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Oral Glucose Administration after Circuit Resistance Exercise Induced Plasma Ghrelin Suppression

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ABSTRACT

The aim of this study was investigation of effect of oral glucose administration after circuit resistance exercise on plasma ghrelin and some glucoregulatory hormones. Thirteen physical education students volunteered to participate in the present study. Subjects were asked to perform nonstop weight circuit exercises (10exercise at 60% 1RM, 20s time for each, 3 circuits with 3min rest between circuits) while the subjects were overnight fast (at least 12h). Blood samples were taken at immediately after exercise, and then subjects divided randomly to two groups [Glucose Group (GG, n = 7) and Water Group (WG, n = 6)]. GG fed glucose solution (0.5gr in 2.5cc distilled water per 1kg body weight) and WG fed distilled water (2.5 cc/kg body weight), and then blood samples were taken further at 30min, and 90min after exercise. Plasma ghrelin, cortisol, GH, c-peptide, insulin and glucose were determined with RIA, RIA, IRMA, IRMA, IRMA and enzymatic method respectively. Repeated measure ANOVA revealed that changes of plasma ghrein, glucose, insulin, and cortisol in response to glucose solution feeding in compare with water feeding after circuit resistance exercise was significant while for plasma GH and c-peptide were not. In conclusion, plasma ghrelin level suppressed due to administration of glucose solution after circuit resistance exercise, it means that administration of glucose solution perhaps could induce a positive energy balance that involvements of plasma glucose, insulin and cortisol is assumed.

Keywords: ghrelin, insulin, cortisol, glucose administration, circuit resistance exercise

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INTRODUCTION

Based on literature, ghrelin, a recently discovered 28-amino acids peptide hormone isolated from human and rat stomach [1], is sensitive to alteration of energy balance; in other word, ghrelin is a short-term index of energy balance; so that, up- and down-regulation of ghrelin expression in negative and positive energy balance situations respectively is demonstrated a negative feedback mechanism for energy homeostasis [2]. In addition, the interesting biological role of ghrelin, a growth hormone (GH) secretagogue, is control of glucose homeostasis; in other word, it stimulates an increase in blood glucose [3-5]. It seems that ghrelin could be involved in glucose metabolism because ghrelin and growth hormone receptor is coexpressed within the endocrine pancreas [6-8]. Indeed, ghrelin may play a developmental role, as well as regulate release of insulin and glucagon [9].

Exercise increases energy expenditure therefore it lowers the energy balance [10]; so that, long term exercise is accompanied by a decrease in glycogen and ATP of muscle and liver [11, 12]; also, It is showed that a muscle energy deficiency occurred after intensive resistance exercise due to elevation of muscle glycogenolysis resulted in decline of muscle glycogen and ATP capacity by 20%-40% and muscle P-Cr by 50%-62% [13-18]. So, acute exercise and physical activity disturb energy balance and homeostasis [19] in muscle cells and increase cell energy demands. Therefore, a negative balance occur with a energy resource decline in cell levels and in this situation ghrelin role can highlight in regulation of energy homeostasis and also it can exposure in serum and plasma to compensate and restore the removed energy resource; so that; this process help to carbohydrate resources reconstruction [20].

Researches on ghrelin responses to a single session acute exercise have contradictory results. number of studies found no changes in plasma ghrelin [21-23]; but, other evidences showed both significant depression [24-27] and elevation [28-30]. Beside, evidence suggests that a ghrelin level is decreased in response to either glucose administration [2, 31, 32], or acute resistance exercise in both circuit [33] and eccentric-concentric [34] manner. But, there not only aren't enough data about the effect of CHO feeding on ghrelin behavior in post-exercise, but also these studies have conflicting result [11, 19, 25, 35]; as some found a decreased response [11, 25, 35], and another didn't see any changes in plasma ghrelin [19].

Regarding to examine the effect of glucose feeding after exercise on plasma ghrelin, we measured ghrelin levels at immediately after circuit resistance exercise, 30 and 90 min after oral glucose administration during recovery. The plasma glucose changes and other parameters involved in glucose metabolism, such as plasma GH, insulin, cortisol, C-peptide, were also analyzed at each time-point of test.

MATERIALS AND METHODS

Subjects and Research Design

The ethic committee of the School of Medical Sciences of Islamic Azad University (IAU) approved the study and it was conducted in accordance with the policy statement of the Declaration of the Iranian Ministry of health. Written informed consent was acquired from the male physical education students (n = 13, age 22.8 ± 2.3 year, height 184 ± 5 cm, body weight 78.5 ± 2.3 kg, and body mass index (BMI) 22.13 ± 1.2 kg/m2) with experience of recreational weight training. All subjects were asked to complete a medical questionnaire with a medical examination to ensure that they were not taking any regular medication, were free of cardiac, respiratory, renal, and metabolic diseases, and were not using steroids. Also, all the subjects were completely familiarized with all of the experimental procedures and had their one repetition maximum (1-RM) determined for each of the 10 exercises used in the circuit resistance exercise protocol.

Exercise Testing Procedures

Before the main trial, participants were taken to the weight room three times. The first and second visits of all the participants performed strength test to determine their one repetition maximum (1-RM) for each of the 10-resistance exercises, employed in the study. The 1-RM value was determined by trial and by adding or removing weight after each attempt as per required. The subjects were allowed to take as long time as they felt necessary to recover from each attempt. On the third visit, the subjects completed a practice session to insure that each participant was able to complete the entire exercise session and also to confirm that the weight lifting was producing fatigue at the end of the session. This was confirmed by visual and verbal feedback from the participants. The resistance exercise session was started at 08:30 AM to 11:00 AM to avoid the effects of circadian rhythm. It included 3 circuits of 10 exercises with 8–12 repetitions at 60% 1-RM. All the exercises were conducted after an overnight fast state and also with the use of free weights. The subjects were instructed to follow a normal lifestyle maintaining daily habits, to avoid any medications, and to refrain from exercise 3 days before the experiment session, as described previously [36-38].

Biochemical Analyses

First blood sample was obtained from antecubital vein immediately after the exercise and at this time participants separated to two groups randomly that the one group (n = 7) fed glucose solution (0.5gr in 2.5cc distilled water per 1kg body weight) and the other group (n = 6) fed distilled water (2.5 cc/kg body weight), then, 30 min and 90 min following the exercise another blood samples were taken. Plasma was separated by centrifugation within 20 min of collection and the samples were analyzed for glucose, insulin, C-peptide, GH, Cortisol, and ghrelin. Glucose was determined using an enzymatic method (glucose oxidase and peroxidase, Man Co. Tehran, Iran). Plasma insulin, C-peptide and GH were determined by immunoradiometric assay (IRMA, Immunotech, Beckman Coul. Com, Prague, Czech Republic and Marseille Cedex, France, respectively). Plasma cortisol was determined by radioimmunoassay (RIA, Immunotech, Beckman Coul. Com. Prague. Czech Republic). Plasma immunoreactive ghrelin was measured in duplicate using a commercial radioimmunoassay (RIA, Phoenix Pharmaceuticals, Belmont, CA), as described previously [33]. Hemoglobin (Hb) and Hematocrit (Hct) were also determined using the system K-4500 automated hematology analyzer. The changes in plasma volume and correction of plasma volume changes in our parameters which were measured in plasma were calculated by using the Dill and Costill method based on hemoglobin and hematocrit estimations [Dill and Costill. 1974] as described previously [39-41].

Statistical Analysis

The data analysis performed using SPSS software. The data were analyzed using a two-way ANOVA (SOLUTION and TIME) with repeated-measures design. All data were presented as means with standard error of mean and statistical significance level was accepted at $P \leq 0.05$.

RESULTS

Plasma Ghrelin

Mauchly's test of sphericity for plasma ghrelin isn't met (Mauchly's W = 0.362, p = 0.006); so according to Greenhouse-Geisser df adjustment, the main effect of TIME was significant (F = 4.919, p = 0.039) and this effect was linear (F = 6.579, p = 0.026). But, the main effect of SOLUTION wasn't significant (F = 2.965, p = 0.113); and in the other hand, the interaction of TIME and SOLUTION with Greenhouse-Geisser df adjustment was significant (F = 5.459, p = 0.03) and this effect was linear (F = 6.744, p = 0.025) [Figure 1].

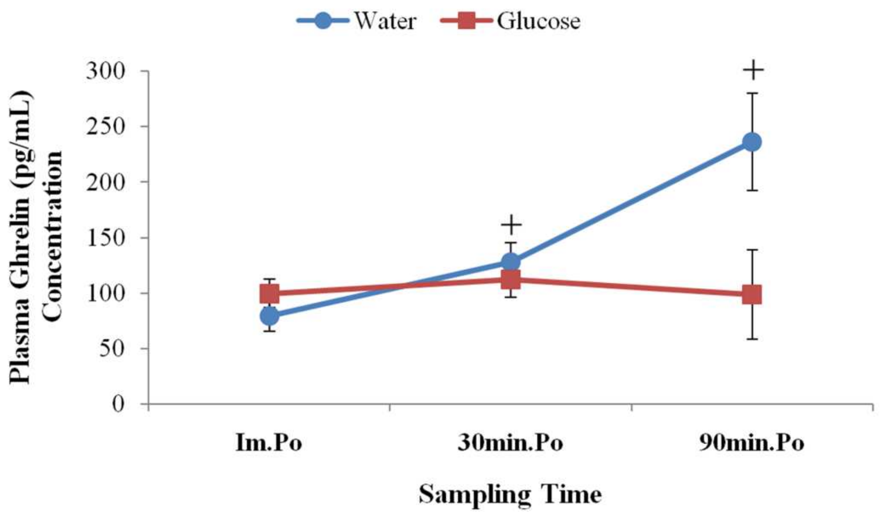

Figure 1. plasma Ghrelin concentration in post circuit resistance exercise after water and glucose feeding for within and between group effects. Im.Po: immediately post-exercise and before solutions feeding. 30min.Po: 30 minutes post-exercise and after solutions feeding. 90min.Po: 90 minutes post-exercise and after solutions feeding. +: Significant linear interaction of TIME and SOLUTION in P ≤ 0.05.

Plasma Glucose

Mauchly's test of sphericity for plasma glucose is met (Mauchly's W = 0.96, p = 0.817). The main effect of TIME with assumption of sphericity was significant (F = 3.399, p = 0.05) and this effect was linear (F = 5.8, p = 0.035). But, the main effect of SOLUTION wasn't significant (F = 1.84, p = 0.202); but, the interaction of TIME and SOLUTION with assumption of sphericity was significant (F = 3.7, p = 0.046) and this effect was linear (F = 4.001, p = 0.045) [Figure 2].

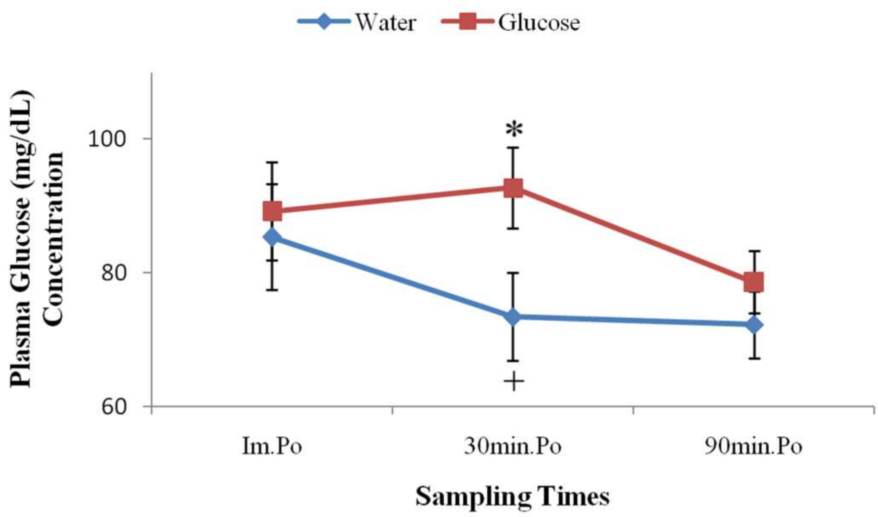

Figure 2. plasma Glucose concentration in post circuit resistance exercise after water and glucose feeding for within and between group effects. Im.Po: immediately post-exercise and before solutions feeding. 30min.Po: 30 minutes post-exercise and after solutions feeding. 90min.Po: 90 minutes post-exercise and after solutions feeding. ∗: Significant linear effect of TIME than Im.Po in P ≤ 0.05. +: Significant quadratic interaction of TIME and SOLUTION in P ≤ 0.05.

Plasma Insulin

Mauchly's test of sphericity for plasma insulin is met (Mauchly's W = 0.949, p = 0.769). The main effect of TIME with with assumption of sphericity was significant (F = 3.944, p = 0.034) and this effect was quadratic (F = 6.308, p = 0.029); so that, this effect was significant only in time of 30min.Po in comparison with Im.Po (Mean Difference = 8.87, p = 0.037). But, the main effect of SOLUTION wasn't significant (F = 0.335, p = 0.575); and in the other hand, the interaction of TIME and SOLUTION with assumption of sphericity was significant (F = 4.412, p = 0.024) and this effect was linear (F = 7.218, p = 0.029) [Figure 3].

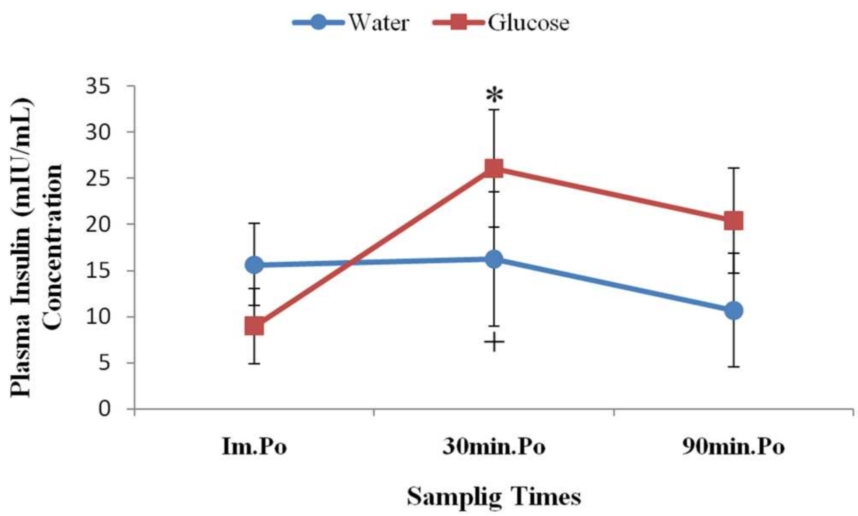

Figure 3. plasma Insulin concentration in post circuit resistance exercise after water and glucose feeding for within and between group effects. Im.Po: immediately post-exercise and before solutions feeding. 30min.Po: 30 minutes post-exercise and after solutions feeding. 90min.Po: 90 minutes post-exercise and after solutions feeding. ∗: Significant quadratic effect of TIME than Im.Po in P ≤ 0.05. +: Significant linear interaction of TIME and SOLUTION in P ≤ 0.05.

Plasma Cortisol

Mauchly's test of sphericity for plasma cortisol was met (Mauchly's W = 0.704, p = 0.173). The main effect of TIME with assumption of sphericity was insignificant (F = 0.787, p = 0.468); and also, the main effect of SOLUTION wasn't significant (F = 0.529, p = 0.482); but, the interaction of TIME and SOLUTION with assumption of sphericity was significant (F = 3.761, p = 0.039) and this effect was linear (F = 11.675, p = 0.006) [Figure 4].

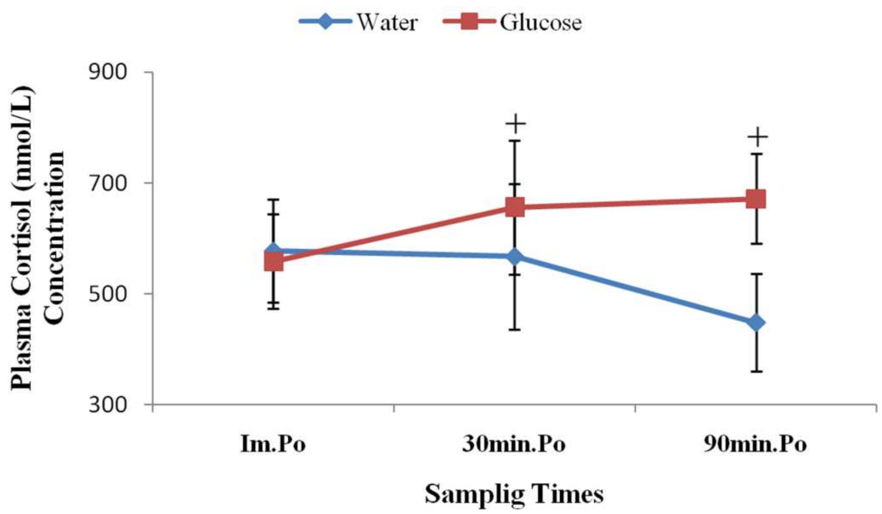

Figure 4. plasma Cortisol concentration in post circuit resistance exercise after water and glucose feeding for within and between group effects. Im.Po: immediately post-exercise and before solutions feeding. 30min.Po: 30 minutes post-exercise and after solutions feeding. 90min.Po: 90 minutes post-exercise and after solutions feeding. +: Significant linear interaction of TIME and SOLUTION in P ≤ 0.05.

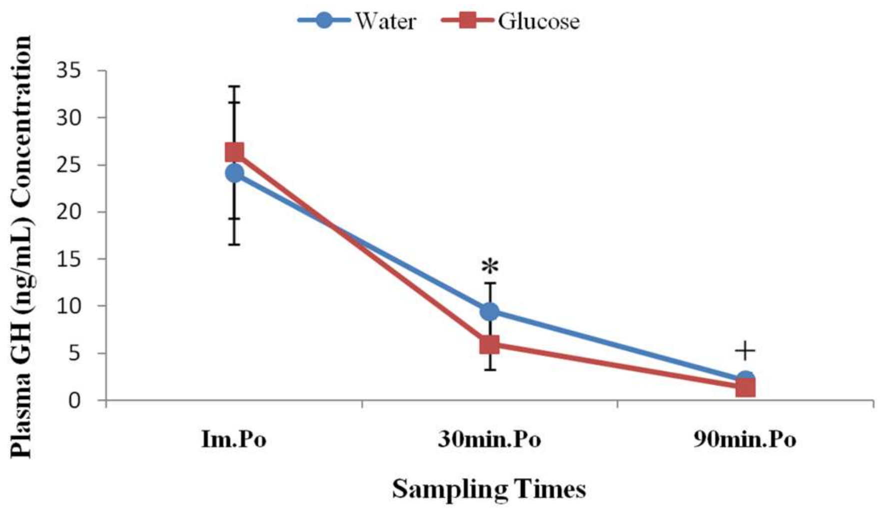

Figure 5. plasma GH concentration in post circuit resistance exercise after water and glucose feeding for within and between group effects. Im.Po: immediately post-exercise and before solutions feeding. 30min.Po: 30 minutes post-exercise and after solutions feeding. 90min.Po: 90 minutes post-exercise and after solutions feeding. ∗: Significant both linear and quadratic effect of TIME than Im.Po in P ≤ 0.01. +: Significant both linear and quadratic effect of TIME than Im.Po and 30min.Po in P ≤ 0.01.

Plasma GH

Mauchly's test of sphericity for plasma GH isn't met (Mauchly's W = 0.252, p = 0.001), so according to Greenhouse-Geisser df adjustment, the main effect of TIME was significant (F = 22.743, p = 0.000) and this effect was either linear (F = 25.208, p = 0.000) or quadratic (F = 10.244, p = 0.008); so that, this effect was significant in all times in comparison with together [(Mean Difference of Im.Po and 30min.Po = 17.48, p = 0.003), (Mean Difference of Im.Po and 90min.Po = 23.46, p = 0.001) and (Mean Difference of 30min.Po and 90min.Po = 5.97, p = 0.009)]. But, the main effect of SOLUTION wasn't significant (F = 0.019, p = 0.894); and in the other hand, the interaction of TIME and SOLUTION with Greenhouse-Geisser df adjustment was insignificant (F = 0.312, p = 0.616) [Figure 5].

Plasma C-peptide

Mauchly's test of sphericity for plasma insulin is met (Mauchly's W = 0.658, p = 0.123). The main effect of TIME with assumption of sphericity was insignificant (F = 1.179, p = 0.326). The main effect of SOLUTION also wasn't significant (F = 3.628, p = 0.083). The interaction of TIME and SOLUTION with assumption of sphericity was insignificant (F = 0.396, p = 0.678) [Figure 6].

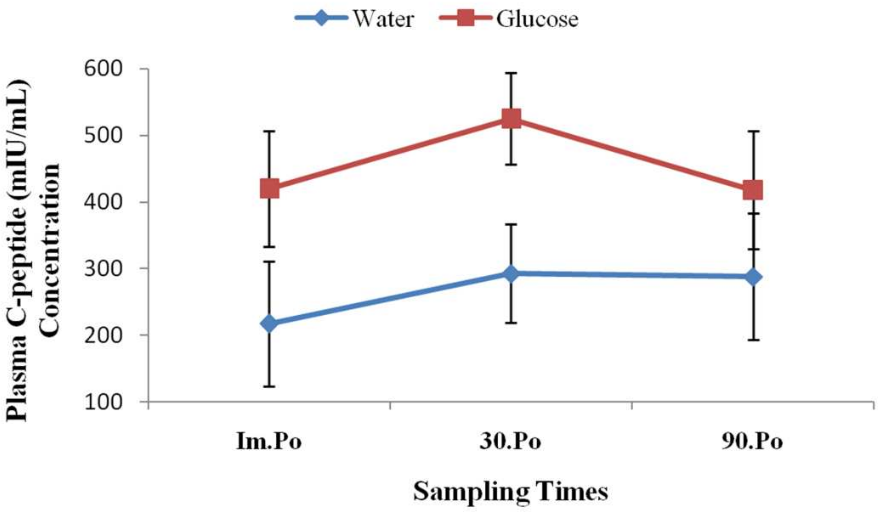

Figure 6. plasma C-peptide concentration in post circuit resistance exercise after water and glucose feeding for within and between group effects. Im.Po: immediately post-exercise and before solutions feeding. 30min.Po: 30 minutes post-exercise and after solutions feeding. 90min.Po: 90 minutes post-exercise and after solutions feeding.

DISCUSSION

The major findings of the present study were that plasma ghrelin concentrations was increased and plasma glucose level was decreased insignificantly during recovery in water group; but, plasma ghrelin had a linear manner in all time of recovery, and plasma glucose first had a insignificant elevation then a significant decrease at 30min and 90min after glucose feeding respectively, along with approximately such manner in plasma insulin suggesting that feeding of glucose solution during recovery maybe can change the negative energy balance resulted from acute resistance exercise toward positive energy balance. It is known that ghrelin secretion is up-regulated under conditions of negative energy balance and down-regulated in the setting of positive energy balance; so that, reflects an acute feeding state and may also serve as an indicator of short-term energy balance [2].

In consistent with our results, it is reported that oral and intravascular administration of glucose to overnight fast normal subjects decreased their plasma ghrelin levels, while intake of an equal volume of water did not [2]. Also, oral glucose solution in overnight obese children increased plasma glucose and decreased plasma ghrelin, with a maximum occurring at 60m after administration in both factor [32], suggesting that ghrelin concentration is suppressed by circulating glucose levels and ghrelin-producing cells maybe response to plasma glucose concentration directly [2, 32]. In the other hand, the plasma ghrelin levels of rats rose significantly following the 1h treadmill running (22 m/min, 10% slope), fall during the 1 h recovery period. Administration of glucose (oral gavage: 3 g/kg body weight) during recovery caused ghrelin concentration returning to the control value. Levels of plasma glucose and insulin were not significantly changed by the exercise, even though there was a tendency towards reduced insulin concentration following the exercise session. But, there was a significant elevation in both plasma insulin and glucose subsequent administration of glucose [11]. In the other hand, however some studies showed that the maximum decrease in concentration of plasma ghrelin occurred before insulin concentration reached their maximum [32, 42]; others reported that intravascular injection of insulin suppress total levels of plasma ghrelin in humans [43]; also, insulin injection in subjects with type 1 diabetes that fed a meal suppressed total plasma ghrelin concentration while in subjects without insulin injection did not [44]. We know that glucose feeding can increase plasma insulin levels as in this study plasma insulin increased significantly at 30m after glucose solution administration while an equal volume of water did not, and also in 90m after glucose feeding it declined in parallel with plasma glucose fall, suggesting that endogenous elevation of plasma insulin maybe suppress the plasma concentration of total ghrelin. Also, it found that 60 min running at 72% of maximum oxygen uptake suppressed plasma acylated ghrelin during, immediately after exercise rather than without training control group, and it elevated during 2h recovery but depressed in control group; in continuance, plasma acylated ghrelin of both experimental and control groups are decreased at 1h after feeding of a high-fat content meal at 2h after finishing of exercise in parallel manner. Plasma glucose during first 2h of recovery period decreased in experimental group to lower than baseline. It elevated in both groups at 30 min and 1h after feeding of meal at 2h after cessation of exercise exactly similar to plasma insulin. After this elevation of plasma glucose and insulin, they decreased slowly to baseline during 5h in both group [25]. Indeed, it is reported that that Ghrelin decreased in response to resistance exercise (3 sets of 10 repetitions of 8 different lift exercises at 70% of 1 repetition maximum, and 1 set of as possible repetitions at 55% of 1 repetition maximum) compared with an increase in the no-exercise condition. Plasma ghrelin concentrations remained significantly lower for the group that consumed 150 mL of CHO beverage 5 min after resistance exercise (ExCHO) and the group that consumed placebo 5 min after resistance exercise (ExPLA) conditions than for the without exercise control group (NoExCHO) at 90 min after exercise; and it insignificantly was lower for ExCHO than ExPLA. Glucose concentrations were lower for ExCHO 90 min post-exercise compared with ExPLA and NoExCHO. Also, ExPLA had significantly lower plasma insulin than ExCHO and NoExCHO immediately after exercise. We notice that all three groups didn't fast; so that, they ate a standard breakfast meal at 2.5 h before starting of trials [19].

Our finding show that plasma cortisol had changes approximately inverse with ghrelin, meaning that plasma cortisol opposite with ghrelin increased and decreased over the time insignificantly in glucose and water group respectively, but these changes was significant simultaneously (Interaction of time and group) same as ghrelin. However, it reported that vein injection of acylated ghrelin [45] and increased ghrelin levels result from a single session resistance exercise [33] didn't alter plasma cortisol; but others showed strong negative relationship between ghrelin and cortisol [46]; and also, plasma ghrelin concentration decreased under endogenous and exogenous hypercortisolism [47].

The ghrelin may have direct hypothalamic effects and perhaps trigger the vagal afferents for further secretion of GH [48, 49]. Beside, GH can interfere in the regulation of ghrelin secretion by suppression of Gastric-Pituitary feedback, indeed, circulating levels of ghrelin decreased in rats by injection of GH [50]. But, data analysis showed that plasma GH changes were independent from administration of glucose solution (it reduced significantly in both groups), suggesting that ghrelin presumably had no effect on GH secretion and vice versa. A study concluded that plasma ghrelin and plasma GH decreased and increased respectively following a single session of circuit resistance exercise and GH changes not related to level of plasma ghrelin [33]. Plasma c-peptide didn't change in our study and this results support by others [33, 34].

In conclusion, plasma ghrelin level suppressed due to administration of glucose solution after circuit resistance exercise, it means that administration of glucose solution perhaps could induce a positive energy balance that involvements of plasma glucose, insulin and cortisol is assumed.

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