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Original Article

Natural Killer Cell Activity Following 6 Weeks of Strength Training in Healthy Young Males With/Without Testosterone Enanthate Administration

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There is limited information on the acute immune response to resistance-training programs in combination with short-term administration of the anabolic androgenic steroid, testosterone enanthate (TE), in healthy young males. Eighteen healthy young men were match-paired and randomly assigned in a double-blind manner to either a TE or a placebo (PG) group. All subjects performed a structured resistance-training program while receiving injection of either TE at the dosage of 3.5 mg per kilogram body mass, or saline as placebo, once weekly for 6 weeks. A 10-second all-out cycle sprint test was conducted at the beginning (Week 0) and end (Week 6) of the treatment period. NK, B and T lymphocyte populations were counted and natural killer cytotoxic activity (NKCA) was measured prior to and 5 minutes post the cycle sprint at Weeks 0 and 6. The TE group significantly increased their total work in the 10-second cycle sprint test from Week 0 to Week 6 ($p < 0.04$), while there was no significant increase for total work in the PG group. There was a significant increase in NKCA from Week 0 to Week 6 ($p < 0.05$) in the PG group. A significantly higher NKCA in the PG group than in the TE group was found in the post exercise sample in Week 6 ($p < 0.04$). No significant differences were found between groups for the lymphocyte subsets. The 6-week strength training increased acute NKCA response to anaerobic type of exercise as shown in the PG group. Although dosing of TE enhanced anaerobic performance, the NKCA response in the TE group was lower than that in the PG group. The impact of this altered immune response on athletes' health requires further investigation. [*J Exerc Sci Fit* • Vol 6 • No 2 • 106–114 • 2008]

Keywords: anabolic steroid, immune function, testosterone enanthate

Introduction

Use of anabolic androgenic steroids (AAS) has been found to increase muscle strength and power, which has led to reports of abuse by athletes participating in sports requiring these performance attributes (Giorgi et al. 1999; Bhasin et al. 1996). Hence, AAS have been classified as prohibited substances in sport as their use can offer an unfair performance advantage. While AAS are able to increase performance, serious adverse effects on liver function, cardiovascular and reproductive systems, and psychological status have been reported (American College of Physicians 1984).

To date, there is very limited information on immune function changes that may occur following anaerobic exercise and AAS use. Studies performed using animal

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models have produced equivocal results (Mendenhall et al. 1990; Duschaux et al. 1982; Henney et al. 1981; Fuji et al. 1975). Natural killer cells are a type of lymphocyte that responds rapidly to foreign substances in the body by exerting a cytotoxic activity. This cytotoxic activity is known as natural killer cytotoxic activity (NKCA), which is the first defence against viruses. In a study on humans by Calabrese et al. (1989), both NKCA and lymphocyte proliferation were increased in a group of 13 body builders, indicating improved immune responsiveness after the use of AAS. However, the report is not conclusive because the types of AAS used varied across the subjects and there was no control for the varying training intensities for each subject when determining the effect of AAS on immune responsiveness.

The acute immune responses to anaerobic exercise following a short-term resistance training program has also received little attention in healthy males (Nieman et al. 1994, 1992; Gabriel et al. 1992), and the previous studies did not demonstrate a clear pattern of the acute effects of anaerobic exercise on lymphocyte numbers and NKCA. Significant increases in natural killer cell numbers and other lymphocytes have been found after maximal cycle tests of 30–60 seconds duration in healthy male athletes (Nieman et al. 1993; Gabriel et al. 1992). However, Nieman et al. (1994) examined chronic levels of NKCA as well as the proportion of circulating natural killer cells in weight-lifters and sedentary controls, and found no significant increase in NKCA or natural killer cell numbers. An important function of natural killer cells is to mediate non major histocompatibility complex (MHC) restricted cytotoxicity to virally infected cells and some malignant cells. Hence, decreasing natural killer cell numbers or their function may increase the rate of growth of tumors and the severity of viral diseases.

Given that there have been reported increases in performance after the use of AAS (Giorgi et al. 1999; Bhasin et al. 1996) while there is limited information available in respect of the acute immune responses to all-out anaerobic exercise and short-term resistance training with combination of use/abuse of AAS, the objectives of this study were to establish: (1) the acute immune response following 6 weeks of resistance training in moderately strength-trained young men; and (2) whether 6 weeks of administration of testosterone enanthate at a dosage of 3.5 mg per kilogram body mass would have an acute effect on lymphocyte count and NKCA following a 10-second all-out cycle exercise.

Methods

Experimental approach

A double-blind, placebo-controlled design was used. Baseline testing (Week 0) included total T ($CD3^+$), total B ($CD3\text{-}CD19^+$), T helper/inducer ($CD3^+/CD4^+$), T cytotoxic/suppressor ($CD3^+/CD8^+$), natural killer ($CD3\text{-}CD16^+$ $CD56^+$) cell number counts and NKCA measurement prior to, and 5 minutes post, a 10-second all-out cycle sprint test, and measurement of body mass. Following this baseline testing, subjects were paired based on weight, height, performance measures, chronological age, training age and nationality. The two subjects in a pair were then randomly allocated to either a testosterone enanthate (TE) or a placebo (PG) group and followed by a common 6-week strength and conditioning program. During training, the TE group received testosterone enanthate (Primoteston Depot, Schering AG, Germany) intramuscularly at the dosage of 3.5 mg per kilogram body mass once per week for 6 weeks (Figure 1). The dose of testosterone enanthate used represented a moderate dose that exceeded clinical replacement levels and had been administered previously without serious side effects (Giorgi et al. 1999). The PG group received intramuscularly an equivalent volume of saline solution (AstraZeneca, Australia). Body mass, lymphocyte count and NKCA measurements were repeated at the conclusion of the 6-week testosterone enanthate/placebo administration period.

Subjects

Eighteen healthy young males were recruited (see screening process below); however, only 13 (mean age, 24.6 ± 2.1 years) completed the immune function part of the study. Two subjects withdrew due to personal reasons not related to the study itself and three subjects were not included due to technical problems in obtaining blood samples. Subjects' characteristics for the testosterone enanthate ($n = 9$) and placebo groups

Fig. 1 Schematic of the experimental design of the study.

Table 1. Age, body mass and height of subjects ($n=16$)

	Testosterone group ($n=9$)	Placebo group ($n=7$)
Age (yr)	24.8±2.9	25.1±4.7
Weight (kg)	79.2±6.8	77.6±5.7
Height (cm)	181.2±6.8	182.1±7.9
Weight training frequency (sessions/wk)†	2.7±1.5	2.9±0.9

*Data are presented as mean±standard deviation; †weight training frequency was the mean number of strength training sessions that subjects performed per week during the 12 months prior to the study.

($n=7$) are presented in Table 1. All subjects were fully informed of the experimental procedures and signed an informed consent document which had been approved by the Human Research Ethics Committee of Southern Cross University (ECN-04-99).

Prior to administration of each AAS injection, each subject's height (to the nearest 0.5 cm using a wall mounted stadiometer, Inter 16, Seca, Hamburg, Germany) and body mass (to the nearest 0.1 kg using an electronic scale, Mettler ID2 Multirange, August Sauter, Germany) was measured (data published in Rogerson et al. 2007). During the study, accommodation was provided for the subjects and physical activity outside of training was limited to organized social activities, thus minimizing any interference with the experimental procedure.

At each weekly intramuscular injection, heart rate and blood pressure were measured prior to each injection along with a number of health indicators including mood, acne development, libido and other potential steroid-influenced factors monitored by a structured questionnaire.

Screening

Criteria for study inclusion were: age between 21 and 35 years, had not used any prohibited substances for sport or performance-enhancing supplements in the previous 6 months, and demonstrated no contraindications to participation with a screening device.

The screening process included recording relevant family medical history, past and present medical conditions, current medication, and nutritional supplement use. A medical practitioner conducted a physical examination, which included cardiovascular, respiratory, neural, abdominal, and musculoskeletal assessments. All subjects had a full blood count, lipid profile, liver function test, and a resting 12-lead electrocardiogram to identify any pre-existing conditions that would have contraindicated participation in the study. At the commencement of the study, no subject reported the use of any nutritional supplements or non-prescription drugs. A urine sample was analyzed for the presence of prohibited substances according to WADA protocols. All subjects showed negative results in the urine testing.

All subjects reported previous resistance training experience, and were considered moderately trained based on self-reported training background.

Strength and conditioning program

The strength and conditioning program was designed to improve general strength and stimulate muscle mass development. The program prescribed a total of 16 weight-lifting sessions in a split-routine format across the 6 weeks of the experimental period. Sessions alternated between upper body and lower body emphasis, allowing a minimum of 48 hours recovery between sessions utilizing the same body part. Each subject was required to use a load that would allow them to work within a prescribed repetition range for a designated number of sets of each exercise. Repetition maximum per set across the training period ranged from six to 12 using a periodization approach to the overall manipulation of training load. Interset recoveries were standardized between 2 and 3 minutes. All training sessions were closely supervised by an accredited strength and conditioning coach.

Ten-second all-out cycle sprint test

Prior to performing the cycle sprint test, each subject performed a 5-minute standardized warm-up by cycling at 30 watts. The cycle sprint test was conducted on an air-braked front-access cycle ergometer (Exertech Exercise Technology, Australia). The subject's feet were secured to the pedals using both toe clips and tape to prevent excess movement. A 5-second countdown was provided and each subject was instructed to start cycling at maximum pace on the count of zero. The subject was instructed to maintain maximal power output for the full 10 seconds. Strong verbal encouragement was provided to all subjects to ensure maximum effort (McNair et al. 1996). Peak power (W) and total work (kJ) were monitored by way of a photo-optically sensitive diode connected to the flywheel with outputs being received by an AMLAB data acquisition and analysis system (Associated Measurement, Australia). The 10-second cycle test was selected as it has previously been reported to be a highly reliable measure of anaerobic performance and less likely than longer duration tests to be influenced by pacing (Zajac et al. 1999).

Lymphocyte counts

Blood samples were collected from an antecubital vein. Each blood sample was taken from subjects prior to the 10-second cycle test and 5 minutes after the test in Week 0 and Week 6. One hour prior to each cycle test, subjects consumed a standardized meal in the form of a meal replacement powder (Mass Monster™, Body Science®, Sydney, Australia), and then 30 minutes prior to testing subjects were seated in the testing laboratory. Following the 30 minutes seated rest and just prior to the commencement of the 10-second cycle test, a resting blood sample was collected. Another sample was taken at 5 minutes after the exercise. Full blood counts were performed using a Beckman Coulter GenS instrument (Coulter Electronics, Inc., Hialeah, FL, USA). Lymphocyte subsets were analyzed to determine absolute cell numbers/mm^3 for total T (CD3$^+$), total B (CD3-CD19$^+$), T helper/inducer (CD3$^+$/CD4$^+$), T cytotoxic/suppressor (CD3$^+$/CD8$^+$), natural killer (CD3-CD16$^+$/CD56$^+$) cells. Determination of lymphocyte subsets was performed by lyse-no wash methodology using Multiset IMK-Lymphocyte Kit (Becton Dickinson Immunocytometry Systems, San Jose, CA, USA). Multiple labeled samples (FITC, PE, PerCP, APC) were assayed using excitation wavelengths of 488 nm and 635 nm. Analysis was carried out on a Becton Dickinson FACSCalibur flow cytometer using Becton Dickinson MultiSET software. The staining and flow cytometry procedure has been described elsewhere (Dohi et al. 2001).

NKCA

The flow cytometry method of NKTEST Kit (ORPEGEN Pharma, Heidelberg, Germany) was used to assess NKCA on the human erythroblastic cell line K-562 as target (Scharhag et al. 2005). Briefly, peripheral blood mononuclear cell (PBMC) suspensions were prepared from each specimen using Ficoll-Isopaque procedure. PBMC (effectors) + target cell (K-562) suspensions (effector: target ratio of 25:1) were prepared from each sample. A target cell control tube (no effectors) was also prepared to monitor spontaneous target cell (K-562) death. Cells were incubated for 2 hours at 37°C in a humidified CO_2 incubator, then placed on ice. Cells were stained with a red fluorescent DNA dye to label the target cells permeabilized by NK activity. The samples were then run on a FACSCalibur flow cytometer using an excitation wavelength of 488 nm. Analysis was carried out using CELLQuest Pro software, gating on the green (FL1) fluorescent target cells then determining the percentage of FL2 positive (red DNA dye) events in the gated region. The percentage of dead K-562 target cells being equivalent to the percentage of FL2 positive cells in the gated FL1 region. Percent specific cytotoxicity was determined by subtracting the percentage of dead cells in the target control tube from the percentage of dead target cells in each test sample. Becton Dickinson Calibrite beads and FACSComp software were used daily to set the PMT voltages, fluorescence compensation, and check instrument sensitivity before use. Results were expressed as the percent lysis of NKCA.

Dietary standardization

All meals were provided throughout the duration of the study. This was to ensure a standardized dietary intake for all subjects. Supplementary proteins were allocated to both groups to control for inadequate protein intakes. The supplementary proteins consisted of *Whey Protein Concentrate* (Body Science®) administered at a dosage of 60 g/day. All subjects were instructed to consume 30 g of the proteins in the morning and 30 g in the evening.

One hour prior to the 10-second cycle test, each subject was provided with and required to consume a standardized meal in the form of a meal replacement powder (Mass Monster™, Body Science®). The consumption of this meal replacement powder was conducted under the supervision of research personnel and the meal replacement powder was used to ensure that the final meal prior to each testing session was standardized for its total energy content in addition to its nutrient profile.

Dose administration blinding

Both testosterone enanthate and saline injections were administered intramuscularly to the gluteal area in order to ensure that all subjects were unable to view the process. All injections were performed by a registered nurse and the blinding procedures were conducted under strict double-blind conditions.

Statistical analyses

All data were summarized using descriptive statistics (mean ± SD) and all statistical analyses were performed using SPSS version 10.1 (SPSS Inc., Chicago, IL, USA). Statistical analysis (mean ± SD) for total T (CD3$^+$), total B (CD3-CD19$^+$), T helper/inducer (CD3$^+$/CD4$^+$), T cytotoxic/suppressor (CD3$^+$/CD8$^+$), natural killer (CD3-CD16$^+$/CD56$^+$) cell subsets and NKCA was conducted using a 2 × 2 [Group (testosterone, placebo) × Time (Week 0, Week 6)] analysis of variance (ANOVA) with repeated measures. When a significant F ratio was identified, Fisher's least significant difference test was used to

locate the pair-wise differences between means. Prior to the first dose, subjects were match-paired and a one-way ANOVA was applied to the potential groups to ensure that there were no differences between groups on any variable (Table 1).

Results

Statistical analysis of the variables for body mass, peak power and total work are presented for 16 subjects (TE, $n = 9$; PG, $n = 7$) in Figures 2 and 3. Lymphocyte count and NKCA were determined for 13 subjects (TE, $n = 7$; PG, $n = 6$) because two subjects withdrew and a blood sample could not be obtained in three due to inability to locate a suitable vein. The dietary assessment of each subject was not assessed prior to their inclusion into the study. However, for the duration of the study, protein, carbohydrate and fat intake was maintained to the recommended daily intake as all meals were supplied to all subjects. There were no adverse side effects reported for blood pressure or heart rate for subjects in either the TE or PG groups. In the TE group, acne occurred in six of the nine subjects (67%) and the duration was greater than 4 weeks, appearing in the majority of cases 2 weeks after the initial injection. In contrast, the PG group only developed mild acne, which occurred in five of the seven subjects (71%) and the symptoms disappeared after 2 weeks. No subject in either group reported serious steroid-related side effects during the study period.

Body mass

The body mass data are presented in Figure 2. A significant group × time interaction was identified for body mass ($p < 0.01$). Further analysis of this effect indicated that body mass was greater at Week 6 than Week 0 ($p < 0.01$) in the TE group. No statistically significant

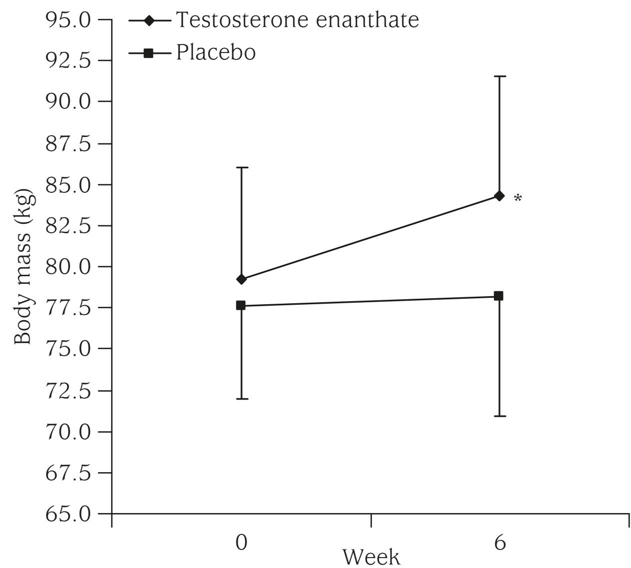

Fig. 2 Body mass for testosterone enanthate ($n = 9$) and placebo ($n = 7$) groups before (Week 0) and after (Week 6) weekly (×6) intramuscular injections of 3.5 mg testosterone enanthate per kilogram body mass or placebo. Data are presented as mean ± standard deviation. *Significantly different between Week 0 and Week 6 for the testosterone group ($p < 0.01$).

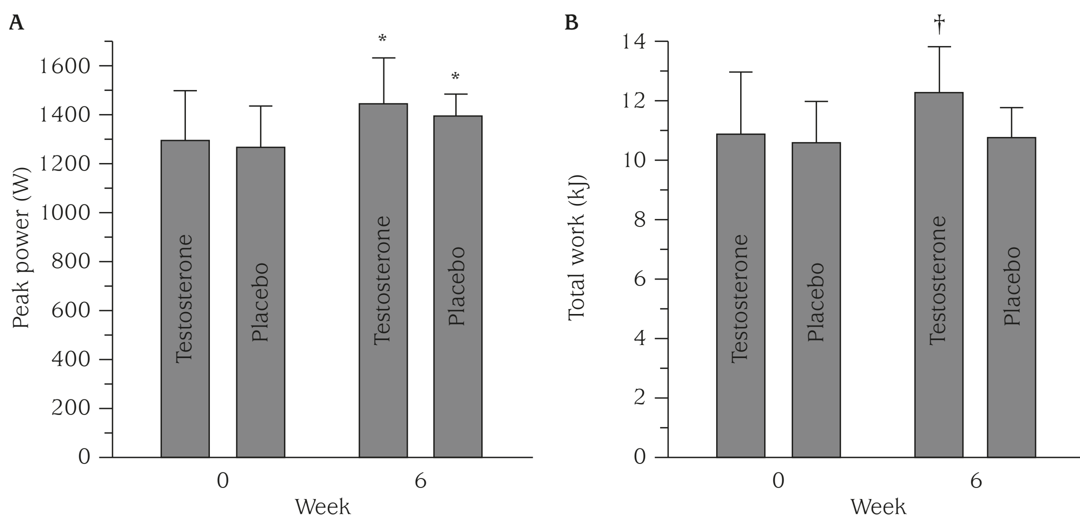

Fig. 3 (A) Peak power and (B) total work during the 10-second all-out cycle test for testosterone enanthate ($n = 9$) and placebo ($n = 7$) groups at Weeks 0 and 6 after weekly (× 6) intramuscular injections of 3.5 mg testosterone enanthate per kilogram body mass or placebo. Data are presented as mean ± standard deviation. *Peak power at Week 6 was significantly higher than at Week 0 ($p < 0.01$) in both groups; †significantly different between Week 0 and Week 6 for testosterone enanthate group only.

Table 2. Lymphocyte subpopulations pre and post exercise at Week 0 and Week 6 following intramuscular administration of $3.5\,mg \cdot kg^{-1}$ testosterone enanthate (TE) or placebo (PG) weekly for 6 weeks ($n = 13$)*

Cell number/mm^3	Group	n	Week 0		Week 6	
			Pre	Post	Pre	Post
Total T	TE	7	1214.5±435.4	1790.6±643.2	1388.8±304.7	1541.6±500.7
	PG	6	1432.6±324.6	2289.2±409.5	1463.0±490.8	1775.6±392.3
T helper/inducer	TE	7	815.7±156.7	865.6±168.6	945.8±238.6	976.6±304.7
	PG	6	776.8±234.5	881.4±235.6	793.5±198.7	834.5±273.1
T cytotoxic/suppressor	TE	7	695.8±90.7	640±140.6	783.3±115.9	745.1±211.5
	PG	6	558.4±170.9	519.4±170.9	789.6±216.6	699.3±175.3
Total B	TE	7	346.5±112.3	378.1±156.4	354.6±165.1	376.5±101.6
	PG	6	401.5±154.3	441.8±222.1	359.6±124.4	391.4±131.3
Natural killer	TE	7	453.4±114.5	478.1±176.2	387.8±191.3	408.4±176.3
	PG	6	376.3±163.5	398.5±116.1	402.1±143.6	423.6±132.6

*Data are presented as mean ± standard deviation.

changes in body mass were noted in the PG group over the 6 weeks.

Ten-second all-out cycle sprint test

Data for peak power and total work performed during the 10-second cycle test are presented in Figure 3. Peak power at Week 6 was significantly higher than at Week 0 irrespective of group ($p < 0.01$). Total work performed during the 10-second cycle test significantly increased from Week 0 to Week 6 in the TE group ($p < 0.04$), but no significant increase was found in the PG group.

Immune cell measures

There were no statistically significant differences between groups for absolute cell numbers for total T (CD3$^+$), total B (CD3-CD19$^+$), T helper/inducer (CD3$^+$/CD4$^+$), T cytotoxic/suppressor (CD3$^+$/CD8$^+$), natural killer (CD3-CD16$^+$CD56$^+$) cell subsets pre- and post-exercise at Week 0. There was no statistical significant group × time interaction effect for absolute immune cell numbers (Table 2).

NKCA

There was no significant difference between groups for either pre- or post-exercise NKCA at Week 0, and pre-exercise at Week 6 (Figure 4). However, there was a significant difference between groups for post-exercise NKCA at week 6 ($p < 0.05$). Pre-exercise NKCA within the PG group increased significantly from Week 0 to Week 6 ($p < 0.05$), whilst there was no significant difference within the TE group from Week 0 to Week 6.

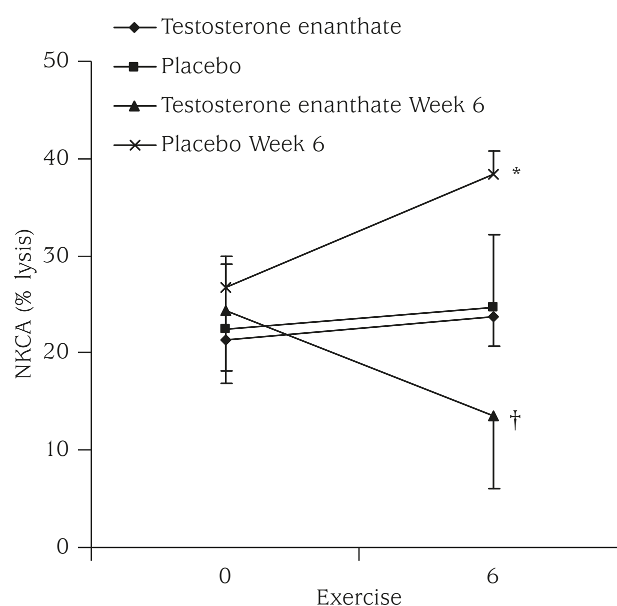

Fig. 4 Natural killer cytotoxic activity (NKCA) (% lysis) at Week 0 and Week 6 for testosterone enanthate ($n = 7$) and placebo ($n = 6$) groups before and after a 10-second all-out cycle test. Data are presented as mean ± standard deviation. There was a significant difference between groups from Week 0 to Week 6. *Significant difference in placebo group between Week 0 and Week 6; †difference is approaching significance in testosterone enanthate group between Week 0 and Week 6 ($p = 0.06$).

There was a significant difference in NKCA between groups for post exercise at Week 6 ($p < 0.04$). It was noted however, that the 10-second cycle test produced a reduction in NKCA from pre to post exercise at Week 6 ($p = 0.06$) in the TE group (Figure 4).

Discussion

This is the first double-blind placebo-controlled study to report a reduction in NKCA following acute anaerobic exercise after AAS administration to young healthy men. This reduction in acute NKCA pre to post exercise after testosterone enanthate administration for 6 weeks suggests an undesirable outcome on an aspect of immune function which is contrary to the performance gains that were found in these subjects. The performance results from this study are supported by previous studies that found a significant increase in leg power and performance after administration of 300 mg and 600 mg of testosterone enanthate per week (Storer et al. 2003; Giorgi et al. 1999; Bhasin et al. 1996). Collectively, these reported findings and our study's data have demonstrated that testosterone enanthate significantly increases performance outcomes that rely on anaerobic power. In addition, this study reports an acute increase in NKCA in the placebo group following 6 weeks of resistance training, outlining enhanced immune responsiveness which may be best explained by the 6-week strength and conditioning program. While not statistically significant, there was an increase in circulating numbers of $CD3^+/CD4^+$, $CD3^-/CD16^+/CD56^+$ and $CD3^-/CD19^+$ lymphocytes and a decrease in $CD3^+/CD8^+$ lymphocytes after short duration maximal anaerobic exercise, which is consistent with previous studies (Gabriel et al. 1992; Nieman et al. 1992).

It has been documented that different AAS can act in either an immunosuppressive or immunostimulatory manner (Hughes et al. 1995; Mendenhall et al. 1990; Duschaux et al. 1982; Fuji et al. 1975). In contrast to this report, a previous study showed that NKCA was augmented in AAS users (Calabrese et al. 1989). However, the results from that study are difficult to interpret because the AAS users were self administering different types of AAS, the dosages varied considerably, and the training volumes and intensities were less controlled. In the present study, the daily activity, diet, training and administration of TE were all rigorously controlled, and the study may therefore have produced more reliable outcomes.

Mendenhall and coworkers (1990) have shown that AAS, such as testolactone, oxandrolone and stanozolol enhanced immune function, while testosterone and the testosterone ester testosterone propionate were immunosuppressive in rodents. They also demonstrated that the duration of AAS administration could either positively or negatively influence immune function (1990). Further evidence for immunosuppression by AAS has been demonstrated by Fuji et al. (1975) with testosterone reducing immune function in mice, by Duschaux et al. (1982) with testosterone inhibiting NKCA after treatment with thymosin in mice, and Hughes et al. (1995) with 17-β nandrolone decanoate and 17-α oxymethenelone inhibiting immune function. However, Hughes et al. (1995) were unable to show dehydroepiandrosterone (DHEA) affecting immune function. In the study reported here, NKCA after short maximal anaerobic exercise was reduced in the testosterone enanthate group from Week 0 to Week 6, suggesting an undesirable effect in acute immune function and potentially decreasing immunocompetence in AAS users.

A possible mechanism for this undesirable effect may be the interaction of testosterone receptors with interleukin-2 (IL-2) release. Testosterone receptors are present on the surface of T cells (Benten et al. 1999), particularly T helper/inducer ($CD3^+/CD4^+$) and T cytotoxic/suppressor ($CD3^+/CD8^+$) cells whose function is to produce IL-2 which influences NKCA. Natural killer cells are large granular cells that depend upon IL-2 production from T lymphocytes to increase numbers of high affinity IL-2 receptors which subsequently influence NKCA (Shephard et al. 1994; Suzuki et al. 1983). Low affinity and high affinity IL-2 receptors on natural killer cells are a regulating factor in NKCA, where upregulation of high affinity IL-2 beta receptors enhances NKCA (Nagao et al. 2000; Nagler et al. 1990; Graham et al. 1986). In response to acute exercise, previous studies have shown that epinephrine acts upon T lymphocytes to produce IL-2 (Henney et al. 1981), which then leads to an enhanced NKCA, via the high affinity IL-2 beta receptors (Nagao et al. 2000; Nagler et al. 1990; Graham et al. 1986). Hence, the enhanced NKCA activity in the PG group supports these findings. In contrast, NCKA activity for the TE group was reduced, suggesting that testosterone enanthate (or its metabolites) may reduce circulating lymphocytes being released into circulation or bind to testosterone receptors on T lymphocytes, downregulating T lymphocyte activities (Grossman & Russell, 1986).

Acute natural killer cell number did not significantly increase in the PG group after 6 weeks of strength training. This outcome is consistent with the literature, where acute response on natural killer function and natural killer cell numbers vary depending on the intensity and duration of the exercise (Gannon et al. 1995; Nieman et al. 1994, 1993; Ullum et al. 1994; Tvede et al. 1993). However, the results from this study showed that NKCA in the PG group was enhanced even though natural killer cell numbers were not increased significantly. It is speculated that this might be due to an effect

mediated by the production of catecholamines, such as epinephrine, and to a lesser extent norepinephrine, which increase with acute exercise (Kappel et al. 1991) and where natural killer cells have been found to contain the highest number of receptors to these hormones which are upregulated during exercise (Maisel et al. 1990). In addition, β-adrenergic receptor agonists have been shown to cause selective recruitment of natural killer cells from blood vessels, and during acute exercise, epinephrine acts upon T lymphocytes to produce IL-2 (Kappel et al. 1991), which is responsible for enhanced NKCA (Shephard et al. 1994; O'Shea & Ortaldo 1992). Similarly, previous studies have found that natural killer cells with high IL-2 response are recruited to the blood and this recruitment may be due to the large numbers of β-adrenoceptors on these cells which are upregulated by exercise (Nagoa et al. 2000; Pedersen et al. 1998; Galant et al. 1978) and induce selective detachment of natural killer cells from endothelial cells (Nagao et al. 2000; Pedersen et al. 1997; Benschop et al. 1993). Therefore, the production of epinephrine after an acute bout of exercise in the PG group may promote natural killer cells with a high IL-2 response capacity to be recruited from the spleen or other sites to the circulating pool, thus causing increased NKCA.

This work, together with data from previous studies, suggests that acute immune response is significantly increased, demonstrating a positive effect of the strength training as shown in the PG group. In addition, this study outlines that a supraphysiological dose of testosterone enanthate can elicit measurable increase in anaerobic performance. However, testosterone enanthate also mediates a contrary effect of reducing immune function, specifically acute NKCA responses which might reduce immunocompetence in AAS users.

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