in hospital. In addition, although the energy from fat was correct in gymnasts, the calories coming from protein were very high, and the calories from carbohydrates, although reached the highest levels, were lower than they would require.

Both sportswomen and anorexia nervosa patients showed lower BMI levels than controls, and all of these values were below BMI of 19, that means they were within low weight range; gymnasts and patients showing 10% and 30% of emaciation, respectively.

Regarding the immunocompetent cells, the outcome is very similar to that found in the anorexia nervosa patients with the exception of the NK cells, whose levels are similar to the control group. These cells are known to be usually increased after physical activity, and probably this is the reason why these cells still maintain normal levels, in spite of the depletion of the rest of the immunocompetent cells.

Cytokine alterations are not the same as in the case of eating disorders. Proinflammatory cytokines such as TNF-α and IL-6 were at the same level as controls, although IL-1 levels were higher than in controls. However, IL-2 secretion was lower than controls, the same as in anorexia nervosa, but IFN-γ was higher than in controls and in patients with anorexia nervosa.

Probably, this different outcome from the one observed in patients with anorexia nervosa, could lead to a higher susceptibility of athletes to be more prone to infections, although the main features of both situations are very similar.

Therefore, it is important to find out not only the mechanisms involved in eating disorders and in athletes but also the biomarkers which can be helpful to know to what extent the state of malnutrition is severe. In both cases, a multidisciplinary group of professionals should be in charge of these situations of malnutrition in order to avoid future risks of developing other diseases.