Interleukin-6 and Cortisol Responses to One and Two Weeks of Tapering in Endurance Male Swimmers

Zehsaz Farzad and Farhangi Negin

Department of Physical Education and Sport Sciences, Tabriz Branch, Islamic Azad University, Tabriz, Iran

Abstract: This study investigated the effect of one and two week tapering periods on concentrations of plasma interleukin-6, cortisol and performance in the well trained male swimmers. After 8 weeks of progressive training, swimmers were randomly assigned to either: control group (n=13) who continued performing intense training for 2 more weeks or taper group (n=13) who continued with a 50% reduction in daily training distance relative to the control group. Blood interleukin-6 and cortisol levels were assayed from analysis obtained via standard ELISA. All data were collected immediately after a 1500m freestyle front crawl swimming test performed before, during and after the 8 week training protocol and after the one and two week tapering/running periods. 1500m swimming test time in the taper group decreased significantly (p < 0.01) and equally in both the one and two week taper periods relative to the control group. There were significant reductions in interleukin-6 levels in the taper group relative to the control group at the end of both one and two week tapering periods. There was significant reduction in cortisol level in the taper group relative to the control group at the end of two week tapering period. Hence, taper periods are effective in improving performance and decreasing blood interleukin-6 and cortisol levels.

Key words: Interleukin-6 • Cortisol • Endurance training • Swimming

INTRODUCTION

The obvious goal of athletic training is to enhance performance. However, it is well documented that overtraining will lead to significant performance decrement. Overtraining induces performance reduction is often accompanied and characterized by specific immunological and hormonal changes. Some studies report that 10-30% of professional athletes, exhibit reduced performance as a characteristic of overtraining syndrome [1], which is accompanied by immunological and hormonal alterations such as, elevated cytokines [2] and cortisol levels in blood [1, 3, 4].

Prolonged exercise induces an inflammatory response that is expressed by an increase in circulating anti-inflammatory and pro-inflammatory molecules. Thus, moderate activity may enhance the immune’s functional capacity, while prolonged and intense exercise may impair the immune function, which finally, results in a decline in exercise performance and the ability to undergo heavy training [5].

Athletes engaged in heavy training programs, particularly those involved in endurance events, appear to be more susceptible to infection. For example, sore throats and flu-like symptoms are more common in such athletes than in the general population and once infected, colds may last for longer in athletes who are training hard. There is some evidence that this increased susceptibility to infection arises due to a depression of immune system function. The causes of this and the reasons for the common association of recurrent infections with heavy training are the subject of current research worldwide [6].

On the other hand, one of the mainly suggested pathophysiological mechanisms of exercise–induced impaired immune function is the elevated levels of stress hormones (catecholamines, cortisol and growth hormone) during repeated bouts of prolonged exercise [5].

Functional bi-directional communication exists between the endocrine and immune systems and cytokines play a major role in these interactions [7]. The endocrine and immune systems seem to be so intimately
linked with each other that they could be regarded as a single network rather than separate systems [7]. During exposure to stress (physical, psychological, chronic, acute), these systems (or networks) are challenged. However, information about mechanisms of adaptation to repeated physically stressful conditions in man is lacking. Most of the results of experiments in exercise/sport physiology have indicated a harmful effect of intensive physical training [7].

Intense and prolonged exercise induces high levels of circulating inflammatory cytokines, especially interleukin-6 (IL-6) and it has been suggested that the release of IL-6 in exercise is related to the occurrence of muscle damage [2] and/or to the depletion of muscle glycogen [8]. The plasma concentration of IL-6 increased after 30 min of the beginning of the exercise training and peaked at the end of it with a 25-fold increase compared with the pre-exercise value [2]. Another research showed that plasma levels of interleukin-6 (IL-6) increased up to 100-fold from baseline values in response to physical exercise [9]. Interestingly, a major contributor to circulating IL-6 appears to be the contracting skeletal muscle. This increase in circulating IL-6 concentration in athletes is similar to that seen in patients with infections [10]. Also the results suggest that the cytokine response to exercise has similarities to that observed after trauma [2].

However, it is not known whether exercise that causes substantial elevations in plasma cortisol levels has a similar effect on spontaneous and stimulated monocyte intracellular cytokine production, but elevations in cortisol may affect cytokine production [11]. It is well known that interleukin-6 (IL-6) has the ability to activate the hypothalamo-pituitary-adenocortical (HPA) axis influencing each level of the axis. Higher basal IL-6 concentration would be associated with the higher cortisol response to the stimulation [12]. IL-6 is an important stimulator of the HPA axis. It has the ability to influence each level of the HPA axis. IL-6 induces CRH release from the hypothalamus of rats in a dose-dependent manner. In CRH knockout animals, IL-6 stimulates ACTH release, presumably by binding to its own receptor on corticotrophs [12]. Humans IL-6 administration induced a dose-dependent increase in ACTH and cortisol [12]. Therefore, subjects with higher plasma IL-6 concentration had higher cortisol response to ACTH stimulation. This implies that, even under physiologic conditions, IL-6 modulates adrenal cortex response to ACTH stimulation [12].

In order to improve endurance performance and to decrease symptoms of overreaching and overtraining including immune system suppression and hormonal alterations, many athletes reduce their training load for 6-21 days before the major competitions (a training procedure known as tapering). Planned tapering generally consists of high intensity exercise, with low volumes [13]. After a period of tapering, improved performance times have been reported in numerous athlete groups including swimmers [14], runners [15] and cyclists [13].

Coaches and sports scientists involved in the preparation of elite athletes for major competitions are well aware of the performance-enhancing potential of a well designed taper period. Tuan et al. (2008) reported that one week of decreasing of training volume and/or sessions, resulted in plasma IL-6 concentrations returning to normal pretraining values in previously intensely trained athletes [16]. Mujika et al. (1996) reported that the 4 weeks of taper resulted in a 2.3% improvement in competition performance and improvements in endurance swimming performance during the taper correlated with changes in the T/C ratio (r = 0.81) [17]. Decrease in cortisol and increases in testosterone levels during the taper have been proposed as a means of monitoring positive performance capacity in athletes. Collegiate swimmers’ cortisol values declined by 23-36% during a taper and the athletes’ competition performance improved by an average of 3.2% in two different 2- to 3-week tapers within a season [18].

The overall aim of this study was to determine the effect of shorter (7 day) and longer (14 day) taper periods on the concentration of post-exercise plasma levels of IL-6 and cortisol in athletes. We hypothesized that longer taper periods could improve indicators of athletes’ acute immune function without compromising the taper induced benefits to their performance capacity. We were particularly interested in the post-exercise values as these are reflective of the acute stress of the exercise on cytokine and cortisol production. While monitoring of chronic non-exercise induced or resting changes in plasma cytokine and cortisol levels would have further informed this study, we were not able to perform these measures in the study design.

MATERIALS AND METHODS

Subjects: Twenty six well-trained swimmers from North-West of Iran took part in this study. They were informed of the purposes and methods of the study before giving written consent to participate. None were taking any drugs. The experimental protocol was approved by the local ethics committee. After completing 8 weeks of progressive endurance training exercise, the subjects were randomly assigned to two groups (control and taper groups) for taper periods lasting 1 or 2 weeks (for a total

\(^1\)Corticotropin-Releasing Hormone
of 10 weeks of taper and training in the study. Table 1 gives the physical and training characteristics of the subjects at the start of the study. Figure 1 outlines the time-course of the testing, training and taper periods.

**Determination of Endurance Exercise Capacity and VO_{2max} Assessment:** To induce realistic training and tapering programs, Twenty six well-trained swimmers were fully trained as if preparing for a competition season. The training status of every subject over the preceding 8 weeks and their training histories were obtained by questionnaire, training records and personal interview. Swimmers were considered as well trained if they had trained for at least 3 years, 2 hours a day, 4 to 5 times a week. Only subjects who met these criteria were included in the study.

Three days before the start of the 10 week training/tapering period, each subject performed an incremental VO_{2max} test on a calibrated Monark cycle ergometer (Monark, Sweden). Following a 2-min rest period of sitting stationary on the cycle ergometer, each swimmer began pedalling at an initial work rate of 80 W for 2 min, followed by 45 W increments every minute up to 260 W. Thereafter, work rate was increased each minute by 20 W increments to volitional fatigue. This test lasted approximately 10-14 min.

Expired gases were collected and analyzed by open circuit spirometry (Sensor Medics, Yorba Linda, CA) by using an automated metabolic analysis system. The data were averaged in 20 sec intervals. The gas analyzer was calibrated with primary standard gas (16.0% O_{2}, 4.0% CO_{2}, balance N_{2}) before each test [19].

![Graph](image1)

![Graph](image2)

![Graph](image3)

**Fig. 1:** The comparison of the means (SD) of the plasma IL-6 and cortisol concentrations in the control and taper groups immediately after the 1500m freestyle front crawl swimming test at various time points

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Table 1: Anthropometric and swimming experience data for the control and taper group swimmers at the start of the study

<table>
<thead>
<tr>
<th>Variable</th>
<th>Taper (mean ±SD)</th>
<th>Control (mean ±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm)</td>
<td>177.1 (3.7)</td>
<td>177.4 (3.6)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.31 (5.3)</td>
<td>68.7 (5)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>23.6 (1.7)</td>
<td>24.5 (2.9)</td>
</tr>
<tr>
<td>VO_{2max} (ml.kg⁻¹.min⁻¹)</td>
<td>64.8 (1.7)</td>
<td>64.27 (1.4)</td>
</tr>
<tr>
<td>Swimming experience (years)</td>
<td>4 (1.1)</td>
<td>4.1 (1.1)</td>
</tr>
</tbody>
</table>

Table 2: Swimming distance at the sessions of the exercise training

<table>
<thead>
<tr>
<th>Week</th>
<th>Distance at 50% VO_{2max} before every session of training</th>
<th>Distance at 60% VO_{2max} in the 1st session of a day</th>
<th>Distance at 70% VO_{2max} in the 2nd session of a day</th>
<th>Sessions per week</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>V_{2max} before every session of training</td>
<td>V_{2max} in the 1st session of a day</td>
<td>V_{2max} in the 2nd session of a day</td>
<td></td>
</tr>
<tr>
<td>First</td>
<td>200 m</td>
<td>1500 m</td>
<td>-</td>
<td>6 (one session/day)</td>
</tr>
<tr>
<td>Second</td>
<td>200 m</td>
<td>1500 m</td>
<td>-</td>
<td>6 (one session/day)</td>
</tr>
<tr>
<td>Third</td>
<td>200 m</td>
<td>1500 m</td>
<td>-</td>
<td>6 (one session/day)</td>
</tr>
<tr>
<td>Forth</td>
<td>200 m</td>
<td>1500 m</td>
<td>-</td>
<td>6 (one session/day)</td>
</tr>
<tr>
<td>Fifth</td>
<td>200 m</td>
<td>1500 m</td>
<td>2 x 550 m</td>
<td>12 (two sessions/day)</td>
</tr>
<tr>
<td>Sixth</td>
<td>200 m</td>
<td>1500 m</td>
<td>2 x 600 m</td>
<td>12 (two sessions/day)</td>
</tr>
<tr>
<td>Seventh</td>
<td>200 m</td>
<td>1500 m</td>
<td>2 x 650 m</td>
<td>12 (two sessions/day)</td>
</tr>
<tr>
<td>Eighth</td>
<td>200 m</td>
<td>1500 m</td>
<td>2 x 700 m</td>
<td>12 (two sessions/day)</td>
</tr>
<tr>
<td></td>
<td>Training program for control group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ninth</td>
<td>200 m</td>
<td>1500 m</td>
<td>2 x 750 m</td>
<td>12 (two sessions/day)</td>
</tr>
<tr>
<td>Tenth</td>
<td>200 m</td>
<td>1500 m</td>
<td>2 x 750 m</td>
<td>12 (two sessions/day)</td>
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<tr>
<td></td>
<td>Training program for control group</td>
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<td>100 m</td>
<td>1500 m</td>
<td>-</td>
<td>6 (one session/day)</td>
</tr>
</tbody>
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Swimming Performance Measurement: A 1500m freestyle front crawl swimming test was used as the standard test (i.e., index of performance) at the beginning of week 1 and after week 4, 8, 9 and 10 (before and after tapering period) to evaluate the physiological and performance effects of training and of the length of the taper protocol. Each swimmer was asked to complete the performance test as fast as possible with no information provided on how well he was performing until the end of the test.

Exercise Program: All training programs progressively increased training volume (swimming distance) over the 2 months, followed by a 2 weeks taper phase (Table 2). During progressive training volume, both groups exercised 6 days/wk. After 1 month, subjects were swimming twice a day, generally for six sessions per week. During 8 weeks, the control and taper groups performed the same training regimen together. The highest volumes of training for both groups occurred during the week 8. After 8 weeks progressive training and before the taper period began, each swimmer was randomly assigned to one of two protocols: the control group swimmers continued performing the intense progressive weekly training volume (n=13) for 2 more weeks. The taper group swimmers proceeds with a 50% reduction in training volume relative to the weekly training volume performed by the control group (n=13) for this 2 weeks period. Training volume in this study is defined as a combination of the distance and the frequency. Frequency can be defined as the number of training sessions over a period of time.

Blood Sampling: Blood samples were collected from 26 participants at the beginning of week 1 and the end of weeks 4, 8, 9 and 10, immediately after 1500m freestyle swimming test. Venous blood samples were drawn from a forearm vein into sodium heparin tubes chilled on ice. Blood was centrifuged at 700 rpm at 23°C for 10 min. Plasma was separated and stored at -70°C.

Plasma IL-6 and Cortisol Measurements: IL-6 level were analyzed in duplicate with all values expressed as a mean of the two determinations, using validated ELISA kits (Quantikine; R & D Systems, Minneapolis, MN). The minimum detectable dose (MDD) of IL-6 ranged from 0.016 to 0.110 pg.mL⁻¹. A standard curve was made by using standards provided in the kits and the cytokine concentrations were appointed from the standard curves by use of linear regression analysis. The assays were a

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two-step "sandwich" enzyme immunoassay in which samples and standards were incubated in a 96-well microtiter plate coated with polyclonal antibodies for the test cytokine as the capture antibody. After the proper incubation time, the wells were washed and a second detection antibody conjugated to either alkaline phosphatase (IL-6 high sensitivity) was added. The plates were incubated and washed and the amount of bound enzyme-labeled detection antibody was measured by adding a chromogenic substrate. The plates were then read at the proper wave length (490 minus 650 nm for IL-6 high sensitivity). The minimum detectable dose of IL-6 is typically less than 0.016 - 0.110 pg/mL.

Circulating concentration of total cortisol was determined using commercially available enzyme-linked immunosorbent assay (ELISA) kits (DRG, Marburg, Germany). The sensitivity of the cortisol assay was less than 0.196 nmol/L. The intra-assay and inter-assay precisions of cortisol were 3.59±0.33 nmol/L and 3.06±0.65 nmol/L. Samples were only thawed once before the analysis for all procedures. A standard curve was made using standards provided in the kits and the hormone concentration was appointed from the standard curves by use of linear regression analysis.

**Statistical Analysis:** Means and standard deviations were used to describe quantitative variables. Two-way repeated measures analysis of variance (ANOVA) was used to determine significant differences between taper and control plasma IL-6 and cortisol concentrations and 1500m performance time means. Also the significant differences between the 1 week and 2 week taper periods for the performance, IL-6 and cortisol concentrations were determined using two-way repeated measures analysis of variance (ANOVA). Data in text and figures are given as the mean ± sem. P<0.05 considered statistically significant. All data was analyzed by using SPSS for windows software version 17.0 (SPSS Inc, Chicago, IL).

**RESULTS**

There were no physical, training experience or VO2max differences between the control or taper group subjects (Table 1). All 26 subjects completed the 10 week training period and the data from all subjects were included in the analyses. Figure 1 indicates the comparison of the means (SD) of plasma IL-6 and cortisol concentrations and their performance time in the control and taper groups.

IL-6 levels between the two training groups were also significantly different at various collecting periods (p < 0.05). In the taper group alone there were also significant differences at various time points (p < 0.05). The mean IL-6 concentrations at the end of week 8 were 138.4% more than those at the day before the beginning of the training protocol (p<0.01). Mean IL-6 concentrations in the tapering group at the end of weeks 9 and 10 were 20.47% and 31.04% less than those at the end of week 8 (p<0.04 and p<0.01). Additionally, 13.29% decreases were observed when comparing levels of IL-6 at the end of week 9 with those at the end of week 10 in the taper group (p<1.00).

Cortisol levels between the two training groups were also significantly different at various collecting periods (p < 0.05). In the taper group alone there were also significant differences at various time points (p < 0.05). The mean cortisol concentrations at the end of week 8 were 32.28% more than those at the day before the beginning of the training protocol (p<0.01). Mean cortisol concentrations in the tapering group at the end of weeks 9 and 10 were 5.13% and 4.44% less than those at the end of week 8 (p<0.68 and p<0.01). Additionally, 9.81% decreases were observed when comparing levels of cortisol at the end of week 9 with those at the end of week 10 in the taper group (p<0.01). See Figure 1 for all of the IL-6 and cortisol data.

The 1500m swimming performance time between the two training groups were significantly different at several time points (p < 0.05). The 1500m swimming performance times at the end of weeks 9 and 10 were 0.17% and 0.25% less than those at the end of week 8 (p<0.01 and p<0.01) in taper group but the 1500m swimming performance times at the end of weeks 9 and 10 were 0.17% and 0.25% more than those at the end of week 8 (p<0.07 and p<0.01) in the control group. Non-significant differences were observed when comparing the 1500m swimming performance time at the end of week 9 with those at the end of week 10 in the taper group (p > 0.05). The performance data is also depicted in Figure 1.

**DISCUSSION**

The findings from this research revealed a significant decrease in mean 1500m swimming (free style) performance time following both one and two week taper periods in elite swimmers relative to swimmers who continue with a regular training load (intense training). These findings support previous studies which have reported that improved performance time was maintained during taper periods of 7-14 days in trained endurance athletes [14, 20, 21].

These findings also indicated that continuous training sessions performed in this study can induce increases in circulating pro-inflammatory cytokine, IL-6,
immediately post-exercise suggesting that intense training performed by swimmers in this study may have temporarily compromised their immune system [22]. Nevertheless, significant increases in the post-exercise IL-6 concentration after 8 weeks of the endurance training in both groups and the continued elevation of these cytokines at 9 and 10 weeks in the control group, suggesting a greater pro-inflammatory profile in these athletes. Previous studies have reported that 10 to 30 percent of professional athletes exhibited negative physiological signs indicative of increased training volume during final preparation for championships events [23]. Previous studies have also reported that there was significant increase in IL-6 post-exercise plasma concentrations after the prolonged endurance training [24, 25] that may be an indicator of acute inflammation. Elevation of this plasma cytokine is related to increase susceptibility to infection [6]. Smith (2000) has suggested that prolonged endurance exercise training may induce a long-term inflammatory state and may also indicate muscle damage [26]. Previous studies have also noted that the cytokine responses to the training are similar to the cytokine responses to the injuries. Clinical research has found that the cytokines also play an important role in the initiating of fatigue in disease states [27] and in the prolonged fatigue syndrome [28]. Elite athletes often suffer from the excessive and chronic fatigue and upper respiratory tract infection (URTI) and their exercise performance is consequently compromised [29]. Following sustained endurance training, the elevation of plasma IL-6 concentrations might be factors in elevating the muscular proteolysis. Some studies have also suggested that exercise associated leakage of intestinal endotoxins may also directly cause increased plasma IL-6 level [2]. Elevated IL-6 concentration may also decrease cellular glucose metabolism and thereby also possibly limiting optimal athletic performance [30].

The plasma IL-6 response to intense exercise has been shown to activate the anti-inflammatory and catabolic effects of cortisol; which may in part be responsible for changes in leukocyte subpopulations [8]. Whereas the initial changes can be ascribed to the effect of catecholamines, the prolonged changes in leukocyte numbers are most likely mediated through an effect of muscle-derived IL-6 on cortisol production [31]. Furthermore, IL-6 stimulates cortisol release and thus produces neutrocytosis and lymphopenia of the same magnitude and pattern as are seen during intense exercise [31].

This study illustrated that the increasing of the training load volume results in increased post-exercise levels of circulating cortisol. The elevated oxygen consumption (VO2) and associated stress during aerobic exercise is reported to result in increased neuroendocrine stress (increased cortisol, prostaglandins (PGs), interferon-(IFN-γ) and the generation of free radicals. Both the intensity and duration of the exercise determine the level of these stresses [32]. Since our measures were only obtained immediately following 400m free style race, it is difficult to attribute how long these reductions and elevations may have lasted or if they also resulted in chronic resting alterations. While monitoring of chronic non-exercise induced or resting changes in plasma hormone levels would have further informed this study, we were not able to perform these measures in the study design.

Our findings support suggestions that for a period of weeks before competition, athletes should significantly reduce their training levels. Other studies have also demonstrated that limiting endurance training for four days a week reversed the fatigue and infection symptoms induced by the prolonged endurance training [33]. In our results, there were significant reductions in plasma IL-6 concentrations of the taper relative to the control groups following exercise at the end of week 9 and 10 of training.

After one and two weeks of the tapering program (at the end of week 9 and 10), there were significant differences between the cortisol concentrations between the two groups. The mechanism underlying this declined plasma cortisol concentration post-taper is thought to be related to enhanced pituitary response to the preceding period of intense training, resulting in a positive influence on androgenic-anabolic activity during the subsequent taper, characterized by reduced levels of physiological stress [14]. This drop is probably relevant for inhibition of the protein catabolism and enhancement of proteins aggregation through the reduction of their degradation. This response may be of particular importance for type I muscle fibers, which may depend more on reduction of protein degradation rather than acceleration of protein synthesis as the primary mechanism responsible for hypertrophy [34]. It is believed that cortisol level reduction would be a physiological indicator of overtraining but it does not necessarily indicate the presence of a complete overtraining syndrome [35].

One of the important effects of systemic inflammation is induction of disease like symptoms including sleepiness, weakness and tiredness, which by limiting the work and effort an athlete can produce can also serve to protect athletes from exhaustion and excessive injuries and thereby help heal damaged tissues. Hence if elevated pro-inflammatory cytokine and cortisol levels are present in athletes prior to a major competition this could
indicate possible negative effects on maximum physical performance, a greater susceptibility to post-competition infection and possibly a slower and longer post-competition recovery period. Our findings of increase in acute elevation of post-exercise cytokine and cortisol levels support such contentions, however further study is needed to determine if a longer taper period will also affect prolonged and resting plasma cytokine and cortisol levels in these athletes. Given that competition performance is the result of a conscious effort, positive physiological and motivational changes taking place during the taper can make a worthwhile contribution to athletic performance [14].

CONCLUSION

A prolonged high training volume for 8 weeks in well-trained male swimmers revealed significant elevation of post-exercise plasma levels of IL-6 and cortisol. Interestingly, a taper period of 1-2 weeks will essentially reverse these elevations while at the same time improving swimming performance. It is important to note that no major differences were observed in any of these variables between 1-2 weeks of taper. Therefore, coaches can safely taper their athletes for up to 1 week before major competition in order to optimize competition performance.

REFERENCES


