SPORTS MEDICINE

Effect of a Six-Hour Marathon Ultra-Race on the Levels of IL-6, LIF, and SCF

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The effects of 6-h marathon ultra-race (long aerobic work below the lactate threshold level) on the levels of IL-6, leukemia inhibiting factor (LIF), and stem cell growth factor (SCF) were studied. The athletes participating in the study had different endurance levels evaluated by the distance covered over 6 h. The level of IL-6 sharply increased after exercise. The degree of IL-6 increase correlated with the length of the distance covered (r=0.83, p=0.042). The concentration of LIF after exercise inversely correlated with the distance covered (r= -0.75), but this correlation was statistically insignificant. The IL-6/LIF proportion exhibited the highest correlation with the result in the marathon ultra-race. This parameter most fully characterized athlete endurance (r=0.92, p=0.009). Hence, the relationship of LIF with physical endurance was demonstrated. Involvement of LIF in antibody production processes can be responsible for it.

Key Words: *IL-6; LIF; physical endurance; cytokines; malonic dialdehyde*

Studies of the reaction of the immune system to long-term exercise are focused on IL-6. However, the results of evaluation of its impact for physical working capacity are ambiguous. This cytokine is involved in the formation of fatigue sensation, which is regarded as muscle protection from damage by limiting their motor activity [7]. Injection of IL-6 to athletes (runners) led to deterioration of their results by 1 min for a 10-km distance [8].

On the other hand, IL-6 stimulates myoblast proliferation [1], blocks catabolic processes during long exercise, and is characterized by a potent angiogenic effect [4]. These effects improve physical working capacity and endurance.

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The mechanism of IL-6 action is mediated through its receptor (IL-6R) [7]. Receptors for IL-6, leukemia inhibitory factor (LIF), and stem cell growth factor (SCF) belong to the same superfamily of type 1 cytokine receptors (hemopoietin receptors) due to high homology of these molecules [9]. These cytokines act as a complex in many cases. A unique common receptor for LIF, SCF, and IL-6 is exposed on the surface of proliferating fetal stem cells. However, the role of LIF and SCF in body reaction to physical stress remains virtually not studied.

We studied changes in the levels of IL-6, LIF, and SCF during long exercise.

MATERIALS AND METHODS

The study was carried out on 6 athletes of different qualification, who took part in a 6-hour marathon ul-

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tra-race. This exercise is a long-term work of aerobic type below the threshold lactate value.

All athletes signed informed consent to participation in the experiment approved by the Ethic Committee of Institute of Physical Culture and Athletics.

Physical training of athletes was evaluated by the distance they covered during 6-h racing.

The blood was collected after overnight fasting 24 h before the competition and directly after race. Control blood specimens were collected 24 h after race. The levels of LIF and SCF were measured by the immunofluorescent method on a Bio-Plex 2200 device (Bio-Rad) using commercial test systems. The level of IL-6 was measured by enzyme immunoassay using IL-6-EIA-BEST (Vector-Best).

Malonic dialdehyde was evaluated by the reaction with thiobarbituric acid [6] in all blood samples.

The median was selected as the central trend in statistical processing of the results; the upper and lower quartiles were selected for interval evaluation, as the studied samples did not conform to normal distribution.

The significance of differences was evaluated by Mann–Whitney *U* test.

RESULTS

The mean pulse rate during racing was 144-154 bpm. The distance covered by the athletes was 51.56-85.36 km. High negative correlation of the distance covered and changes in the level of MDA (one of the most important LPO final products) was detected (r=-0.90, p=0.015). The relationship between MDA and level of physical training is well known [3], and hence, we confirmed the possibility to objectively evaluate athlete endurance by measuring the distance he/she passed.

Before the marathon ultra-race, the level of IL-6 was low: 2.4 (1.3-5.9) pg/ml, while directly after exercise it increased to 79.1 (66.9-114.1) pg/ml (p=0.028). One day after the race, the level of IL-6 dropped below the initial level, reaching 0.7 (0.2-1.2), though these values did not differ significantly from the initial level. Evaluation of the athletic results showed a positive correlation between the distance covered and IL-6 level directly after exercise (Fig. 1). High physical endurance was associated with high levels of IL-6 (r=0.83, p=0.042).

The mean level of LIF changed little after exercise in the group: 33 (19-36) pg/ml *vs.* 29 (26-36) pg/ml before the marathon ultra-race. This effect was explained by different direction of changes: in some athletes LIF level decreased after exercise, while in others it increased. A negative correlation between the distance covered and LIV level was noted directly after the end of exercise (Fig. 2), but the resultant coefficient of correlation was statistically negligible (r=-0.75, p=0.09), because of the small size of the sampling.

The IL-6/LIF proportion was calculated. This value varied from 0.57 to 14.11 in the athletes. Evaluation of the relationship between the distance passed and the IL-6/LIF proportion showed a 0.92 coefficient of correlation, which was statistically significant (p=0.009). Hence, the IL-6/LIF proportion after exercise more adequately characterizes athlete endurance than any of these parameters alone.

The level of SCF virtually did not change in response to exercise and was 101.1 (99.8-108.0) pg/ml before race, 114.6 (102.5-120.0) pg/ml after exercise, and 105.4 (98.3-114.9) pg/ml after recovery.

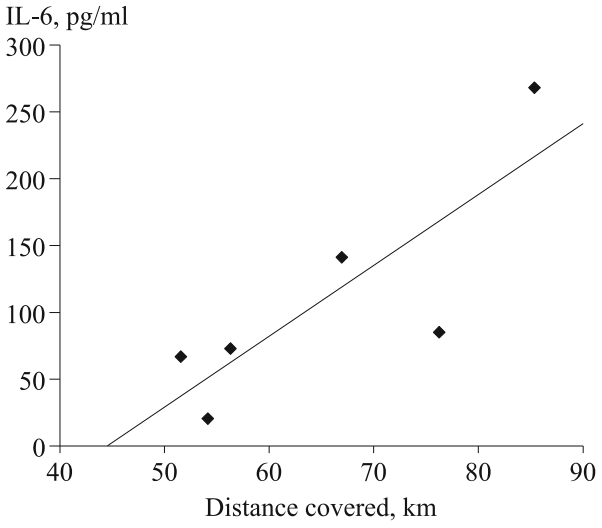

Fig. 1. Relationship between the distance covered and IL-6 level directly after marathon ultra-race.

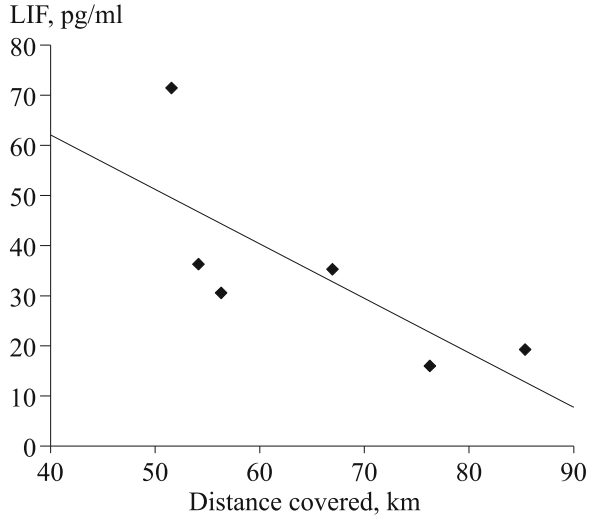

Fig. 2. Relationship between the distance covered and LIF level directly after the marathon ultra-race.

Our data confirm the positive role of IL-6 in adaptation to long-term exercise. The degree of physical endurance correlates with the intensity of the cytokine response, manifesting by an increase in IL-6 level in response to physical stress, and does not depend on the basal cytokine level.

The relationship between LIF and physical endurance was demonstrated.

The role of LIF in the regulation of cell differentiation in health and in tumor diseases is now actively studied. This factor is characterized by low basal secretion, but its level increases drastically in response to inflammation. We did not observe pronounced elevation of LIF concentration in response to exercise, which indirectly confirms that changes in the cytokine levels were not caused by inflammatory response to cell microinjuries during exercise.

In addition to immunocompetent cells, LIF is secreted in the CNS, where it is involved in astrocyte differentiation [10]. Involvement of this cytokine in neoangiogenesis processes has been shown. Inhibitory effect of LIF on VEGF in mice has been detected [5]. It has been also shown that the density and length of vessels are greater in the LIF gene knockout mice [2,10]. Presumably, high level of LIF is an unfavorable factor in angiogenesis in the muscle tissue. Hence, individuals with low production of this cytokine in response to physical stress are less sensitive to this unfavorable factor during training and are characterized by better physical endurance due to better muscular trophics.

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