

Exercise induced-changes in insulin-like growth factor 1 following fasting compared to glucose administration

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Abstract

Introduction: Carbohydrate supplement intake might change exercise induced-insulin-like growth factor 1 (IGF-1); however it is not well known. The purpose of the present study was to determine exercise induced-changes in IGF-1 following fasting compared to glucose administration.

Material & Methods: Eleven non-athletes healthy men (aged: 21.0 ± 2.1 years; body mass index (BMI): 22.6 ± 3.3 kg/m²; mean \pm 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 IGF-1 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 IGF-1 levels were measured at the same times of the first week.

Results: The results showed that glucose levels were higher in hyperglycemia condition than hypoglycemia condition ($P < 0.05$). Glucose level was decreased by 54.8% after the exercise but it was higher than the baseline until 30 min after the exercise ($P < 0.05$). The results, also indicated that IGF-1 level had no significant changes after the exercise at both of hypo and hyperglycemia conditions and no significant differences were observed during blood sampling between hypo and hyperglycemia conditions.

Conclusions: In conclusion, it seems that exercise in hypo or hyperglycemia conditions had no significant effect on IGF-1 levels.

Keywords: Hyperglycemia, Hypoglycemia, Insulin-like growth factor 1, Exercise

1. Introduction

Insulin-like growth factor 1 (IGF-1) is known as somatomedin C. IGF-1 belongs to polypeptide hormones, which are functionally and structurally similar to the insulin (1). IGF-1 is metabolic mediates of growth hormone (GH) (2,3). Growth hormone is produced by the anterior pituitary gland, is essential for growth in the postnatal period. Growth hormone affects the tissue by the IGF1. IGF-1 stimulates all growth processes. Researches show that IGF-1 can be synthesized in vivo and in vitro in some tissues, but the main IGF-1 synthesizing organ is the liver (4). IGF-1 is secreted from hepatocytes into the serum, where it binds to insulin-like growth factor binding protein –IGFBP (5).

IGF-1 plays a key role in exercises associated muscle growth and development. Several of clinical studies have shown increased (6), decreased (7), or unchanged levels of IGF-I after endurance or resistance training (8). IGF-1 response is related to the intensity and duration of exercise. After short-term (20 min) ergometer exercise reported increased IGF-I but after 3 h endurance exercise, IGF-1 level was decreased and no change after interval training. In the same study, IGFBP-3 seems to increase during exercise (9). This suggests that more prolonged exercise

causes decreasing in total IGF-1 level.

On the other hand, fasting strikingly stimulates somatotroph secretion in normal healthy humans; (10,11) reduction in the negative IGF-1 feedback action as well as CNS-mediated mechanisms such as concomitant reduction in somatostatin activity and GHRH hyperactivity are likely to play major role (12,13). Maccario et al. (2001) reported that IGF-1 level had no significant changes after 36 h fasting in adult hypopituitary patients with severe GH deficiency while it decreased in obese patients as well as in normal subjects (14). Although clinical studies indicated that IGF-1 might decrease after calorie restriction (12,15), hyperglycemia induces a signaling that results in enhanced IGF-1 concentration (16). The effects of exercise on IGF-1 levels in hypo and hyperglycemia are not well known. Previously Vendelbo et al. (2015) reported that there were no significant differences in IGF1 mRNA expression after a bout of exercise during fasting or glucose administration (17). Thus the aim of present study was to examine exercise induced-changes in IGF-1 following fasting compared to glucose administration.

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/m²; mean \pm SD) were participated in this study as the subject. 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.

Protocol

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 IGF-1 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 IGF-1 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 IGF-1 was analyzed using enzyme-linked immunosorbent assay (ELISA) kit (LDN, Germany). The sensitivity of kit was <9.75 ng/ml.

Statistical analysis

Results were expressed as the mean \pm SD and distributions of all variables were assessed for normality using Shapiro-Wilk test. Repeated measures of ANOVA test (Time \times 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 $P \leq 0.05$. Data analysis was performed using SPSS software for windows (version 17, SPSS, Inc., Chicago, IL).

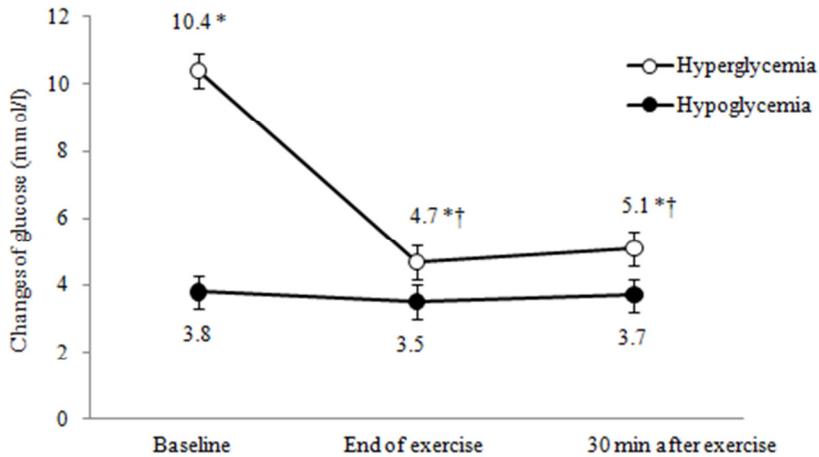
3. Results

Anthropometrical measurements of the subjects are presented in the Table 1. The results indicated that the young men with normal weight were participated in the study as the subject.

Table 1. Anthropometric characteristics (mean \pm 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

The changes of plasma glucose at baseline and after the exercise at 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 hyperglycemia condition than hypoglycemia condition ($P < 0.05$). Glucose level had not significant changes immediately and 30 min after the exercise in hypoglycemia condition but it was decreased significantly immediately after the exercise and it was higher than the baseline until 30 min after the exercise in hyperglycemia condition ($P < 0.05$).



* Significant differences with baseline ($P < 0.05$)

† Significant differences between two conditions ($P < 0.05$)

Figure 1. Changes of plasma glucose at baseline and after the exercise at hypo and hyperglycemia conditions

The changes of serum IGF-1 at baseline and after the exercise at hypo and hyperglycemia conditions are presented in the Figure 2. Repeated measures of ANOVA test showed that IGF-1 level had no significant changes after the exercise at both of hypo and hyperglycemia conditions and no significant differences were observed during 3 times of blood sampling between hypo and hyperglycemia conditions.

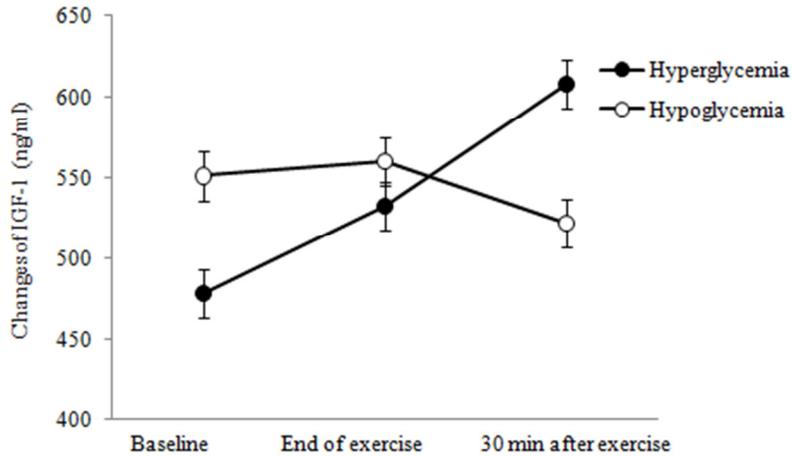


Figure 2. Changes of IGF-1 at baseline and after the exercise at hypo and hyperglycemia conditions

4. Discussion

This study was designed to test whether exercise-induced changes in IGF-1 after fasting compared to a glucose infusion. The results indicated that glucose level was higher in hyperglycemia condition than hypoglycemia condition at baseline ($P < 0.05$). Glucose level had not significant changes immediately and 30 min after the exercise in hypoglycemia condition but it was decreased significantly immediately after the exercise and it was higher than the baseline until 30 min after the exercise in hyperglycemia condition ($P < 0.05$). 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 hypoglycemia condition but glucose levels were increased after glucose intake and it had been decreased during the exercise and 90 min after this (17,19).

While plasma glucose does not normally decrease during exercise in hypoglycemia condition, a significant decrease in plasma glucose can occur when carbohydrates are consumed as a pre-exercise meal (19-22). 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 (22). It seems that the effect of the carbohydrate meal on plasma glucose was due to the additive effect of insulin and exercise (23,24). This effect has been explained in previous studies and reviews (25,26).

The results, on the other hand, indicated that IGF-1 level had no significant changes after the exercise at both of hypo and hyperglycemia conditions and no significant differences were observed during 3 times of blood sampling between hypo and hyperglycemia conditions. In line with the present study results, Vendelbo et al. (2015) also reported that 36 h of fasting had not significant effect on IGF-1 mRNA levels (17). In another study, Vendelbo et al. (2010) observed that more prolonged fasting tends to increase IGF1 mRNA levels in muscle (27). They noted that myocellular GH signaling is stimulated after exercise and fasting in terms of increased STAT5 phosphorylation and/or IGF-1 gene expression. This suggests that exercise with brief, well-defined GH peaks leads to distinct STAT5 phosphorylation and subsequent IGF-1 gene expression, whereas fasting induces more sporadic GH bursts and less distinct but more persistent activation of the GH signal (27). These discrepant results may be attributed to differences in exercise intensity, blood sampling frequency, time of fasting and study population. GH and insulin levels did not measured in this study. It is suggested that the GH and insulin concentrations measure in the future studies.

5. Conclusion

The results indicated that IGF-1 level had no significant changes after the exercise at both of hypo and hyperglycemia conditions thus it seems that exercise in hypo or hyperglycemia conditions had no significant effect on IGF-1 levels.

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References

1. Monzavi R, Cohen P. IGFs and IGFBPs: role in health and disease. *Best Pract Res Clin Endocrinol Metab* 2002; 16: 433-447.
2. LeRoith D, Bondy C, Yakar S, Liu JL, Butler A. The somatomedin hypothesis: 2001. *Endocr Rev* 2001; 22: 53-74.
3. Richman C, Kutilek S, Miyakoshi N, Srivastava AK, Beamer WG, Donahue LR, et al. Postnatal and pubertal skeletal changes contribute predominantly to the differences in peak bone density between C3H/HeJ and C57BL/6J mice. *J Bone Miner Res* 2001; 16: 386-897.
4. Ohlsson C, Mohan S, Sjögren K, Tivesten A, Isgaard J, Isaksson O, et al. The role of liver-derived insulin-like growth factor-I. *Endocr Rev* 2009; 30: 494-535.
5. Jones JJ, Clemmons DR. Insulin-like growth factors and their binding proteins: biological actions. *Endocr Rev* 1995; 16: 3-34.
6. Koziris LP, Hickson RC, Chatterton Jr RT, Groseth RT, Christie JM, Goldflies DG, et al. Serum levels of total and free IGF-I and IGFBP-3 are increased and maintained in long-term training. *J Appl Physiol* 1999; 86: 1436-1442.
7. Eliakim A, Brasel JA, Mohan S, Wong WLT, Cooper DM. Increased physical activity and the growth hormone-IGF-I axis in adolescent males. *Am J Psychol* 1998; 275: 308-314.
8. Fontana L, Klein S, Holloszy JO. Long-term low protein, low-calorie diet and endurance exercise modulate metabolic factors associated with cancer risk. *Am J Clin Nutr* 2006; 84: 1456-1462.
9. Nguyen UN, Mouglin F, Simon-Rigaud ML, Rouillon JD, Marguet P, Regnard J. Influence of exercise duration on serum insulin-like growth factor and its binding proteins in athletes. *Eur J Appl Physiol* 1998; 78: 533-537.
10. Ho KY, Veldhuis JD, Johnson ML, Furlanetto R, Evans WS, Alberti KG, et al. Fasting enhances growth hormone secretion and amplifies the complex rhythms of growth hormone secretion in man. *J Clin Invest* 1988; 81: 968-975.

11. Hartman ML, Veldhuis JD, Johnson ML, Lee MM, Alberti KG, Samojlik E, et al. Augmented growth hormone (GH) secretory burst frequency and amplitude mediate enhanced GH secretion during a two-day fast in normal men. *J Clin Endocrinol Metab* 1992; 74: 757-765.
12. Thomas GB, Cummins JT, Francis H, Sudbury AW, McCloud PI, Clarke IJ. Effect of restricted feeding on the relationship between hypophysial portal concentrations of growth hormone (GH)-releasing factor and somatostatin, and jugular concentrations of GH in ovariectomized ewes. *Endocrinology* 1991; 128: 1151-1158.
13. Maccario M, Grottoli S, Procopio M, Oleandri SE, Rossetto R, Gauna C, et al. The GH/IGF-I axis in obesity: influence of neuroendocrine and metabolic factors (Review). *Int J Obes Relat Metab Disord* 2000; 24: S96-99.
14. Maccario M, Aimaretti G, Grottoli S, Gauna C, Tassone F, Corneli G, et al. Effects of 36 hour fasting on GH/IGF-I axis and metabolic parameters in patients with simple obesity. Comparison with normal subjects and hypopituitary patients with severe GH deficiency. *Int J Obes Relat Metab Disord* 2001; 25: 1233-1239.
15. Dreval A, Trigolosova I. Diabetes Mellitus influence on GH and IGF-1 levels in acromegalic patients. *Endocrine Abstracts* 2010; 22: 656.
16. Clemmons D, Maile L, Xi G, Shen X, Radhakrishnan Y. Igf-I signaling in response to hyperglycemia and the development of diabetic complications. *Curr Diabetes Rev* 2011; 7: 235-245.
17. Vendelbo MH, Christensen B, Grønbaek SB, Høgild M, Madsen M, Pedersen SB, et al. GH signaling in human adipose and muscle tissue during 'feast and famine': amplification of exercise stimulation following fasting compared to glucose administration. *Eur J Endocrinol* 2015; 173: 283-290.
18. Kasim-Karakas SE, Tsodikov A, Singh U, Jialal I. Responses of inflammatory markers to a low-fat, high-carbohydrate diet: effects of energy intake. *Am J Clin Nutr* 2006; 83: 774-779.

19. Shin YH, Jung HL, Ryu JW, Kim PS, Ha TY, An JY. Effects of a pre-exercise meal on plasma growth hormone response and fat oxidation during walking. *Prev Nutr Food Sci* 2013; 18: 175-180.
20. Sherman WM, Peden MC, Wright DA. Carbohydrate feedings 1 h before exercise improves cycling performance. *Am J Clin Nutr* 1991; 54: 866-870.
21. Wright DA, Sherman WM, Dernbach AR. Carbohydrate feedings before, during, or in combination improve cycling endurance performance. *J Appl Physiol* 1991; 71: 1082-1088.
22. Horowitz JF, Mora-Rodriguez R, Byerley LO, Coyle EF. Lipolytic suppression following carbohydrate ingestion limits fat oxidation during exercise. *Am J Physiol* 1997; 273: E768-E775.
23. Brozinick JT Jr, Etgen GJ Jr, Yaspelkis BB 3rd, Kang HY, Ivy JL. Effects of exercise training on muscle GLUT-4 protein content and translocation in obese Zucker rats. *Am J Physiol* 1993; 265: E419-E427.
24. Wallberg-Henriksson H, Constable SH, Young DA, Holloszy JO. Glucose transport into rat skeletal muscle: interaction between exercise and insulin. *J Appl Physiol* 1988; 65: 909-913.
25. Cortright RN, Dohm GL. Mechanisms by which insulin and muscle contraction stimulate glucose transport. *Can J Appl Physiol* 1997; 22: 519-530.
26. Ivy JL. 1997. Role of exercise training in the prevention and treatment of insulin resistance and non-insulin-dependent diabetes mellitus. *Sports Med* 24: 321-336.
27. Vendelbo MH, Jørgensen JO, Pedersen SB, Gormsen LC, Lund S, Schmitz O, et al. Exercise and fasting activate growth hormone-dependent myocellular signal transducer and activator of transcription-5b phosphorylation and insulin-like growth factor-I messenger ribonucleic acid expression in humans. *J Clin Endocrinol Metab* 2010; 95: E64-E68.