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EFFECTS OF SELF-ADMINISTERED GH OR IGF-1 HORMONES ON RESTING OXIDATIVE STRESS AND ANTIOXIDANT MARKERS IN MEN WITH OR WITHOUT RESISTANCE EXERCISE

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Abstract

Introduction. Some athletes and non-athletes use peptide hormones to increase lean body mass and fat loss, but those effects on oxidative stress and antioxidant markers are unknown. The aim of this study was to show the physiological profile of oxidative stress and antioxidant markers in athletes and non-athletes following long-term self-administration of GH or IGF-1 ***Material and Methods.*** Seventy-five healthy young men with the history of peptide hormone (i.e., GH or IGF-1) use for at least 1 year (i.e., 3 to 4 times a year) or resistance exercise (RE) experience for at least 3 years volunteered to participate in this study and were divided into 5 selected groups including 1) GH use plus RE (GH+RE, n = 15), 2) IGF-1 use plus RE (IGF-1+RE, n = 15), 3) GH use (GH, n = 15), 4) IGF-1 use (IGF-1, n = 15), and 5) RE only (RE, n = 15). Blood sample was obtained one time in order to evaluate the resting concentration of oxidative stress markers including 8-hydroxy-2-deoxyguanosine (8-OHdG), malondialdehyde (MDA), nitric oxide (NO) and antioxidant defense systems (i.e., glutathione peroxidase [GPx], catalase [CAT], and glutamate [GLU]). ***Results.*** There were no significant ($p > 0.05$) differences among the groups in the 8-OHdG, MDA, NO, GPx, CAT, and GLU levels. ***Conclusions.*** Self-administration of peptide hormone and RE for at least 1 year is not accompanied by alterations in resting oxidative stress and the antioxidant system in male athletes and non-athletes.

Key words: reactive oxygen species, defense system, peptide hormones, resistance training

Introduction

To date, peptide hormone is one of the most commonly used drugs among athletes to improve physical performance, muscle size, strength, and protein metabolism [1]. It appears that growth hormone (GH) is an anabolic hormone that plays a crucial role in improving muscle hypertrophy and also tissue repair throughout the body [2]. In addition, insulin-like growth factor 1 (IGF-1) is another peptide hormone that plays an important role in increasing muscle mass and also facilitating the body's response to exercise [3].

Although some amounts of peptide hormones may be useful in some pathological conditions, they are often abused by humans desiring to build muscle mass and enhance physical performance [4, 5]; however, World Anti-Doping Agency (WADA) prohibited the use of peptide hormones such as GH and IGF-1 because some individuals used them for purposes other than clinical or therapeutic [6].

In fact, there was not enough evidence to show potentially adverse effects in the immune system, cardiovascular and endocrine responses following peptide hormone use. In a systematic review, Liu et al. [3] reported that GH use could improve body composition and increase lean mass; 2 mg dose of GH could increase body composition and performance adaptations following athletic exercise compared to the control group [4]. Saugy et al. [6] noted that GH and IGF-1 use had anti-catabolic and anabolic effects on increasing beneficial impacts of training; however, the effects of peptide hormones use on oxidative stress and antioxidant markers are unknown.

In normal conditions, free radicals production and their subsequent antioxidant defense system work together for normalizing human homeostasis, but increases in free radical expression above physiological condition could induce oxidative stress in the body [7, 8]. Longitudinal administration of peptide hormones provides imbalance between free radicals production and the antioxidant defense system resulting in increasing ROS generation and also oxidative stress and cell damage [9, 10, 11].

Several athletes have used peptide hormone to increase muscle size and hypertrophy; however, side effects of longitudinal self-administration of peptide hormone on oxidative stress biomarkers and antioxidant defense systems in humans are unknown and no information is available on this subject. Therefore, the aim of this study was to show the physiological profile of oxidative stress (8-hydroxy-2-deoxyguanosine (8-OHdG), malondialdehyde (MDA), nitric oxide (NO)) and antioxidant (glutathione peroxidase (GPx), catalase (CAT) and glutamate (GLU)) markers following the longitudinal self-administration of peptide hormone (i.e., GH and IGF-1) in male athletes and non-athletes.

Material and Methods

Participants

Seventy-five healthy young men with the history of peptide hormone (i.e., GH or IGF-1) use or resistance exercise (RE) experience participated in this study (Tab. 1). The subjects were divided into 5 selected groups including, 1) GH use plus RE (GH+RE, n = 15), 2) IGF-1 use plus RE (IGF-1+RE, n = 15), 3) GH

Table 1. Characteristics of the study participants

	GH+RE	IGF-1+RE	GH	IGF-1	RE	Significant P value
Age (y)	26.6 ± 4.8	30.1 ± 5.6	28.6 ± 5.7	27.9 ± 4.8	29.5 ± 2.6	0.326
Height (cm)	177.9 ± 5.8	182.2 ± 6.7	180.3 ± 6.9	179.5 ± 5.7	180.2 ± 5.4	0.326
Weight (kg)	90.1 ± 10.7	91.9 ± 9.2	94.9 ± 9.7	90.4 ± 10.9	89.4 ± 8.3	0.562

GH+RE: growth hormone use plus resistance exercise; IGF-1+RE: Insulin like growth factor-1 use plus resistance exercise; GH: growth hormone use; IGF-1: Insulin like growth factor-1 use; RE: resistance exercise. Values are mean ± SD.

use (GH, n = 15), 4) IGF-1 use (IGF-1, n = 15), and 5) RE only (RE, n = 15). The inclusion criteria for the selected groups were as follows: 1) self-administration (determined by the interview) of GH or IGF-1 in a cyclic fashion (three to ten mcg daily in three doses daily using a liquid form by injection, at least three to four times in one year with at least two months of washout between periods), 2) at least 3 years of resistance training program, 3) no orthopedic or upper- and lower-body injuries. The exclusion criteria were as follows: 1) the presence of known respiratory, cardiovascular or musculoskeletal diseases, 2) any systemic diseases inducing fatty liver, etc. (determined by an internist physician), 3) no use of any supplement for at least 3 months before inclusion in the study. After screening for nutritional and drug-related information via a health-history questionnaire and an interview, the subjects that had similar macro/micronutrient content and caloric intake (25% protein, 55% carbohydrates and 20% fat) were included in the study. The participants in the GH+RE and IGF-1+RE groups had experience in resistance training programs during peptide hormone use, whereas the GH and IGF-1 groups only used peptide hormones and did not participate in any resistance training program. In addition, the RE groups did not have any experience of the peptide hormone use and only performed RE for at least 3 years before inclusion in the study. Before taking part in the study, the participants were notified about the potential risks involved and gave their written consent. This study was approved by the University human research committee.

Study design

A cross-sectional design was used in this study. After familiarization with the study procedure during subject selection, the subjects had their blood samples taken in order to analyze oxidative stress biomarkers and the antioxidant defense system. The blood sampling was performed in the morning (9:00-12:00 a.m.) following 12 h fasting, under the same conditions. The participants were advised to avoid any vigorous activities on the day before the test.

Measurements

Height was measured to the nearest 0.1 cm with the use of a wall-mounted stadiometer (Seca 222, Terre Haute, IN). Weight was measured to the nearest 0.1 kg using a medial scale (Camry, EF921, China).

Blood sample was obtained via venipuncture, after 5 mins in a supine position, from an antecubital vein by using a 20-guage needle and vacutainer tubes. The blood was allowed to clot at room temperature for 30 mins and centrifuged at 1500 × g for 10 mins. The serum layer was removed and frozen at -20°C in multiple aliquots for further analyses. Serum 8-hydroxy-2-deoxyguanosine (8-OHdG), nitric oxide (NO) and malondialdehyde (MDA) were analyzed in duplicate using enzyme-linked immunosorbent assay (ELISA) kits (Eastbiopharm Co., Ltd., Hangzhou, China). Serum antioxidant biomarker levels (glutathione peroxidase (GPx), catalase (CAT) and glutamate (GLU)) were analyzed in duplicate using commercially available ELISA kits (Eastbiopharm Co., Ltd., Hangzhou, China). The intra-assay coefficients of variances were < 7% for all blood measurements.

Statistical analysis

Descriptive statistics (mean ± standard deviation [SD]) for each of the variables were calculated. The normality distribution of each variable was examined using the Shapiro-Wilk test. Assumptions of sphericity were assessed using Mauchly's test of sphericity, with any violations adjusted with the use of the Greenhouse-Geisser (GG) correction. The analysis of variance (ANOVA) was applied to identify the differences between the groups. The level of significance was set at $p \leq 0.05$.

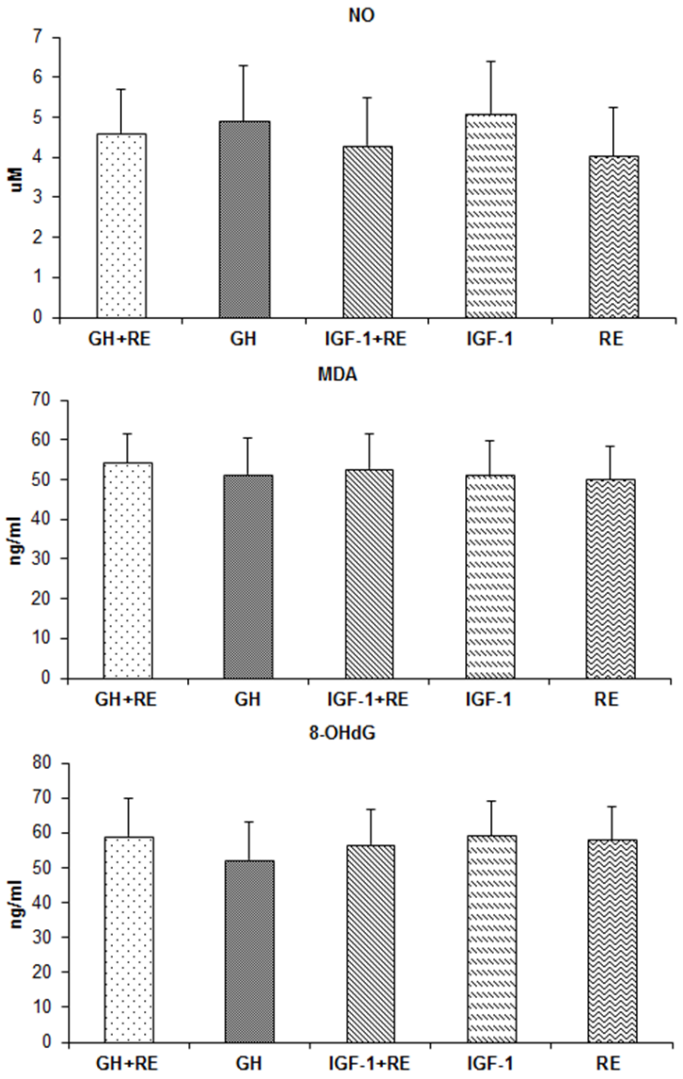
Results

There were no significant differences between groups at baseline in oxidative stress biomarkers (8-OHdG, p = 0.261; MDA, p = 0.733; and NO, p = 0.329) and the antioxidant defense system (GPx, p = 0.352; CAT, p = 0.935; and GLU, p = 0.736) (Fig. 1 and 2).

Discussion

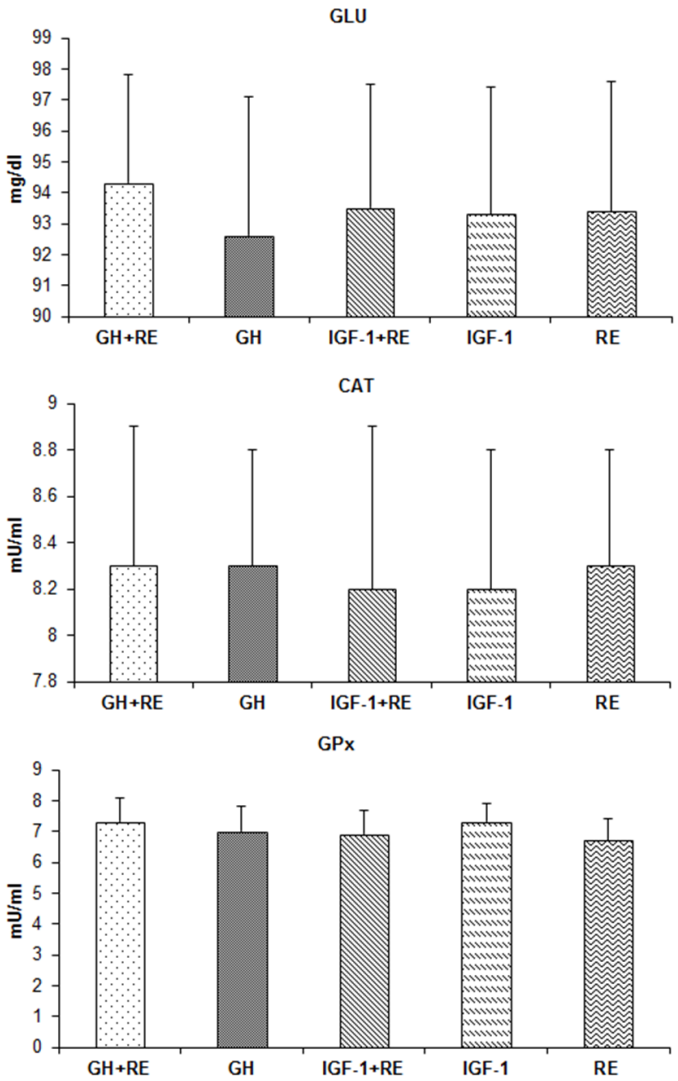
The aim of this study was to show the influence of self-administration of peptide hormone on oxidative stress and antioxidant markers in male athletes and non-athletes. We found no potential effects of longitudinal self-administration of peptide hormone and/or long-term RE on resting 8-OHdG, MDA, NO, GPX, CAT, and GLU levels were observed for the groups. In fact, longitudinal resistance training and/or one year GH or IGF-1 hormone use did not have any main or interaction effects on resting oxidative stress and antioxidant markers.

To date, oxidative stress is a biological phenomenon marked by an imbalance between reactive free radicals (often oxygen-based molecules) and antioxidant defenses [12]. The term oxidative stress indicates some combination of accelerated free radical production and/or exhaustion of antioxidant defenses [13]. A severe or prolonged oxidative stress can lead to oxidatively modified lipids, proteins, and DNA due to xanthine-xanthine oxidase pathway, respiratory burst of neutrophils, catecholamine autooxidation, local muscle ischemia-hypoxia, conversion of the weak superoxide to the strong hydroxyl radical by lactic acid, and alteration of calcium homeostasis [14, 15]. In relation to changes in oxidative stress biomarkers, 8-OHdG as a biomarker of oxidative DNA damage, MDA as a biomarker of lipid peroxidation, and NO were evaluated [14, 16]. To the authors' knowledge, it was the first study that explored the resting levels of oxidative stress variables following peptide hormone use plus RE in male bodybuilders and, for this reason, the discussion could be limited. The results indicated no significant differences among the groups for those variables. It seems that long-term resistance training and 1-year use of peptide hormone induced similar cellular adaptions to control free radicals throughout life time in bodybuilders who used GH or IGF-1 hormones and/or performed RE with peptide hormones; however, the information and knowledge about this subject is limited and more stud-



GH+RE: growth hormone use plus resistance exercise; IGF-1: insulin like growth factor-1; 8-OHdG: 8-hydroxy-2-deoxyguanosine; MDA: malondialdehyde; NO: nitric oxide. Values are mean ± SD.

Figure 1. Oxidative stress markers in the groups



GH+RE: growth hormone use plus resistance exercise; IGF-1: insulin like growth factor-1; GPx (D): glutathione peroxidase; CAT (E): catalase; GLU (F): glutamate. Values are mean ± SD.

Figure 2. Antioxidant markers in the groups.

ies are needed to explore the effects of long-term use of peptide hormones on oxidative stress markers in other populations and animals.

In order to evaluate the changes in antioxidant biomarkers, CAT, GPx and GLU, as the primary defense against ROS, were measured [12, 17], and all the groups manifested similar values for the antioxidant defense system. In the literature, some studies showed that the body defense system plays an important role in controlling the oxidant and antioxidant properties. In the body, one of the crucial defense system elements are antioxidant enzymes including GPX, CAT and GLU [9, 10, 18]. It appears that performing resistance training could have a critical impact on improving antioxidant enzymes, and long-term use of peptide hormones such as GH or IGF-1 may produce more oxidative status in the body resulting in greater antioxidant capacity for controlling cell metabolism [3, 8]; however, more studies are needed to clarify the effects of long-term peptide hormone use and resistance training combined with peptide hormone use on antioxidant variables in human and animal subjects.

This study has a few methodological limitations that warrant discussion. The first limitation includes a low number of male bodybuilders, which prevents generalization of the results. Furthermore, the results of the current investigation are based on a male population, and further research is needed to determine if similar effects can be obtained in female subjects. In addition, we used male bodybuilders, so more studies are needed to clarify the effects of peptide hormone use in other sports disciplines. In this study, there were some limitations regarding an increase in other blood oxidative and antioxidant variables such as total antioxidant capacity or protein carbonyl and/or the use of other peptide hormones such as GHRP-6. Therefore, more studies are necessary to clarify other effects of peptide hormone use on oxidative stress and antioxidant variables.

Conclusion

In conclusion, longitudinal use of peptide hormones for 1 year or RE for at least 3 years had no potential effects to indicate differences in resting oxidative stress and antioxidant markers.

The present study did not report a range of negative redox status consequences of peptide hormone use in combination with resistance training. On the other hand, GH and IGF-1 use and RE for at least 1 year did not induce greater oxidative stress and antioxidant properties in men. It can be concluded that peptide hormone use or performing RE did not induce further changes in resting oxidative stress markers and the antioxidant defense system in male athletes and non-athletes.

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