ABSTRACT

The aim of sports training is the increase and the improvement of the physical performance. Whenever the intensity, duration and the daily working load are not appropriate, positive physiological adaptations occur. However, there is a fairly subtle delimitation between an outstanding performance and a decrease in it due to overtraining. Overtraining may include: lesion and muscular weakness; cytokine activation; hormonal and hematological alterations; mood swings; psychological depression and nutritional problems which may lead to loss appetite and diarrhea. Several studies about overtraining have been conducted with the effort to identify its causes, symptoms, hypotheses, besides the markers that could identify it. Nevertheless, its diagnosis is very difficult since the overtraining symptoms are similar to the ones from pre-overtraining and to the ones from normal training, making it difficult to dissociate them. Currently, there is not a single marker that could predict overtraining, thus, the decrease in physical performance is still considered the gold-standard. Hormonal, biochemical, immune and psychological markers, besides the oxidative stress, may provide relevant information for an accurate and trustworthy diagnosis on overtraining.

INTRODUCTION

The aim of sports training is the increase and the improvement in physical performance. Whenever an excessive and extended training is simultaneously applied with inadequate recovery, several of the positive physiological alterations associated with physical training are reverted to overtraining (OT)(1). Nonetheless, there is a subtle limit between an optimum performance and a chronic decrease due to OT(2).

OT may be defined as an increase in the training volume or intensity which results in a long period of performance decrease(3), or even characterized by the decrease of specific performance of the sport associated with mood disturbances(3). Conversely to OT, pre-overtraining (POT) is a short term performance decrease, but which is followed in a few days by a complete recovery or even an increase in physical performance (supercompensation)(4). Thus, many coaches affirm that it is necessary to induce a state of POT during the training process(5).

Since there is a continuous risk of imbalance among training, competition and recovery, OT is a recurrent problem(6). Six percent of long distance runners, 21% of Australian swimmers and more than 50% of soccer players have been classified with OT(6,9) and it is estimated that 70% of high level endurance athletes have been in OT during their careers (7). Nowadays the only known treatment is followed in a few days by a complete recovery or even an increase of performance, which is usually verified in the POT. Later, in a stage previous to OT, despite an increase of the ACTH, there is a decrease of the adrenal responsiveness, which results in a decrease of the cortisol indices. After that, in a further stage of the OT, the hypophysis also decreases the release of ACTH. In that stage there is further evidence on the occurrence of a decrease of the intrinsic sympathetic activity and the sensitivity of the organic markers of the catecholamines(12).

Moreover, Newsholme(13) proposes the glutamine theory. In response to the decrease of the immune responses and associated with an increase of infections rate presented during OT(14), the glutamine suffers a decrease in its blood indices, once it is the first fuel used by the lymphocytes and macrophages for its proliferation(15-17).

Further investigation has focused on the modification of the circulating indices of the tryptophan amino acid. The reduction of the blood indices of tryptophan has been interpreted as a reflex of an increase of the use of this amino acid by the nervous system. The tryptophan is a precursor of the synthesis of the serotonin neurotransmitter. It is believed that an increase of the serotonin indices in the nervous system results in mood and sleep alterations, decrease of the excitability of the motor neuron, decrease of appetite and inhibition of hormones release by the hypothalamus(18), all evident in OT(19).

However, there are few or none trustworthy markers that could diagnose OT(12,4,9,10).

The OT markers are defined as the physical, physiological or psychological characteristics alterations associated with OT and the stimuli that precede or follow the occurrence of the current OT syndrome(20). Consequently, some of these physiological, biochemical and immunological alterations commonly associated with heavy training have been proposed as potential OT markers.

THEORIES AND HYPOTHESES OF OVERTRAINING

A myriad of hypotheses have been proposed for OT. Some of these hypotheses remain viable; others however, have no support at all. Thus, plenty of investigation has focused on the hypothalamus, since it acts in the activation of the autonomous nervous system, in the adrenal and gonadal glands as well. These actions result in alterations in the blood catecholamines, glucocorticoids and in the testosterone indices. Doubtfully, there is the involvement of these systems in the OT, as long as heavy training represents an extreme physical and psychological stress(11).

Based on the premises that OT is an imbalance between training and recovery, it has been argued that a neuroendocrine imbalance is one of the main reasons of OT. During intense endurance training or periods of POT, the majority of the results give evidence of an increase of the ACTH by the hypophysis, generating an increase of the cortisol indices, which is usually verified in the POT. Later, in a stage previous to OT, despite an increase of the ACTH, there is a decrease of the adrenal responsiveness, which results in a decrease of the cortisol indices. After that, in a further stage of the OT, the hypophysis also decreases the release of ACTH. In that stage there is further evidence on the occurrence of a decrease of the intrinsic sympathetic activity and the sensibility of the organic markers of the catecholamines(12).

2. Received in 4/10/05. Final version received in 6/3/06. Approved in 15/6/06.
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Keywords: Overtraining. Pre-overtraining. Hormonal markers.

of physical performance which has been frequently observed in OT\textsuperscript{[10]}. Foster and Lehman\textsuperscript{[17]} suggested that OT may be induced by repetitive trainings in which there are not physical activities variation (daily training boredom). Theoretically, it is assumed that this psychological training boredom could cause a negative impact in the athlete's physiological performance, increasing thus, the possibility of lesion. Such theory is known as OT monotony.

Currently, it has been suggested that OT is a response to the excessive muscle-skeletal stress associated with insufficient periods of resting and recovery, which can induce an acute local inflammation, developing to a chronic inflammation, producing a systemic inflammation as well. Part of this systemic inflammation involves the activation of the circulating monocytes, which can synthesize large amounts of inflammatory cytokines (IL-1\textbeta, IL-6 and TNF-\alpha). These cytokines act in the CNS inducing a sum of behaviors, among them decrease of appetite and depression. They also act in the sympathetic nervous system and in the hypothalamus-hypothysis-adrenal axis suppressing its activity, which causes alterations in the blood indices of the catecholamines, glucocorticoids and gonadal hormones. Immune alterations may be related to an immune suppression, possibly due to antiinflammatory factors that follow the pro-inflammatory response, which occurs due to the muscular trauma.

On the same flow of thinking, Tildus\textsuperscript{[23]} show the oxygen free radicals (OFR) as one of the primary factors of the inflammatory response generating, induced by post-exercise muscular lesions and its subsequent recovery. Once the OFR are present, the neutrophils and macrophages infiltrate in the muscular tissue in order to recuperate it, generating more OFR (via respiratory burst), as well as cytokines that, through a large number of inter-related mechanisms promote the post-exercise inflammatory response and the removal of the damaged tissue and its recovery.

### OVERTRAINING DIAGNOSIS

Several studies about OT were conducted in the last decade in an effort of identifying its causes, symptoms and hypotheses as well as markers that could identify it. However, such diagnosis is extremely difficult, since the OT symptoms mix with the ones from the POT and with the ones from normal training, being many times of difficult dissociation.

One of the most important symptoms, fatigue, which is defined as the inability of keeping given training intensity, may be considered as a warning of the body in response to excessive stress. Conversely, fatigue plays an important role in sports training, since it is the first step for the training adaptation process, which stimulates an increase of the organic functions of the athlete, where the balance between stress and recovery defines the quality of the training program\textsuperscript{[9]}.

Several other symptoms have been reported in the literature, being divided into physiological (decrease of physical performance, muscular strength, coordination, increase of the perceived exertion and the recovery period, alterations of the lactate curve, sleep and anorexia), biochemical (decrease of muscular glycogen, bone mineral content, free testosterone and testosterone/cortisol ratio higher than 30\%, as well as increase of cortisol and urea), psychological (depression, emotional stress, fear of competition, general apathy), immune (increase of infections and diseases, decrease of neutrophils and macrophages activity)\textsuperscript{[19]}.

The evaluation of the specific performance decrease still represents the gold-standard in the diagnosis of OT and needs sports specific tests. Therefore, maximal tests up to exhaustion may identify a decrease in sports specific performance, since athletes in OT usually present a lactic anaerobic performance decrease, a decrease in the exhaustion time in high intensity tests and a slight decrease in the maximal heart rate. The lactate also presents a decrease during submaximal exercise resulting in a slight increase of the anaerobic threshold\textsuperscript{[31]}. Thus, high intensity and short duration tests and the running velocity have represented the most sensitive instruments for OT detection, especially the so called stress test. Such test is conducted in an intensity 10\% above the individual anaerobic threshold and induces exhaustion within 15 to 45 minutes approximately\textsuperscript{[30]}. The Medical Center of the British Olympic Committee has reported that athletes in OT present a low power peak in the 20 seconds Wingate test\textsuperscript{[13]}

Other important instruments such as resting measurement of selected blood markers as urea, uric acid, ammonia, enzymes activity as the creatine kinase and hormones as the testosterone/cortisol ratio may serve in order to reveal circumstances that in the long run would harm physical performance. Yet, these are not widely used for OT diagnosis. The urinary excretion of catecholamines at night, ACTH, GH, cortisol and plasma catecholamines may provide interesting information for the OT diagnosis\textsuperscript{[30]}.

Within this context, Halson et al.\textsuperscript{[20]} verified the cumulative effects of exercise stress and its subsequent recovery over physical performance and the fatigue indicators in 8 cyclists. Significant decrease in the produced power was verified and an increase in the performance time of the test occurred, joined with the increase of 29\% in the global mood disturb. The decrease of physical performance was associated with a decrease of 9.3\% of the maximal heart rate, 5\% of reduction in the oxygen consumption, and an increase of 8.6 points in the perceived exertion according to the Borg's scale.

Lac and Maso\textsuperscript{[24]} suggest some important instruments for the training control, as well as its hierarchy and the easiness of its completion. The training control of the athlete should have a minimum basis including the body mass control, sleep quality, fat % and cardiac control. The authors consider important: a systemized nutritional supervision, the use of self-questionnaires (psychological profile), as well as other biological markers in order to confirm the OT suspect.

More recently, from the view point of physical performance, Meeusen et al.\textsuperscript{[21]} suggested a protocol with two maximal tests in order to clarify the real differences between highly trained athletes in POT or OT. In this study, two maximal tests were performed by 7 cyclists before and after 10 days of field training. The results were compared with the results of an athlete clinically diagnosed in OT. A decrease of 6\% in the physical performance of the cyclists was verified between the 1\textsuperscript{st} and the 2\textsuperscript{nd} maximal test, while for the athlete in OT; a decrease of 11\% of the performance was verified. Moreover, a suppression of the hormones secreted by the hypothalamus-hypothysis (GH, PRL and ACTH) in the athlete in OT after the 2\textsuperscript{nd} maximal test was observed.

Some important factors make an OT immediate diagnosis complex: (1) the intraindividual variation; (2) the different symptoms for acute (POT) and chronic (OT) decreases of the physical performance; (3) the excessive training volume affecting the body differently from the excessive training intensity, (4) two kinds of OT: sympathetic and parasympathic, each one presenting differentiated symptoms; (5) the OT symptoms in endurance athletes are also different from the strength athlete's\textsuperscript{[25]}; (6) repeated blood samples before and after exercise are needed; (7) the exercise causes alterations in the plasma volume and it should be corrected; (8) the physiological and biochemical markers present different characteristics according to the sport and are influenced by psychological, social or cultural aspects\textsuperscript{[10]}.

While a simple marker could not be used in order to identify and avoid OT, the best identification strategy for athletes at risk of acquiring it, is to regularly monitor the athletic performance as well as the physiological, biochemical, immunological and psychological variables.
Among the biochemical markers, the most mentioned are plasma glutamine, creatine kinase activity, urea and blood lactate.

The plasma glutamine concentration has been suggested as a possible stress indicator due to excessive training, once low indices of plasma glutamine are usually reported in athletes with OT. The plasma glutamine concentration decreases after acute or extended exercise, but not after high intensity and short duration exercise. The glutamine decrease may occur after physical trauma, burns, inflammations and infections. The plasma glutamine concentrations temporarily increase after protein food intake, but they decrease 25% after some days with low carbohydrates intake.

The evaluation of the activity of the creatine kinase enzyme has been widely used, not as an OT marker, but rather as an instrument for identification of a recent stage of muscular lesion or POT. This fact is explained once well-trained athletes that perform eccentric muscular contractions do not present large increases in the creatine kinase activity, even if they present muscular pain, maybe due to the fact that they are result of a lesion or inflammation in the conjunctive muscular tissue. On the other hand, the diagnosis based on the determination of the creatine kinase seems to be sensible and evaluates an increase of the muscular stress or an individual tolerance to the muscular effort.

It has been suggested that the nitrogen residues concentration in the blood plasma (urea and uric acid) may indicate a decrease of muscular proteins, being able thus to be an OT marker due to its association with a catabolic state. The largest problem is that the extended acute exercise is associated with a temporary increase of the urea and uric acid indices and can even be influenced by a diet with proteins intake. For these reasons, urea, uric acid and creatine kinase are not trustworthy parameters for the definite diagnosis of the OT.

A decrease in the maximal physical performance parallel to a reduction in the maximal lactate concentration has been described in runners, swimmers, cyclists and triathletes. A decrease of blood lactate in response to submaximal tests is also observed in athletes with OT, probably due to a decrease of the muscular glycogen indices, decrease of the catecholamines in response to exercise, or decrease of the catecholamines effect over the muscular tissue. The determination of blood lactate is a training routine for gen indices, decrease of the catecholamines in response to exercise. The lactate/perceived exertion ratio was hence proposed.

In this context, Bosquet proposed the investigation about the physiological responses in endurance athletes in 4 weeks with increase of the training volume and intensity. The lactate and the perceived exertion ratio were evaluated and it was concluded that the athletes who entered in OT for this sudden increase of the working load, presented a lower lactate production during a maximal test, and that the perceived exertion ratio did not significantly alter. Similar results for the lactate were found by J eukendraup. In this case, a lactate control could be an important instrument for OT prevention, since it is an accessible and widely used technique in the sports field.

**HORMONAL MARKERS: TESTOSTERONE/CORTISOL RATIO**

The balance between anabolic and catabolic activities is represented by the ratio between testosterone and cortisol, which is known as testosterone/cortisol or free testosterone/cortisol. Based on the premise that the testosterone has anabolic effects and the cortisol catabolic ones, the testosterone/cortisol ratio has been proposed as a great marker for OT. Adlercreutz et al. suggest ed that a decrease of this ratio be higher than 30%, the athlete would be in OT. Despite of that, the athlete’s performance should be considered, since not necessarily when the ratio is higher than 30% the athlete will face a decrease in his physical performance. Moreover, the principle of the athlete’s individuality should be considered, once he will be able to differently react to an anabolic and catabolic state.

Based on this evidence, massive research was conducted with the testosterone/cortisol ratio in order to verify the sports training anabolic/catabolic state, however, the results are contradictory and vary a lot among these studies.

Filaire et al. examined the salivary testosterone/cortisol ratio in 17 soccer players before the season (T1), before (T2) and after (T3) high intensity program and 16 weeks later, during the competition season (T4). It was observed a decrease higher than 30% in the testosterone/cortisol ratio in the (T3) period compared with the (T2) period; however, the team performance did not decrease (71.4% of wins in the championship) in this period.

Gorostiaga et al. verified the same ratio in soccer players training simultaneously to an explosive strength training during 11 weeks. An inverse correlation between the testosterone/cortisol ratio with the experimental group was observed. Nonetheless, the authors suggest that a transitory decrease of 45% of this ratio cannot be always interpreted as an OT signal.

In another study, the salivary testosterone/cortisol ratio in basketball players was evaluated with differences in the training volume during 2 maximal tests; the first before (PS1) and another during (PS2) the basketball season in two periods (T1 and T2). T1 presented training volume higher than T2. As a result, it was seen that the decrease in the salivary testosterone/cortisol ratio was negatively correlated with the training volume. T1 presented a decrease in this ratio, while T2 presented an increase in the testosterone/cortisol ratio, both in relation to (PS2) x (PS1), which suggests that T2 better adapted to training, with predominance of an anabolic state, contrary to (T1) which established a predominance of the catabolic state. Before that, the same author observed in basketball players that there was no influence from the game result over the salivary concentrations of testosterone and cortisol. However, the winners presented a brief increase in both, while the losers presented a decrease of testosterone and an increase in cortisol.

Mujika et al. examined the effects of 12 weeks of intensive training added to 4 weeks of training progressive reduction (polishing) over the hormonal concentrations and over the performance in a group of 8 highly trained swimmers. As a result, they verified that no significant alterations occurred in the plasma concentrations of total testosterone, cortisol, LH, creatine kinase and ammonia during training and polishing. The physical performance had a brief decrease during intense training and increased during polishing, showing a correlation between performance and the testosterone/cortisol ratio (r = 0.86, p < 0.01). Hence, the authors concluded that testosterone/cortisol ratio was the most efficient marker of the physical performance of swimmers during intense training.

In another study, Tremblay et al. studied the anabolic and acute catabolic effects in response to strength and endurance exercises with the same volume in individuals with different training levels. The sample consisted of sedentary subjects, strength and endurance athletes. These groups completed 3 sessions – one of resting, another of 40 minutes of running at 50-55% VO2 max and one extra session of strength exercise. It was observed that there were not significant differences between the testosterone/cortisol and the free testosterone/cortisol between the groups. However, significant differences occurred between the resting and endurance sessions compared with the strength ones.

Fry et al. examined the hormonal responses in a protocol of high intensity and low strength training volume. Two groups par-
ticipated in the study, OT (n = 11) and control (n = 6). The OT group daily trained for 2 weeks at 100% of 1RM, while the control group trained at 50% of 1RM once a week during the same period. It was observed that the testosterone, the cortisol, the testosterone/cortisol and the free testosterone/cortisol are not affected by this protocol. Despite of that, a decrease in the physical performance was verified. In another study, the influence of strength training of multiple series in 5 women before and after and after 8 weeks of training in the testosterone/cortisol ratio was verified. An increase of 20% in the resting testosterone/cortisol and a decrease of 35% post-exercise were seen after training. Nevertheless, some authors suggest that the testosterone/cortisol ratio may be an extremely useful instrument for the prediction of an imbalance between anabolic/catabolic metabolism.

**OXYGEN FREE RADICALS**

The interest on the oxygen free radicals generation and adaptation mechanisms (OFR) to exercise significantly increased from the demonstration of its relation with the oxygen consumption. The OFR are made by the incomplete reduction of oxygen, generating species that present high relativity for other biomolecules, especially lipids and proteins of the cellular membranes and even DNAs. Injuries caused by oxidative stress present cumulative effects and are related to a series of diseases, such as cancer, atherosclerosis and diabetes.

Acute physical exercise, due to its increase in the oxygen consumption, promotes the increase of the OFR formation. These molecules increase in extentuated and of high intensity exercises, however, physical training is able to generate adaptations capable of preventing the harmful effects by the OFR.

Margaritis et al. proposed that the magnitude of the increase of the antioxidant defense system depends on the training loads. The same authors still demonstrate that the higher the VO2max of triathletes, the higher the activity of the GPx antioxidant enzyme will be in the erythrocytes, protecting thus the body from the cellular membrane damage. Leeuwenburgh et al. add that the exercise induced-oxidative stress may trigger adaptations to response to training and that such adaptations would be tissue-specific. It was demonstrated in our laboratory that the aerobic training, performed in rats through treadmill running, increases the myocardial oxidative stress, which may interfere in the physical performance and lead to OT.

**FINAL CONSIDERATIONS**

The main objective of the sports training is the most physical performance; however, there is a threshold between the training optimum adaptations and the overtraining negative adaptations. Currently there is not a simple marker that can predict it; nevertheless, a suitable control of the physical performance is still considered the gold-standard in the overtraining diagnosis. Hormonal, biochemical, immune and psychological markers may provide relevant information for an accurate and trustworthy overtraining diagnosis. Nonetheless, there is not a trustworthy standardized protocol for this diagnosis, but a long term follow-up of the physical performance and of the balance between anabolic and catabolic balance has been suggested. So far, the best control measure for keeping this balance seems to be the testosterone/cortisol rate. Yet, its results are still contradictory, ranging according to sport, training intensity, volume and level.

Further studies should be conducted on overtraining, since recent studies have shown evidence that the primary factors of overtraining are highly connected with alterations in the hypothalamus/hypophysis axis, the immunological system and the oxidative stress.

**ACKNOWLEDGMENTS**

To CNPq, CAPES and CENESP for the financing for the development of this work.

All the authors declared there is not any potential conflict of interests regarding this article.
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