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Exercise induced-changes in growth hormone in hypo and hyperglycemia conditions

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Abstract

Introduction: Fasting stimulates, whereas glucose suppresses growth hormone (GH) secretion, but the effect of doing exercise in hypo or hyper condition on GH concentration is unclear. The purpose of the present study was to determine exercise induced-changes in GH in hypo and hyperglycemia conditions.

Material & Methods: Eleven non-athletes healthy men (aged: 21.0 ± 2.1 years; body mass index (BMI): 22.6 ± 3.3 kg/m^2; mean ± SD) were participated in this study as the subject. At the first week, the subjects were consumed 1 g/kg body weight of glucose in 200 mL water 30 min prior to exercise (hyperglycemia condition) and subsequently walked on a treadmill at 50% of heart rate reserve (HRR) for 60 min. Glucose and GH levels were measured at baseline, immediately and 30 min after the exercise. After a week, the subjects were performed the same exercise after at least 14 h

of fasting (hypoglycemia condition) and glucose and GH levels were measured at the same times of the first week.

Results: The results showed that glucose level had not significant changes in response to exercise at the hypoglycemia condition but it was decreased significantly immediately after the exercise at the hyperglycemia condition and it was lower than the baseline until 30 min after the exercise. Repeated measures of ANOVA test showed that there were no significant differences in the GH concentration in the hypo and hyperglycemia conditions at the baseline. The results revealed that GH concentration was increased significantly immediately after the exercise at the hypo and hyperglycemia conditions and the increases of the GH was higher in the hypoglycemia condition in compare to the hyperglycemia condition ($P<0.05$). GH concentration was returned to the baseline levels 30 min after the exercise at the hypo and hyperglycemia conditions.

Conclusions: In conclusion, it seems that exercise induced-GH is higher in hypoglycemia condition.

Keywords: Hyperglycemia, Hypoglycemia, Growth hormone, Exercise

1. Introduction

Growth hormone (GH) is a 191 amino-acid single chain polypeptide, which is secreted by the somatotrophs in the anterior pituitary. GH acts both directly through its own receptors and indirectly through the induced production of Insulin-like Growth Factor I (IGF-I). Its physiological effects have been demonstrated not only in tissue growth, but also in glucose / lipid metabolism, coronary disease, diabetes mellitus and vascular aging (1). GH is a dynamic hormone, which like most other hormones in the human body, varies in concentration and action under the influence of numerous factors. Exercise is the most potent physiologic stimulus for GH release (2,3) and the magnitude of the GH response to exercise is influenced by various factors such as age,

gender, body composition, substrate intake, physical fitness, and intensity, nature, and duration of the exercise (2). Studies indicated that consecutive hypoglycemic episodes separated by several hours equally stimulate GH responses even in the absence of exercise (4), so the progressively attenuated GH response to repeated exercise may depend on the occurrence of hypoglycemia or glycogen depletion (5). There is evidence that oral glucose administration affects GH secretion, initially decreasing and subsequently stimulating GH secretion and in human obesity GH secretion after oral glucose is decreased (6). Other clinical studies indicated that acute hyperglycemia suppresses basal growth GH secretion (7,8) and the GH response to GH releasing hormone (GHRH) in normal subjects (9-11). Garrel et al. (1989) reported that hyperglycemia decreases (57%) peak plasma GH concentration in a group of healthy men (12). Murao et al. (1994) were examined the effects of acute hypo and hyperglycemia on hypothalamic GH-releasing hormone and somatostatin gene expression in the rat. The results indicated that acute changes in the plasma glucose concentration stimulated hypothalamic somatostatin mRNA. The researchers found that hypoglycemia completely inhibited pulsatile GH secretion, whereas hyperglycemia partially inhibited GH secretion (13). Previous studies indicated that fasting lowers somatomedin C levels (14) and in so doing removes feedback inhibition of GH release (15). While hypo or hyperglycemia conditions may play a mediating role in the GH responses, the effects of doing exercise in these conditions on GH levels are still unclear. For example, Shin et al. (2013) examine the effects of a pre-exercise meal on the plasma GH response and fat oxidation during walking. They reported that plasma GH concentration was higher in the subjects whom received 1 g/kg body weight of glucose in 200 mL water in compare to the subjects that consume 200 mL water alone 30 min prior to exercise and subsequently walked on a treadmill at 50% of VO_{2max} for 60 min (16). On the other hand, Cappon et al. (1993) had been reported modest decreases but not significant statistical in GH response to exercise after the high-glucose meal (17). The aim of present study was to determine exercise induced-changes in GH in hypo and hyperglycemia conditions.

2. Materials and Methods

Subjects

Eleven non-athletes healthy men (aged: 21.0 ± 2.1 years; body mass index (BMI): 22.6 ± 3.3 kg/m^2; mean ± SD) were participated in this study as the subject. The personal characteristics of the subjects are presented in the Table 1. All the subjects were asked to complete a personal health and medical history questionnaire, which served as a screening tool. All the subjects were complete inactive at least 6 month before the study and they were nonsmokers and free from unstable chronic condition including dementia, retinal hemorrhage and detachment; and they have no history of myocardial infarction, stroke, cancer, dialysis, restraining orthopedic or neuromuscular diseases. All the subjects were given 3-day diet recall form (18) to complete and were instructed to maintain their normal dietary habits throughout the study. The Islamic Azad University, Marvdasht branch Ethics Committee approved the study and written informed consent was obtained from all subjects.

Table 1. Personal characteristics (mean ± SD) of the subjects

	mean	SD
Age (yr)	21.0	2.1
Height (cm)	174.1	11.9
Weight (kg)	68.6	11.0
BMI (kg/m^2)	22.6	3.3

Study design

At the first week, the subjects were consumed 1 g/kg body weight of glucose in 200 mL water 30 min prior to exercise (hyperglycemia condition) and subsequently walked on a treadmill at 50% of heart rate reserve (HRR) for 60 min. Each participant was equipped with a heart rate monitor (Beurer, Germany) to ensure accuracy of the exercise level. Glucose and GH levels were measured at baseline, immediately and 30 min after the exercise. After a week, the subjects were performed the same exercise after at least 14 h of fasting (hypoglycemia condition) and glucose and GH levels were measured at the same times of the first week.

Blood analyses

Plasma glucose was immediately measured (Beckman Instruments, Brea, CA, USA). Serum samples were stored at –20 °C, and GH was analyzed using enzyme-linked immunosorbent assay (ELISA) kit (Monobind Inc, USA). The sensitivity of kit was <0.5 μg/L.

Statistical analysis

Results were expressed as the mean ± SD and distributions of all variables were assessed for normality using Shapiro-Wilk test. Repeated measures of ANOVA test (Time × condition) was used to evaluate time-course change in variables. Post hoc analyses (Bonferroni) were then performed when warranted. The level of significance in all statistical analyses was set at $P \leq 0.05$. The statistical software program SPSS.17 was used for all data analysis.

3. Results

The changes of plasma glucose at baseline and after the exercise at the hypo and hyperglycemia conditions are presented in the Figure 1. Repeated measures of ANOVA test showed that there were significant differences between times of blood sampling and between hypo and hyperglycemia conditions. Post hoc analyses (Bonferroni) indicated that glucose level was higher in the hyperglycemia condition than the hypoglycemia condition at baseline and after the exercise ($P<0.05$). Glucose level had not significant changes in response to exercise at the hypoglycemia condition but it was decreased significantly immediately after the exercise at the hyperglycemia condition and it was lower than the baseline until 30 min after the exercise ($P<0.05$).

The changes of serum GH level at baseline and after the exercise at hypo and hyperglycemia conditions are presented in the Figure 2. Repeated measures of ANOVA test showed that there were no significant differences in the GH concentration in the hypo and hyperglycemia conditions at the baseline. The results revealed that GH concentration was increased significantly immediately after the exercise at the hypo and hyperglycemia conditions and the increases of the GH was higher in the hypoglycemia condition in compare to the hyperglycemia condition ($P<0.05$). At the end, the results indicated that GH concentration was

returned to the baseline levels 30 min after the exercise at the hypo and hyperglycemia conditions.

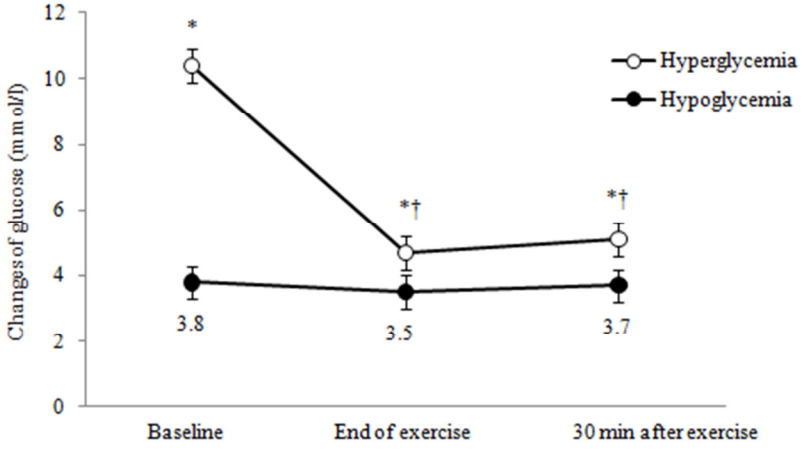

Figure 1. Changes of plasma glucose at baseline and after the exercise at hypo and hyperglycemia conditions
† Significant differences with baseline (P<0.05)
* Significant differences between two conditions (P<0.05)

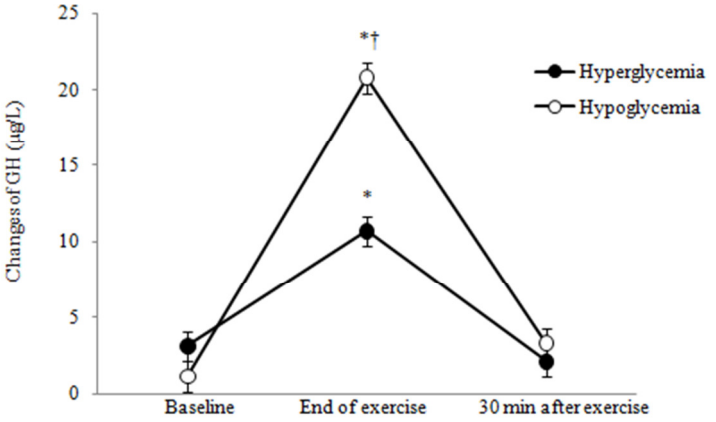

Figure 2. Changes of GH at baseline and after the exercise at hypo and hyperglycemia conditions
* Significant differences with baseline (P<0.05)
† Significant differences between two conditions (P<0.05)

4. Discussion

The fact that exercise stimulates GH secretion is well known (19) and the magnitude of the GH response to exercise is influenced by various factors such as substrate intake prior the exercise, mode of exercise and personal characteristics of the people (2). Fasting stimulates, whereas glucose suppresses GH secretion (12-15), but the effect of doing exercise in hypo or hyper condition on GH concentration is unclear. This study was designed to test whether exercise-induced changes in GH after fasting compared to a glucose infusion. The results indicated that glucose level had not significant changes in response to exercise at the hypoglycemia condition but it was decreased significantly immediately after the exercise at the hyperglycemia condition and it was lower than the baseline until 30 min after the exercise. Previously Shin et al. (2013) and Vendelbo et al. (2015) also demonstrated that the plasma glucose had not significant changes until 90 min after the exercise at the hypoglycemia condition but glucose levels were increased after glucose intake and it had been decreased during the exercise and 90 min after this (16,20).

While plasma glucose does not normally decrease during exercise at the hypoglycemia condition, a significant decrease in plasma glucose can occur when carbohydrates are consumed as a pre-exercise meal (16,21-23). This phenomenon reflects an imbalance between the rate of carbohydrate oxidation and the rate of carbohydrate supplementation in muscle during exercise. In the present study, the reduction in plasma glucose levels after the exercise following carbohydrate intake was due to a significant increase in muscle glucose uptake without a compensatory increase in glucose supplementation into blood (24). It seems that the effect of the carbohydrate meal on plasma glucose was due to the additive effect of insulin and exercise (24,25). This effect has been explained in previous studies and reviews (26,27).

The results of the present study revealed that there were no significant differences in the GH concentration in the hypo and hyperglycemia conditions at the baseline. The results demonstrated that GH concentration was increased significantly immediately after the exercise at the hypo and hyperglycemia conditions and the increases of the GH

was higher in the hypoglycemia condition in compare to the hyperglycemia condition. GH concentration was returned to the baseline levels 30 min after the exercise at the hypo and hyperglycemia conditions. Fasting is associated with a pronounced increase in both endogenous GH production (28) and lipolytic responsiveness to exogenous GH (29). The insulin antagonistic effects of GH are preserved during fasting, which constitutes an important adaptation by reducing glucose oxidation and thereby the need for gluconeogenic precursors from muscle protein (30). By contrast, IGF-I declines progressively during fasting (31,32) and thus the anabolic and insulin-like effects, which makes teleological sense in a condition with nutritional deprivation (33).

In line with the study results of Vendelbo et al. (2015) (20) and Shin et al. (2013) (16), we did not detect increased baseline levels of GH after 14 h of fasting, which could relate to the relatively short period of fasting and the 'elusive' pulsatile nature of GH secretion. Previous studies with more frequent blood sampling have shown increased GH concentrations after 72 h of fasting (34), and GH levels during exercise were increased after fasting in the present study. It is therefore likely that the increased intracellular GH signal following exercise on the fasting examination day to a large extent is a direct consequence of increased circulating levels of GH (20). We had some limitation in the present study. We did not measure the levels of free fatty acids (FFAs) and STAT-5b in this study. Previous studies indicated that high levels of FFA during fasting leads to dampen of muscle STAT-5b phosphorylation by up to 40%, which may counterbalance stimulation of the intracellular signal for release of GH (20,35).

The elevation of plasma GH during exercise has been shown to be affected by the intensity and duration of exercise, work output during exercise, muscle mass used during exercise, and carbohydrate intake (36,37). The exercise stimulus used in this study was mild, at only 50% HRR, but was long enough to promote a significant increase in plasma GH levels (See Figure. 1). Dore et al. (1991) demonstrated that when subjects consume carbohydrates during aerobic exercise, GH declines in comparison to those subjects who do not consume carbohydrates (38). However, in the present study, GH levels were found to be significantly elevated in the hyperglycemia condition. According to the results of

previous studies, this elevation in the hyperglycemia condition was a result of a reduction in plasma glucose levels induced by the intake of carbohydrates as a pre-exercise meal (16,39,40).

5. Conclusion

Our result suggest that although GH concentration increases significantly immediately after the exercise at the hypo and hyperglycemia conditions, the increases of the GH was higher in the hypoglycemia condition in compare to the hyperglycemia condition. Thus doing exercise in hypoglycemia condition introduces to stimulate higher GH secretion.

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Conflict of interests: None of the authors declare competing financial interests.

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