NUTRITIONAL SUPPLEMENTATION, PERFORMANCE, AND OXIDATIVE STRESS IN COLLEGE SOCCER PLAYERS

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ABSTRACT

Arent, SM, Pellegrino, JK, Williams, CA, DiFabio, DA, and Greenwood, JC. Nutritional supplementation, performance, and oxidative stress in college soccer players. *J Strength Cond Res* 24(4): 1117–1124, 2010—The purpose of this study was to examine changes in performance and metabolic parameters in collegiate soccer players during preseason preparation and to determine the impact of a nutraceutical blend proposed to reduce oxidative stress. Male Division I college soccer players ($n = 22$) performed a progressive maximal treadmill test at the beginning and end of preseason to assess changes in $\dot{V}O_2$max, velocity at lactate threshold (V_{LT}), time-to-exhaustion, lipid hydroperoxide (LPO), 8-isoprostane, and creatine kinase (CK) response. After baseline testing, athletes were randomly assigned to receive the nutraceutical blend (EXP; $n = 12$) or an isocaloric equivalent (CON; $n = 10$) for 20 days of preseason training. $\Delta\dot{V}O_2$max (2.1 ± 3.3 ml·kg^{-1}·min^{-1}, $p = 0.007$), ΔV_{LT} (0.8 ± 1.4 km·h^{-1}, $p = 0.045$), and Δtime-to-exhaustion (39.4 ± 77.4 seconds, $p = 0.033$) were improved across groups, but a significant effect of supplementation on performance was not seen. Changes in resting levels of CK from the beginning to end of preseason were significantly lower ($p = 0.044$) in EXP (64.8 ± 188.4 U·L^{-1}) than in CON (292.8 ± 304.8 U·L^{-1}). Additionally, EXP demonstrated a significant decrease in the magnitude of the 8-isoprostane response at Trial 2 compared with Trial 1 (effect size [ES] = −0.74), whereas CON had an increased response (ES = 0.20). A similar pattern was seen for LPO ($p = 0.067$). Preseason training in male college soccer players resulted in significant improvements in $\dot{V}O_2$max, V_{LT}, and time-to-exhaustion. Supplementing with a proprietary antioxidant and nutraceutical blend may enhance some of these effects as indicated by magnitude of the responses. However, it appears that the most notable effects of supplementation were seen for reduced CK and oxidative stress, at least with short-term supplementation.

KEY WORDS antioxidant, lactate threshold, 8-isoprostane, reactive oxygen species, superoxide dismutase

INTRODUCTION

Preseason training places an extreme demand on athletes requiring them to engage in frequent high-intensity workouts with limited time devoted to recovery. This is particularly pronounced in many college sports, especially fall–season sports, faced with trying to maximize athlete readiness during progressively shortened preparatory periods. College soccer players, for instance, typically have only a few weeks to train as a team before dealing with the rigors of the competitive season and therefore engage in multiple high-intensity, high-volume sessions per day during the preseason period. Furthermore, peak performance is not just determined by the soccer-specific conditioning that takes place in preparation for the season, but also by the ability of the neuromuscular and endocrine systems to recover and adapt after the loads placed on them (16).

Even without the added preseason stressors, soccer itself is physiologically demanding. The athletes need to possess aerobic endurance, power, speed, and strength simultaneously. Elite soccer players spend a considerable portion of a match at intensities averaging 80–90% of HR_{max} and rely on anaerobic metabolism and power during brief burst of sprinting, kicking, and jumping (27). They need to be able to perform near maximal capacity for extended periods, which results in increased oxidative stress (1). Although the generation of reactive oxygen species (ROS) is a natural by-product of cellular respiration, their formation increases as the intensity of exercise increases (1). Oxidative stress has been related to fatigue and muscle damage (2,8), and increased recovery time (1), all of which can negatively impact performance. Furthermore, decreased mitochondrial

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efficiency has been indicated as a potential side effect of repeated cell membrane peroxidation (16).

Although exercise training can enhance endogenous antioxidant resources, these protective mechanisms are typically insufficient to adequately deal with ROS resulting from high-intensity or prolonged intermittent aerobic or anaerobic exercise (4,13). Because of this, various antioxidant or anticatabolic supplements have been investigated to determine their potential use in the protection from oxidative stress, corresponding muscle damage, or resultant performance decrements. Perhaps the compounds that have received the most attention as potential ergogenic aids because they relate to the mitigation of oxidative stress due to exercise are antioxidants such as vitamins A, C, and E. There is evidence that the requirements for these antioxidants increase with exercise (13). Previous research has demonstrated that antioxidants, obtained through either antioxidant-rich diets or antioxidant supplementation, can reduce the lipid hydroperoxide (LPO) response (14) and attenuate exercise-induced muscle damage (22), indicating reduced oxidative stress. These effects appear to be most pronounced when multiple antioxidant sources are combined, suggesting a synergistic effect (23). Furthermore, these findings have been shown to extend to polyphenols and other phytochemicals high in antioxidant capacity (24,31). It has been suggested that the reduced oxidative response may be achieved by enhancing the organism's own endogenous antioxidant capacity, as evidenced by positive changes in the antioxidant enzymes glutathione peroxidase and superoxide dismutase (SOD) (5,24). Recent research has also indicated that direct supplementation with SOD may be possible and highly effective at combating oxidative stress and enhancing endogenous resources.

Gastric breakdown has been the primary limitation for providing orally administered forms of antioxidant enzymes, such as SOD (25). However, recent advancements using a wheat gliadin polymer system to coat plant-derived (*Cucumis melo*) SOD appears to have circumvented this problem and provided an effective oral form of SOD (Glisodin®). Research using this form of SOD has demonstrated antioxidant and antiinflammatory properties (19,28,29). This orally available form of SOD is part of a proprietary antioxidant and anticatabolic nutriceutical mixture that has been incorporated into a dietary supplement (Resurgex® and Resurgex Plus®) that was developed to improve immune functioning, spare lean muscle, and reduce oxidative stress in patients suffering from muscle-wasting diseases. Both Resurgex® and Resurgex Plus® have been used as an adjunct to medical care in patients with HIV or AIDS, cancer, Hepatitis C, and other chronic illnesses, but they have received no direct testing on performance in high-level athletes despite the potential application as a nutritional aid.

The purpose of this study was to examine changes in performance, muscle damage markers, and oxidative stress in collegiate soccer players over the course of preseason preparation and to determine the impact of supplementing the diet with a proprietary nutriceutical blend. It was hypothesized that preseason training in college soccer players would result in improvements in fitness and that supplementing with Resurgex® would enhance these effects. It was also hypothesized that those athletes receiving Resurgex® would demonstrate lower oxidative stress and creatine kinase (CK) responses compared with an isocaloric control group in response to a maximal exercise test.

METHODS

Experimental Approach to the Problem

This study was run as a blinded, placebo-controlled design using 24 fit male Division I college soccer players. Performance tests were administered at the beginning (Trial 1) and end (Trial 2) of preseason camp (during the month of August) 20 days apart using a progressive maximal treadmill test to exhaustion. Preseason was chosen because of the fact that the training stimulus during this period of time was extremely high and because all athletes were living off-campus in a hotel and eating each meal as a team. In this way, diet was controlled as much as possible without interfering with the team's preparation. A 3-day dietary recall log was also completed before each Trial and analyzed using commercially available dietary analysis software (FoodWorks, Xyris Software, Queensland, Australia). Because of the preseason status of the athletes, they could not limit activity the day preceding the posttest. However, they did not perform a training session on the day of the testing, and each athlete was tested at the same time of the day for each trial. After Trial 1, the athletes were matched on maximal oxygen consumption ($\dot{V}O_2max$) and randomly assigned to either an experimental group ($n = 12$) or a control group ($n = 12$), which were matched for calories. The supplement drinks were administered twice a day by the research team after morning and evening training. Approximately 5 minutes before (t_0) and 5 minutes after (t_1) each performance test, blood samples were collected. Dependent variables included lactate threshold (V_{LT}), $\dot{V}O_2max$, time-to-exhaustion, CK, LPO, and 8-isoprostane (8-iso $PGF_{2\alpha}$).

Subjects

Members of a men's Division I college soccer team ($n = 24$; $M_{age} = 19.5 \pm 1.5$ years.; $M_{height} = 175.5 \pm 7.3$ cm; and $M_{weight} = 74.8 \pm 7.3$ kg) volunteered to participate in the study. Risks and benefits were explained to the subjects, and each of them gave written informed consent before participation in the study. All athletes were free from current injuries limiting their ability to train and complete physiological testing. Goalkeepers were excluded from analysis because of different training demands. After baseline testing, athletes were matched on $\dot{V}O_2max$ and randomly assigned to either an experimental group ($n = 12$) or a control group ($n = 12$). Two participants in the control group were injured during the preseason and unable to complete posttesting. Therefore, all analyses are based on 12 participants in the experimental group ($M_{\text{age}} = 19.5 \pm 0.4$ years; $M_{\text{height}} = 175.4 \pm 2.6$ cm; $M_{\text{weight}} = 76.0 \pm 2.0$ kg) and 10 participants in the control group ($M_{\text{age}} = 19.4 \pm 0.4$ years; $M_{\text{height}} = 175.6 \pm 1.4$ cm; $M_{\text{weight}} = 73.3 \pm 2.1$ kg). These procedures were approved by the Rutgers University Committee for the Protection of Human Subjects.

Procedures

Supplementation Protocol. Subjects in the experimental group received Resurgex Plus® (Millennium Biotechnologies Inc., Basking Ridge, NJ, USA), whereas those in the control group received an isocaloric equivalent without the proprietary nutriceutical blend. The nutriceutical blend in Resurgex Plus® consists of 75 mg CoQ_{10}, 500 U SOD/Gliadin, 1,750 mg ornithine ketoglutarate, 300 mg L-Carnitine, 100 mg nucleotides, 750 mg d-ribose, 500 mg L-glutamine, 100 mg beta glucans, 12.5 mg fruit polyphenols, and 1,750 mg branched chain amino acids (BCAA). To keep the athletes blind to the group assignment, the drinks were premixed and administered in generic, unlabeled bottles by the research team twice daily for 20 days after morning (1000–1100 hours) and evening (1900–2000 hours) training.

Exercise Test. On the day of each performance test, all athletes reported to the Rutgers University Human Performance Laboratory. Athletes were asked to arrive for testing normally hydrated and to refrain from ingesting substances that could affect normal physiological functioning (i.e., tea, coffee, alcohol, and nicotine). Subjects did not receive their assigned supplement on the day of each test to avoid acute effects.

The exercise performance test consisted of a graded maximal treadmill test to exhaustion. Athletes completed a series of 3-minute stages with 1-minute rest intervals between stages for the sampling of capillary blood to determine blood lactate values. The speed at Stage 1 was set at 8 $km \cdot h^{-1}$ and the grade was set at 1%. Speed was increased by 2 $km \cdot h^{-1}$ with each incremental stage, and grade was maintained at 1% throughout the test to maintain biomechanical demands similar to flat-level running during a soccer game. This process continued until volitional exhaustion. Heart rate was continuously monitored using a Polar S610 HR monitor (Polar Electro Co., Woodbury, NY, USA), and direct gas exchange was measured using a Max-1 gas analysis system (Physiodyne Instrument Corporation, Quogue, NY, USA).

Performance Measures. Capillary blood samples (5 μL) were taken from the fingertip at rest and at the end of each 3-minute stage to analyze blood lactate accumulation. The Lactate Scout (SensLab GmbH, Leipzig, Germany) portable analyzer was used to determine whole-blood lactate content. The Lactate Scout has previously demonstrated a variation coefficient between 3 and 8%. Lactate concentration was plotted against treadmill speed to determine the velocity at which lactate threshold (V_{LT}) occurred using the D_{MAX} method (6). $\dot{V}O_2$max was determined using the direct breath-by-breath gas exchange data from the Max-1 system (Physiodyne Instrument Corporation) and was established as the maximal average oxygen consumption over 30-second monitoring intervals. Additionally, total time spent running for each test was determined and used to establish total time-to-fatigue for each participant.

Biochemical Measures. Approximately 5 minutes before (t_0) and 5 minutes after (t_1) each performance test, blood samples were collected via venipuncture of a superficial forearm vein using a vacutainer system (Becton Dickinson, Rutherford, NJ, USA). Pretest blood draws were initiated after the subject had rested in a supine position for 30 minutes after arrival at the laboratory. Approximately 8 mL was collected in a serum separator tube, 8 mL in a sodium heparin coated tube, and 6 mL in an ethylenediaminetetraacetic acid (EDTA)-coated tube. The serum separator tubes were placed on ice and left to stand for 30 minutes to facilitate clotting before being centrifuged at 3,500*g* for 15 minutes at 4°C to obtain serum for CK analysis, used as an indicator of muscle membrane permeability change. Samples collected in the sodium heparin and EDTA vacutainer tubes were centrifuged immediately at 3,500*g* for 15 minutes at 4°C to obtain plasma for later analysis of lipid peroxidation markers indicating oxidative stress (8-iso $PGF_{2\alpha}$ [8-isoprostane] and [LPOs]). It has been suggested (10) that F2-isoprostanes are promising biomarkers for examining the influence of antioxidant intake on chronic conditions. All samples were stored at −80°C until analysis of the dependent measures. Assays were performed in duplicate. Serum samples were shipped to Labcorp (Raritan, NJ, USA) on dry ice for analysis of serum CK using a kinetic spectrophotometric assay read at 340 nm (Test #: 001362).

To analyze plasma free 8-iso $PGF_{2\alpha}$, plasma from the EDTA tubes was first purified by diluting the sample in a 1:5 ratio with Eicosanoid affinity column buffer (Cayman Chemical, Ann Arbor, MI, USA). A known amount of tritiated 8-iso $PGF_{2\alpha}$ was added before purification to determine recovery rates. Ethanol was added to the solution, and the sample was chilled at 4°C for 5 minutes to precipitate proteins and then centrifuged at 1,500*g* for 10 minutes at 4°C. The supernatant was decanted, and the remaining ethanol was evaporated by vacuum centrifugation. The pH was lowered to 4.0 using dropwise addition of HCl. Samples were then passed through a C-18 affinity column (Cayman Chemical) previously activated with methanol and UltraPure water. After addition of the sample, the column was washed with 5 mL UltraPure water followed by 5 mL high performance liquid chromatography grade hexane (Sigma Chemical, St. Louis, MO, USA). The sample was eluted with 5 mL of an ethyl acetate:methanol solution (Cayman Chemical). The elution solution solvents were evaporated again using vacuum centrifugation, and the samples were then reconstituted in 450 μL enzyme immunoassay (EIA) buffer (Cayman Chemical). For each purified sample, 50 μL

Table 1. Performance changes before (Trial 1) and after (Trial 2) preseason training for the experimental and control group (mean ± *SD*).*

	Experimental group ($n = 12$)			Control group ($n = 10$)		
	Trial 1	Trial 2	ES	Trial 1	Trial 2	ES
VLT ($km \cdot h^{-1}$)	11.58 ± 0.8	12.57 ± 1.3	0.93	11.96 ± 1.1	12.46 ± 1.1	0.44
Time-to-exhaustion (min)	16.44 ± 1.9	17.32 ± 1.6	0.51	16.95 ± 1.6	17.33 ± 1.4	0.26
$\dot{V}O_2max$ ($ml \cdot kg^{-1} \cdot min^{-1}$)	49.83 ± 4.1	52.46 ± 5.1	0.57	49.57 ± 4.5	50.95 ± 3.6	0.34

*ES = effect size; VLT = velocity at lactate threshold; $\dot{V}O_2max$ = maximal oxygen consumption.

was analyzed using a commercially available 8-isoprostane EIA kit (Cayman Chemical), with each sample assayed in duplicate. Absorbance values were determined with a Spectramax 340 microplate reader (Molecular Devices, Sunnyvale, CA, USA) between 405 and 420 nm and the raw data corrected using the recovery rates of tritiated $PGF_{2\alpha}$.

The LPO concentrations of plasma from the sodium heparin tubes were determined using the modified PCA-FOX assay (9). Each plasma sample was divided into a blank and a test sample. Catalase (Sigma Chemical) was then added to both to eliminate H_2O_2 interference, followed by incubation for 2 minutes at room temperature (21). After this, 20 mM Tris(2-carboxyethyl)phosphine HCl (Sigma Chemical) was used to reduce LPOs in the blank sample to their organic alcohols (21). UltraPure water was added to the test sample followed by incubation for 30 minutes at room temperature. All samples then received the PCA-FOX assay reagent consisting of 100 μM xylenol orange (MP Biomedicals, Aurora, OH, USA) and 20 μM ferrous ammonium sulfate (Sigma Chemical) in 110 mM perchloric acid (Fisher Scientific, Fairlong, NJ, USA) (9) and incubated at room temperature for 45 minutes. The reaction mixture was then centrifuged at 10,000*g* for 10 minutes. The supernatant was aliquotted into a micotiter plate and read at 560 nM with a Spectramax 340 microplate reader (Molecular Devices). Concentrations were determined by dividing the net absorbance by the molar extinction coefficient of lipid hydroperoxide in perchloric acid (9).

Statistical Analyses

A 2 × 2 (Group × Trial) multivariate analysis of variance (MANOVA) with repeated measures on the second factor was used to assess effects of training and supplementation on V_{LT}, $\dot{V}O_2max$, and time-to-exhaustion. Significant multivariate effects were followed by univariate follow-up tests.

To control for baseline values and examine the differences in overall response to the exercise tests, change scores were computed for each of the biochemical measures at each testing time (Trial 1 or Trial 2). Creatine kinase changes were examined using a 2 × 2 (Group × Trial) ANOVA with repeated measures on the second factor. A 2 × 2 (Group × Trial) MANOVA with repeated measures on the second factor was conducted to assess effects on the oxidative stress biomarkers (8-iso $PGF_{2\alpha}$ and LPO). Univariate follow-up tests were conducted in the event of a significant multivariate effect.

For each univariate analysis, examination of the Huynh–Feldt (H–F) epsilon for the general model was used to test the assumption of sphericity. If this statistic was greater than

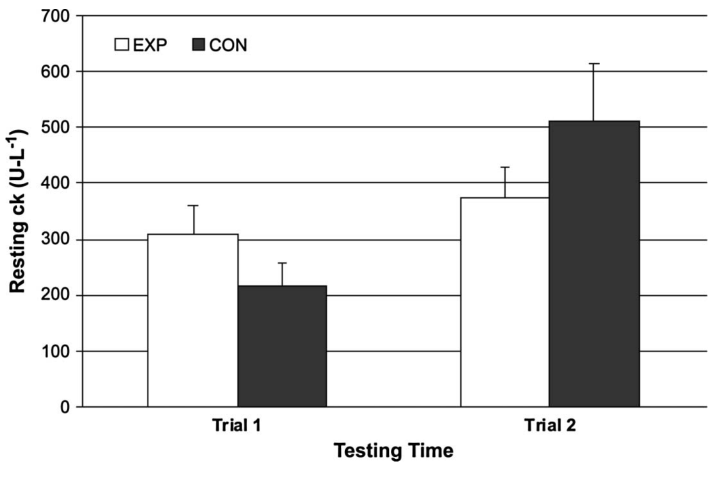

Figure 1. Resting levels of creatine kinase ($U \cdot L^{-1}$) before (Trial 1) and after (Trial 2) preseason camp in the experimental (EXP; $n = 12$) and the control (CON; $n = 10$) group. Change from Trial 1 to Trial 2 was significantly lower in the EXP group than in the CON group ($p = 0.044$).

Table 2. Biochemical responses to performance testing at the beginning (Trial 1) and the end (Trial 2) of preseason training for the experimental and control groups before (t_0) and after (t_1) exercise (mean ± *SD*).*

	Experimental group ($n = 12$)				Control group ($n = 10$)			
	Trial 1		Trial 2		Trial 1		Trial 2	
	t_0	t_1	t_0	t_1	t_0	t_1	t_0	t_1
CK ($U \cdot L^{-1}$)	306.9 ± 183.9	372.6 ± 224.3	371.8 ± 197.9	458.6 ± 247.5	216.4 ± 127.7	272.3 ± 168.4	509.2 ± 309.3	589.7 ± 332.1
8-Iso $PGF_{2\alpha}$ ($pg \cdot mL^{-1}$)	31.3 ± 16.4	43.9 ± 15.1	32.0 ± 18.9	40.2 ± 18.9	26.7 ± 12.1	43.3 ± 21.2	32.1 ± 13.6	53.5 ± 19.8
LPO ($\mu M \cdot L^{-1}$)	1.2 ± 0.8	2.7 ± 1.4	1.5 ± 0.8	2.8 ± 1.4	1.6 ± 0.9	3.1 ± 0.6	1.7 ± 0.8	3.3 ± 0.5

*CK = creatine kinase; 8-iso $PGF_{2\alpha}$ = 8-isoprostanes; LPO = lipid hydroperoxides.

0.75, sphericity was considered to have been met, and the unadjusted univariate statistic was used. If epsilon was less than 0.75, a violation of the assumption of sphericity was considered to have occurred, and the H–F adjusted statistic was used to determine significance.

Because of the impact that even small effects may have on overall performance of athletes at this level and in accord with recent recommendations for statistical follow-up (20), effect sizes (ESs) were calculated to compare magnitude of changes in the experimental and control groups using Hedges' *g* formula for ES computation. This ES computation was used for all variables. Group data are expressed as mean ± *SD*, and statistical significance was set at the $p \leq 0.05$ level.

RESULTS

After accounting for differences in the micronutrient profiles of the assigned supplements, dietary analysis revealed no significant differences between groups ($p = 0.72$). There was a significant multivariate main effect for Trial for the performance measures ($p = 0.02$). The multivariate main effect for Group ($p = 0.36$) and the multivariate Group × Trial interaction ($p = 0.72$) were not significant. Follow-ups indicated significant improvements across both groups for V_{LT} ($p = 0.045$), $\dot{V}O_2max$ ($p = 0.007$), and time-to-exhaustion ($p = 0.033$) from the beginning to the end of preseason. There was an average increase in V_{LT} of 0.8 ± 1.4 $km \cdot h^{-1}$ (ES = 0.43). $\dot{V}O_2max$ increased by an average of 2.1 ± 3.3 $ml \cdot kg^{-1} \cdot min^{-1}$ (ES = 0.49), and there was also an average increase of 39.4 ± 77.4 seconds (ES = 0.46) in time-to-exhaustion. No significant changes in performance were seen as a function of supplementation ($p > 0.10$). Means ± *SD* and ESs as a function of supplement group can be found in Table 1.

Biochemical Measures

CK Response. There were no significant changes in the degree of CK response to the exercise test, with CK increasing in response to the test regardless of Group or Trial. There were, however, different trends in the magnitude of changes in baseline values between the groups (Figure 1). Although both groups had elevated CK at rest at Trial 2 compared with Trial 1, this increase was significantly smaller ($p = 0.044$) in the experimental group ($\Delta CK = 64.8 \pm 188.4\ U \cdot L^{-1}$; ES = 0.33) than in the control group ($\Delta CK = 292.8 \pm 304.8\ U \cdot L^{-1}$; ES = 1.24). Means ± *SD* as a function of group can be found in Table 2.

Oxidative Stress. There was a significant multivariate Group × Trial interaction for the oxidative stress measures ($p = 0.01$). The primary contributor to this multivariate effect was a significant Group × Trial interaction for 8-iso $PGF_{2\alpha}$ ($p = 0.004$). The Group × Trial interaction for LPO also approached significance ($p = 0.067$). The experimental group demonstrated a significant decrease in the magnitude of 8-iso $PGF_{2\alpha}$ response during testing at Trial 2 (Δ8-iso $PGF_{2\alpha} = 8.2 \pm 16.3\ pg \cdot mL^{-1}$) compared with Trial

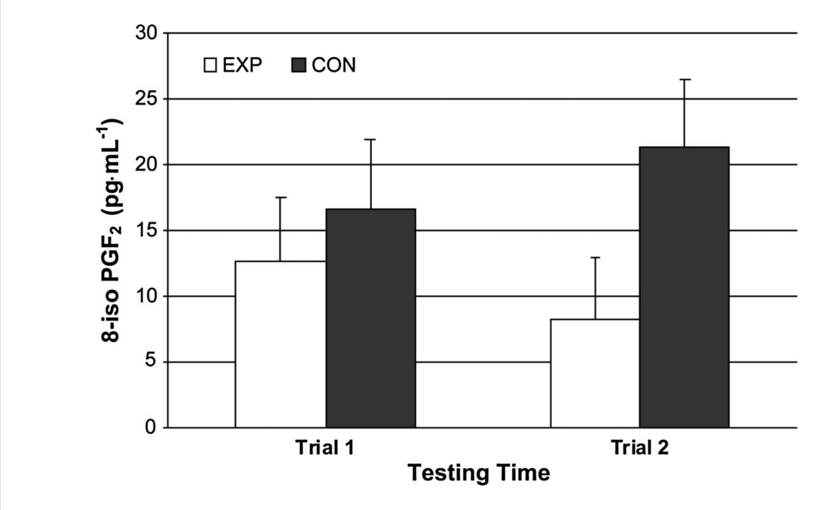

Figure 2. 8-Isoprostane (Δ8-iso $PGF_{2\alpha}$; pg·mL^{-1}) response to exercise testing before (Trial 1) and after (Trial 2) preseason camp in the experimental and the control group. There was a significant Group × Time interaction ($p = 0.004$).

1 (Δ8-iso $PGF_{2\alpha}$ = 12.6 ± 17.0 pg·mL^{-1}), ES = −0.74 (Figure 2). In contrast, the control group had an elevated 8-iso $PGF_{2\alpha}$ response at Trial 2 (Δ8-iso $PGF_{2\alpha}$ = 21.4 ± 16.1 pg·mL^{-1}) compared with that at Trial 1 (Δ8-iso $PGF_{2\alpha}$ = 16.6 ± 16.8 pg·mL^{-1}), ES = 0.20. The pattern of response was essentially identical for LPO. The experimental group showed a slight decrease in LPO response during testing at Trial 2 (ΔLPO = 1.31 ± 0.7 μmol·L^{-1}) compared with that at Trial 1 (ΔLPO = 1.52 ± 0.7 μmol·L^{-1}), ES = −0.27. The control group, though, had a slight increase in LPO response from Trial 1 (ΔLPO = 1.50 ± 0.6 μmol·L^{-1}) to Trial 2 (ΔLPO = 1.61 ± 0.6 μmol·L^{-1}), ES = 0.19. Means ± *SD* as a function of group can be found in Table 2.

DISCUSSION

The findings of this study indicate that preseason training in male Division I college soccer players resulted in significant improvements in performance as indicated by increased V_{LT}, $\dot{V}O_2max$, and time-to-exhaustion. Any additional benefit to improvement on these measures as a function of supplementing with Resurgex® did not reach statistical significance. However, supplementation with Resurgex® resulted in blunted oxidative stress in response to maximal exercise and lower resting CK compared with the control group.

Results revealed that those in the experimental group had an attenuated F_2-isoprostane response at Trial 2 compared with that at Trial 1. In contrast, those in the control group had an elevated F_2-isoprostane response. The pattern of response for LPO was identical, though not statistically significant. Interestingly, Halliwell (10) has suggested that F_2-isoprostanes hold particular promise as biomarkers for studies examining the influence of antioxidant intake on chronic disease. Their formation has also been identified as a better indicator of oxidative stress than other markers of lipid peroxidation (17). The attenuated oxidative stress response is consistent with other studies using high antioxidant diets in athletes. For example, Schroder et al. (26) found that, compared with placebo, an antioxidant combination decreased LPO response in professional basketball players over the course of a season, and similar responses have also been seen with supplementation in swimmers (5). These results are also consistent with previous studies using isolated Glisodin® supplementation that have demonstrated a protective effect on DNA and reduced 8-isoprostane levels when exposed to hyperbaric oxygen-induced cell stress (19), enhanced antioxidant status and resistance to oxidative stress-induced apoptosis (28), and reduced inflammatory responses when injected with the proinflammatory cytokine IFN-gamma (29).

Despite the lack of statistical significance, it may be premature to conclude that there is no added benefit to performance when supplementing with Resurgex®, particularly in light of the biochemical findings. Examination of the performance ESs for the 2 groups demonstrates that, in all cases, the magnitude of the change in performance was larger for the experimental group vs. control group (V_{LT} ES = 0.93 vs. 0.44; $\dot{V}O_2max$ ES = 0.57 vs. 0.34; time-to-exhaustion ES = 0.51 vs. 0.26). Given these trends coupled with the biochemical findings and the relatively short duration of the administration period, it is conceivable that the influence of Resurgex® or its constituent nutriceutical components is clinically significant despite lack of statistical significance. For example, previous findings have indicated that just a 5% increase in running economy can result in as much as a 1,000-m increase in distance covered during a soccer game (11). During the course of an intense training regimen, reductions in acute oxidative stress responses may allow for improved recovery and enhanced mitochondrial functioning. Given a longer period of supplementation, it is conceivable that the cumulative effects would become apparent in performance outcomes. Of course, it is entirely possible that this would not be the case and that oxidative stress attenuation may not be tightly coupled to performance improvements in this group of athletes. It has been noted (30) that studies in humans have not been able to demonstrate that antioxidant *restriction* impacts exercise performance. It may also be that chronic administration of the supplement would exert effects on performance via indirect means. For example, Davis et al. (7) found that administration of oat-beta glucan, which is also found in Resurgex®, offset immunosuppressive effects of exercise in mice. This effect may be further magnified by the resistance to proinflammatory cytokines such as tumor necrosis factor-α resulting from Glisodin® supplementation (29). Immune support would allow an athlete to stay healthy and continue training, thus leading to further performance improvements. Future research is clearly warranted to examine these issues.

The change in CK response during recovery instead of immediately following the exercise itself is consistent with previous research on BCAA supplementation and protein metabolism (3). As noted by Hoffman et al. (12), CK appears to be a particularly effective marker of muscle damage as a result of chronic exercise. This would explain why differences were seen in resting CK values at Trial 2 as opposed to immediately following the acute exercise test. It may be that the supplement does not attenuate acute muscle breakdown in response to exercise, but rather improves the rate of recovery from the acute bouts by modifying the anabolic vs. catabolic environment. Although it would have been ideal to perform a 24-hour follow-up with the athletes after each Trial to assess this, it was impossible given the context of the study. Any biochemical responses seen at 24 hours would likely not have been solely attributable to the exercise test itself as it would not have been feasible to require the athletes to refrain from any other physical training over this period.

To evaluate these proposed modifications to the anabolic vs. catabolic environment as a result of supplementation with Resurgex®, future research should consider directly assessing endocrine responses contributing to this effect. Both testosterone and cortisol have been found to be important markers of training stress and indicators of the predominance of either anabolic or catabolic processes, respectively (18). Previous research with college soccer players (15) suggests that a catabolic environment, evidenced by a decreased ratio of testosterone to cortisol, at the beginning of a competitive season can lead to progressive performance deterioration over the course of the season. A nutritional supplement capable of assisting in promoting an optimal biochemical and hormonal environment for recovery and fitness improvements should be of considerable interest to athletes and coaches alike.

Future research needs to examine the optimal dosage required to produce adaptive benefits, particularly for compounds such as Glisodin® that have not yet had dose–response effects established. The biochemical and performance effects of relatively short-term supplementation with Resurgex® may be meaningful effects for athletes of this level (and higher) and warrant further, long-term investigation into the adaptations that may occur and the mechanisms driving these responses.

PRACTICAL APPLICATIONS

With exogenous supplementation of protective nutriceuticals such as those found in Resurgex®, it appears possible to reduce acute and chronic oxidative stress and muscle damage. Supplementing with Resurgex® also appears to provide some benefit for enhancing performance changes resulting from intense training, though these performance effects appear modest. The coach or athlete should consider whether these performance differences warrant use of Resurgex® during training and whether there may be long-term benefit to demonstrated reductions in markers of oxidative stress and CK response. Although the current research did not support a statistically significant enhancement because of supplementation with this particular product, it may be that even small benefits can prove advantageous for higher-level athletes seeking a competitive edge.

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