THE EFFECT OF ONE BOUT OF EXHAUSTIVE EXERCISE ON IgA AND TNFα

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SUMMARY

In vivo depletion of lymphocyte subsets allows investigation of the role of specific subsets in protective immunity. The immune system has potent intracellular mediators that regulate inflammatory and immune response. This study examined the effect of exhausting exercise on IgA and TNFα in 20 recreationally active female volunteers of normal health, with no positive clinical finding. After fully explaining the procedures, their written consent was taken. Following physical measurements and VO2max determination, subjects performed an exhaustive exercise according to the Bruce protocol. Blood samples were obtained before and following the exercise. Statistical analysis revealed that IgA concentrations increased significantly, and TNFα levels remained stable. The observed effect of exhaustive exercise may be transient and related with intensity and duration. The results suggest that the given exhaustive exercise can not induce suppression of the immune function.

Key words: Immune system, exhaustion, immunoglobins, cytokines, exercise

ÖZET

BİTKİNLEŞTİRİCİ AKUT EGZERSİZİN IgA VE TNFα DÜZEYLERİNE ETKİSİ

Lenfosit alt birimlerinin in vivo yüküm süreçleri bu birimlerin immün korunma sistemindeki rollerinin araştırılmasına olanak verir. Immün sistemin hücreci mediatörleri enflamatuar ve immün yanıtlan regüle eder. Bu çalışmada herhangi klinik bulgusu bulunmayan sağlıklı ve rekreasyonel düzeyde aktif 20 kadın gönnülünde bitkinleştirici egzersizin IgA ve TNFα düzeylerine etkisi incelendi. Yöntemler açıklanıldktan sonra deneklerin yazılı onayları alındı. Fiziksel parametrelerin ve VO2max

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düzeylerinin ölçümünden sonra bireyler Bruce protokolünü tükenene kadar sürdürdüler. Egzersiz öncesi ve sonrasıda kan örnekleri alındı. İstatistiksel analiz IgA konsantrasyonlarının anlamlı düzeyde arttığını, TNFα seviyelerinin ise değişmedğini ortaya koydu. Çalışmada uygulanan bitkinleştirme egzersizin etkilerinin geçici olduğu, şiddet ve süresine bağlı olarak immün fonksiyonun baskılanması yol açmadığı söylenebilir.

**Anahtar sözcükler:** Immün sistem, bitkinlik, immünoglobulinler, sitokinler, egzersiz

**INTRODUCTION**

The integrated cytokine response to infection and injury is complex and tissue responses depend not only on absolute concentrations of tumor necrosis factor TNFα and IgA (1,17), but also on the simultaneous presence of naturally occurring cytokine inhibitors and anti-inflammatory cytokines (7,9,23). The local response to tissue injury involves the production of cytokines that are released at the site of inflammation (2). These cytokines facilitate an influx of lymphocytes, neutrophils, monocytes and other cells, which participate in the clearing of antigens and healing of tissue (8,15,18). Increases in the circulating concentration of pro-inflammatory cytokine TNFα have been reported following endurance exercise (13,21).

Starkie and coworkers (21) demonstrated that monocyte intracellular IL6 protein expression was unchanged following a bout of prolonged strenuous exercise, and exercise had no significant effects on TNFα or IL6 production. The local inflammatory response is accompanied by a systemic response known as the acute phase response (11). It has also been suggested that IgA may play a role in the apparent altered susceptibility to URTI associated with moderate exercise (4,17). Secretory IgA, the predominant immunoglobulin in mucosal secretion, is a major effector of resistance against pathogenic microorganisms causing URTI.

Previous work has shown that salivary IgA levels decrease after a single bout of intense prolonged exercise (7,10,19). The purpose of these studies was to examine IgA response to various exercise conditions. IgA secretion rate decreased 20 to 50% following exercise (p<0.001). Post-exercise IgA secretion rates were significantly lower (p<0.05) on days two and three compared with day one. Elite swimmers were followed over a six month season, IgA concentrations being measured five times. Throughout the season, IgA concentrations were significantly lower (p<0.05) in stale swimmers compared with well-trained ones (5).
IgA and IgM concentrations relative to total protein decreased following each exercise session. IgA, IgM and IgG flow rates decreased 50-65% after interval exercise. There was no effect of training on any immune parameter measured, although total work performed in the five 60s bouts increased after training (6). Concentrations of IgA decreased further following the competition (20 km for females) to very low levels. Changes in serum IgA, IgG and IgM concentrations were also not found significant following an acute bout of strenuous resistance exercise in both trained and untrained women.

Conversely a 45 min walk at 60% VO$_2$max was associated with significant increases in IgA, IgG and IgM compared with resting over the same period (4). There was also a significant increase in the percentage of B cells in the athletes after the race compared with the controls. The mechanism responsible for these changes is unknown, but the low salivary IgA levels may result from depletion of nasal fluid and/or malfunction of the mucosal plasma cells due to decreased temperature in the mucous membranes. A temporary antibody deficiency on the mucosal surface might lead to susceptibility to acquire viral and bacterial infections, especially during the period immediately following strenuous exercise.

Injection of TNFα, IgA into laboratory animals or humans produces most, if not all, aspects of the acute phase response. A pivotal advance in the past years has been the discovery and identification of at least two classes of biological inhibitors of the pro-inflammatory cytokines (17,20,22). These include the IL-1 receptor antagonist (IL-1ra) and the two soluble receptors for TNFα (3). Early studies demonstrated that exercise induced an increase in TNFα, although it was later pointed out that the biological assay used in the early studies may not distinguish it. Inconsistent findings have been reported for TNFα. Researchers reported increased plasma TNFα 2 h after completing a 2.5 h run, and 1 h after a 5 km race, respectively; but other studies have failed to detect TNFα changes after exercise (12,14). The present study provides time course of change in measurements of TNFα and IgA in the post-exercise period. Furthermore, it was investigated to what extent exercise induces cytokine inhibitors.

**MATERIAL and METHODS**

A total of 20 female subjects (22.0 ± 4.3 yrs of age, 56.1 ± 5.8 kg, 162.8 ± 4.0 cm, VO$_2$max of 34.2 ± 2.8 ml.min$^{-1}$.kg$^{-1}$, and body fat ratio of 23.1 ± 0.6 %) participated in the study. The experimental protocol...
was approved by the local ethics committee, and all subjects were informed of the risks and purposes of the study before their written informed consent was obtained. All subjects were identified as healthy on the basis of their medical history and the results of physical examination. Ambient temperature during running was 27°C. Subjects performed the Bruce protocol until exhaustion as the exercise.

Blood samples were drawn from the antecubital vein before and immediately after the exercise. The tubes were kept on ice until being centrifuged. Plasma was separated from the cells and stored at -80°C until being analyzed by commercially available enzyme-linked immune sorbent assay (ELISA, R&D Systems). Changes in plasma volume were calculated from measurements of haemoglobin and haematocrit, and results were corrected. Statistical analysis included means ± SD and paired t-tests to compare TNFα and IgA response, α being set at p<0.05.

RESULTS

Plasma concentrations of TNFα increased from 0.35 ± 0.64 pg/ml to 0.55 ± 1.76 pg/ml (t=-0.448, p=0.66), and that of IgA from 200.6 ± 93.2 mg/dl to 225.7 ± 118.2 mg/dl (t=-3.456, p=0.03) following exhaustive exercise (Fig. 1 and 2, respectively), thus reaching significance (p<0.05) for the IgA response.

![Figure 1. Plasma TNFα response following exercise.](image-url)
**Figure 2.** Plasma IgA response following exercise.

**DISCUSSION**

Previous studies demonstrated that strenuous, intensive and prolonged exercise induces change in the pro-inflammatory cytokine TNFα, and a dramatic increase in IgA. This effect is balanced by the release of cytokine inhibitors (4,15). The recent finding of TNFα in muscle biopsies obtained after strenuous exercise without increase of the TNFα protein in plasma, and the finding of TNFα in the urine of runners supports this latter idea. Studies proved that exercise induces a cascade of cytokine inhibitors and the anti-inflammatory cytokine, and that carbohydrates restrict increase of cytokine levels in plasma (2,4,16). It has also been shown that carbohydrate loading diminishes the exercise-induced increase in TNFα, and that with carbohydrate restriction, an even more pronounced increase in plasma cytokine levels may be found (3). As the exercise was not very intense or prolonged, and that carbohydrate intake was not controlled in the present study, subjects can be assumed to be well loaded with respect to glycogen. This might have contributed to the fact that changes in TNFα were not significant.

Output of IgA decreases after brief supramaximal interval exercise, which is partly due to the decrease in circulating fluids. In addition, there appears to be a specific effect of intense exercise on IgA
concentration greater than that due to decreased saliva flow alone. The increases might be due to exercise induced influx of IgA into the blood from the lymph and extracellular pools (4). In response to an acute bout of high intensity exercise, many studies report a decrease in s-IgA concentration following exercise that recovers to resting levels within 1 h of exercise completion, although some studies have reported either no change or even increases in s-IgA concentration (4). The effect of exhaustive exercise on IgA was significant, which may be transient and related with exercise intensity and duration. The results suggest that the exhaustive exercise in question induced changes in lymphocyte subsets, but may not have induced suppression of immune function. The present study does not provide information about changes in the plasma concentration of the cytokine TNFα.

In conclusion, exhausting exercise caused plasma IgA and TNFα to increase in recreationally active women. It is suggested that exhaustive exercise of 8-12 min duration may not have induced suppression of immune function.

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