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Effect of curcumin supplementation on inflammatory status and muscle damage in competitive female soccer players: a placebo-controlled, single-blind, nonrandomized, crossover pilot study

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[Purpose] Curcumin, a major component of turmeric, has anti-inflammatory and antioxidative properties, which are associated with protective effects against muscle damage. This study examined the effects of dietary curcumin on inflammation and muscle damage in female competitive soccer players.

[Methods] A single-blinded, placebo-controlled, nonrandomized, crossover pilot study was conducted. Six competitive female soccer players (20.0 ± 2.0 years-old) who participated in a 2-week preseason training program were assigned to two conditions: placebo and curcumin. The participants ingested a placebo or curcumin dosage (270 mg/day) during 2 weeks of preseason training, with 1 week of washout. Fasting blood samples were collected under resting conditions before (day 0) and after (day 15) the training period to examine changes in the concentration of interleukin 6 (IL-6), an inflammatory marker, and indices reflective of muscle damage.

[Results] Curcumin decreased the concentration of IL-6 released (mean decrease, −30.2 ± 28.1%), whereas no decrease was observed in the placebo condition (13.4 ± 17.4%). Changes in plasma IL-6 concentrations were significantly greater in the curcumin condition than in the placebo condition ($P < 0.05$). However, curcumin supplementation had no significant effects on muscle damage indices.

[Conclusion] The present study shows that curcumin supplementation could attenuate inflammation, as indicated by IL-6 concentrations, in competitive female soccer players during the training period.

[Keywords] athletes, curcumin, inflammation, muscle damage, supplementation, plasma IL-6

INTRODUCTION

Skeletal muscle damage following intensive training induces cumulative muscle fatigue and a sensation of discomfort, which can lead to underperformance or reduced motivation for subsequent training. Strenuous physical activities, especially those involving high-intensity or eccentric muscle contraction, can induce muscle damage, and consequently, inflammatory responses[1,2]. Therefore, it is important to determine effective strategies to prevent muscle damage between intensive training sessions and avoid loss of athletic performance.

Curcumin, commonly used as a spice and yellow pigment in foods, is the main phenolic compound present in turmeric (*Curcuma longa* L.), which possesses beneficial properties, including antioxidant and anti-inflammatory effects[3,4]. Evidence from animal models highlights the beneficial effects of curcumin supplementation on physical activity and sports performance[5], supporting a decrease in inflammation[6] and oxidative stress[7], and the prevention of muscle damage and fatigue[5,8]. Furthermore, we and others have reported that acute curcumin ingestion before or after a single bout of resistance exercise attenuates muscle damage and inflammation following exercise in healthy individuals[9-11], as well as in those performing other types of acute exercise (e.g., aerobic exercise)[12]. Based on these findings, it is believed that dietary curcumin supplementation could be an effective tool for reducing or minimizing inflammation caused by intensified training-induced muscle damage, as well as acute exercise. However, the effects of curcumin supplementation on the inflammatory response and muscle damage in athletes performing sports activities have not been investigated.

Soccer is an intermittent sport requiring athletes to execute a variety of physical demands, such as cardiorespiratory fitness, muscle strength and power, and speed[13]. During the preseason soccer training period, intense and sustained physical activities, including aerobic and strength training, can increase inflammatory response to muscle damage. Therefore, in this study, we aimed to examine the effects of dietary curcumin supplementation on an inflammatory marker and other muscle damage indices in competitive female soccer players during a training period. The study was designed to investigate the effect of curcumin supplementation on the concentrations of interleukin-6 (IL-6), an inflammatory marker, and muscle damage indices, namely creatine kinase (CK) activity, myoglobin, aspartate aminotransferase (AST), and lactate dehydrogenase (LDH) levels. We hypothesized that curcumin supplementation may have a positive effect in reducing inflammation and muscle damage in competitive female soccer players.

METHODS

Participants

Six competitive female soccer players participated in this study. All the players were members of the same university soccer team, and are international- or national-level athletes, with 11.8 ± 1.3 years of soccer experience. All athletes had regular menstrual periods (24–29 days), and none had a history of overt chronic illnesses or showed any signs or symptoms of such illness. All participants provided written informed consent to participate in the study, and all procedures were reviewed and approved by the Ethics Committee of the University of Tsukuba. This study conformed to the principles outlined in the Declaration of Helsinki.

Experimental design

The present study employed a single-blind, placebo-controlled, nonrandomized, crossover design. The participants were tested under two different conditions for 14 days: placebo supplementation and curcumin supplementation, in which each condition was followed by 7 days washout period (Figure 1). The athletes were instructed to consume their capsules after breakfast, lunch, and dinner daily throughout the study. All athletes generally performed technical soccer and strength training during the preseason soccer training period. The participants' rating on the Borg Rating of Perceived Exertion scale was 12–15 points, indicating a heavy exertion (the scale ranges from 6 to 20 points; a rating of 6 indicates "no exertion at all" and a rating of 20 indicates "maximal exertion"). Physical activity levels were assessed for 14 consecutive days using a uniaxial accelerometer (Life-Corder; Suzuken Co., Nagoya, Japan) for each condition at all times while the participants were awake except during sleeping and bathing[14]. Based on the magnitude and frequency of accelerometer, data for 14 consecutive days were used to assess the total daily energy expenditure (kcal/day) and daily physical activity energy expenditure (kcal/day).

Supplementation procedures

Participants orally ingested three 90 mg curcumin capsules (Theracurumin; Theravalues Corporation, Tokyo, Japan) or an equivalent oral placebo after every meal (3 times per day, total 270 mg/d) for 14 days during the preseason training period. This daily ingestion dose was determined based on our previous study and was sufficient to increase the plasma curcumin concentration[9]. Theracurumin consists of highly absorptive curcumin dispersed in colloidal nanoparticles and is associated with a much higher plasma concentration after intake than achieved with the intake of conventional curcumin powder[15,16]. The placebo was ingested as placebo capsules, which were similar in shape and color, and contained equivalent doses of starch (dextrin and maltose) to prevent the participants from distinguishing between the capsules.

Resting blood pressure and heart rate

Systolic and diastolic blood pressures (mmHg) and heart rate were measured from the nonexercised arm in the supine position using oscillometry and echocardiogram (form PWV/ABI; Colin Medical Technology, Japan).

Blood sampling and assessment of biochemical parameters

At baseline and after 14 days, fasting morning blood

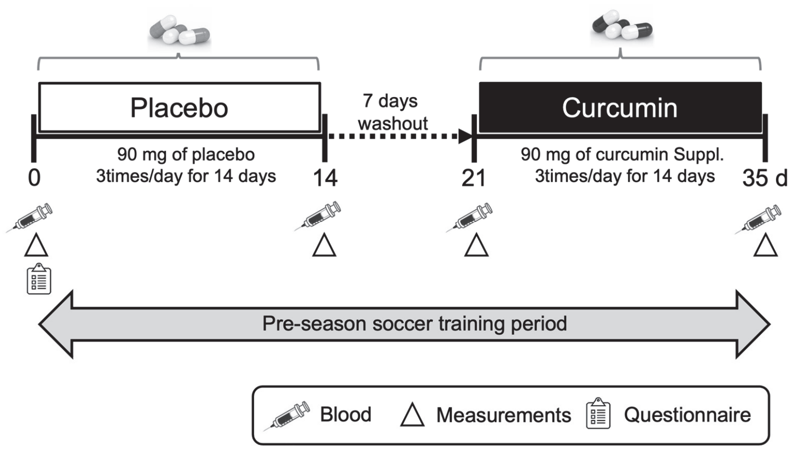

Figure 1. Schematic illustration of the experimental protocol. Suppl, supplementation; Blood, blood sampling; Measurements, measurements of resting blood pressure and heart rate; Questionnaire, questionnaire including participant characteristics and preseason soccer training.

samples were obtained from the antecubital vein under resting conditions using the standard venipuncture technique. Blood samples were immediately centrifuged at 3,000 rpm for 15 min at 4 °C, and the serum and plasma samples were stored at –80 °C until analysis. The serum cholesterol and plasma glucose concentrations were determined using standard enzymatic techniques. The plasma IL-6 concentration was determined using a commercial enzyme-linked immunosorbent assay kit (Quantikine Human IL-6, R&D System Inc., Minneapolis, USA). Serum CK activity was measured by a commercial laboratory using a test kit (Wako Pure Chemical Industries, Osaka, Japan). Serum myoglobin, AST, and LDH concentrations were analyzed using the Japan Society of Clinical Chemistry consensus methods[17].

Statistical analysis

All data are expressed as mean ± standard deviations (SD). The Kolmogorov–Smirnov test was performed to check the normality of distribution of parameters. The paired *t*-test (parametric test) or Wilcoxon test (nonparametric test) was used to test the mean differences between the conditions at baseline, as appropriate. Changes in plasma IL-6 concentrations between the two conditions were compared using a paired *t*-test. All statistical analyses were performed using IBM SPSS Statistics 22 (SPSS Inc., Chicago, IL, USA), with statistical significance set at $P < 0.05$. Hedge's g effect size was also calculated to determine the magnitude of changes in plasma IL-6 concentration between conditions, and $g > 0.80$ was accepted as a large effect[18].

RESULTS

The participants' characteristics are presented in Table 1. The mean age, height, weight, and body mass index of participants was 20.0 ± 2.0 years, 162.1 ± 8.7 cm, 58.1 ± 6.3 kg, and 22.1 ± 0.9 kg/m^2, respectively. The serum lipid levels of all participants were within the clinically normal range. The total daily energy expenditure (2,279 ± 211 for placebo vs. 2,288 ± 230 kcal/day for curcumin; $P = 0.465$) and daily physical activity energy expenditure (483 ± 149 for placebo vs. 489 ± 162 kcal/day for curcumin; $P = 0.588$) during the daily training period did not differ between the placebo and curcumin conditions.

Hemodynamic parameters before and after training are shown in Table 2. There were no differences in systolic blood pressure, mean blood pressure, diastolic blood pressure, or heart rate between the two conditions. In addition, no changes were observed in these parameters after pretraining in either group.

The differences in the concentrations of plasma IL-6, a circulating inflammatory marker, between the two conditions are shown in Figure 2. There was no difference in plasma IL-6 concentrations between the two conditions before training (0.71 ± 0.26 for placebo vs. 1.04 ± 0.41 pg/mL for curcumin). Curcumin decreased the concentration of IL-6 released (mean decrease, −30.2 ± 28.1%), whereas no decrease was observed in the placebo condition (13.4 ± 17.4%). Changes in plasma IL-6 concentrations were significantly greater in the curcumin condition than in the placebo condition ($P < 0.05$, Hedge's $g = 1.69$).

Several biochemical parameters, including CK, LDH, myoglobin, and AST, have been proposed as candidate markers for investigating the impact of strenuous physical exercise on skeletal muscle damage[19]. In the present study, the serum CK activity and serum myoglobin, AST, and LDH concentrations did not differ between the two conditions before training (Table 3). These markers did not change significantly after training, and no significant differences were observed between the two conditions.

Table 1. Characteristics of participants.

Variable	n = 6
Age, years	20.0 ± 2.0
Height, cm	162.1 ± 8.7
Weight, kg	58.1 ± 6.3
Body mass index, kg/m^2	22.1 ± 0.9
Total cholesterol, mg/dl	186.7 ± 14.0
HDL cholesterol, mg/dl	75.7 ± 10.7
LDL cholesterol, mg/dl	97.7 ± 15.8
Triglyceride, mg/dl	60.5 ± 6.7

Values are means ± SD
HDL, High density lipoprotein; LDL, Low density lipoprotein

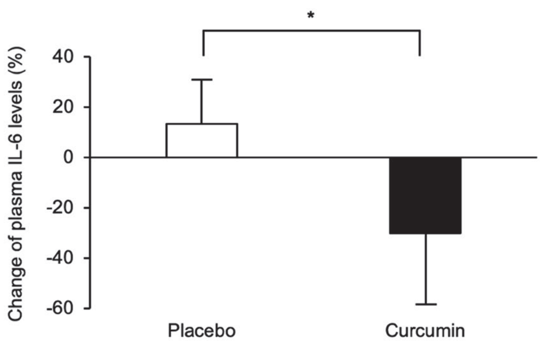

Figure 2. Changes in plasma IL-6 levels in the curcumin and placebo conditions. *$P < 0.05$ vs. placebo condition.

Table 2. Hemodynamic parameters before and after training.

	Placebo		Curcumin	
	Pre-training	Post-training	Pre- training	Post-training
Systolic blood pressure, mmHg	104.4 ± 2.5	103.5 ± 4.0	103.8 ± 4.2	102.1 ± 3.0
Mean blood pressure, mmHg	77.2 ± 3.4	76.6 ± 2.0	76.1 ± 3.8	76.2 ± 3.2
Diastolic blood pressure, mmHg	58.0 ± 3.2	57.6 ± 3.1	58.9 ± 3.2	57.3 ± 3.7
Heart rate, beats/min	51.2 ± 10.1	48.6 ± 10.1	49.2 ± 11.5	47.5 ± 7.4

Values are means ± SD

Table 3. Changes in biomarkers of muscle damage before and after training.

	Placebo		Curcumin	
	Pre-training	Post-training	Pre-training	Post-training
Creatine kinase (CK) activity, IU/L	306 ± 250	258 ± 83	298 ± 275	238 ± 142
Myoglobin (Mb), ng/mL	31 ± 10	38 ± 12	36 ± 12	33 ± 14
Lactate dehydrogenase (LDH), IU/L	211 ± 37	208 ± 27	202 ± 28	208 ± 37
Aspartate aminotransferase (AST), IU/L	25 ± 12	24 ± 7	25 ± 13	27 ± 9

Values are means ± SD.

DISCUSSION

The major finding of the present study was that dietary curcumin supplementation decreased the inflammatory response, as measured using plasma IL-6 concentrations, during intense training periods in competitive female soccer players. However, curcumin supplementation did not change the muscle damage indices in competitive female soccer players. We previously identified the beneficial effects of acute curcumin supplementation on muscle damage induced by a single bout of resistance exercise[9]. Therefore, in this study, we aimed to determine the effects of curcumin as a dietary supplement on muscle damage and inflammatory responses in athletes engaged in regular strenuous exercise training. Our results indicate that dietary curcumin supplementation for 14 days during an intense training period has a beneficial effect on the inflammatory response associated with muscle damage in female athletes.

During exercise, inflammation is related to muscle metabolism and damage. Exercise induces an increase in free radical production, which acts as a key effector of inflammation and DNA damage. IL-6, which acts as both a cytokine and myokine, is a critical circulating inflammatory marker that is produced and released into the circulation during exercise[20]. IL-6 is the most prominent muscle-derived protein, and its circulating levels increase in response to exercise without causing muscle damage[21]. Additionally, Chaffin et al. suggested that IL-6 levels after exercise were not affected by hormonal variations throughout the menstrual cycle in women[22]. Therefore, in this study, we measured plasma IL-6 concentration as an inflammatory marker in female athletes, and found a decrease in IL-6 levels following dietary curcumin supplementation during regular strenuous exercise training periods.

Regular strenuous athletic training, which is commonly performed during the preseason soccer period, is expected to induce inflammation and muscle damage in the participants. In this study, although there was a significant decrease (approximately −30.2%) in plasma IL-6 levels in the curcumin condition, the levels did not change from pre-training to post-training in the placebo condition. Furthermore, biochemical markers of skeletal muscle damage, including CK, LDH, myoglobin, and AST, did not change under either condition. In contrast to the findings of increased muscle damage or inflammation in response to acute exercise in untrained individuals[9-11], these observations may be less evident in trained athletes engaged in regular strenuous exercise. Plasma IL-6 concentrations are ~1 pg/mL or even lower at rest but not immediately after exercise in young athletes[23]. Under strenuous prolonged exercise, our findings of decreased IL-6 levels in the curcumin condition also provide evidence that supplemental curcumin may partly prove beneficial, even with slightly increased inflammation, in response to training. Further research is required to confirm this issue.

The present study had some limitations. This study had a small sample size. The effect size was calculated using Hedge's g for significant results (i.e., plasma IL-6 concentration) to determine the magnitude of change. We observed large effect sizes (Hedge's $g = 1.69$) for the changes in plasma IL-6 concentrations between the placebo and curcumin conditions. Another limitation was that this study was not randomized. For a randomized study, participants who first ingested curcumin would require an adequate wash-out period, resulting in extended experimental time, which is problematic for a field study.

In conclusion, the present study is the first field study to investigate the dietary effects of curcumin on markers of inflammation and muscle damage during a strenuous training period in competitive female soccer players. This study revealed that the anti-inflammatory effect of curcumin protects against training-associated inflammation, at least partly, and that curcumin may be useful as a dietary supplement for individuals engaged in regular exercise. However, future studies investigating the dietary effects of curcumin on inflammation and muscle damage in exercise-trained subjects should consider using a protocol with higher intensity and longer duration to produce a more robust inflammatory response.

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