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Study of Some Immunity Parameters in Patients Receiving Low-Caloric Diets

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The immunoregulatory effect of low-caloric diets on various components of the immune system was demonstrated. Serum content of TNF-α increased after the diet. Seasonal fluctuations in this parameter were observed in patients receiving these diets. A relationship between the increase in TNF-α level and body weight loss during low-caloric diet was detected. Presumably, transition to endogenous nutrition triggers not only catabolic hormones, but also cytokines with catabolic effects.

Key Words: *immunity; low-caloric diet; neutrophils*

The effects of fasting on the immune system and the relationship between the immune system and metabolism are important scientific and practical problems. Wide use of low-caloric diets (LCD) as therapeutic and rehabilitation methods implies LCD effects on the immune system. Effects of some food components on the immune system are well known [4,5].

However, the effects of food restriction on the state of different components of the immune system are little studied. Some experimental data demonstrate the important role of cytokines during fasting, which manifests by their influence on the endocrine system [10]. Moreover, they possess intrinsic catabolic activity, which is very important during fasting [2,7].

We studied the effects of LCD on oxygen-dependent bactericidal function of neutrophils, level of circulating immune complexes (CIC), and level of TNF-α in the serum.

MATERIALS AND METHODS

We examined 274 men and women aged 16-45 years hospitalized at Rehabilitation Center. The patients received LCD for 10 days according to the method developed at the Research Center of Clinical and Experimental Medicine, Siberian Division of Russian Academy of Medical Sciences [1]. Oxygen-dependent bactericidal function of neutrophils was evaluated by spontaneous and stimulated (zymosan, 20 μg/ml blood) NBT test [3]. CIC were measured by the standard method using 4% polyethylene glycol (PEG-6000). TNF-α was assayed using commercial kits (Protein Contour Firm). All measurements were carried out 1 day after hospitalization (before LCD) and on day 9 (after LCD). In parallel with these measurements, common clinical examinations, blood and urine tests, blood glucose measurements, and body weight control were carried out.

RESULTS

The mean body weight loss during LCD was 7.0±0.1%, with individual fluctuations within 5-10%. CIC levels underwent different changes in patients receiving LCD. Two groups can be distinguished: with decrease (1) and increase (2) in CIC levels in response to LCD (Fig. 1).

The individual decrease varied from negligible to more than 3-fold. This type of reaction was regarded as stabilizing. It was observed mainly in patients with initially high CIC levels. In some patients this parameter returned to normal during LCD, *i. e.* the for-

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mation of immune complexes decreased in response to LCD.

In the other group of patients the reaction to LCD was opposite: the level of CIC increased during LCD (immunostimulatory effect). This type of reaction was more incident in the patients with initially low levels of CIC. These patients felt subjectively better. An important result of this study was detection of a seasonal pattern of CIC fluctuations. The maximum levels were observed in spring (March-April), which can be explained by seasonal exacerbation of chronic inflammatory processes. It was more difficult to carry out LCD in spring than during other seasons, because the patients worse tolerated fasting.

Bactericidal activity of neutrophils underwent similar changes during LCD (Fig. 2).

The parameters of spontaneous NBT test decreased by 2.1 times in one group, but increased by 1.5 times in the other. Stimulated NBT test characterizing the reserve potentialities of this system increased after LCD. The neutrophil capacity to respond to the stimulus increased after LCD. The increase in CIC level and parameters of spontaneous NBT test was observed in patients with initially low and medium values of these characteristics, while the decrease was more often seen in patients with high levels of CIC and spontaneous NBT test values.

The reactions of these two subsystems (B-cellular and phagocytic) were not always synchronous during LCD. The decrease of CIC level did not always coincide with the decrease of NBT test values, that is, LCD acted as a selective immunoregulator, modulating activity of the immune system depending on body status.

Measurements of TNF-α levels were carried out 3 times during different seasons (in autumn, winter, and spring). Serum concentration of TNF-α increased more than 1.5-fold during LCD (Fig. 3).

The level of TNF-α did not increase in some patients, but in general this parameter increased in both groups. This increase was more significant in the fall and winter and less pronounced in spring. Body weight loss was more pronounced in the group with appreciably increased TNF-α compared to group 2, where this parameter increased less markedly. In subgroup 1 body weight loss was 7.41±0.40% from the initial body weight, while in subgroup 2 it was 6.74±0.30%. Cases of more than 10% body weight loss were observed only in subgroup 1. A trend to a more pronounced body weight loss was observed in patients with higher production of TNF-α. Parallel measurements of CIC and TNF-α revealed no correlation between these parameters: the level of CIC decreased during LCD, while the level of TNF-α increased. Seasonal fluctuations were observed for both parameters, more pronounced for CIC and less so for TNF-α level.

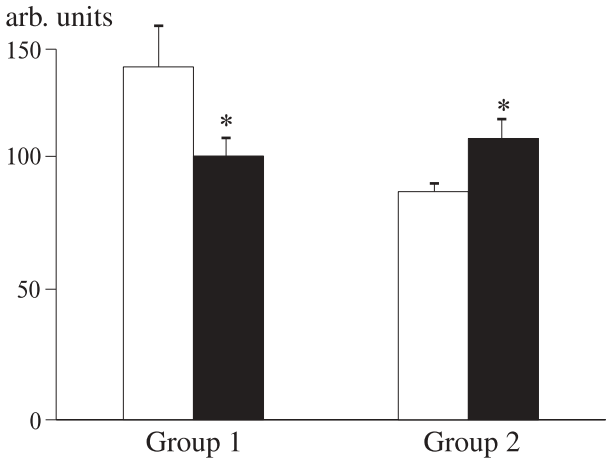

Fig. 1. Levels of circulating immune complexes before (light bars) and after (dark bars) low-caloric diet (LCD). *$p<0.05$ compared to level before LCD.

Hence, the effects of LCD on different levels of the immune system are different. It is obvious that the effect of the diet is immunoregulatory. The increase in TNF-α level during LCD is a principally new fact, which can be interpreted as follows. The realization of fasting involves not only catabolic hormones, but also cytokines with catabolic effects (TNF-α). Body weight loss in experimental animals after induction of TNF-α was demonstrated by many researchers [9]. It can be hypothesized that production of TNF-α increases during fasting. This cytokine activates catabolism in various tissues, including adipose tissue. This process provides energy material for body functioning during fasting. Presumably, it is an important mechanism of switching over to endogenous nutrition during fasting. The capacity of TNF-α to stimulate both proteolysis and lipolysis was demonstrated in animal experiments [6]. Adipocytes can produce and release TNF-α [8]. During fasting adipocytes are activated and production

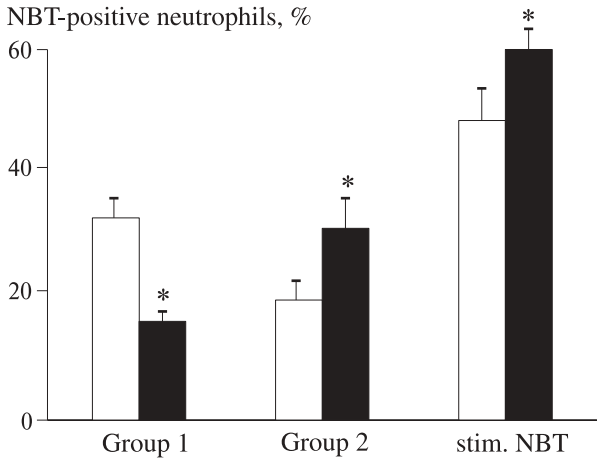

Fig. 2. Spontaneous and stimulated NBT test before (light bars) and after (dark bars) LCD. *$p<0.05$ compared to values before LCD.

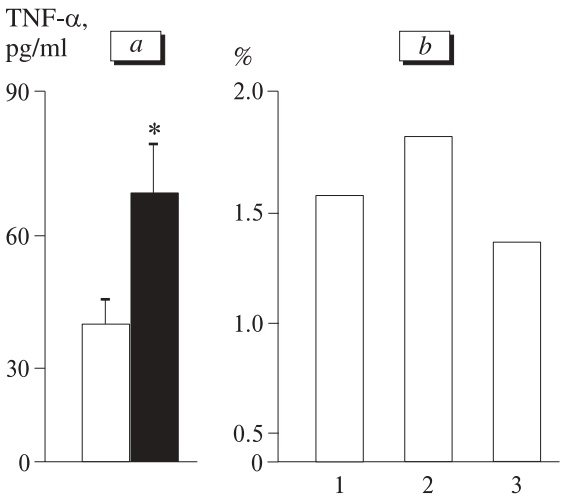

Fig. 3. Levels of TNF-α before (light bars) and after (dark bars) LCD (*a*), its relative increase (*b*) in autumn (*1*), winter (*2*), and spring (*3*). *$p<0.05$ compared to level before LCD.

of TNF-α increases. TNF-α acting via the autocrine mechanism stimulates lipolysis and adipocyte apoptosis, which explains why body weight loss is more pronounced in patients with higher TNF-α levels.

Hence, we found a new mechanism of body weight loss during fasting in humans receiving LCD: due to increased production of TNF-α as a catabolic cytokine. On the other hand, being a polyfunctional cytokine TNF-α can stimulate neutrophils and B-cells, this probably reflected the observed changes. The mechanism underlying the increase in TNF-α level during fasting can be principally important for the development of new technologies for body weight loss in humans.

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