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CHARACTERISTICS OF SYSTEMIC INFLAMMATORY MARKERS IN ATHLETES ON INTENSIVE PHYSICAL TRAINING PROGRAM

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Regular physical activity and good physical fitness are widely accepted as factors that reduce all-cause mortality and improve a number of health outcomes. The aim of this study was to investigate the effects of intensive aerobic exercise training program on systemic inflammatory markers in young healthy athletes.

The investigation involved fifteen healthy athletes with the aim to investigate the effect of intensive physical training program on inflammatory response, and systemic inflammatory markers. Mean age of athletes was 16–20 years. The training period lasted minimum six months. All athletes trained 3 times/week. Blood samples were taken from the antecubital vein, in the morning, immediately before training; post-exercise blood samples were taken 5–10 min immediately after the exercise session. Cardiovascular parameters, inflammatory markers and physical exercise-related symptoms were determined.

Ten male and five female athletes with mean age 18.03±1.4 years were included in the investigation. There was not a significant difference in systolic blood pressure, but significant reduction of diastolic blood pressure and increasing of heart rate ($p<0.05$) were registered after completion of exercise. Significant increase in SE I and lukocyte count as well as neutrophile predomination were found after the exercise. The lymphocyte stake was significantly decreased after intensive training. The training-related symptoms were more frequent at the beginning of the training program. Breathlessness was experienced more frequently (36%) than wheezing (12%), cough (16%), weakness (16%) or chest tightness (12%) at the beginning of the program.

Regular physical activity reduces the risk of cardiovascular and atherosclerotic diseases. The concentration of CRP during exercise training program is a useful marker for determination of athletes' physical condition and their response to the training program intensity. Only well-balanced exercise training programs result in favorable effects on the immune system, which is manifested through reduction of inflammation, increased immune response and reduction of physical exercise-related symptoms. *Acta Medica Medianae 2009;48(4):50-54..*

***Key words**: inflammation, inflammatory markers, athletes, physical training*

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Introduction

Athletes represent the healthiest segment of society. Regular physical activity and good physical fitness are widely accepted as factors that reduce all-cause mortality and improve a number of health outcomes (1).

Physical activity is generally divided into two large categories: isotonic or dynamic exercises and isometric or static exercises. Isotonic or dynamic exercises, such as running, lead to an increase in stroke volume, left ventricular end-diastolic volume, and oxygen consumption. The result is a mass-to-volume ratio that is unchanged. Left ventricular end-diastolic diameter is a compensatory measure to reduce the stress of the left ventricle wall. The athlete requires a greater cardiac output during exercise and this is accomplished through a larger stroke volume, a lower heart rate and myocardial wall thickening (2). A recent study has shown that low maximal aerobic capacity is closely associated with unwanted cardiac events (3). Therefore, physical training has been proposed to reduce these events by improving aerobic capacity.

However, the association between training response and cardiovascular autonomic function is largely unknown. Yet, there are still reports on sudden death occurring on athletic field. Any athlete who 'goes to ground' or experiences syncope should be sent to immediate examination. The term 'goes to ground' simply means that while an athlete is performing in competitive sports, the athlete has a syncopal event or may have an aborted sudden death event (2).

The most common causes of sudden death in athletes are hypertrophic cardiomyopathy,

anomalous coronary arteries, arrhythmogenic right ventricular cardiomyopathy, myocarditis, dilated cardiomyopathy and unexplained arrhythmogenic episodes-atrial and ventricular fibrillation. Patho-physiology of each abnormality and how it contributes to symptoms of syncope and sudden death are still unknown (4).

Further searching and literature analysis revealed that excessive endurance exercise or overtraining can lead to chronic systemic inflammation and, separately, that there is a solid association between C reactive protein (CRP) and atrial fibrilation (AF) (5), and that anti-inflammatory agents have been reported to lower CRP and ameliorate AF (6).

It is of particular interest to extend our knowledge about inflammmation in athletes, because athletic behavior that can induce inflammation may contribute to appereance of syncope and sudden death as well as other health problems in athletics. On the other hand, we can make better decision about frequency and the intensity of the exercise programs measuring inflammatory response markers. In that way, we can improve perfomance of athletics and get better sports results minimising the health risks.

Aims

The aim of this study was to investigate the effects of intensive aerobic exercise training program on systemic inflammatory markers in young healthy athletes.

Participants and methods

The investigation involved fifteen healthy athletes, conducted with the aim to investigate the effect of intensive physical training program on inflammatory response and systemic inflammatory markers. Mean age of athletes was 16–20 years. The training period lasted minimum six months. All athletes trained 3 times/week.

Exercise training protocol

The pre-exercise blood samples were taken at 7 AM in the fasting state (12 hour food deprivation during night period) from participants. Blood samples were taken from the antecubital vein prior to training after assuming a sitting position. They were then allowed to participate in the endurance training. This involved three repetitions of 20-min running sessions, with two breaks of 3-min rest intervals inbetween. The athletes were aiming for a heart rate of around 120–140 bpm. Completion of exercise was defined as completion of the training session. Post-exercise blood samples were taken immediately after the exercise session within 5–10 min. All participants gave informed consent.

Cardiovascular examination

Cardiovascular parameters comprise measuring of systolic and diastolic arterial tension and heart rate. Upon arrival (completion of the training session), the subjects remained resting in the sitting position for 5 min before the start of measuring. Blood pressure was measured by auscultation (sphygmomanometer and stethoscope, Becton Dickinson, USA) three times accordingly to American Heart Association procedure, on the occasion of which the mean value of three measurings was taken as valid (7).

Biochemical examination

Sedimentation rate was determined in the first and the second hour after collection of whole blood samples into polypropylene tubes.

Inflammatory risk factors comprise determination of leukocyte count by autoanalyser for blood samples Haematolog H1-Technicon.

Determination of high sensitive C reactive protein was done by commercial tests Dade Behring on Dimension Expand analyser. Serum values of hsCRP are expressed in mg/l.

The exercise-related symptoms were collected by anonymous questionnaire. They comprised the symptoms occurring during the last 3 months.

Individuals who had some infection in the past month were excluded from the study. Individuals with allergic diathesis, metabolic diseases or any other condition, which influence the immune system, were excluded. Four weeks prior to the study the subjects were advised to avoid the use of vitamin supplements.

The data were analysed by standard descriptive methods (mean, standard deviation and percent frequency). Results were obtained by using the paired Student's t test, χ^2 test and Fisher test depending on specimens and type of data.

Statistical analysis was done by software package SPSS 11.0.

Results

Ten male and five female athletes were included into the investigation. Mean age of examinees was 18.03±1.4 years, with no significant variation between gender (Table 1).

There was not a significant difference in systolic BP at the beginning and at the end of training. Significant reduction of diastolic blood pressure ($p<0.05$) and increase of HR ($p<0.05$) were registered after completion of exercise (Table 2).

Significant increase of SE I and lukocyte count as well as neutrophil predomination were found after completion of exercise. The lymphocyte stake was significantly decreased after intensive training (Table 3).

Physical exercise-related symtoms reported in the last three months of training program are shown in Graph 1.

Table 1. Characteristics of examinees

	N	%	Weight (kg)	Height (cm)	Age (year)
Male	10	66	78.1±10.3*	180±6.5*	18.3±1.5
Female	5	34	65.3±9.8	175±7.1	17.4±1.2
Total	15	100	74.2±10.1	178.2±6.8	18.03±1.4

Data are presented as the N/% or mean±S.D.;*p<0.05

Table 2. Cardiovascular parameters

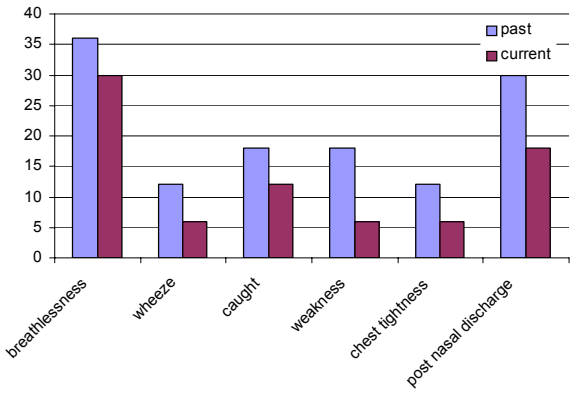
	start	end	p
sTA (mmHg)	116.1±4.3	131±6.4	NS
dTA (mmHg)	82.5±5.2	77.6±13	<0.05
HR (/min)	72.3±5.6	77.6±7.5	<0.05

Data are presented as the mean±S.D.
sBP- systolic blood pressure;
dBP- diastolic blood pressure; HR-heart rate

Table 3. Inflammation markers before and after completion of exercise

	start	end	p
SE I (mm)	5.2±1.4	8.1±3.2	<0.05
SE II (mm)	10.5±2.1	12.1±4.5	NS
Leu (G/L)	6.4±2.7	12.9±4.6	<0.05
Neu (%)	55.2±6.8	66.4±7.8	<0.05
Eo (%)	2.7±1.4	2.9±1.5	NS
Ba (%)	0.2±0.1	0.2±0.2	NS
Ly (%)	32.3±3.8	24.6±5.4	<0.01
Mo (%)	5.1±3.9	6.3±3.7	NS
hsCRP (mg/dL)	2.3±0.7	3.5±1.1	NS

Data are presented as the mean±S.D.;
SE I-sedimentation rate in 1st hour,
SE II-sedimentation rate in 2nd hour;
Leu-Leukocyte count;
Neu-neutophylic leukocytes;
Eo-eosinophylic leukocytes;
Ba-basophylic leukocytes;
Ly-lymphocytes; Mo-monocites



Graph 1. Physical exercise- related symptoms reported in last three months

Discussion

The study investigated the effects of intensive aerobic exercise training program on systemic inflammatory markers in young healthy athletes. Especially, we wanted to prove the hypothesis that improvement in aerobic capacity and balanced physical load during training would prevent significant increase of inflammatory markers.

The values of cardiovascular parameters were within normal range at the begining and after completion of exercise (Table 2). Moreover, diastolic blood presure showed significant reduction after completion. There is consistent evidence that regular rhythmic physical exercise of the lower extremities decreases both systolic and diastolic blood pressure by 5–7 mm Hg apart from weight loss, alcohol intake or salt intake (8).

Inflammation and normal intensive exercise

Significant increase of SE I and lukocyte count were found after completion of exercise. The rearragement patern was characterised by neutrophil domination and limphocyte depletion (Table 3). As for acute exercise, there are several consistent patterns that emerge regarding leukocyte subpopulations in the blood. The neutrophil concentration increases during exercise and continues to increase post-exercise (9,10). The lymphocyte concentration increases during exercise and falls below preexercise values following intense long-duration exercise, but is not suppressed after moderate exercise (9). The increased lymphocyte concentration is due to recruitment of all lymphocyte subpopulations to the blood. Thus, both the CD4+ T cells, CD8 + T cells, CD19 + B cells, CD16 + natural killer (NK) cells, and CD56 + NK cells increase in number during exercise and decline following intense exercise lasting at least one hour. Furthermore, following intense long-lasting exercise, the function of NK and B cells is suppressed. Thus, the NK cell activity (the ability of NK cells to lyse a certain number of tumor target cells) is inhibited. Furthermore, antibody production in the circulation is inhibited and the local production of secretory IgA in mucosa is inhibited (11). The importance of well-designed training programe lies in the fact that opposite to these results, T cell function and NK activity were significantly greater in a group of highly conditioned female endurance competitors when compared with age-matched sedentary controls (10).

C-reactive protein (CRP) is an example of an acute phase protein and is a sensitive marker of inflammation regardless of etiology. It has been believed that both IL-6 and IL-1 induce the synthesis of CRP. Synthesis of acute phase proteins in the liver following pro-inflammatory cytokine stimulation is associated with higher risk of cardiovascular events as well (12). It has been shown that CRP promotes vascular inflammation and thrombosis and is involved in the progression of atherosclerosis. Increased CRP level is thus associated with increased cardiac morbidity (13).

Several studies have suggested that physical exercise induces muscle damage and a complex cascade of nonspecific inflammatory responses. They have demonstrated acute short-term increases in IL-6 and CRP released in the brain, skeletal muscle, and/or connective tissue in response to intensive or prolonged exercise, particularly to long-distance running (14). Increases in IL-1 receptor antagonist and in some anti-inflammatory cytokines were also detected (15).

In the examined athletes, a significant increase in CRP concentration after completion of training was not found; CRP levels were in the lowest quartile of normal range (Table 3), which is in line with results that under certain circum-stances such as endurance training, acute, pulsatile release of IL-6 does not stimulate synthesis of CRP (16), during which the CRP levels stay reduced at least up to 6 weeks after heavy physical activity (17) .

Long-term controlled training exercise in general results in a decline of inflammatory markers, putting aside questions of running injuries and overtraining. A 9-month study of 14 runners training for marathon showed a distinct downward trend in their baseline C-reactive protein (CRP) during the training period (18). Two major reviews support the distinction between acute pro-inflammatory and long-term anti-inflammatory response in case of normal intensive exercise (19).

The association of physical activity with lower levels of inflammation and CRP may provide another cardioprotective mechanism, because high levels of CRP have been found to be associated with increased risk of cardiovascular events (20).

Excessive training that results in deterioration of performance is called ''overtraining''; similar to ''burnout''. There were data which indicate that systemic inflammation ''is the central underpinning of the overtraining syndrome''. Musculoskeletal trauma results in local inflammatory reactions; with continued and excessive high intensity training, local inflammation becomes chronic and systemic (21).

Overtraining induces immunologic dysfunction and neuro-endocrine-immune dysregulation (5). Because of that, we investigated the frequency of respiratory and other disorders during physical training program and found the impact of the training program on inflammatory diseases. The training-related symptoms were more frequent at the beginning of the training program, breathlessness as the most common response to intense exercise (Graph 1).

Breathlessness, exercise-induced phlegm production, wheezing and cough, in order of frequency, were the most prevalent respiratory symptoms in athletes according to Turcotte H et al. These findings were independent of training environment and duration of training, and were not always associated with obstructive respiratory diseases (22) and muscular strenght achivemment (23).

The fact that a larger number of athletes reported respiratory symptoms in the past compared with current symptoms, in relation to exercise, could be attributed to a reduction in inflammation, increased immune response and tolerance to symptoms over time, or to a better control of symptoms through training techniques, such as warming up before exercise.

Conclusions

Dynamic training can improve blood pressure and decrease systemic inflammation thus reducing the risk for cardiovascular and atherosclerotic diseases development.

Concentration of CRP during exercise training program is a useful marker for determination of an athlete's physical condition, and its determination after completion of daily exercise points to the balance between athlete's physical capacity and intensity of training procedures.

Having in mind that intense long-lasting exercise is followed by impairment of the immune system, only well-balanced exercise training programs result in favorable effects on the immune system, which is manifested through reduction of inflammation, increased immune response and reduction of physical exercise-related symptoms.

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KARAKTERISTIKE INFLAMATORNIH POKAZATELJA KOD ATLETIČARA NA INTENZIVNOM PROGRAMU SPORTSKIH PRIPREMA

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Redovna fizička aktivnost i dobra fizička kondicija su faktori koji redukuju ukupni mortalitet i sprečavaju razvoj mnogih oboljenja. Cilj rada bio je da se ispita uticaj intenzivnog aerobnog treninga na inflamatorne markere kod mladih atletičara na intenzivnom programu sportskih priprema.

U ispitivanje je uključeno petnaest zdravih atletičara kako bi se odredio efekat intenzivnog fizičkog treninga na imuni odgovor i sistemske markere inflamacije. Prosečna starost atletičara bila je između 16 i 20 godina. Period treninga trajao je minimum 6 meseci, a učestalost treninga bila je tri puta nedeljno. Uzorci krvi sakupljani su iz kubitalne vene našte neposredno pre treninga i 5–10 minuta nakon treninga. Određivani su kardiovaskularni parametri, inflamatorni markeri i simptomi vezni za fizičku aktivnost.

U ispitivanje je uključeno deset atletičara muškog i pet ženskog pola prosečne starosti 18.03□1.4 godina. Vrednosti sistolnog krvnog pritiska (TA) se nisu značajnije razlikovale pre i nakon treninga ali je registrovana značajana redukcija dijastolnog TA i porast srčane frekvencije ($p<0.05$). Značajan porast vrednosti sedimentacije u prvom satu i broja leukocita, kao i predominacija neutrofila, registrovani su nakon treninga. Udeo limfocita bio je značajno manji nakon treninga ($p<0.05$). Simptomi vezani za trening bili su znatno češći na početku programa priprema. Nedostatak daha je najčešće navođeni simptom (36%) i češći je od zviždanja u grudima (12%), kašlja (16%), slabosti (16%) ili stezanja u grudima (12%) na početku priprema.

Regularna fizička aktivnost redukuje rizik za kardiovaskularna i aterosklerotska oboljenja. Koncentracija CRP tokom programa priprema je koristan pokazatelj fizičke kondicije kod etletičara i njihovog odgovora na intenzitet treninga. Jedino dobro odmereni program priprema tokom vremena dovodi do poželjnih efekata na imuni sistem, koji se ispoljavaju kroz redukciju inflamacije, porast imune otpornosti i redukcije simptoma vezanih za fizički napor. Acta Medica Medianae 2009;48(4):50-54.

Ključne reči: *inflamacija, inflamatorni pokazatelji, atletika, fizički trening*